National Institute for Health and Care Excellence

Kidney cancer: diagnosis and management

[B] Evidence review for management of localised renal cell carcinoma using non-surgical interventions or active surveillance

NICE guideline NG256

Evidence underpinning recommendations 1.5.1 to 1.5.2 and 1.5.6 to 1.5.11, and a research recommendation in the NICE guideline

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1.1 Review question

What is the clinical and cost effectiveness of different non-surgical interventions or active surveillance, compared to each other or surgical interventions, for localised renal cell carcinoma in adults?

1.1.1 Introduction

There is variation in practice in the NHS for the management of renal cell carcinoma (RCC). Treatment options for early, localised RCC include surgery (partial and radical nephrectomy), non-surgical interventions (ablative therapies and stereotactic ablative radiotherapy (SABR)), or active surveillance. This review focuses on the non-surgical options and active surveillance and is related to review A which compares partial and radical nephrectomy.

Thermal ablation destroys cancerous tissue using extreme temperatures (hyperthermia or hypothermia). The types of thermal ablation included in this review are cryotherapy, microwave ablation and radiofrequency ablation. SABR, also called stereotactic body radiotherapy or SBRT, is a way of delivering radiation very precisely to the tumour. Active surveillance involves a set program of follow up to monitor the development of the tumour, often using imaging. Active surveillance is currently used in practice for people with very small or slow growing tumours.

This review aims to evaluate the clinical and cost-effectiveness of non-surgical interventions and active surveillance compared with each other or with surgery.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	**Inclusion**: • Adults (18 years or over) with (histologically confirmed or suspected on imaging) localised renal cell carcinoma (RCC) Localised RCC diagnosis can be defined according to the clinical or pathological TNM classification, stage 1 and stage 2. **Exclusion**: • Adults with locally advanced or metastatic disease
Interventions	• Non-surgical interventions: 　o Thermal ablation using the following methods:

	▪ Radiofrequency ablation ▪ Cryotherapy ▪ Microwave ablation ○ Stereotactic ablative radiotherapy (SABR) ○ Active surveillance
Comparator	• Surgical intervention (partial or radical nephrectomy) • Non-surgical interventions compared to each other
Outcomes	• Disease-free survival, including cancer-free survival or if not reported: ○ Local recurrence ○ Distant metastases • Overall survival or if not reported: ○ Mortality • Cancer-specific survival • Severe adverse events and complications: ○ observed in the intraoperative period ○ observed in postoperative period • Long-term severe adverse events ○ Renal function impairment ○ Cardiovascular events • Duration of hospital stay • Quality of life
Study type	• Randomised controlled trials (RCTs) • Any controlled, non-randomised studies • Cohort studies (prospective and retrospective observational studies) • Systematic reviews of the above studies

For the full protocol see appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document.

Methods and technical decisions specific to this review are summarised below. Many align with the methods detailed in review A.

1. Four systematic reviews (SRs) were used in this evidence review (Guo et al. 2019, Hu et al. 2019, Patel et al. 2017, and Yanagisawa et al. 2022). Of these, 1 was assessed as low risk of bias (Yanagisawa et al. 2022) and the remaining 3 at moderate risk of bias, mainly due to protocols and full search strategies not being provided, and limitations on selection criteria such as only accepting English language only studies. Risk of bias of included studies was assessed using varied tools across the SRs. Where ROBINS-I or a tool considered to be similar to ROBINS-I was used (for example the Cochrane Risk of Bias

Assessment Tool for Non-Randomized Studies of Interventions), the systematic review assessment is used. Two systematic reviews (Guo et al. 2019 and Xu et al. 2019) used the Newcastle Ottawa scale. Assessments of study risk of bias from these SRs were downgraded by two levels (e.g. from low risk of bias to high risk of bias) in order to bring them in line with the ROBINS-I tool.

2. The population for this review is people with localised RCC, defined as stage 1 or stage 2 (T1-T2) cancer according to the clinical or pathological TNM classification. Some studies had broader eligibility criteria that included stage 3 (T3) and above. In this scenario, studies were excluded where ≥10% of the sample had clinical T3+ RCC and the outcomes could not be disaggregated.

3. Included studies used different definitions for each outcome. Therefore, the way the study described an outcome was compared to the outcomes agreed by the committee in the protocol to determine what each study was reporting. For consistency, outcomes were renamed in the analysis to match the protocol outcomes. This particularly applied to the following:

    a. Disease-free survival: time to event outcomes of disease-free survival, cancer-free survival, recurrence-free survival and relapse-free survival were combined in the analysis.

    b. Recurrence: event data reported as recurrence, local recurrence, and distant metastases. These three outcomes were analysed separately. Recurrence was interpreted as any recurrence, with local recurrence and distant metastases as subsets of these.

    c. Overall survival: time to event outcomes reported in studies as survival, mortality and all-cause mortality were combined in the analysis.

    d. Cancer-specific survival: time to event outcomes reported in studies as cancer-specific survival, cancer death or similar were combined in the analysis.

4. Outcomes for partial and radical nephrectomy separately were preferred to outcomes for nephrectomy as a combined arm. Results for nephrectomy combined were only presented where results could not be disaggregated (Cheung et al. 2023 and Grant et al. 2020).

5. Where studies reported hazard ratios for relevant outcomes from both Kaplan-Meier analyses and multivariate models assessing association between surgery method and the outcome, the result considered to be at least risk of bias from confounding was preferred. Both types of results were combined in analyses.

6. Where more than 1 timepoint was reported we reported data at up to 5 years and more than 5 years. Where several time points were reported that could fit in the same category, the latest time point was used.

7. The search was limited to OECD countries only, because studies from these countries were considered to be more directly applicable to the UK healthcare setting.

8. For the comparisons of active surveillance versus partial nephrectomy and active surveillance versus thermal ablation, the systematic review Guo et al. (2019) presented data for the outcomes overall survival (Figure 60 and Figure 74) and cancer-specific survival ≤ 5 years (Figure 62 and Figure 76). However, the data was pooled and it was not possible to determine what studies were included in the analyses. Therefore, these forest plots include the pooled data from Guo et al. (2019) as a single line.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 18/01/2024 and re-run on 14/02/2025. The following databases were searched: Central Register of Controlled Trials (Wiley), Cochrane Database of Systematic Reviews (Wiley), Embase (Ovid), Epistemonikos (Epistemonikos) and MEDLINE ALL (Ovid). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to OECD countries, systematic reviews, randomised controlled trials and observational studies.

The searches for the cost effectiveness evidence were run on 05/01/2024 and 07/01/2024 and re-run on 06/05/2025. The following databases were searched: EconLit (Ovid), Embase (Ovid), HTA (CRD), International HTA database (INAHTA), MEDLINE ALL (Ovid) and NHS Economic Evaluations Database (CRD). Limits were applied to remove animal studies, conference abstracts, editorials, letters, news items and commentaries, as well as papers not published in the English language. Filters were used to limit to OECD countries and cost utility studies.

A NICE senior information specialist (SIS) conducted the searches. The MEDLINE strategy was quality assured by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement. Further details and full search strategies for each database are provided in appendix B.

1.1.3.2 Protocol deviations

1. For outcomes where the line of no effect was defined as the minimal important difference (MID), we planned to use a power calculation from a robust RCT to determine the minimum sample size needed for consideration for the second downgrade criteria for the imprecision domain in GRADE. No relevant RCTs reporting power calculations were identified, so the minimum sample sizes used for review A were used for this review. For overall survival, a sample size of 1300 was used. For all other outcomes, a sample size of 420 was used.

2. For outcomes comparing active surveillance with another treatment, the committee requested that a sensitivity analysis be undertaken to remove studies which did not require participants to have confirmed renal cell carcinoma. The results of this are discussed in section 1.1.11.3 Benefits and harms. Duration of hospital stay was only reported for thermal ablation versus partial nephrectomy The committee noted that open partial nephrectomy would be expected to result in a longer hospital stay than minimally

invasive partial nephrectomy and requested sensitivity analysis to show only studies with using minimally invasive surgical techniques for partial nephrectomy.

3. In the protocol, overall survival and cancer-specific survival were only listed as time to event outcomes, however, some studies reported related outcomes such as all-cause mortality or cancer death. Where time to event data was not available for these outcomes event data was extracted instead. See section 1.1.3 Methods and process for more details.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

A single systematic search was carried out to identify potentially relevant studies for the current review (review B) and reviews A, C, H1 and H2 combined (review A: surgical interventions for localised RCC, review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC, reviews H1 and H2: non-pharmacological management of advanced RCC). The search found 19, 882 references (see appendix B for the literature search strategy).

These 19,882 references were screened at title and abstract level against the protocols for the 4 reviews, with 19,208 excluded at this level. 674 studies were taken forward for full text assessment for any of the four review questions listed above. Of these, 172 were relevant to review B. 10% of references were screened separately by two reviewers with 99.9% agreement. Discrepancies were resolved by discussion.

The full texts of 172 references were ordered for closer inspection. A total of 69 articles (4 systematic reviews [SR] of cohort studies, 1 randomised controlled trial [RCT] and 64 cohort studies, 22 of which were also included in the 4 relevant SRs) met the criteria specified in the review protocol (appendix A). The clinical evidence study selection is presented as a PRISMA diagram in appendix C.

The four included SRs (Guo et al. 2019, Hu et al. 2019, Patel et al. 2017, and Yanagisawa et al. 2022) were all used as a source of studies and data. They included a total of 22 cohort studies. Additional data from 43 studies (1 RCT and 42 cohort studies) identified in the literature searches were combined with data from the SRs. A total of 65 primary studies and 4 SRs were therefore included.

The SRs all reported different relevant outcomes, (see the full evidence tables, and a table listing studies and data taken from included SRs, in appendix D):

- Patel et al. (2017) reported data on renal function for comparisons including active surveillance, partial nephrectomy and radical nephrectomy.

- Hu et al. (2019) reported data on survival and recurrence outcomes for thermal ablation versus partial nephrectomy.

- Guo et al. (2017) reported survival outcomes for active surveillance versus partial and radical nephrectomy.
- Yanagisawa et al. (2022) reported postoperative complications and duration of hospital stay for thermal ablation versus partial nephrectomy.

For a summary of the 69 articles included in this review see Table 2, Table 3 and Table 4. Table 5 shows the studies and outcomes that were included for each comparison. Data for all comparisons apart from SABR versus radical nephrectomy were identified.

See section 1.1.13 References – included studies for the full references of the included studies.

1.1.5 Summary of studies included in the effectiveness evidence

Table 2 Summary of characteristics of the included systematic reviews

Author (year)	Primary studies included from this review	Population	Interventions	Outcomes	Risk of bias
Guo (2019) Search date: Jan 2000 to Sept 2018 N=4,807	• Alam (2018) • Lane (2010) • Miller (2018) • Patel (2012) • Tang (2017) • Patel (2015)	People with localised renal masses who underwent 'nephron sparing intervention' (enucleation, PN, and TA, like radiofrequency ablation, cryoablation, microwave ablation, etc.) or active surveillance.	• Partial nephrectomy • Thermal ablation • Active surveillance	• Overall survival • Cancer-specific survival	Moderate Partially applicable (did not include all relevant interventions)
Hu (2019) Search date: Nov 2018 N=3,269	• Alam (2018) • Park (2018) • Fossati (2015) • Thompson (2015) • Emara (2014) • Guillotreau (2012) • Olweny (2012) • Klatte (2011)	People with cT1a renal masses who underwent partial nephrectomy or thermal ablation.	• Partial nephrectomy • Thermal ablation	• Overall survival • Disease-free survival • Recurrence • Cancer-specific survival	Moderate Partially applicable (did not include all relevant interventions and limited to

	• Takaki (2012) • Ko (2008) • Lucas (2008) • Stern (2007) • Desai (2005)				cT1a tumours)
Patel (2017) Search date: Jan 1997 to May 2015 N=2,503	• Guillotreau (2012) • Klatte (2011) • Takaki (2010) • Cooper (2015) • Danzig (2015) • Deklaj (2010) • Foyil (2008) • Lucas (2007) • Takaki (2014) • Faddegon (2013) • Kiriluk (2011) • Mitchell (2011) • Mues (2012) • Pascal (2011) • Tanagho (2013) • Turna (2009)	People with localised renal tumours who underwent radical nephrectomy, partial nephrectomy, thermal ablation or active surveillance.	• Partial nephrectomy • Radical nephrectomy • Thermal ablation • Active surveillance	• Renal functional outcomes	Moderate Partially applicable (did not include all relevant interventions)

Yanagisawa (2022) Search date: Aug 2021 N=2,416	• Park (2018) • Fossati (2015) • Guillotreau (2012) • Klatte (2011) • Ko (2008) • Stern (2007) • Desai (2005) • Garcia (2021) • Haramis (2012) • Yanagisawa (2018) • Rembeyo (2019) • Shapiro (2019) • Acosta Ruiz (2019) • Caputo (2017) • Kim (2015) • Anglickis (2019) • Park (2019)	People with cT1a or cT1b renal tumours who underwent partial nephrectomy or thermal ablation.	• Partial nephrectomy • Thermal ablation	• Postoperative complications • Duration of hospital stay	Low Partially applicable (did not include all relevant interventions and limited to studies presenting cT1a and cT1b tumours separately)

Table 3 Summary of characteristics of the included RCT

Study details	Population	Intervention	Comparison	Outcomes	Risk of bias
Neves (2023) UK Follow up time: 6 months	N=50 Adults with a diagnosis of a small renal mass (tumour <4cm with an imaging appearance consistent with stage T1a). Key exclusion criteria: Advanced disease or a concurrent medical or surgical condition or indication that meant that the tumour board/multidisciplinary team recommended one treatment modality over another.	Partial nephrectomy (robot-assisted) (n=25)	Cryoablation (percutaneous) (n=25)	• Postoperative complications • Renal functional impairment	High

Table 4 Summary of characteristics of the included non-randomised studies

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Acosta Ruiz (2021) Retrospective cohort study Sweden October 2007 and December 2016 Median = 38 months; range = 2.5 - 99 months	People with non-hereditary T1a RCC aged ≤75 years with two kidneys. Exclusion criteria: Tumours treated by multiple treatment methods.	Percutaneous radiofrequency ablation (RFA) (N = 60)	Laparoscopic partial nephrectomy (LPN) (N= 31)	Treatment (LPN/RFA), the pre-value of the response variables, and confounders (pre-treatment eGFR, BMI, age, tumour size, tumour nearness [distance to the collecting system or sinus] and Charlson Comorbidity Index) were included in the models as explanatory variables.	Renal functional impairment Postoperative severe adverse events	Serious
Aikawa (2023) Retrospective cohort study Japan	People with de novo cT1b renal tumour Exclusion criteria: Missing data on long-term survival or renal function.	Percutaneous cryoablation (N = 29)	Partial nephrectomy (open or laparoscopic) (N=90)	Inverse probability weighting was used for balancing patient demographics, including renal function and tumour complexity.	Recurrence Survival Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
January 2011 to November 2021 Median follow-up was 43 months (IQR: 29-59) in the percutaneous cryoablation group and 36.5 months (IQR: 18-59) in the partial nephrectomy group.	Synchronous metastasis or renal tumour accompanied by The Von Hippel-Lindau (VHL) disease					
Alam (2019) Prospective cohort study US Since January 1, 2009 The median follow-up time was 3.0	People aged ≥18 years; People with T1a RCC Contrast-enhancing renal mass ≤4.0 cm in diameter on axial imaging. Exclusion criteria: Not reported	Ablation (N= 27) or Active surveillance (N=339)	Partial nephrectomy (PN) (N=231)	Analysis controlled for age, sex and comorbidity index.	Renal functional impairment	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
years [IQR 1.6-5.0], and 158 People (24.7%) were followed for ≥5 years.						
Almadalal (2022) Retrospective cohort study Sweden January 2005 to December 2012 Follow up: At least 5 years for disease recurrence. Overall survival data available until December 2019.	People with clinical T1aM0 RCC registered in the National Swedish Kidney Cancer Register Exclusion criteria: Metastatic disease at diagnosis	Ablative treatments (radiofrequency ablation, cryoablation) (N=169)	Radical nephrectomy (N= 938) Partial nephrectomy (N=738)	Multivariable Cox regression model, factors adjusted for not specified.	Recurrence Survival	Serious
Andrews (2019)	People with localised cT1 renal tumour	Radiofrequency ablation (RFA) and cryoablation (CA)	Partial nephrectomy (PN)	Propensity score adjusted results used.	Survival Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Retrospective cohort study US Between 2000 and 2011 Follow up: Among cT1a, the median clinical follow-up was 9.4, 7.5, and 6.3 years, respectively. Among cT1b, the clinical follow-up was 8.7 and 6.0 years, respectively.	Exclusion criteria: Renal masses with radiographic evidence of extension beyond the kidney or extension into the renal or segmental veins; People with a history of prior RCC; People with genetic syndromes	cT1a: RFA (N=180) CA (N=187) cT1b: CA (N=52)	cT1a: (N=1055) cT1b: (N=324)			
Anglickis (2019) Retrospective cohort study	People aged ≥70 years with exophytic solitary small (<4 cm) renal mass, T1a	Microwave thermal ablation (MWT) (N=15)	Open partial nephrectomy (OPN) (N=18)	No adjustment for confounders.	Recurrence Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
January 2012 to January 2019 Median follow up was 40 months. microwave ablation 40 (IQR: 34 to 47) PN 40.10 (IQR: 38 to 43)	Exclusion criteria: Uninformative or benign biopsy result					
Attawettayanon (2023) Retrospective cohort study USA 1975 to 2022 Median overall follow-up was 59 months in the thermal ablation cohort and 41	People with clinical stage T1 renal mass in a solitary kidney. Exclusion criteria: People with familial disease	Thermal ablation (N= 66)	Partial nephrectomy (N=66)	Propensity score matching was used to balance differences in relevant baseline characteristics (age, sex, preoperative glomerular filtration rate, body mass index, diabetes, hypertension, cardiovascular disease, R.E.N.A.L. nephrometry score, and tumour diameter).	Recurrence Postoperative severe adverse events	Moderate

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
months in the partial nephrectomy cohort.						
Beksac (2022) Retrospective cohort study USA February 1998 to March 2020 Median follow-up was 59.4 months	People with a solitary kidney who underwent treatment for a cT1a renal mass Exclusion criteria: Multiple tumours; Tumours larger than 4 cm; Von Hippel Lindau disease; Previous ipsilateral partial nephrectomy; Previous ipsilateral thermal ablation; Previous kidney transplantation	Cryoablation (laparoscopic or percutaneous) (N=43)	Partial nephrectomy (open or robotic) (N=31)	Linear mixed-effects models used to assess association between treatment type while adjusting for confounders. No propensity score matching was described.	Recurrence Renal functional impairment	Serious
Bertolo (2019) Retrospective cohort study US	People older than 75 years who underwent robotic PN or cryoablation for renal tumour. Exclusion criteria: Not reported	Cryoablation (N=65)	Robotic partial nephrectomy (N=65)	People were matched according to age, sex, race, BMI, ASA score, diabetes, hypertension, pre-existing CKD, Charlson’s Comorbidity Index, clinical tumour size, R.E.N.A.L. score and	Renal functional impairment	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
June 2006 to December 2016 Median follow-up of 37 (29 to 44) and 46 (38 to 53) months for robotic partial nephrectomy and cryoablation, respectively				preoperative serum creatinine.		
Bhindi (2018) Retrospective cohort study US 2005 to 2015 Follow up: Median (IQR) Whole cohort: 47 (18, 74) months.	People with solitary kidney and single localised non-cystic primary renal tumour; node-negative, non-metastatic Exclusion criteria: Multiple tumours; Salvage procedures; Inherited tumour syndromes; Tumour in a transplanted kidney	Percutaneous cryoablation (CRA) (N = 64)	Partial nephrectomy (PN) (N = 54)	Inverse probability treatment weighting (IPTW) was used to adjust the cohort for confounders. The propensity to undergo CRA versus PN was estimated using a logistic regression model based on age, sex, Charlson comorbidity index, treatment year, RENAL nephrometry score, tumour size (maximum tumour diameter in centimetres), baseline eGFR, renal cell carcinoma (RCC) tumour	Recurrence Survival Postoperative severe adverse events	Moderate

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
				histology, and history of prior contralateral nephrectomy for RCC.		
Bianchi (2021) Retrospective cohort study Italy January 2007 and July 2019 Follow up: Median (IQR) Overall: 61 (33-93) PN: 63 (32-100) RFA: 48 (35-66) CA: 63 (44-85)	People with cT1aN0M0 renal masses Exclusion criteria: Not reported	Radiofrequency ablation (RFA) and cryoablation (CA) RFA (N=68) CA (N=83)	Partial nephrectomy (PN) (N=665)	Covariates consisted of patient's characteristics (age, CCI and gender), preoperative tumour's features (PADUA score, size, side, local stage and number of synchronous renal masses), histologic data (non-clear cell RCC versus clear cell RCC) and type of procedure (PN versus RFA versus. CA).	Recurrence Survival	Serious
Bird (2009) Retrospective cohort study	People with localised renal tumour Exclusion criteria: Not reported	Radiofrequency ablation (RFA) (N= 36)	Partial nephrectomy (PN) (N=33)	No adjustment for confounders.	Duration of hospital stay Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
US 2002 to 2007 Follow up: RFA: mean 12 months, range 6 to 23 months PN: mean 27 months, range 6 to 58 months						
Caputo (2017) Retrospective cohort study US 1999 to 2014 Median follow up, months (IQR) Cryoablation: 30.1 (13.2-64)	People with cT1b renal mass (between 4 and 7cm) Exclusion criteria: Not reported	Cryoablation (Laparoscopic and percutaneous techniques) (N=31)	Robot-assisted partial nephrectomy (PN) (N=161)	Matching was based on key baseline variables (tumour size, Charlson comorbidity index, age, BMI, ASA score, preoperative serum creatinine, preoperative eGFR, gender and solitary kidney). RENAL scores were not included in the matching algorithm.	Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
PN: 13 (3.19-19.2)						
Cazalas (2023) France 2010 to 2020 Mean follow-up was 28.8 ± 17.4 months for the RAPN People and 31.4 ± 28.8 months for the TA People.	People with sporadic, biopsy-proven, stage cT1b renal cell carcinoma Exclusion criteria: Benign renal tumour on histology; Presence of metastases; People with a genetic predisposition to cancer (Von Hippel-Lindau syndrome)	Percutaneous thermal ablation (including cryoablation, radiofrequency ablation, and microwave ablation) (N = 75)	Robotic-assisted partial nephrectomy (N = 75)	Retrospective 1:1 propensity-score matched analysis adjusting for tumour size, histology results, and RENAL score.	Recurrence Postoperative severe adverse events Renal functional impairment	Serious
Chan (2022) Retrospective cohort study UK 2003 to 2016 The	People with cT1N0M0 histology-confirmed RCC Exclusion criteria: Multiple tumours; Inherited tumour syndromes;	Cryoablation and radiofrequency ablation Cryoablation (N = 72) Radio-frequency ablation (N = 87)	Laparoscopic partial nephrectomy (N = 79)	Cox multivariable model adjusted for age, sex, R.E.N.A.L nephrometry score, lesion size, RCC type, grade and t-stage.	Survival Recurrence Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Median (IQR) follow-up duration is 72.5 (42.0 to 100.9) months, 59.5 (27.5 to 99.39) months, and 67.9 (50.8 to 91.3) months for CRYO, RFA, and LPN, respectively.	People with a history of LPN, CRYO, or RFA of the same kidney; People with solitary kidney or tumour recurrence					
Cheung (2023) Retrospective cohort study Canada 2000 to 2020 Median follow-up for people alive at the end of follow-up was 4.6 years in the active surveillance group and 4.9 years	People with a small renal mass (≤4 cm, T1a solid renal mass); Aged 55-75 years Exclusion criteria: Symptomatic lesions; Personal history of cancer; Family history of renal cancer; Undergoing radiofrequency ablation	Active surveillance (N = 53)	Nephrectomy (N = 57)	People undergoing active surveillance or nephrectomy were exactly matched for age, sex, Eastern Cooperative Oncology Group (ECOG) performance status score, biopsy status, and histology.	Survival	Moderate

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
in the nephrectomy group.						
De Angelis (2024) Retrospective cohort study US 2004 to 2020 Follow-up: not reported	People older than 18 years, with T1aN0M0 renal cell carcinoma who underwent either partial nephrectomy or exclusive radiotherapy (external beam radiotherapy) Exclusion criteria: People with metastatic disease, unknown histological subtype, and unknown tumour size.	Radiotherapy (N=92)	Partial nephrectomy (N=92)	Propensity score matching applied to age, tumour size, and histology.	Survival	Serious
Duus (2023) Prospective cohort study Denmark	People with clinical stage T1 (cT1) renal cell carcinoma (RCC) treated with RAPN or PCA Exclusion criteria: Under 18 years old;	Percutaneous cryoablation (PCA) (N = 38)	Robot-assisted partial nephrectomy (RAPN) (N = 18)	No adjustment for confounders.	Renal functional impairment	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
June 2019 to January 2021 Follow up: 6 months	Benign tumour; Conversion of RAPN to open surgery or radical nephrectomy; Salvage treatment within 6 months					
Emara (2014) Retrospective cohort study UK 2008 to 2012 Mean follow-up (months): Cryoablation: 25.59 PN: 32.78	People diagnosed with small renal masses (T1). Exclusion criteria: Not reported	Laparoscopic cryoablation (N = 56)	Robot-assisted partial nephrectomy (RAPN) (N = 47)	No adjustment for confounders or matching undertaken.	Postoperative severe adverse events Recurrence	Serious
Fraisse (2019) Retrospective cohort study France	People with T1 renal tumour Exclusion criteria:	Percutaneous cryoablation (PCA) (N = 177)	Robot-assisted partial nephrectomy (RAPN) (N = 177)	To reduce differences between the two groups attributable to selection bias and confounding was performed a 1:1 matched analysis on radiological	Survival Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Between 2009 and 2016 Median follow-up was 39.03 months for the RAPN group and 62.59 months for the PCA group.	People with other metastatic cancers or with a history of contralateral kidney tumour			tumour stage and RENAL nephrometry score.		
Grant (2020) Retrospective cohort study US 2004 to 2014 Follow-up Surgery (median: 57 months), tumour ablation (median: 50 months), SBRT	People with T1N0M0 kidney cancer (7 cm or less with no nodal or distant metastases) Exclusion criteria: People who receive conventionally fractionated radiation or non-standard procedures; People who received systemic therapy; People with benign or rare histology, bilateral disease, or involving	Tumour ablation (including cryoablation and thermal ablation) (N = 17,196) Stereotactic body radiation therapy (SBRT) (N=104) Observation (N=18,241)	Surgery (including partial and total nephrectomy) (N = 165,298)	No adjustment for confounders.	Survival	Moderate

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
(median: 37 months), and observed (median: 19 months)	renal pelvis; People with stage T2-T4, nodal or metastatic disease					
Haber (2012) Retrospective cohort study US February 1998 to September 2008 Mean follow-up PN: 42.7 months Cryoablation: 60.2 months	People with radiologically suspicious enhancing mass 7cm or less (clinical stage 1); Exclusion criteria: Not reported	Laparoscopic cryoablation (N = 30)	Laparoscopic Partial nephrectomy (N = 48)	No adjustments for confounders or matching.	Recurrence Duration of hospital stay	Serious
Jasinski (2024) Retrospective cohort study	People aged under 67 years with functional contralateral kidney, no significant comorbidities that	Partial nephrectomy (laparoscopic or open) (N=44)	Percutaneous radiofrequency ablation (N=41)	Not reported.	Duration of hospital stay	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Retrospective cohort study Poland August 2016 to February 2022 Median follow-up: 28 months	would be a contraindication to partial nephrectomy People with exophytic lesions and one of the following: not larger than 30 mm and located in the central part of the kidney; not larger than 30 mm and located in the lower pole of the kidney; not larger than 25 mm. Exclusion criteria: People without confirmed renal cell carcinoma or missing data.					
Junker (2022) Prospective cohort study Denmark	People aged ≥18 years with histologically verified primary renal cell carcinoma stage cT1N0M0;	Percutaneous cryoablation (N = 104)	Partial nephrectomy (N = 86)	Univariate and multivariable logistic regression analyses were performed, adjusted for age and sex. No propensity score matching was described.	Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
June 2019 to February 2021 All people had a follow-up period of 90 days.	Exclusion criteria: Metastatic disease at the time of diagnosis; Conversion from partial to radical nephrectomy; Salvage procedures					
Junker (2022) Prospective cohort study Denmark June 2019 to February 2021 All people had a follow-up period of 90 days.	People aged ≥18 years with histologically verified primary renal cell carcinoma clinical stage cT1; Exclusion criteria: People with diagnosed dementia or under evaluation for dementia; People with multiple tumours treated with nephron-sparing	Percutaneous cryoablation (N = 86)	Partial nephrectomy (N = 79)	Adjusted models included age and sex as covariates as these were considered potential confounding factors.	Quality of life	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
	surgery more than once within 3 months					
Kawaguchi (2022) Retrospective cohort study Japan October 2016 to December 2021 The mean follow-up period was 24.3 (2 to 60) months for the RAPN group and 20.1 (2 to 60) months for the PCA group.	People aged ≥70 years diagnosed with RCC Exclusion criteria: Not provided	Percutaneous cryoablation (N = 49)	Robot-assisted partial nephrectomy (RAPN) (N = 50)	No adjustment for confounders.	Survival Postoperative severe adverse events Renal functional impairment	Serious
Kiriluk (2011) Retrospective cohort study US	People who underwent nephron sparing surgery Exclusion criteria: Not reported	Thermal ablation Laparoscopic radiofrequency ablation (N=21)	Partial nephrectomy (laparoscopic) (N=51)	People were matched by preoperative estimated glomerular filtration rate (eGFR), comorbidities, age, comorbidities, BMI and tumour size to 51 people who underwent	Postoperative severe adverse events Renal functional impairment	Moderate

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
November 2002 to December 2008 Follow up: PN: mean 18 months (range 13.0-26.8) TA: mean 27 months (range 0.4-40.0)		Laparoscopic cryoablation (N=30)		LPN. Pairwise matching was performed individually between the groups. The bigger LPN group was used as controls. This is not named as propensity score matching.		
Kitley (2019) Retrospective cohort study US Between 1998 and 2012 Follow up: 96 months	People with T1a RCC Exclusion criteria: cN(+) and cM(+)	Cryoablation (CA) (N = 6229)	Partial nephrectomy (PN) (N = 6229)	Propensity score matching was performed in a 1:1 nearest neighbour fashion using tumour diameter, Charlson score, race, age, geographic region, facility type, insurance type, and income to generate the conditional treatment probability.	Survival	Serious
Lane (2010)	People older than 75 years with suspected cT1 renal cancer	Active surveillance (N = 105)	Radical nephrectomy.	Adjusted for age, sex, race, presence of solitary kidney, eGFR using Cox	Recurrence Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Retrospective cohort study US January 2000 to December 2006 Follow up Median years [IQR] AS: 3.7 [2.4-5.1] RN: 4.4 [2.8-5.50]	Exclusion criteria: People who underwent nephrectomy for reasons other than renal cancer		(N = 146)	proportional hazard models.	Renal functional impairment	
Lehrer (2023) Retrospective cohort study France January 2010 to January 2021	People older than 75 years treated for a T1 renal cell cancer Exclusion criteria: Suspected or presence of metastases; Multiple tumours on the same kidney	Percutaneous thermal ablation (radiofrequency ablation, cryoablation, and microwave ablation) (N = 66)	Robot-assisted partial nephrectomy (N = 143)	A Cox proportional hazards regression model was used to measure the association between treatment and oncological outcomes, adjusting for relevant prognostic factors. No propensity score matching was performed.	Recurrence Survival Duration of hospital stay	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Mean follow-up (months) RAPN: 22 ± 16.1 TA: 22 ± 15.5						
Long (2017) Retrospective cohort study France 2000 to 2015 Mean follow-up (months) PN: 43 (SD 53.70) TA: 38 (SD (24.17)	People undergoing thermal ablation or partial nephrectomy for a renal tumour in an imperative indication Exclusion criteria: Not reported	Thermal ablation Radiofrequency ablation (N = 104) Cryoablation (N = 8)	Partial nephrectomy (PN) (N = 172)	No adjustment for confounders.	Survival Recurrence Postoperative severe adverse events Renal functional impairment Duration of hospital stay	Serious
Lucignani (2023) Retrospective cohort study Italy	People older than 18 years with small renal mass (< 4 cm) Exclusion criteria: Masses showing	Microwave ablation (N = 62)	Robot-assisted partial nephrectomy (N = 109)	No adjustment for confounders.	Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
January 2016 to October 2022 Follow up period was 24 (7-24) and 24 (12-36) months for MWA and RAPN, respectively.	extrarenal and vascular invasion					
Mason (2018) Retrospective cohort study US 1974 to 2013 Follow up (years): Median (IQR) PN: 3.2 (1.5-7.5) Cryoablation: 1.2 (0.3, 3.6)	People with synchronous bilateral tumours Exclusion criteria: Presence of metastases	Cryoablation (N = 12)	Partial nephrectomy (PN) (N = 76)	No adjustments for confounding or matching carried out.	Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Millan (2022) Retrospective cohort study Canada 2011 to 2021 Median follow up: PN was 2.0 years (IQR 0.6-4.2) AR was 2.6 years (IQR 1.1-4.2)	People aged ≥18 years with cT1a N0 M0 renal cancers Exclusion criteria: Multiple tumours	Percutaneous ablation therapy (AT), including radiofrequency ablation (RFA) or cryoablation (N = 275)	Partial nephrectomy (PN) (N = 2001)	Inverse probability of treatment weighting (IPTW) using propensity score (PS) was used.	Recurrence Survival	Serious
Mues (2012) Retrospective cohort study US 1990 to 2010	People with solitary kidney or who underwent nephron-sparing surgery for one or more renal masses	Thermal ablation (TA) Laparoscopic and percutaneous cryoablation or	Robot-assisted partial nephrectomy (PN) (N = 100)	No adjustments for confounders or matching was undertaken.	Postoperative severe adverse events Recurrence Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Follow up TA: mean 31 months PN: mean 24 months	Exclusion criteria: Presence of metastases	radiofrequency ablation. (N = 98)				
Palumbo (2020) Retrospective cohort study US From 2004 to 2015 Follow up not reported	People with T1a RCC Exclusion criteria: All autopsy or death certificate cases and those with missing follow-up data	Local tumour ablation (LTA) (N = 4524) Non-interventional management (NIM) (N = 1654)	Partial nephrectomy (PN)	Adjustment variables consisted of age at diagnosis, gender, race, year of diagnosis, population density, marital status, socioeconomic status, tumour grade, histology and tumour size.	Survival	Serious
Pandolfo (2023) Retrospective cohort study USA and Europe	People with renal mass Exclusion criteria: People with previous kidney cancer surgery	Percutaneous tumour ablation (PTA) (cryoablation, radiofrequency, or microwave ablation)	Robot-assisted partial nephrectomy (RAPN) (N = 60)	No adjustment for confounders.	Recurrence Survival Postoperative severe adverse events Renal functional impairment	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
2010 to 2020 Mean follow-up was 44.4 (32) months for RAPN and 35.6 (35.1) months for PTA.	or multiple renal tumours	(N = 92)			Duration of hospital stay	
Pantelidou (2016) Retrospective cohort study UK 2005 to 2013 Follow up (months): median (range) RFA: 47.5 (11.8 to 80.2) PN: 18.5 (6.2 to 29.5)	People with T1 stage histologically confirmed RCC <7cm; Exclusion criteria: Lost to follow-up or no post-procedure follow-up imaging;	Percutaneous radiofrequency ablation (RFA) (N = 63)	Robot-assisted partial nephrectomy (RAPN) (N = 63)	Adjustments for baseline tumour size, PADUA score, age and type of treatment offered. Unclear how type of treatment offered was adjusted for. Did not adjust for baseline eGFR or RCC type.	Recurrence Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Panumatrassamee (2013) Retrospective cohort study US 2000 to 2012 Follow up: Cryoablation: median IQR: 41 (26-59) PN: median IQR: 17 (5-62)	People with solitary kidney Exclusion criteria: Not reported	Cryoablation (N = 43)	Partial nephrectomy (PN) (N = 33)	No adjustment for confounders.	Postoperative severe adverse events	Serious
Park (2018) Retrospective cohort study South Korea 2008 to 2016	People with solitary renal mass and histologically confirmed RCC Exclusion criteria: Small (<4 cm) pT3a RCC, multiple RCC, bilateral RCC,	Radiofrequency ablation (RFA). (N = 63)	Robot-assisted Partial nephrectomy (RAPN). (N = 63)	Propensity score matching was undertaking with the following variables: age, sex, American Society of Anaesthesiologists (ASA) score, tumour size, tumour laterality, tumour histology, R.E.N.A.L. nephrometry score and preoperative	Renal functional impairment	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Median follow up (months) PN: 24.6 RFA: 21	metastatic RCC and hereditary RCC			estimated glomerular filtration rate (eGFR).		
Park (2019) Retrospective cohort study Korea January 2005 and October 2014 Average follow-ups were 60 and 68 months for RFA and PN, respectively	People with histologically confirmed T1a RCC (small [< 4 cm] solitary tumour, followed up for at least 2 years after surgery People with a small (< 4 cm) solitary tumour Exclusion criteria: People with bilateral renal masses, metastatic disease or hereditary renal tumour	Radiofrequency ablation (RFA) (N = 62)	Partial nephrectomy (PN) (N = 53)	No adjustment for confounders.	Recurrence Survival	Serious
Patel (2012) Retrospective cohort study UK 2005 to 2010	People with suspected cT1 renal cancer or solid or cystic enhancing T1a small renal mass	Active surveillance (AS) (N = 71)	Radical nephrectomy (RN). (Open or laparoscopic) (N = 41)	No adjustments or matching conducted.	Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Mean follow up: AS: 34 months RN: 37 months	Exclusion criteria: Not reported					
Pecoraro (2019) Retrospective cohort study US From 2004 to 2015 Median follow up was 38 months	People aged ≥18 years with T1b histologically confirmed RCC Exclusion criteria: People with missing or inadequate survival follow-up data	Cryoablation (CA) (N = 228)	Partial nephrectomy (PN) (N = 434)	The 1:2 PS matched cohort was balanced by age, gender, ethnicity, educational status, socioeconomic status, marital status, population density by patient residence type, tumour size, tumour grade, histological type and diagnosis year. Additional multivariable adjustment was made for age, tumour size, tumour grade and histological type.	Survival	Serious
Pedraza-Sanchez (2023) Retrospective cohort study	People older than 18 years with radiologic imaging diagnoses of small renal mass (SRMs) including benign lesions.	Percutaneous radiofrequency ablation (PRFA) (N = 111)	Partial nephrectomy (PN) (robotic-assisted, laparoscopic, and open)	Multivariate analysis carried out; factors adjusted for not reported.	Recurrence Survival Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Spain June 2014 to June 2021 Median follow-up time was 38 months (range, 12-109) for PRFA and 48 months (range, 12-78) for PN.	Exclusion criteria: Metastatic disease Radiological evidence of tumour extension beyond the kidney or vascular involvement; Inability to undergo any of these two surgical procedures		(N = 180)		Renal functional impairment Duration of hospital stay	
Qiu (2023) Retrospective cohort study Prospective cohort study US Data were collected retrospectively from	People with biopsy proven T1a RCC ≤4 cm Exclusion criteria: Metastatic disease at diagnosis; Lack of follow-up; Genetic predispositions to multiple renal masses such as VHL or Lynch syndrome	Microwave ablation (MWA) (N = 126)	Partial nephrectomy (PN) (robotic-assisted laparoscopic partial nephrectomy and open partial nephrectomy) (N = 80)	No adjustment for confounders.	Recurrence Survival Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
2009 to 2015 and prospectively since 2015 Median follow-up for PN <3 cm was 35.9 months (IQR 18.7 to46.4) and 25.6 months (IQR 18.5 to49.9) for MWA. Median follow-up for SRMs 3-4 cm was 36.1 months (IQR 18.8 to50.7) for PN and 27.3 months (IQR 12.3 to48.6) for MWA.						
Rembeyo (2020) Retrospective cohort study France	People with cT1bN0M0 RCC (solitary renal mass > 4cm) Exclusion criteria:	Cryoablation (CA) (N = 55) Radiofrequency ablation (RFA) (N = 11)	Robot-assisted partial nephrectomy (RAPN) (N = 36)	The propensity score of each patient was calculated using preoperative variables, which included age, pretreatment eGFR, American Society of Anesthesiologists score,	Renal functional impairment Survival Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Between February 2010 and May 2016 Follow up: Median (range): 23.7 months (15.5-32.2), 19.9 months (15.5-27.2), and 51.3 (31.1-56.5) in the groups RARP, CA, and RFA, respectively	People with multiple RCC; People with an ASA>4			RENAL score, Charlson comorbidity index, diabetes, and hypertension.		
Rusinek (2022) Retrospective cohort study Poland 2014 to 2017 Follow up: 3 years	People with T1a Exclusion criteria: Not reported	Percutaneous thermal ablation (N = 84)	Nephron sparing surgery (N = 56)	Multiple regression Cox proportional hazards model was used considering only those variables which were significant or almost significant (p < 0.1) in single regression model.	Survival Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Ryoo (2022) Retrospective cohort study Korea 2005 to 2019 Follow up 43 to 54 months	People with cT1aN0M0 renal masses Exclusion criteria: People with bilateral or multiple renal masses or a history of hereditary renal cell carcinoma	Radiofrequency ablation (RFA) (N=188)	Partial nephrectomy (PN) (N=323)	Propensity scores were estimated using a logistic regression model.	Renal functional impairment	Serious
Shapiro (2020) Retrospective cohort study US Between January 2000 and June 2018 Median follow-up was 34-, 35-, and 49-months following	People with cT1b renal mass (between 4 and 7cm) Exclusion criteria: Advanced RCC People with hereditary RCC syndromes	Microwave Ablation (MW) (N = 40)	Partial nephrectomy (PN) (N = 74) Radical nephrectomy (RN) (N = 211)	No adjustment for confounders.	Recurrence Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
MW, PN, and RN, respectively.						
Staehler (2022) Retrospective cohort study Germany January 2009 and December 2017 Median follow-up was 28.1 months in both groups (range 6.0-78.3 months).	People with histologically proven clear cell RCC Exclusion criteria: Not reported	High-dose local stereotactic robotic radiosurgery (RRS) (N = 35)	Open partial nephrectomy (N = 35)	Nonparsimonious and multivariate logistic regression was utilized to calculate the propensity scores on the basis of ECOG performance status, age, and tumour size.	Survival Recurrence	Moderate
Takaki (2010) Retrospective cohort study	People with a single RCC of ≤ 4cm maximum diameter (T1a) with at least 6 months follow up	Radiofrequency ablation (RFA) (N = 51)	Radical nephrectomy (RN) open or laparoscopic	No adjustment for confounders.	Survival Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Japan 2002 to 2008 Follow up et al. (months, mean SD) RFA: 34.0 ± 23.2 RN: 40.9 ± 23.2	Exclusion criteria: People with RCCs with vascular invasion or extrarenal spread		(N = 54)			
Takaki (2014) Retrospective cohort study Japan 2002 to 2012 Follow up (months, mean SD) RFA: 41.3 (31.1) RN: 48.6 (33.2)	People with a single RCC measuring 4.1-7.0cm, with at least 6 months follow up Exclusion criteria: Not reported	Radiofrequency ablation (RFA) (N = 21)	Radical nephrectomy (RN) (N = 39)	No confounders adjusted for in the analysis.	Survival Recurrence	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Tanagho (2013) Retrospective cohort study US 2000 to 2012 Mean radiographic follow up (SD), months Cryoablation: 39.8 (34.3) PN: 21.9 (18.8)	People with contrast enhancing renal masses concerning for RCC on preoperative imaging Exclusion criteria: Not reported	Cryoablation (laparoscopic and percutaneous) (N = 267)	Robot-assisted partial nephrectomy (PN) (N = 233)	Authors report that model adjusted for baseline patient and tumour characteristics but does not specify which.	Recurrence Postoperative severe adverse events Survival	Serious
Tang (2017) Retrospective cohort study US 2000 to 2013	People aged 80 to 89 with incidental enhancing solid renal mass. Exclusion criteria: Metastatic disease at evaluation	Active surveillance (AS) (N = 31)	Partial nephrectomy (N = 31) Radical nephrectomy (N = 53)	The variables included in the multivariable analysis were age, Charlson comorbidity index, clinical stage, and management type.	Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Median follow-up period: 51 months (IQR, 23-81 months).						
Turna (2009) Retrospective cohort study US September 1997 to October 2006 Median follow up: PN: 42.5 months Cryoablation: 24 months RFA: Not reported	People with solitary kidney Exclusion criteria: Not reported	Cryoablation (N = 36) Radiofrequency ablation (N = 29)	Laparoscopic partial nephrectomy (PN) (N = 36)	Multivariate regression analysis using the ordinal logistic fit model included variables with p 0.20 on univariate analysis.	Survival Recurrence Duration of stay	Serious
Uemura (2021)	People with cT1 renal tumour	Percutaneous cryoablation (PCA)	Robot-assisted partial nephrectomy (RAPN)	No adjustment for confounders.	Recurrence Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Retrospective cohort study Japan Between March 2016 and November 2019 Median follow up (IQR) RAPN: 18.5 months (12-30) PCA: 12 months (6-32)	Exclusion criteria: Not reported	(N = 48)	(N = 78)			
Uhlig (2020) Retrospective cohort study US Between 2004 and 2015	People with stage I RCC Exclusion criteria: Under 18 years old at the time of treatment; Unknown cancer histology	Cryoablation (N = 5446) Radiofrequency or microwave (MW) ablation (N = 3432)	Partial nephrectomy (PN) (N = 82913)	People were propensity score–matched to account for potential confounders, including patient age, sex, race, comorbidities, tumour size, histology, grade, tumour sequence, administration of systemic therapy, treatment in academic versus non-academic centres,	Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Median follow-up time was 58.1 months (IQR: 34.7 to 86.6 months)	Radiation to metastatic RCC sites	Stereotactic body radiotherapy (SBRT) (N = 174)		treatment location, and year of diagnosis.		
Umari (2022) Retrospective cohort study Italy Percutaneous cryoablation data were collected and analysed since 2011 and active surveillance since 2010 Mean follow up 35.31 (SD = 21.19)	People with a single cT1a renal tumour Exclusion criteria: Not reported	Active surveillance (AS) (N = 75)	Percutaneous cryoablation (PCA) (N = 59)	No adjustment for confounders.	Recurrence	Serious
Weinberg (2015)	People with contrast enhancing renal masses concerning for	Laparoscopic cryoablation (N = 4421)	Robotic partial nephrectomy (PN) (N = 10034)	No adjustment for confounders.	Duration of hospital stay	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
Retrospective cohort study US 2008 to 2010 Follow up: Not reported.	RCC on preoperative imaging Exclusion criteria: With diagnoses of transplant, renal pelvis tumour or pyelonephritis; Admission types other than elective; People undergoing concomitant procedures: splenectomy, liver resection, pancreas resection, bowel or colon resection, or thrombectomy with vascular reconstruction.					
Xing (2018) Retrospective cohort study	People at least 66 years old with node-negative, nonmetastatic T1a RCC (≤4cm)	Thermal ablation (N = 898) Active surveillance (AS) (N = 1978)	Radical nephrectomy (N = 4522)	Propensity scores were calculated on the basis of 17 predefined covariates: age, sex, race, Charlson comorbidity index,	Survival Cardiovascular events	Moderate to serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
US 2002 to 2011 Median follow up in months AS versus TA: 42.2 versus 42.3 AS versus RN: 60.1 versus 63.0 RN versus TA: 46.9 versus 46.8	Exclusion criteria: Pre-existing end-stage renal disease before diagnosis			cardiovascular disease, hypertension, diabetes, moderate or severe renal disease, socioeconomic status, marital status, region, urban or rural location, tumour size, histologic characteristics, Fuhrman grade, year of diagnosis, and length of follow-up.		
Yamanoi (2024) Retrospective cohort study Japan	People with cT1 renal cell carcinoma Exclusion criteria: People with non-renal cell carcinoma histology, prior histology of renal cell carcinoma, intrarenal metastasis of other	Robot-assisted partial nephrectomy (N=108)	Percutaneous cryoablation (N=108)	Participants were matched 1:1 with the nearest neighbour propensity score. Confounders not reported.	Distant metastasis Complications Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
June 2012 to May 2021 Follow-up: PN: 53 months TA: 61 months	cancers, no control imaging, and history or renal replacement therapy such as dialysis and transplantation.					
Yanagisawa (2020) Retrospective cohort study Japan September 2011 to December 2019. Median follow-up was 26.5 months for PCA and 18 months for LPN	People with cT1 renal tumour Exclusion criteria: People with benign tumours, diagnosed by biopsy or resection	Percutaneous cryoablation (N = 90)	Laparoscopic partial nephrectomy (N = 90)	Propensity scores were calculated through logistic regression modelling based on the following covariates: Age, gender, Charlson's comorbidity index (CCI), the R.E.N.A.L nephrometry score, clinical T-stage, tumour diameter, and pre-operative eGFR.	Duration of hospital stay Postoperative severe adverse events	Serious
Yang (2024) Retrospective cohort study	People diagnosed with renal cell carcinoma by positive histology who underwent partial	Radiofrequency ablation (N=300)	Partial nephrectomy (N=15392)	Age Race Gender	Survival	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
US January 2004 to December to 2015 Follow-up: RA: median 45.5 months PN: median 55 months	nephrectomy or radiofrequency ablation. People with tumour size no more than 4 cm, consistent with TNM stage T1a. Exclusion criteria: People with metastatic disease or unknown tumour grade.			Year of diagnosis		
Yasuda (2023) Retrospective cohort study US People were identified from the Cleveland Clinic kidney cancer database (IRM 20-	People with solitary kidney Exclusion criteria: People with horseshoe kidneys	Cryoablation (N = 102) Active surveillance (N = 26)	Partial nephrectomy (PN) (N = 842)	No adjustment for confounders.	Recurrence Survival Postoperative severe adverse events	Serious

Study details	Population	Intervention	Comparator	Confounders the study adjusted for	Outcomes	Risk of bias
836) between 1975 and 2022 Follow-up (months), median (IQR) PN: 57.4 (47.2 to 71.1) CA: 31.2 (6.8 to 114.9) AS: 39.4 (11.8 to 74.2)						

Table 5 Summary of the studies included for each comparison and the available outcomes

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
Thermal ablation versus partial nephrectomy (non-randomised evidence)	Acosta Ruiz (2021) Aikawa (2023) Alam (2019) Almadalala (2022) Andrews (2019) Anglickis (2019)	N=69,622 Retrospective cohort studies	Recurrence • Disease free survival • Recurrence • Local recurrence-free survival • Local recurrence • Metastasis-free survival	Moderate to serious

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
	Attawettayanon (2023) Beksac (2022) Bertolo (2019) Bhindi (2018) Bianchi (2021) Bird (2019) Caputo (2017) Cazalas (2023) Chan (2022) Duus (2023) Emara (2014) Fraisse (2019) Haber (2011) Junker (2022a) Junker (2022b) Kawaguchi (2022) Kiriluk (2011) Kitley (2019) Lehrer (2023) Long (2017)		• Metastasis Survival • Overall survival • Mortality • Cancer-specific survival • Cancer-specific mortality Postoperative complications • All complications • Minor complications • Major complications Duration of hospital stay Renal function • Change in eGFR • New onset eGFR <60 mL/min/1.73 m^2 • New onset eGFR <45 mL/min/1.73 m^2 • New onset eGFR <30 mL/min/1.73 m^2 • New onset eGFR <15 mL/min/1.73 m^2 Quality of life • EORTC global health score 14 days • EORTC global health score 90 days	

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
	Lucignani (2023) Mason (2018) Millan (2022) Mues (2012) Palumbo (2020) Pandolfo (2023) Pantelidou (2016) Panumatrassamee (2013) Park (2018) Park (2019) Pecoraro (2019) Pedraza-Sanches (2023) Qiu (2023) Rembeyo (2019) Rusinek (2022) Ryoo (2022) Shapiro (2020) Takaki (2010) Tanagho (2013) Turna (2009)			

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
	Uemura (2021) Uhlig (2020) Weinberg (2015) Yanagisawa (2020) Yasuda (2022)			
Thermal ablation versus radical nephrectomy	Almadalal (2022) Takaki (2010) Takaki (2014) Shapiro (2020) Xing (2018)	N=2,999 Retrospective cohort studies	Recurrence • Disease free survival • Recurrence • Local recurrence • Metastasis Survival • Overall survival • Mortality • Cancer-specific survival • Cancer-specific mortality Renal function • Change in eGFR Cardiovascular events	Moderate to serious
Active surveillance versus partial nephrectomy	Alam (2019) Cheung (2023)	N=29,869	Recurrence • Recurrence	Moderate to serious

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
	Palumbo (2020) Yasuda (2022)	Retrospective cohort studies	• Local recurrence • Metastasis Survival • Overall survival • Mortality • Cancer-specific survival Postoperative complications • Major complications Renal function • New onset eGFR <45 mL/min/1.73 m^2	
Active surveillance versus radical nephrectomy	Cheung (2023) Lane (2010) Patel (2012) Tang (2017) Xing (2018)	N=3,962 Retrospective cohort studies	Recurrence • Metastasis Survival • Overall survival • Mortality • Cancer-specific survival • Cancer-specific mortality Renal function • New onset eGFR <60 mL/min/1.73 m^2	Moderate to serious

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
SABR versus partial nephrectomy	Staehler (2022) Uhlig (2020)	N=388 Retrospective cohort studies	Recurrence • Local recurrence Survival • Overall survival	Moderate to serious
Active surveillance versus thermal ablation	Grant (2020) Umari (2022) Yasuda (2022)	N=35,699 Retrospective cohort studies	Recurrence • Recurrence • Local recurrence • Metastasis Survival • Overall survival • Mortality • Cancer-specific survival Postoperative complications Major complications	Moderate to serious
SABR versus thermal ablation	Uhlig (2020)	N=477 Retrospective cohort studies	Survival • Overall survival	Serious
SABR versus active surveillance	Grant (2020)	N= 18,345 Retrospective cohort studies	Survival • Overall survival	Moderate

Comparison	Contributing studies	Study details	Outcomes presented	Risk of bias for included outcomes
Active surveillance versus nephrectomy (all)	Cheung (2023) Grant (2020)	N=183,649 Retrospective cohort studies	Survival • Overall survival	Moderate

Note: Table 4 and Table 5 include primary non-randomised studies only and do not include non-randomised studies which are reported on in the included systematic reviews.

See appendix D for full evidence tables

1.1.6 Summary of the effectiveness evidence

Assessing publication bias

Funnel plots were constructed for outcomes contributed to by ten or more studies (see the methods chapter for more details and see appendix E for funnel plots alongside the relevant forest plot). Publication bias was strongly suspected for the outcome of local recurrence ≤5 years for thermal ablation compared with partial nephrectomy based on a visual assessment of the distribution of studies on the funnel plot. This outcome was downgraded for publication bias as part of the GRADE assessment. The forest plot and funnel plot are presented in appendix E, Figure 12 and Figure 13.

Interpreting the effectiveness evidence

In the absence of published minimally important differences (MIDs) clinical decision thresholds were agreed with the committee and used to interpret the evidence. The line of no effect (in this case represented by 1.0) was used as a clinical decision threshold for the outcomes of disease-free survival and recurrence, overall survival and mortality, cancer-specific survival and cancer-specific mortality, post-operative severe adverse events, renal function impairment, quality of life using the EORTC questionnaire, cardiovascular events and duration of hospital stay as detailed in the protocol. No data was identified for quality of life using the EQ-5D or VAS scores (the only outcomes with a published MID), hospital admissions or intra-operative adverse events.

The following criteria were used to interpret the effect (column of ‘Interpretation of effect’ below) in the summary GRADE tables:

For outcomes without a published MID or where the clinical decision thresholds is set as the line of no effect evidence statements are divided into 2 groups as follows:

- We state that the evidence showed that there is an effect if the 95% CI does not cross the line of no effect.
- It is not possible from the evidence to differentiate between comparators if the 95% CI crosses the line of no effect.

Further details on GRADE assessment are described in appendix F.

Thermal ablation versus partial nephrectomy

Table 6 Thermal ablation versus partial nephrectomy RCT

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Neves 2023)	Postoperative severe adverse events - Clavien-Dindo I	50	RR 0.67 (0.12 to 3.65)	Very low	Could not differentiate
1 (Neves 2023)	Postoperative severe adverse events - Clavien-Dindo 2	50	RR 0.25 (0.03 to 2.08)	Very low	Could not differentiate
1 (Neves 2023)	Postoperative severe adverse events - Clavien-Dindo 3-5	50	Not estimable (0 events in both arms)	Very low	Not estimable
1 (Neves 2023)	Renal functional impairment: Change in eGFR at 6 months (mL/min/1.73 m2)	50	MD 0.8 (-6.46 to 8.06)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Table 7 Thermal ablation versus partial nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
4 (Fossati 2015, Lehrer 2023, Millan 2022, Pantelidou 2016)	Disease-free survival ≤5 years	2,363	HR 1.96 (1.24 to 3.08)	Low	Effect favours partial nephrectomy
1 (Olweny 2012)	Disease-free survival >5 years	74	HR 0.85 (0.23 to 3.15)	Very low	Could not differentiate

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
10 (Almadalal 2022, Anglickis 2019, Bird 2009, Caputo 2017, Long 2017, Qiu 2023, Rembeyo 2019, Tanagho 2013, Uemura 2021, Yasuda 2022)	Recurrence ≤5 years	2,983	OR 2.13 (1.07 to 4.22)	Very low	Effect favours partial nephrectomy
4 (Aikawa 2023, Fraisse 2019, Millan 2022, Pedraza-Sanchez 2023)	Local recurrence-free survival ≤5 years	2,420	HR 2.57 (1.50 to 4.40)	Low	Effect favours partial nephrectomy
2 (Andrews 2019, Chan 2022)	Local recurrence-free survival >5 years	1,901	HR 0.69 (0.14 to 3.38)	Very low	Could not differentiate
21 (Almadalal 2022, Attawettayanon 2023, Beksac 2022, Cazalas 2023, Desai 2005, Emara 2014, Fossati 2015, Guillotreau 2012, Haber 2011, Klatte 2011, Lucas 2008, Mues 2012, Pandolfo 2023, Park 2018, Qiu 2023, Shapiro 2020, Stern 007, Takaki 2010, Thompson 2015, Turna 2009, Yasuda 2022)	Local recurrence ≤5 years	6,038	OR 3.24 (1.74 to 6.03)	Very low	Effect favours partial nephrectomy
3 (Bianchi 2021, Olweny 2012, Park 2019)	Local recurrence >5 years	1,005	OR 3.07 (0.48 to 19.70)	Very low	Could not differentiate
2 (Aikawa 2023, Bhindi 2018)	Metastasis-free survival ≤5 years	204	HR 0.83 (0.45 to 1.54)	Very low	Could not differentiate
2 (Andrews 2019, Chan 2022)	Metastasis-free survival >5 years	1,798	HR 0.44 (0.15 to 1.35)	Very low	Could not differentiate
12 (Attawettayanon 2023, Cazalas 2023, Haber 2011, Mason 2018, Mues 2012, Pandolfo 2023, Pedraza-Sanchez 2023, Shapiro 2020, Turna 2009, Takaki 2010, Yasuda 2022, Yamanoi 2024)	Metastasis ≤5 years	2,510	RR 1.28 (0.77 to 2.14)	Very low	Could not differentiate

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Bianchi 2021)	Metastasis >5 years	816	RR 1.17 (0.40 to 3.49)	Very low	Could not differentiate
10 (Aikawa 2023, Alam 2019, Bhindi 2018, Lehrer 2023, Millan 2022, Pedraza-Sanchez 2023, Takaki 2012, Thompson 2015, Uhlig 2020, Yang 2024)	Overall survival ≤5 years	19,959	HR 1.89 (1.53 to 2.34)	Low	Effect favours partial nephrectomy
4 (Andrews 2019, Chan 2022, Kitley 2019, Olweny 2012)	Overall survival >5 years	14,433	HR 1.69 (1.22 to 2.35)	Very low	Effect favours partial nephrectomy
13 (Almadalal 2022, Kawaguchi 2022, Long 2017, Mues 2012, Qiu 2023, Pandolfo 2023, Rembeyo 2019, Rusinek 2022, Takaki 2010, Turna 2009, Uemura 202, Yamanoi 2024, Yasuda 2022)	Mortality ≤5 years	3,521	RR 1.50 (0.94 to 2.38)	Very low	Could not differentiate
1 (Park 2019)	Mortality >5 years	115	RR 4.29 (0.21 to 87.32)	Very low	Could not differentiate
6 (Aikawa 2023, Alam 2019, Bhindi 2019, Palumbo 2020, Pecoraro 2019, Yang 2024)	Cancer-specific survival ≤5 years	25,430	HR 1.64 (1.28 to 2.110)	Low	Effect favours partial nephrectomy
2 (Andrews 2019, Olweny 2012)	Cancer-specific survival >5 years	1,679	HR 1.29 (0.38 to 4.39)	Very low	Could not differentiate
8 (Fraisse 2019, Long 2017, Pedraza-Sanchez 2023, Rembeyo 2019, Shapiro 2020, Takaki 2010, Turna 2009, Yamanoi 2024)	Cancer-specific mortality ≤5 years	1,508	RR 1.00 (0.32 to 3.12)	Very low	Could not differentiate
1 (Bianchi 2021)	Cancer-specific mortality >5 years	816	RR 4.40 (1.11 to 17.41)	Very low	Effect favours partial nephrectomy

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
31 (Acosta Ruiz 2021, Aikawa 2023, Bhindi 2018, Caputo 2017, Chan 2022, Desai 2005, Emara 2014, Fossati 2015, Garcia 2021, Guillotreau 2012, Haramis 2012, Junker 2022, Kiriluk 2011, Klatte 2011, Ko 2008, Long 2017, Lucignani 2023, Mues 2012, Pandolfo 2023, Pantelidou 2016, Panumatrassamee 2013, Pedraza-Sanchez 2023, Qiu 2023, Rembeyo 2019, Shapiro 2020, Stern 2007, Tanagho 2013, Yamanoi 2024, Yanagisawa 2018, Yanagisawa 2020)	Postoperative severe adverse events - Clavien-Dindo I-V	5,414	RR 0.76 (0.60 to 0.96)	Very low	Effect favours thermal ablation
12 (Chan 2022, Emara 2014, Junker 2022, Kiriluk 2011, Mues 2012, Pandolfo 2023, Pantelidou 2016, Panumatrassamee 2013, Pedraza-Sanchez 2023, Qiu 2023, Rusinek 2022, Tanagho 2013)	Postoperative severe adverse events - Clavien-Dindo I-II	2,341	RR 0.88 (0.73 to 1.07)	Very low	Could not differentiate
36 (Aikawa 2023, Anglickis 2019, Attawettayanon 2023, Caputo 2017, Cazalas 2023, Chan 2022, Desai 2005, Emara 2014, Fossati 2015, Garcia 2021, Guillotreau 2012, Haramis 2012, Junker 2022, Kawaguchi 2022, Kim 2015, Klatte 2011, Ko 2008, Long 2017, Lucignani 2023, Mues 2012, Pandolfo 2023, Panumatrassamee 2013, Pantelidou 2016, Park 2018, Park 2019, Pedraza-Sanchez 2023, Qiu 2023, Rembeyo 2019, Rusinek 2022, Shapiro 2020, Stern 2007,	Postoperative severe adverse events - Clavien-Dindo III-V	6,896	RR 0.83 (0.63 to 1.09)	Very low	Could not differentiate

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
Tanagho 2013, Tanagisawa 2018, Yamanoi 2024, Yanagisawa 2020, Yasuda 2022)					
17 (Bird 2009, Desai 2005, Fossati 2015, Garci 2021, Haber 2011, Jasinski 2024, Kim 2015, Ko 2008, Lehrer 2023, Long 2017, Pandolfo 2023, Park 2018, Pedraza-Sanchez 2023, Turna 2009, Weinberg 2015, Yanagisawa 2018, Yanagisawa 2020)	Duration of hospital stay (days)	16,926	MD -2.70 (-3.68 to -1.73)	Very low	Effect favours thermal ablation
7 (Bird 2009, Haber 2011, Lehrer 2023, Pandolfo 2023, Turna 2009, Weinberg 2015, Yanagisawa 2020)	Duration of hospital stay (days) (sensitivity analysis: minimally invasive surgery)	15,280	MD -1.84 (-2.95 to -0.74)	Very low	Effect favours thermal ablation
25 (Acosta Ruiz 2021, Bertolo 2019, Cazalas 2023, Cooper 2015, Danxig 2015, Deklaj 2010, Duus 2023, Faddegon 2013, Foyil 2008, Guillotreau 2012, Kawaguchi 2022, Kiriluk 2011, Klatte 2011, Long 2017, Lucas 2008, Mitchell 2011, Mues 2012, Pandolfo 2023, Pascal 2011, Pedraza-Sanchez 2023, Takaki 2010, Takaki 2014, Tanagho 2013, Turna 2009, Youn 2013)	Renal function impairment: Change in eGFR ≤5 years	3,611	MD 0.99 (-0.7 to 2.68)	Very low	Could not differentiate
5 (Beksac 2022, Pandolfo 2023, Park 2018, Rembeyo 2019, Ryoo 2022)	Renal function impairment: New onset eGFR <60 mL/min/1.73 m2	859	RR 1.17 (0.82 to 1.69)	Very low	Could not differentiate

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Alam 2019)	Renal function impairment: New onset eGFR <45 mL/min/1.73 m2	258	OR 1.72 (0.39 to 7.56)	Very low	Could not differentiate
1 (Ryoo 2022)	Renal function impairment: New onset eGFR <30 mL/min/1.73 m2	106	RR 1.50 (0.26 to 8.62)	Very low	Could not differentiate
7 (Beksac 2022, Guillotreau 2012, Lucas 2008, Mues 2012, Pascal 2011, Ryoo 2022, Turna 2009)	Renal function impairment: New onset eGFR <15 mL/min/1.73 m2	1,159	RR 1.21 (0.57 to 2.57)	Very low	Could not differentiate
1 (Junker 2022)	Quality of life at 14 days (EORTC questionnaire)	165	MD -9.6 (-15.95 to -3.25)	Very low	Favours thermal ablation
1 (Junker 2022)	Quality of life at 90 days (EORTC questionnaire)	165	MD 0.26 (-6.14 to 6.66)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Thermal ablation versus radical nephrectomy

Table 8 Thermal ablation versus radical nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Almadalal 2022)	Disease-free survival ≤5 years	1,107	HR 5.67 (3.23 to 9.95)	Very low	Favours radical nephrectomy
1 (Takaki 2014)	Recurrence ≤5 years	60	RR 0.93 (0.19 to 4.66)	Very low	Could not differentiate
2 (Shapiro 2020, Takaki 2014)	Local recurrence ≤5 years	311	RR 8.31 (1.24 to 55.51)	Very low	Favours radical nephrectomy
3 (Shapiro 2020, Takaki 2010, Takaki 2014)	Metastasis ≤5 years	426	RR 0.63 (0.18 to 2.18)	Very low	Could not differentiate
1 (Almadalal 2022)	Overall survival ≤5 years	1,107	HR 0.72 (0.49 to 1.05)	Very low	Could not differentiate
2 (Takaki 2010, Takaki 2014)	Mortality ≤5 years	175	RR 11.71 (2.19 to 62.57)	Very low	Favours radical nephrectomy
1 (Xing 2018)	Cancer-specific survival ≤5 years	772	HR 0.89 (0.53 to 1.52)	Very low	Could not differentiate
3 (Shapiro 2020, Takaki 2010, Takaki 2014)	Cancer-specific mortality ≤5 years	426	RR 0.88 (0.11 to 7.14)	Very low	Could not differentiate
7 (Cooper 2015, Danzig 2015, Deklaj 2010, Foyil 2008, Lucas 2008, Takaki 2010, Takaki 2014)	Renal function impairment: Change in eGFR ≤5 years	390	MD 9.06 (3.91 to 14.21)	Very low	Favours thermal ablation
1 (Xing 2018)	Cardiovascular events	1,466	RR 0.82 (0.72 to 0.92)	Low	Favours thermal ablation

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Active surveillance versus partial nephrectomy

Table 9 Active surveillance versus partial nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Yasuda 2022)	Metastasis ≤5 years	842	RR 1.30 (0.33 to 5.04)	Very low	Could not differentiate
5 (Alam 2019, Miller 2018, Patel 2012, Patel 2015, Tang 2017)	Overall survival ≤5 years	3,517	HR 2.50 (2.13 to 2.94)	Very low	Favours partial nephrectomy
1 (Yasuda 2022)	Mortality ≤5 years	868	RR 0.85 (0.52 to 1.39)	Very low	Could not differentiate
6 (Alam 2019, Miller 2018, Palumbo 2020, Patel 2012, Patel 2015, Tang 2017)	Cancer-specific survival ≤5 years	6,629	HR 2.15 (0.99 to 4.66)	Very low	Could not differentiate
1 (Alam 2019)	Renal function impairment: New onset eGFR <45 mL/min/1.73 m2 ≤5 years	570	OR 0.97 (0.37 to 2.53)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Active surveillance versus radical nephrectomy

Table 10 Active surveillance versus radical nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Lane 2010)	Metastasis ≤5 years	251	RR 0.46 (0.02 to 11.24)	Very low	Could not differentiate
2 (Lane 2010, Tang 2017)	Overall survival ≤5 years	335	HR 1.25 (0.83 to 1.87)	Very low	Could not differentiate

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Patel 2012)	Mortality ≤5 years	112	RR 0.87 (0.39 to 1.94)	Very low	Could not differentiate
1 (Xing 2018)	Cancer-specific survival >5 years	3,348	HR 1.08 (0.82 to 1.42)	Very low	Could not differentiate
2 (Lane 2010, Patel 2012)	Cancer-specific mortality ≤5 years	363	RR 0.63 (0.11 to 3.46)	Very low	Could not differentiate
1 (Lane 2010)	Renal function impairment: New onset eGFR <60 mL/min/1.73 m2	251	RR 0.22 (0.09 to 0.54)	Very low	Favours active surveillance

Reasons for downgrading can be found in the full GRADE tables in appendix F.

SABR versus partial nephrectomy

Table 11 SABR versus partial nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Staehler 2022)	Local recurrence ≤5 years	70	RR 3.00 (0.13 to 71.22)	Very low	Could not differentiate
2 (Staehler 2022, Uhlig 2020)	Overall survival ≤5 years	388	HR 1.64 (0.33 to 8.07)	Very low	Could not differentiate
1 (de Angelis 2024)	Cancer-specific mortality	184	HR 4.30 (0.88 to 20.99)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Active surveillance versus thermal ablation

Table 12 Active surveillance versus thermal ablation non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
2 (Umari 2022, Yasuda 2022)	Metastasis ≤5 years	262	RR 0.93 (0.25 to 3.45)	Very low	Could not differentiate
3 (Alam 2019, Grant 2020, Miller 2018)	Overall survival ≤5 years	35,907	HR 1.68 (0.59 to 4.80)	Very low	Could not differentiate
1 (Yasuda 2022)	Mortality ≤5 years	128	RR 1.40 (0.78 to 2.50)	Very low	Could not differentiate
4 (Alam 2019, Larcher 2015, Miller 2018, Xing 2018)	Cancer-specific survival ≤5 years	3,624		Very low	Favours thermal ablation

Reasons for downgrading can be found in the full GRADE tables in appendix F.

SABR versus thermal ablation

Table 13 SABR versus thermal ablation non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Uhlig 2020)	Overall survival >5 years - cryotherapy	318	HR 2.50 (1.65 to 3.80)	Very low	Favours thermal ablation
1 (Uhlig 2020)	Overall survival >5 years - radiofrequency ablation	318	HR 2.17 (1.47 to 3.19)	Very low	Favours thermal ablation

Reasons for downgrading can be found in the full GRADE tables in appendix F.

SABR versus active surveillance

Table 14 SABR versus active surveillance non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
1 (Grant 2020)	Overall survival ≤5 years	18,345	HR 0.56 (0.39 to 0.80)	Low	Favours SABR

Reasons for downgrading can be found in the full GRADE tables in appendix F.

Active surveillance versus nephrectomy

Table 15 Active surveillance versus nephrectomy non-randomised evidence

Number of studies	Outcome	Sample size	Effect estimate	Certainty	Interpretation of effect
2 (Cheung 2023, Grant 2020)	Overall survival ≤5 years	183,649	HR 3.19 (1.27 to 8.01)	Moderate	Favours nephrectomy
1 (Grant 2020)	Overall survival ≤5 years (sensitivity analysis: confirmed RCC)	183,539	HR 4.00 (3.84 to 4.16)	Moderate	Favours nephrectomy
1 (Cheung 2023)	Overall survival ≤5 years (sensitivity analysis: unconfirmed RCC)	167	HR 1.20 (0.19 to 7.71)	Very low	Could not differentiate

Reasons for downgrading can be found in the full GRADE tables in appendix F.

See appendix F for full GRADE tables.

1.1.7 Economic evidence

A single literature search was conducted to identify published economic evaluations of relevance to the review questions on management in this guideline (see appendix B), which includes the present review B for non-surgical interventions for localised RCC, as well as reviews for partial and radical nephrectomy for localised RCC (evidence review A), management of locally advanced RCC (evidence review C) and management of advanced RCC (evidence reviews H1 and H2).

This search retrieved 326 studies, and based on title and abstract screening four studies were identified as potentially relevant for any of the evidence reviews covered by the search. On review of the full text, two studies were included for evidence review B (the present review), and two studies were excluded. For details on study selection, see economic study selection flow chart in appendix G.

1.1.7.1 Included studies

Two studies were included at full text review; however, one study (Xia et al. 2025) was considered as partially applicable with very serious limitations and the committee agreed that it was not suitable for decision making (see Table 38). The other included study (Health Technology Wales 2022) is summarised in Table 16 with further information detailed in Appendix H – Economic evidence tables.

1.1.7.2 Excluded studies

Two studies were excluded at full text review (see Appendix J – Excluded studies for a list of studies and reason for exclusion).

1.1.8 Summary of included economic evidence

Table 16: Economic evidence profile [SABR versus observation in people whose cancer cannot be managed using surgery or thermal ablation]

Study	Applicability	Limitations	Other comments	Incremental			Uncertainty
				Cost (£)	Effects (QALYs)	ICER (£/QALY)	
Health Technology Wales (2022) Evidence Appraisal Report: Stereotactic ablative radiotherapy to treat	Directly applicable only for the subgroup of people with localised renal cancer who are not suitable for surgery or thermal ablation.	Potentially serious limitations, due to the use of separate sources for baseline and relative effects	Partitioned survival analysis over a lifetime time horizon, comparing SABR with observation in people	£2,395	2.02	£1,188	Scenario analysis: SABR was found to be cost-effective in all scenarios. Probabilistic analysis:

Study	Applicability	Limitations	Other comments	Incremental Cost (£)	Incremental Effects (QALYs)	Incremental ICER (£/QALY)	Uncertainty
people with primary kidney cancer.			whose cancer cannot be managed using surgery or thermal ablation.				SABR had a 100% probability of being cost-effective at a threshold of £20,000 per QALY.

1.1.9 Economic model

A costing analysis was conducted to aid in recommendation making for this review question and give context of how costly each treatment option is, weighed against the outcomes in the clinical review and their potential downstream costs across the management pathway. Full details of the analysis are included in the accompanying costing report.

All potential treatment strategies were mapped out by the committee, along with follow-up and management of downstream consequences in line with current practice. A summary of the procedure costs is in Table 18 and the downstream costs are presented in Table 19.

The decision problem for the costing analysis is detailed in Table 17.

Table 17: PICO, costing analysis

Population	Adults (18 years or over) with (histologically confirmed or suspected on imaging) localised renal cell carcinoma (RCC)

Intervention	• Thermal ablation
	  ○ Radiofrequency ablation
	  ○ Cryoablation
	  ○ Microwave ablation
	• Stereotactic ablative radiotherapy (SABR)
	• Active surveillance

Comparator	• Surgery
	  ○ Partial nephrectomy
	  ○ Radical nephrectomy

Outcomes	Costs • Initial treatment • Adjuvant treatment • Follow-up after treatment (based on risk-stratified imaging strategy suggested by GIRFT guidance and expert opinion) • Downstream events (management of recurrence)

Cost of the procedures

The costs of minimally invasive and open radical nephrectomy were estimated from NHS Cost Collection. A minimally invasive nephrectomy can be undertaken as a robot-assisted procedure; however, there is not a specific HRG code for robotic surgery, and so the additional cost of this procedure relative to laparoscopic nephrectomy was estimated from Camp (2018). A weighted average cost was estimated using the relative proportion receiving each of the three surgical approaches as reported in the National Kidney Cancer Audit (2024) and the corresponding episode cost from NHS Cost Collection. The cost of an appointment with a consultant following surgery is also included in these costs. It is expected that length of stay would differ between the different interventions however any difference in costs due to this are assumed to be implicitly captured in the NHS Cost Collection which includes all direct costs associated with a particular episode.

For thermal ablation, Rossi et al. (2021) assumed that 60% of ablation would be cryoablation. Based on this, we assumed that the remaining 40% would be evenly split between microwave and radiofrequency ablation. The committee also mentioned that there would be a follow-up appointment with a consultant surgeon after the procedure. All procedure costs and the cost of follow-up appointment were from NHS Cost Collection. The cost for any ablation was calculated as an average of radiofrequency ablation, cryoablation and microwave ablation.

For SABR the committee advised that people would receive between 1 and 3 fractions of radiation treatment, based on the person's characteristics, and would require the cost of CT preparation prior to treatment. Following the procedure, patients receive a CT scan with contrast of three areas, and an appointment with surgical consultant or a cancer MDT meeting. A range of costs has been calculated, based on whether they receive 1 or 3 fractions, or a consultant or cancer MDT post-surgical appointment.

Table 18: Summary of management costs

Surgery procedure	Type of procedure	Total cost of the procedure
Partial nephrectomy	Open: 9% Laparoscopic: 4% Robotic: 87%	Open: £10,142 Laparoscopic: £9,970 Robotic: £10,172 Surgical consultant: £157 Overall: £10,319
Radical nephrectomy	Open: 20% Laparoscopic: 48% Robotic: 31%	Open: £10,142 Laparoscopic: £9,970 Robotic: £10,172 Surgical consultant: £157 Overall: £10,226
Thermal ablation	Radiofrequency: 20% Cryoablation: 60%	Radiofrequency: £2,118 Cryoablation: £3,632

Surgery procedure	Type of procedure	Total cost of the procedure
	Microwave ablation: 20%	Microwave ablation: £2,118 Overall: £3,026
SABR	Lowest estimate: 1 fraction of radiation, post-surgical appointment with cancer MDT Highest estimate: 3 fractions of radiation, post-surgical appointment with surgical consultant	£2,133 £2,684

Cost of downstream events

Monitoring of patients after treatment comprises imaging, namely CT scans, at regular intervals. Complete blood counts are taken prior to imaging. Follow-up schedules over 5 years for the costing analysis are based on the GIRFT guidance and committee opinion, with costs of scans taken from NHS Cost Collection. Costs were estimated for each risk category, with their risk score based on their RCC subtype (e.g. Leibovich score for clear cell RCC). People previously receiving SABR are assumed to be followed up as if they are intermediate risk.

The cost of a year of adjuvant pembrolizumab treatment was included for people at increased risk of recurrence who were previously treated via nephrectomy, which the committee suggested would be 30% of people who have had surgery. Pembrolizumab does have a confidential access price which has not been included here, and so this cost after surgery is an overestimate. People treated with SABR or thermal ablation are not eligible for adjuvant therapy with pembrolizumab, as per the NHS commissioning guidelines.

Downstream costs associated with recurrences are estimated using the distribution of treatments for stages III and IV RCC as reported by Rossi et al (2021) for local and distant recurrences, respectively. The cost of managing local recurrence was estimated as the weighted average cost of open nephrectomy, laparoscopic nephrectomy and robotic nephrectomy. The cost of managing distant recurrence consisted of cytoreductive nephrectomy, metastasectomy, radiotherapy and systemic therapy. Cost of follow up, which consists of CT scan, blood test and visits of clinical and medical oncologists, were also included in the management of both local and distant recurrence. The committee suggested that 85% of distant recurrences would be treated with systemic therapies, with costs of the systemic therapy pathway extracted from the recent NICE appraisal TA964.

Table 19: Summary of downstream costs

Downstream resource	Costing approach	Total cost
Adjuvant treatment	Assume 30% receive adjuvant pembrolizumab. Cost per vial: £2,630. Admin cost per dose: £398. Dose given every 3 weeks.	Total 1-year cost: £29,522
Follow up	CT scan with contrast of three areas. Low risk: 3 total scans, intermediate risk: 6 total scans, high risk: 8 total scans.	Total 5-year cost: Low risk: £378 Intermediate risk: £757 High risk: £1,009
Recurrence	Local recurrence: 51% managed by open nephrectomy, 24.5% by laparoscopic nephrectomy and robotic nephrectomy, respectively. Distant recurrence: 85% systemic therapy, 37% cytoreductive nephrectomy, 12% radiotherapy, 17% metastasectomy.	Cost per local recurrence (5-year cost): £14,649 Cost per distant recurrence (1-year cost): £77,342 Note that these costs apply onto to those who experience recurrence see Section 1.1.6 for relative effectiveness evidence.

1.1.10 Unit costs

Unit costs of interventions in the scope of this review are listed in Table 20.

Table 20: Unit costs of interventions

Resource	Unit cost	Source
Open nephrectomy	£10,142.10	NHS Cost Collection (2024). Weighted average of codes LB61C-G, Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over
Laparoscopic nephrectomy	£9,970.10	NHS Cost Collection (2024). Weighted average of codes LB62C-D, Major Laparoscopic, Kidney or Ureter Procedures, 19 years and over

Resource	Unit cost	Source
Robot-assisted nephrectomy	£10,172.87	Ratio of robotic to laparoscopic partial nephrectomy costs estimated from Camp et al. (2018), calculated as £4,444 / £4,356 = 1.02. Ratio applied to the laparoscopic nephrectomy unit cost to estimate the robotic nephrectomy unit cost.
CT preparation for SABR therapy	£1,691.27	NHS Cost Collection (2024). SC41Z preparation for intensity modulated radiation therapy with technical support
One fraction of SABR	£237.42	NHS Cost Collection (2024). SC22Z deliver a fraction of treatment on a megavoltage machine
Radiofrequency ablation	£1,960.46	NHS Cost Collection (2024). YL02Z Standard Percutaneous Ablation of Lesion of Kidney
Cryoablation	£3,474.14	NHS Cost Collection (2024). YL01Z Complex Percutaneous Ablation of Lesion of Kidney
Microwave ablation	£1,960.46	NHS Cost Collection (2024). YL02Z Standard Percutaneous Ablation of Lesion of Kidney

SABR: stereotactic ablative radiotherapy, CT: computed tomography.

1.1.11 The committee's discussion and interpretation of the evidence

Evidence review B (the current review) and evidence review A which compares partial and radical nephrectomy are linked. Where the committee's discussion about the evidence for the two reviews contains some overlapping content this is reproduced, or referred to, in both reviews for completeness.

The committee discussed the terminology around nephrectomy and that whilst the evidence identified refers to "radical nephrectomy", the committee preferred to use the term "total nephrectomy" as it is generally more acceptable to people with renal cell carcinoma (RCC). So, the term "total nephrectomy" has been used in the committee's discussion and interpretation of the evidence and in the recommendations. The term "radical nephrectomy" is still used in other sections of this evidence review to reflect the evidence.

1.1.11.1 The outcomes that matter most

The committee discussed the outcomes specified in the protocol. They agreed that the most important outcomes for this review were recurrence and survival, including cancer-specific survival, and quality of life. In their experience, concerns about how likely the cancer is to recur (locally or distant), how this might affect their survival and the likely quality of their life after intervention are usually at the forefront of people's minds in conversations about treatment options for localised renal cell carcinoma (RCC).

Of importance, but less so than the outcomes above, are severe adverse events in the intraoperative and postoperative period, and long term severe adverse events. These outcomes may inform people's quality of life and health status in the short and long term and may still play an important role in deciding which treatment option is best for individuals. Duration of hospital stay is also important both for individuals, and also as an indicator of resource impact of the treatment.

1.1.11.2 The certainty of the evidence

Overall, the outcomes ranged from moderate to very low certainty, with the majority being very low certainty. Much of the evidence was downgraded for imprecision as the 95% confidence interval crossed the line of no effect. The committee agreed that low event numbers, particularly for mortality outcomes which are expected to be rare when considering localised cancer, contributed to wide confidence intervals. Meta-analyses with fewer than 1,300 participants for survival or 420 participants for other outcomes were also downgraded for imprecision as there were likely to be too few participants to reliably detect an effect.

The majority of the evidence for this review comes from non-randomised studies, with only one RCT included. This RCT compared robotic partial nephrectomy with cryoablation. The committee agreed that this comparison was highly relevant, reflecting UK practice in which robotic surgery and cryoablation are increasingly common. Outcomes from the RCT were of very low certainty due to risk of bias (participants not completing thermal ablation treatment due to preferring the control treatment – partial nephrectomy – and lack of blinding) and inconsistency (as the study could not be combined with others in meta-analysis). The study aimed to assess the feasibility of recruitment to a cohort-embedded RCT, not to assess effectiveness of the treatments. The study was therefore very small and underpowered to detect an effect. The committee also noted that as equipoise in treatment selection was required, included participants would be fit for surgery. This removes confounding between the two groups to more clearly indicate the effects of the interventions. However, the committee noted that the baseline eGFR and other health markers were therefore likely to be more favourable in the study sample than the general population with localised RCC, especially than those who receive thermal ablation (as thermal ablation is often reserved for those who cannot have surgery), limiting applicability.

The committee acknowledged the moderate risk of bias of three of the included systematic reviews (Guo et al. 2019, Hu et al. 2019, Patel et al. 2019) but agreed to use the studies as the risk of bias came mainly from a lack of clarity in reporting rather than evidence of methodological flaws (see the Methods and process section for more information about risk of bias of included studies and how this was managed). They also noted that for the systematic review Guo et al. 2019, the included studies could not be disaggregated and therefore the weighting of each individual study in the result could not be determined. However, based on the other available evidence on active surveillance, they were not concerned that including Guo et al. 2019 would affect the interpretation of the effect of the intervention (active surveillance) on outcomes and decision making.

Outcomes from non-randomised evidence ranged from moderate (for one outcome only – overall survival ≤5 years for active surveillance versus nephrectomy, Figure 80) to very low certainty. The committee were particularly concerned about the following issues:

- Confounding in all comparisons: treatment decisions are based on clinical and personal factors which mean that most studies will display systematic differences between the people in each arm. Although most non-randomised studies (40 out of 60) attempted to adjust for confounders either through matching participants across arms or adjusting for confounders in the analysis, adjustments typically did not include all the confounders the committee expected to impact the effect. For studies which did adjust for all major confounders, residual confounding could still bias results. This is incorporated into the risk of bias domain of GRADE.

- Active surveillance studies: active surveillance was defined differently across studies. Some studies specified a clear follow-up protocol and conditions for treatment in the future, others – especially those using data from the SEER database – included anyone without a procedural code into an active surveillance arm. The latter could include both people with small renal masses which are slow growing, and also people who are not suitable for any treatments (for example, due to being very frail or having multiple comorbidities. (The committee agreed that the latter group of people should not be classified as having active surveillance because this option is limited to people who can have some form of active treatment.) Other studies do not describe the details of the active surveillance intervention at all. This makes it difficult to assess the effectiveness of any particular type of active surveillance. (Active surveillance methods, duration and frequency are examined in more detail in review E.) In addition, the committee pointed out that biopsy confirmed RCC was not always a condition of recruitment to active surveillance studies. Where RCC is unconfirmed, the active surveillance arm may be expected to have a higher proportion of benign histology and therefore lower rates of recurrence and death for this reason.

- Relevance of included interventions to current UK practice: the committee pointed out that while evidence on all surgery and thermal ablation types was relevant, robotic surgical techniques are more accessible and becoming increasingly common for performing nephrectomies, replacing open techniques. They also agreed that cryotherapy was more commonly used than radiofrequency or microwave ablation. Most studies did not provide enough detail to enable us to split the results by surgery or ablation type.

It was not possible to carry out most of the planned subgroup analyses due to too few studies in the meta-analysis or insufficient detail in the level of reporting to categorise participants. Although some studies limited participants by age, the mean age of participants in the other studies was not dissimilar and so informative subgrouping could not be conducted. Where possible, subgroups were conducted for TNM stage and for type of ablation (where thermal ablation was one of the interventions being considered in the comparison). Results are described under benefits and harms below.

Sensitivity analyses to look at the effect of removing partially and unadjusted studies were not undertaken due to the lack of studies which fully adjusted for all pre-specified confounders.

The committee noted that there were gaps in the evidence (for discussion of the research recommendation, see other factors the committee took into account):

- There were no studies comparing SABR to total nephrectomy.

- There were no studies reporting on quality of life for any comparison other than thermal ablation versus partial nephrectomy (Junker 2022).

- There were no studies reporting on cardiovascular events for any comparison other than thermal ablation versus total nephrectomy (Xing 2018).

- There were no studies reporting on hospital admissions or intraoperative adverse events for any comparisons. However, data on postoperative adverse events and hospital stay duration informed discussion on benefits and harms of the interventions.

Studies did not specify whether the participants had tumours which were solid or cystic, although as participants had either suspected or confirmed RCC, the committee agreed it was unlikely that many participants had Bosniak 1, 2 or 2F cysts. As Bosniak 3 and 4 cysts are more often malignant than other cysts, the committee agreed to take people with these cysts into account when making recommendations, as well as those with solid renal masses.

1.1.11.3 Benefits and harms

Recurrence and survival outcomes

The committee noted that in people with localised RCC, recurrence outcomes (including local and distant recurrence) are more useful indicators of effectiveness of a treatment than survival outcomes, as survival outcomes are more likely to be influenced by other factors and less likely to occur within the follow-up of a study.

The committee agreed that the certainty of the evidence for oncological outcomes was low to very low, but that evidence suggesting that both total nephrectomy and partial nephrectomy may have better recurrence and local recurrence outcomes than thermal ablation aligned with their clinical experience (Figure 8, Figure 11, Figure 13, Figure 51).

Subgroup analyses could only be carried out for the comparison of thermal ablation compared to partial nephrectomy. Other comparisons either had too few studies, or the included studies were not sufficiently spread across subgroups, or there was insufficient reporting. The following subgroup analyses were undertaken for recurrence outcomes, but no subgroup differences were detected:

- Recurrence ≤5 years: TNM stage (studies including participants with only T1a compared with studies that did not specify T1a only) and ablation type (cryoablation, microwave ablation, radiofrequency ablation, combined ablation types or not reported)
- Local recurrence ≤5 years: ablation type
- Metastasis ≤5 years: ablation type.

The committee discussed the implications of experiencing local recurrence and noted that for people who had undergone thermal ablation, local recurrence could be treated with repeat ablation, a less invasive procedure than surgery. However, they noted the health economics evidence which demonstrated high costs associated with recurrence, especially for metastatic kidney cancer treated with systemic therapy (see cost effectiveness and resource use below). The committee included lay members who were able to share their experiences, and those of the people in the patient networks they are involved in. For individuals with localised RCC local recurrence could be destabilising and cause anxiety even if the subsequent treatment was not clinically complex.

It was not possible from the evidence to differentiate between some comparisons (SABR versus partial nephrectomy, active surveillance versus partial nephrectomy and active surveillance versus total nephrectomy). This may be because there were not enough people in the studies, or events occurring over the follow-up period, to be able to detect an effect. For example, for SABR versus partial nephrectomy, the data for local recurrence is from a single study (Staehler et al. 2022) with 70 participants, and there is 1 event in the SABR arm and none in the partial nephrectomy arm. The committee noted that there were no recurrence outcome data available for all other SABR comparisons (SABR versus thermal ablation or total nephrectomy or active surveillance).

Of the survival outcomes included in this evidence review, the committee agreed that cancer-specific survival was most useful because it does not include people who died from non-cancer related reasons such as old age or due to comorbidities. This is especially important when there is an imbalance in age or comorbidities between study arms, as there was for many studies included in this review. For example, if older people or people with other conditions are more likely to have thermal ablation than surgery, their overall survival would be worse because of other non-cancer conditions.

There was an increase in mortality from cancer with thermal ablation when this was compared to partial nephrectomy for cancer-specific survival ≤5 years (Figure 28) and the related outcome, cancer-specific mortality >5 years (Figure 31). However, it was not possible from the results for cancer-specific survival >5 years and for cancer-specific mortality ≤5 years to differentiate between treatments (Figure 29 and Figure 30). This does not necessarily mean that there is no difference in effect (or that thermal ablation and partial nephrectomy are equivalently effective) as it could be the case that there were insufficient people and studies to be able to detect a difference. The committee noted the smaller volume of evidence contributing to outcomes at over 5 years. Cancer-specific mortality at up to and including 5 years was informed by 7 studies, one of which reported no events. Of the three studies showing lower cancer-specific mortality with thermal ablation compared with partial nephrectomy, Long et al. (2017) and Shapiro et al. (2020) did not adjust for confounders, while Fraisse et al. (2019) did. Subgroup analyses for mortality ≤5 years (by ablation type and TNM stage) and cancer-specific mortality (by ablation type) did not detect subgroup differences. When active surveillance was compared to thermal ablation, there was an improvement in cancer-specific survival at ≤5 years in the thermal ablation group.

For outcomes comparing active surveillance with another treatment, the committee requested that a sensitivity analysis be undertaken to remove studies that did not require participants to have confirmed RCC. The committee recognised that in studies that did not require participants to have confirmed cancer, the active surveillance arm was likely to have a higher proportion of benign lesions than other treatment arms, and therefore artificially positive results. However, no sensitivity analysis could be undertaken due to limitations of the data:

- Active surveillance versus partial nephrectomy: all outcomes either included single studies or included data from the Guo et al. (2019) systematic review. As individual study results contributing to the combined result in Guo et al. (2019), are not presented, it was unclear how to classify the results of this analysis.

- Active surveillance versus total nephrectomy: all outcomes are contributed to by 2 studies, both of which did not require confirmed RCC.

- Active surveillance versus thermal ablation: the metastasis outcome is contributed to by 2 studies, both of which did not require confirmed RCC. All other outcomes are either contributed to by a single study, or by Guo et al. (2019) systematic review (see above).
- SABR versus active surveillance: 1 study contributes to this outcome. The study required confirmed RCC.
- Active surveillance versus nephrectomy: 2 studies contribute to this outcome: Grant et al. (2020) required confirmed RCC, Cheung et al. (2023) did not (see Table 35 and Figure 80).

Complications and duration of stay

The only comparison reporting complications (postoperative severe adverse events using the Clavien-Dindo scale) or duration of hospital stay was thermal ablation versus partial nephrectomy. Data from the included RCT (Neves et al. 2024) could not differentiate for Clavien-Dindo grade 1, grade 2 or grade 3 (there were no events at grade 3 or above in either arm). All participants being eligible for surgery may mean the thermal ablation arm is healthier, and potentially less prone to complications than thermal ablation arms from the cohort studies, which are more likely to reflect usual practice.

The non-randomised evidence showed a statistically significant and potentially clinically meaningful reduction in overall complications (grade 1 to 5) in the thermal ablation group compared to the partial nephrectomy group, although the upper 95% confidence interval was close to the line of no effect (RR 0.76 [95% CI 0.59 to 0.97]). However, when this data was divided into minor complications (Clavien-Dindo I-II) and major complications (Clavien-Dindo III-V) the results were no longer statistically significant as the upper 95% confidence interval for both outcomes moved across the line of no effect. This may reflect a lower statistical power to detect effects as a result of reducing the sample size in the subgroup analyses compared to the pooled analysis. Subgroup analyses for overall complications, minor complications and major complications (all by TNM stage) did not detect subgroup differences.

The committee agreed that the oncological benefits in terms of lower risk of recurrence and metastases of using partial nephrectomy were likely to outweigh the higher risks of complications for most people, especially as they noted that minor complications are more common than major complications. However, for some people, such as people with comorbidities or older people who may be frailer and for whom complications could have large impacts on health, the risk of complications with surgery may be of greater importance than the benefit from lower risk of recurrence. For these people, the committee agreed that thermal ablation might have a better balance of benefits and harms.

Duration of stay was only reported for thermal ablation versus partial nephrectomy. Sixteen studies found a statistically significant reduction in duration of hospital stay by 2.69 days (mean difference, MD - 2.69 [95% CI-3.7 to -1.68]) for thermal ablation compared with partial nephrectomy. The committee noted that open partial nephrectomy would be expected to result in a longer hospital stay than minimally invasive partial nephrectomy. A sensitivity analysis was carried out to remove all studies which included open surgery or did not specify surgery type to determine whether the results for minimally invasive partial nephrectomy alone would be lower and perhaps much closer to that for thermal ablation. This left 7 studies (Turna et al. 2009, Bird et al. 2009, Haber et al. 2011, Weinberg et al. 2015, Yanagisawa et al. 2020, Lehrer et al. 2023, Pandolfo et al. 2023) and showed a smaller but still statistically significant (and therefore clinically significant, as minimal important difference was set as statistical significance, see summary of the effectiveness evidence) reduction in duration of hospital stay for thermal ablation compared with partial nephrectomy (MD -1.84 days [95% CI -2.95 to -0.74]) Figure 40). Longer hospital stays are expensive and can be stressful for patients. However, the lay committee members' experience was that while many will want to recover at home as much as possible, a reduced risk of recurrence would outweigh the desire for a shorter hospital stay for most people.

Long-term adverse events and quality of life

Long-term adverse events include both renal functional outcomes and cardiovascular events. All non-surgical interventions (thermal ablation and SABR), active surveillance and partial nephrectomy are considered to be nephron-sparing, as they are intended to have reduced impact on renal function compared with total nephrectomy.

The committee were not surprised that thermal ablation and active surveillance both resulted in less of a reduction in renal function compared with total nephrectomy. Active surveillance is a form of monitoring and is used without treatment of the lesion, so the only effects on renal function that would be expected for this management option would come from the growth of the renal lesion or the effects of other non- kidney cancer related comorbidities on renal function. There was no evidence comparing SABR to total nephrectomy. The committee acknowledged that they were unable to determine whether and to what extent renal function recovered after each type of treatment from the available evidence, making the longer-term importance of effects on this outcome harder to interpret.

It was not possible from the evidence to differentiate between partial nephrectomy and either thermal ablation or active surveillance for renal functional outcomes. For the comparison including active surveillance, the committee noted that this could be due to the limited amount of evidence (1 study, Alam et al. 2019, with 570 participants, Figure 63) rather than a true effect, because in their experience thermal ablation is usually associated with some reduction in renal function.

Cardiovascular events were reported by one study (Xing et al. 2018, Figure 58) for the comparison of thermal ablation versus total nephrectomy. The results from this study showed a lower risk of cardiovascular events (defined as hospitalisation for coronary disease, heart failure, stroke, or peripheral arterial disease) for the thermal ablation group compared to people who had total nephrectomy. The small volume of evidence, combined with uncertain biological mechanisms for any effect, contributed to the committee's decision not to base recommendations on this evidence.

The committee agreed that understanding the impact of these treatments on quality of life was critical to appreciating their broader impacts on wellbeing. Evidence on quality of life came from one study (Junker et al. 2022, Figure 47and Figure 48) reporting on thermal ablation versus partial nephrectomy. The evidence found that quality of life was statistically significantly reduced in the partial nephrectomy group compared with thermal ablation at 14 days, but that there it was not possible from the evidence to differentiate between the 2 interventions by 90 days (14 days: MD -9.6 [95% CI-15.95 to -3.25]; 90 days: MD 0.26 [95% CI -6.14 to 6.66]). To help compensate for the lack of evidence about effects on quality of life the committee used the experiences of the lay committee members to inform the recommendations.

Drafting the recommendations

Studies did not specify whether the participants had tumours which were solid or cystic. The committee agreed that people with Bosniak 3 and 4 cysts have an increased chance of malignancy compared with Bosniak 1 and 2 cysts. They agreed that, for Bosniak 4 cysts, management should be similar to management of solid masses. Bosniak 3 cysts have a lower chance than Bosniak 4 cysts of being malignant and so may be managed differently. The committee made recommendations on the management of Bosniak 3 and 4 cysts as well as solid renal masses. (These can be grouped under the heading of renal lesions.)

Shared decision making

The committee agreed that people with renal lesions will make different decisions about what treatments they want based on what is important to them. They noted that there is often a lack of clarity about what the different management options available to them entail. They agreed that clearly communicating the practicalities of all interventions as well as their benefits and harms in a balanced way was important to support shared decision making. They drafted a recommendation to help with shared decision making and included some specific points based on the evidence and their clinical expertise and experience:

- surgery may be associated with a lower risk of recurrence than thermal ablation and SABR but there may be a greater risk of short-term complications, and if the whole kidney is removed then a greater reduction in kidney function is expected compared with thermal ablation and SABR
- thermal ablation may have a lower risk of complications than surgery, but a higher risk of recurrence
- there is a lack of evidence for stereotactic ablative radiotherapy (SABR) compared with surgery or thermal ablation, so its relative effectiveness and chance of complications are uncertain, and there may also be a higher risk of recurrence
- active surveillance has a higher risk of renal lesion growth and spread than interventions to treat the lesion.

They also agreed that people who choose active surveillance initially should be told that they may be able to have treatments such as thermal ablation, surgery or SABR in the future if they wish to and these treatments continue to be suitable for them.

The committee were aware of the core NICE guidelines that are intended to facilitate the decision-making process and ensure that patients are able to fully participate. They noted that the sections on enabling patients to actively participate in their care in the NICE guideline on patient experience in adult NHS services, and communicating risks, benefits and consequences in the NICE guideline on shared decision making are particularly relevant. However, they did not include a specific cross reference to these guidelines with these recommendations because there will be a box highlighting them and other core content that applies across guidelines at the start of the kidney cancer guideline. In addition, specific sections from these reviews are cross referred to in the section on information in the guideline (see evidence review D for more details relating to the recommendations in the information and support section of the guideline).

Surgery, thermal ablation, SABR or active surveillance for people with suspected or confirmed localised renal cell carcinoma, and Bosniak 3 and 4 cysts.

Although much of the evidence was not presented in a way that enabled it to be divided into the populations of interest as defined by the planned subgroup analyses, the committee used the main evidence base combined with their clinical expertise and experience to draft the recommendations. For clarity, the committee decided to split their recommendations up by lesion type (solid renal mass or Bosniak 3 or 4 cyst) and size.

The committee had already made recommendations to offer surgery for people with solid renal masses, and Bosniak 4 cysts, 2cm and larger as a result of the evidence in review A (on the management of localised renal cell carcinoma using partial versus total nephrectomy). Using the evidence identified in this review, review A and their expertise, the committee agreed that for people with solid renal masses, and Bosniak 4 cysts, 2 cm and larger surgery remained the most effective management option available for most people. However, they agreed that some people would not want surgery. For others, the risks of complications from surgery might outweigh the potential oncological benefits, or their comorbidities may make surgery unsuitable. In these cases, other management options such as active surveillance, thermal ablation or SABR may be suitable depending on the renal lesions' characteristics (including size) and the person's characteristics (such as comorbidities).

There was limited evidence for thermal ablation, active surveillance and SABR included in this review. Using their clinical expertise and experience, the committee decided to make recommendations about management options for solid renal masses and Bosniak 4 cysts when surgery is not suitable or is declined:

- For people with solid renal masses between 2 cm and 4 cm in diameter: the committee recommended considering thermal ablation or active surveillance. As the evidence for thermal ablation and active surveillance compared with each other was limited, the committee decided not to recommend one over the other. They agreed that whilst SABR should remain an option, thermal ablation is more established in practice and has stronger evidence base, and therefore they specified that SABR only be used when thermal ablation is not suitable and active surveillance is declined. They noted that thermal ablation and SABR should not be used without biopsy confirmation of malignancy.

- For people with solid renal masses larger than 4 cm in diameter: the committee made a recommendation to consider thermal ablation or SABR. They noted that for larger lesions thermal ablation may need multiple treatments and that SABR is not suitable for lesions greater than 7 cm in diameter. They did not include active surveillance in this recommendation because, in their experience, active surveillance would not be offered for people with larger renal masses due to increased risks of growth of the tumour.

- For people with Bosniak 4 cysts 2 cm in diameter or larger: the committee noted that for this group management would depend on the size of the cyst and the size of its solid component, the lesion location and complexity, the person's characteristics (for example frailty), and the person's preferences about management options. The committee also discussed that thermal ablation and SABR would only be suitable treatment options with biopsy confirmation of malignancy, and noted that this is included in an earlier recommendation in the section already. They agreed that due to the lack of evidence specifically about Bosniak 4 cysts they could not rank the treatments. Therefore thermal ablation, SABR and active surveillance are all options to consider.

The committee agreed that due to the lower risk of malignancy with Bosniak 3 cysts compared with Bosniak 4 cysts, surgery may not be a suitable first option given the risks of surgery both in terms of the procedure itself and potential impact on renal function. However, they noted the lack of evidence for management of Bosniak 3 cysts and so made a weak recommendation to consider active surveillance for people with Bosniak 3 cysts 2 cm or larger. They noted that some people may not want active surveillance and may prefer to have the cyst removed entirely, and so included surgery as an option for when active surveillance is declined.

For people with a solid renal mass, or Bosniak 3 or 4 cyst, under 2 cm in diameter the committee agreed that surgery or non-surgical treatment is often unnecessary and may not be possible. Thermal ablation and SABR require a solid component to target, which Bosniak 3 cysts do not have, and should not be used without biopsy confirmation of malignancy, which cannot be conducted on very small solid masses / components. They noted that active surveillance was a particularly useful option for lesions of this size because it involves monitoring the lesion to detect any changes, with treatment as an option if indicated in future. Therefore, the committee chose not to recommend surgery as the preferred option for this group of people. Instead, they recommended that active surveillance be considered after the person has had diagnostic imaging and discussions with the urology–oncology multidisciplinary team. They then made weak recommendations that if active surveillance is declined, people with solid renal masses, or Bosniak 4 cysts, less than 2 cm in diameter could have surgery or thermal ablation, and for people with Bosniak 3 cysts less than 2 cm in diameter surgery could be an option. SABR was not included in this recommendation as it is not standard practice in lesions of this size.

The committee agreed that a number of factors should be taken into account in the decision about which management options are suitable and made a recommendation to summarise them for the clinician to help with decision making. Some of these have been mentioned above already – lesion factors and the person's clinical characteristics; that thermal ablation and SABR should not be used without biopsy confirmation of malignancy before treatment; that for larger lesions thermal ablation may need multiple treatments (and that only certain types of thermal ablation may be suitable, and this may need to be carried out in a specialist centre) and that SABR is not suitable for lesions greater than 7 cm in diameter.

The committee noted that for people with solid renal masses, or Bosniak 4 cysts, of 2 cm and larger in diameter surgery is the preferred option when it is suitable. They highlighted the importance of taking into account whether reducing the risk of complications from surgery is important enough to justify the higher risks from non-surgical options. The evidence suggested that partial or total nephrectomy may result in lower levels of recurrence than thermal ablation. Although there was not enough evidence about SABR compared to surgery to be certain, the committee agreed that partial and total nephrectomy would likely reduce risk of recurrence compared to SABR as well. However, in their experience SABR can achieve high local control with low toxicity.

The committee also noted that because active surveillance is not a treatment to cure or treat RCC it was likely to be associated with worse outcomes in terms of renal lesion growth than surgery and non-surgical interventions. Despite this, the committee were aware that some people who could have treatments to remove or destroy the lesion (surgery, thermal ablation or SABR) choose active surveillance instead. This could be because they want to delay having an intervention to allow them to attend a key life event, such as a family wedding, or because the mass is slow growing or relatively small. The committee noted the importance of taking people’s preferences into account when decisions around management options are being made and included this, as well as the points about active surveillance, thermal ablation, SABR and surgery, in the recommendation mentioned above.

1.1.11.4 Cost effectiveness and resource use

Two economic studies were identified from the evidence review. One study (Xia et al. 2025) was assessed to be only partially applicable with very serious limitations and was not considered useful for the committee in making recommendations. The Health Technology Wales (2022) study suggested that at a threshold of £20,000 per QALY, SABR was more cost-effective compared with observation for people who were not suitable for surgery or ablation. However, the committee noted that there were some uncertainties around some parameters, including an unadjusted comparison of relative effectiveness.

Given this lack of formal economic evidence for other interventions, the committee used their expertise to discuss the relative resource use associated with each type of procedure and the associated impact on downstream events, such as managing recurrence or poor kidney function. This discussion was informed by a costing analysis conducted by NICE.

For SABR, the upfront and follow-up costs were slightly lower than thermal ablation. The upfront cost estimates for nephrectomy were higher than for SABR and for ablation.

The costing analysis estimated that the management of recurrences was likely to be more costly than primary treatment, especially for metastatic kidney cancer treated with systemic therapy. Any intervention that can reduce the risk of recurrence, short-term procedure-related complications, reduced renal function and ultimately renal failure, or progression to metastasis may be cost saving to the NHS. The clinical evidence suggests that both total nephrectomy and partial nephrectomy may have lower rates of recurrence and local recurrence than thermal ablation. Even though the cost of surgery is much higher than the cost of thermal ablation and SABR, this short-term high procedure cost may be offset by the reduction of costs of local recurrence management in future. Thermal ablation and active surveillance may have better renal function outcomes than total nephrectomy, and may therefore have reduced costs of managing reduced renal function, which can be substantial at end stage kidney disease where dialysis or transplantation may be required. The committee noted that partial nephrectomy had a significant increase in duration of hospital stay compared with thermal ablation, and that open partial nephrectomy is expected to have a longer duration of hospital stay than minimally invasive approaches. Longer hospital stays are generally associated with higher costs and can be more stressful for patients.

The committee agreed that surgery is the best option for a resectable tumour and the benefit of the lower likelihood of costly recurrences would be expected to outweigh the higher upfront cost of surgery. However, for people who have multiple comorbidities or are at high risk of complications, the committee acknowledged that thermal ablation and SABR should be considered given that the complication risks associated with surgery outweighs the benefit of reduced risk of local recurrence.

The committee noted that there are some obstacles to getting local access to specific treatments. Robotic-assisted surgery is not available everywhere, and currently it is only provided in NHS centres where surgeons can do it in volume due to the set-up of robotic-related surgery and the training cost for clinicians. Other non-surgical treatments are also not available everywhere, and especially SABR is not routinely commissioned for treatment for localised RCC in the NHS. The use of SABR will require sign off in an MDT with the necessary expertise.

As a result of the new recommendations, it is predicted that SABR will be more widely implemented and replace some current thermal ablation procedures and active surveillance. The recommendations are not expected to replace many partial nephrectomies with non-surgical treatments.

1.1.11.5 Other factors the committee took into account

The committee was aware of and contributed to the Equality and Health Inequalities Impact Assessment (EHIA) for this guideline. They noted that health inequalities impact on the prevalence and incidence of kidney cancer, and also on people's access to and choice of treatment for localised RCC. In particular, they noted that for some people, the costs of attending treatment – especially where multiple treatments are required or where the treatment is not provided locally – could be prohibitive. This problem is exacerbated if the person has less secure employment (for example, if they work on zero hours contacts), but the committee noted that this barrier to treatment also affects a wider population of people who would not be considered to be socioeconomically deprived. The committee acknowledged that many of the issues identified within the EHIA were societal issues and not within the committee's ability to address. However, they were aware of organisations that can offer support and advice about how to access financial help, for example Macmillan Cancer Support and Maggie's.

The committee discussed the importance of taking into account an individual's perspective, circumstances and needs in conversations about treatment choice. They agreed that one person will weigh up the benefits and harms of the available treatments differently than another person, and that major life events, available support, comorbidities, age and other factors would influence this.

The committee had viewed the draft NHS England commissioning policy for SABR for localised RCC and discussed this. They noted that the content could change before publication, but made recommendations taking into account the draft policy, the review evidence and their own experience and expertise, acknowledging that availability is locally dependent currently. They noted that although more research would increase certainty in the effectiveness of SABR in relation to other treatments, it may be a useful option for people who cannot have or do not want surgery. The committee are aware of studies by IROCK (the International Radiosurgery Consortium of the Kidney) about effectiveness of SABR which could not be included in this review as they are single arm studies or compare different methods of delivering SABR to each other. Therefore, the committee made a research recommendation about SABR compared with other interventions for localised RCC (see appendix K). The committee included surgery as a comparator for SABR in the research recommendation due to the lack of evidence on SABR compared to partial or radical nephrectomy. The committee also included thermal ablation in this research recommendation as a comparator for SABR because of the relatively large number of studies that have already been conducted on the effectiveness of this intervention. They also included active surveillance as a comparator because this is not an active treatment and therefore it is expected to have worse outcomes. (The committee drafted a separate research recommendation to look at different approaches to active surveillance as part of review E on active surveillance.)

The committee discussed whether and when biopsy should be undertaken in relation to the treatments covered in this review and in the recommendations. They noted that biopsy prior to thermal ablation is increasingly common in clinical practice (and they included this in their recommendation), but that in published evidence biopsy has often not been undertaken first. (See evidence review J on biopsy for more information about this procedure.)

1.1.12 Recommendations supported by this evidence review

This evidence review supports recommendations 1.5.1, 1.5.2 and 1.5.6 to 1.5.11 and the research recommendation on SABR for localised renal cell carcinoma. Other evidence supporting these recommendations can be found in the evidence reviews on management of localised renal cell carcinoma using partial versus total nephrectomy (Review A).

1.1.13 References – included studies

1.1.13.1 Effectiveness

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Appendices

Appendix A – Review protocols

Effectiveness review protocol

ID	Field	Content
1.	Review title	Clinical and cost-effectiveness analysis of non-surgical interventions or active surveillance in adults with localised renal cell carcinoma (RCC)
2.	Review question	What is the clinical and cost effectiveness of different non-surgical interventions or active surveillance, compared to each other or surgical interventions, for localised renal cell carcinoma in adults?
3.	Objective	To evaluate the clinical effectiveness, safety, and cost effectiveness of different non-surgical interventions (e.g. thermal ablation, stereotactic ablative radiotherapy) or active surveillance, versus each other or surgical interventions, for treating adults with localised RCC.
4.	Searches	The following databases will be searched: Cochrane Central Register of Controlled Trials (CENTRAL) Cochrane Database of Systematic Reviews (CDSR) Embase MEDLINE Epistemonikos INAHTA For the economics review the following databases will be searched: Embase MEDLINE Medline in Process Medline EPub Ahead of Print Econlit HTA (legacy records) NHS EED (legacy records) INAHTA Searches will be restricted by: Date limitations: None

		English language Human studies Abstracts, conference presentations and theses will be excluded The full search strategies for all database will be published in the final review.
5.	Condition or domain being studied	Localised renal cell carcinoma
6.	Population	Adults (18 years or over) with (histologically confirmed or suspected on imaging) localised RCC Localised RCC diagnosis can be defined according to the clinical or pathological TNM classification, stage 1 and stage 2. Exclusion: Adults with locally advanced or metastatic disease
7.	Intervention	Non-surgical interventions: Thermal ablation using the following methods: Radiofrequency ablation Cryotherapy Microwave ablation Stereotactic ablative radiotherapy (SABR) Active surveillance
8.	Comparator	Surgical intervention: (partial or radical nephrectomy) Non-surgical interventions compared to each other
9.	Types of study to be included	Systematic reviews of RCTs and RCTs are preferred where available for a comparison. Where RCTs are not available for a comparison, systematic reviews of non-randomised comparative studies and primary non-randomised comparative studies published after the systematic reviews will be considered. Where good quality systematic reviews of non-randomised studies are identified, these may be used completely or as a source of references (limited to cohort studies only), depending on applicability. Where individual primary non-randomised comparative studies are included to update a good quality systematic review or where a full evidence review is required, these will be limited to prospective and retrospective cohort studies.
10.	Other exclusion criteria	Abstracts, conference presentations and theses Non-human studies

		Non-English language studies
11.	Context	There is currently no national guideline in the UK on the diagnosis and treatment of kidney cancer and audit data indicates variation in the clinical practice within NHS. Stakeholders identified this gap and NICE was commissioned to develop a guideline on kidney cancer by NHSE. A review of the evidence is required to understand which people with localised renal cell carcinoma may benefit from less invasive, non-surgical interventions compared to surgery.
12.	Outcomes	• Disease-free survival, including cancer-free survival (time to event data) Some studies may report disease-free survival as the, local recurrence, or distant metastases (dichotomous data). These will be extracted as proxy outcomes where survival data is not reported in the studies. • Cancer-specific survival (time to event data) • Overall survival (time to event data) • Severe adverse events and complications reported as: For thermal ablation versus surgery: • observed in the intraoperative period (measured according to Intraoperative Adverse Incident Classification – EAUiaiC; dichotomous data) • observed postoperative period (according to Clavien-Dindo Classification of Surgical Classifications at 30-days and 90-days after surgery; dichotomous data) For SABR versus surgery: • Grades 3 or 4 classified by Common Terminology Criteria for Adverse Events (CTCAE); dichotomous data • Long-term severe adverse events • Renal function impairment measured by estimated glomerular filtration rate (eGFR; dichotomous or continuous data) • Cardiovascular events (dichotomous data) • Number of hospital admissions (continuous data) • Duration of hospital stay (continuous data) • Quality of life using: • EORTC Core Quality of Life Questionnaire (EORTC QLQ-C30; (dichotomous or continuous data)) • EuroQol-5 dimensions (EQ-5D; (dichotomous or continuous data))

		Minimal important differences Any statistically significant difference will be used for the following outcomes: • Disease-free survival • Cancer-specific survival • Overall survival • Severe adverse events and complications • Long-term adverse events • Number of hospital admissions • Duration of hospital stay • Quality of life using EORTC QLQ-C30 MIDs for the following quality of life measure was identified in the literature: • EQ-5D: 0.08 for UK-based scores and 0.07 for VAS scores
13.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.2). Study investigators may be contacted for missing data where time and resources allow. This review will make use of the priority screening functionality within the EPPI-reviewer software. The following rules will be adopted to determine when to stop screening: at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) will be screened After this point, screening is only terminated if a threshold of 750 abstracts is met for a number of abstracts being screened without a single new include being identified. if sifting is terminated before the full database has been looked at additional checks will be carried out to ensure that relevant studies have not been missed.
14.	Risk of bias (quality) assessment	Risk of bias will be carried out using the preferred checklists as described in Appendix H of Developing NICE guidelines: the manual. The risk of bias for RCTs will be assessed using the Cochrane Risk of Bias v.2.0 checklist and for systematic reviews, the Risk of Bias in Systematic Reviews (ROBIS) tool will be used.

		The risk of bias for non-RCT studies will be assessed using the Cochrane Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.
15.	Strategy for data synthesis	Where possible, meta-analyses will be conducted to combine the results of quantitative studies for each outcome. RCT and non-RCT data will be pooled separately. Where data can be disambiguated it will be separated into the subgroups identified in section 17 (below). Pairwise meta-analyses will be performed in Cochrane Review Manager V5.3. Continuous outcomes will be analysed as pooled mean differences (using the inverse variance method) unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Where different studies present continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes will all converted to the same scale before meta-analysis is conducted on the mean differences. Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Hazard ratios will be pooled using the generic inverse-variance method. Adjusted, unadjusted and partially adjusted hazard ratios will be pooled. Sensitivity analysis will be carried out to look at the effect of removing partially and unadjusted studies For survival outcomes, time-to-event data is preferred. Where this data is not available, relative risks will be calculated for proxy outcomes as described in section 12. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all outcomes, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions are met: Significant between-study heterogeneity in methodology, population, intervention, or comparator was identified by the reviewer in advance of data analysis. The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

		GRADE will be used to assess the quality of the outcomes. Data from randomised controlled trials and non-randomised comparative trials will be initially rated as high quality where they come from: RCTs and systematic reviews of RCTs (where individual studies have been quality assessed using Cochrane risk of bias) non-randomised comparative trials and systematic reviews of non-randomised studies (where individual studies have been quality assessed using the ROBINS-I assessment tool) The quality of the evidence for each outcome will then be downgraded or not from this starting point based on the other GRADE domains. To assess imprecision, where there are no defined MIDs we will set the MID as the line of no effect for all outcomes except for (1.0 for dichotomous outcomes and 0 for continuous outcomes). A second decision threshold will be applied where the sample size is sufficiently small that it is not plausible any realistic effect size could have been detected. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias.
16.	Analysis of sub-groups	Where the data allows, subgroup analyses may be conducted to explore heterogeneity considering the following: • according to non-surgical interventions received (for thermal ablation interventions only) • age • by TNM classification • by primary RCC type e.g. clear cell, papillary, chromophobe • renal function at baseline • performance status of the person at baseline (e.g. ECOG and Karnofsky)
17.	Type and method of review	X Intervention Diagnostic Prognostic Qualitative Epidemiologic Service Delivery Other (please specify)
18.	Language	English

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<tr><td>23.</td><td>Named contact</td><td colspan="3">Named contact
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Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and Guideline Development Team.</td></tr>
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• Steve Sharp, Technical adviser
• Sarah Boyce, Senior technical analyst
• Olivia Crane, Senior technical analyst
• Agnesa Mehmeti, Technical analyst
• Fernando Zanghelini, Technical analyst
• Lucy Beggs, Health economics adviser
• Hannah Tebbs, Health economist
• Yuanyuan Zhang, Health economist
• Amy Finnegan, Senior Information specialist</td></tr>
<tr><td>25.</td><td>Funding sources/sponsor</td><td colspan="3">This systematic review is being completed by the Guideline Development Team which receives funding from NICE.</td></tr>
<tr><td>26.</td><td>Conflicts of interest</td><td colspan="3">All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of</td></tr>
</table>

		interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: Kidney Cancer (GID-NG10398).
28.	Other registration details	None
29.	Reference/URL for published protocol	None
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
31.	Keywords	Localised renal cell carcinoma, thermal ablation, stereotactic ablative radiotherapy, active surveillance
32.	Details of existing review of same topic by same authors	Not applicable
33.	Current review status	Ongoing Completed but not published X Completed and published Completed, published and being updated Discontinued
34.	Additional information	None
35.	Details of final publication	www.nice.org.uk

Economic review protocol

ID	Field	Content
1.	Review title	A: Cost-effectiveness of partial versus radical nephrectomy in adults with localised renal cell carcinoma B: Cost-effectiveness of non-surgical interventions or active surveillance in adults with localised renal cell carcinoma C: Cost-effectiveness of nephrectomy or stereotactic ablative radiotherapy for treating locally advanced renal cell carcinoma in adults H1: Cost-effectiveness of non-pharmacological interventions, used before systemic anti-cancer therapy for adults with advanced renal cell carcinoma H2: Cost-effectiveness of non-pharmacological interventions, used after systemic anti-cancer therapy for adults with advanced renal cell carcinoma
2.	Objective	To identify economic studies for all relevant guideline review questions on the management of renal cell carcinoma
3.	Inclusion criteria	• Populations, interventions and comparators as specified in the effectiveness review protocol. • Relevant comparative economic study design: cost–utility analysis • Decision analytic model-based or within-trial economic analyses • OECD countries (except USA) • Healthcare and personal social services cost perspective • Studies published from 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs High-quality studies in line with the NICE reference case (recent UK NHS/PSS cost-utility analyses using the QALY as the measure of outcome) are the most applicable to NICE decision making. Not all studies meeting the inclusion criteria will therefore necessarily be used in decision-making - see Review strategy below for details.
4.	Exclusion criteria	• Conference posters or abstract only studies – these do not provide sufficient information for quality assessment. • Studies published before 2010 – this cut off has been applied to restrict the review to more recent studies which will have more applicable resource use and costs • Studies from non-OECD countries or the USA – these are considered unlikely to be applicable to the UK NHS setting due to substantial differences in healthcare delivery and unit costs. • Non-comparative economic analyses including cost-of-illness studies. • Letters, editorials or commentaries, study protocols or reviews of economic evaluations (recent reviews will be ordered and the bibliographies will be checked for relevant individual economic studies, which will then be ordered and checked for eligibility). • Non-English language papers.

		• Studies considering exclusively intervention costs, e.g. medicine acquisition costs, without considering wider healthcare costs associated with the management of renal cell carcinoma. • Studies comparing costs of branded versus generic forms of the same medicine. • Studies only focussing on productivity losses or gains.
5.	Search strategy	An economic study search will be undertaken covering all review questions relating to the management of renal cell carcinoma using guideline population-specific terms and a health economic study filter. For search details see appendix B below. The following databases will be searched: • MEDLINE All, Ovid • Embase, Ovid • International HTA database, International Network of Agencies for Health Technology Assessment (INAHTA) • Econlit • NHS EED and HTA (legacy records)
6.	Review strategy	• Studies meeting the inclusion and exclusion criteria will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist in appendix H of Developing NICE guidelines: the manual. • The NICE economic evaluation checklist assesses: o Applicability to the NICE guideline decision making context with consideration of the NICE reference case relevant to the guideline. Recent UK studies that use the NICE reference case methods are the most applicable when considering cost effectiveness. o Methodological limitations. • The aim is to present the best available economic evidence to inform committee decision-making in the context of the guideline, the current UK NHS setting and NICE methods. Therefore, the health economist may not present all studies that meet inclusion criteria. If recent high quality, UK cost-utility analyses are available for a question, it is often not deemed informative to present studies that are less applicable or lower quality such as older UK analyses or analyses from other countries. A similar principle is deemed to apply more generally when considering applicability and methodological limitations. Some specific examples are given below: o If multiple versions of a model are available for the UK and other countries it is usually reasonable to only present the UK version. o If multiple versions of the same UK model are available, it is usually reasonable to present only the most recent. o If there has been a NICE MTA or guideline model that informs current NHS practice it is usually reasonable not to present older studies, unless they address a different subpopulation or other specific issue. o If a UK model that includes all interventions in the decision space is available it may be reasonable not to present studies that only include

		individual or fewer interventions, if the analysis is sufficiently applicable and of good methodological quality. • Quality and relevance of effectiveness data used in the economic analysis: the more closely the clinical effectiveness data used in the economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline. • Hierarchy of economic evaluation evidence based on quality assessment o 'Directly applicable' and 'Minor limitations' (only recent UK CUAs can get this rating). Usually presented and used in decision-making. o Directly or partially applicable combined with minor or potentially serious limitations (other than 1). Discretion over whether these are presented and used in decision-making, depending on the availability of more relevant evidence. o 'Not applicable' or 'Very serious limitations'. Typically not presented and not used in decision-making. The health economist will make a decision based on the relative applicability and quality of the available evidence for each question, in discussion with the guideline committee if required. All decisions will be transparently reported in the evidence report. Studies that are presented to the committee and used in decision-making when formulating recommendations will be included in the summary tables and will have an evidence extraction. Other studies may not be presented to the committee in detail but will be listed, with the reason for not being presented to the committee and thus not used in decision-making being provided. Committee members can review and query the decision not to present studies with the health economist and will be provided with full details of these studies where requested.

Appendix B – Literature search strategies

Background and development

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches. The MEDLINE strategies below were quality assured (QA) by another NICE SIS. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

This search report is based on the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

A test set of 8 systematic reviews were supplied by the technical analysts, this test set covered the current review (review B) and reviews A, C, H1 and H2 combined (review A: surgical interventions for localised RCC, review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC, reviews H1 and H2: non-pharmacological management of advanced RCC).

Search limits and other restrictions

Formats

Limits were applied in adherence to standard NICE practice and the review protocol to exclude:

- Animal studies
- Editorials, letters, news items and commentaries

- Conference abstracts and posters
- Registry entries for ongoing clinical trials or those that contain no results
- Theses and dissertations
- Papers not published in the English language.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

> Dickersin K, Scherer R & Lefebvre C. (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

Date limits

No date limits were applied, in adherence to the review protocol.

Search filters and classifiers

Effectiveness searches

OECD:

The OECD countries filters were used without modification:

Ayiku, L., Hudson, T., Williams, C., Levay, P., & Jacob, C. (2021). The NICE OECD countries' geographic search filters: Part 2 - Validation of the MEDLINE and Embase (Ovid) filters. Journal of the Medical Library Association, 109(4), 583–589.

Observational filter:

The terms used for observational studies are standard NICE practice that have been developed in house.

Systematic reviews filters:

Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. BMC Medical Research Methodology, 12(1), 51.

- In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.
- In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

RCT filters:

McMaster Therapy – Medline – "best balance of sensitivity and specificity" version:

The standard NICE modifications were used: the MeSH heading *randomized controlled trial/*, which is equivalent *to randomized controlled trial.pt* was exploded to capture newer, narrower *terms equivalence trial/ and pragmatic clinical trial*. The free-text term *randomized.mp* was also changed to the (more inclusive) alternative *randomi?ed.mp.* to capture both UK and US spellings.

Haynes RB e al. (2005) Optimal search strategies for retrieving scientifically strong studies of treatment from Medline: analytical survey. BMJ, 330, 1179-1183.

McMaster Therapy – Embase "best balance of sensitivity and specificity" version:

Wong SSL et al. (2006) Developing optimal search strategies for detecting clinically sound treatment studies in EMBASE. Journal of the Medical Library Association, 94(1), 41-47.

Cost effectiveness searches

In line with the review protocol, the precise version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

Key decisions

A single systematic search was carried out to identify potentially relevant studies for the current review (review B) and reviews A, C, H1 and H2 combined (review A: surgical interventions for localised RCC, review C: nephrectomy or stereotactic ablative radiotherapy for locally advanced RCC, reviews H1 and H2: non-pharmacological management of advanced RCC).

Clinical searches

Database results

Database	Date searched	Database Platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	18/01/2024	Wiley	Issue 1 of 12, January 2024	767
Cochrane Database of Systematic Reviews (CDSR)	18/01/2024	Wiley	Issue 1 of 12, January 2024	8
Embase	18/01/2024	Ovid	1974 to 2024 January 18	13394
Epistemonikos	18/01/2024	Epistemonikos	n/a	1993
INAHTA	18/01/2024	INAHTA	n/a	97
MEDLINE ALL	18/01/2024	Ovid	1946 to January 17, 2024	9991

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Cochrane Central Register of Controlled Trials (CENTRAL)	14/02/2025	Wiley	Issue 2 of 12, February 2025	845
Cochrane Database of Systematic Reviews (CDSR)	14/02/2025	Wiley	Issue 2 of 12, February 2025	8
Embase	14/02/2025	Ovid	1974 to 2025 February 13	14588
Epistemonikos	14/02/2025	Epistemonikos	n/a	2350
INAHTA	14/02/2025	INAHTA	n/a	177

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
MEDLINE ALL	14/02/2025	Ovid	1946 to February 13, 2025	10686

No date limits were applied to the rerun searches due to technical issues in OVID. Duplication of records was managed in EPPI Reviewer 5.

Search strategy history

Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ (85773) 2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (17162) 3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (490) 4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (70604) 5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (808) 6 or/1-5 (118618) 7 exp nephrectomy/ (37938) 8 (nephrectom* or lymphadenectom*).ti,ab,kw. (62205) 9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (204663) 10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (59909) 11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (918105) 12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (21870) 13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2661)

Searches
14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (446) 15 radiotherapy/ or lymphatic irradiation/ or radiosurgery/ or radiotherapy, adjuvant/ or radiotherapy dosage/ or radiotherapy, high-energy/ or re-irradiation/ or Cytoreduction Surgical Procedures/ or Ablation Techniques/ or Radiofrequency Ablation/ or Robotic Surgical Procedures/ or Minimally Invasive Surgical Procedures/ or Metastasectomy/ or Lymph Node Excision/ or Watchful Waiting/ (239644) 16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (933898) 17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (2177) 18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (11) 19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (38472) 20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (5) 21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (279) 22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (26) 23 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (38392) 24 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (266) 25 (delay* adj2 treat*).ti,ab. (20889) 26 (delay* and treat*).kw. (162) 27 (watchful* adj1 wait*).ti,ab. (3238) 28 (watchful* and wait*).kw. (4) 29 or/7-28 (2201330) 30 6 and 29 (38582) 31 animals/ not humans/ (5153512) 32 30 not 31 (36911) 33 limit 32 to english language (30806) 34 limit 33 to (letter or historical article or comment or editorial or news or case reports) (9081) 35 33 not 34 (21725) 36 exp Randomized Controlled Trial/ (608436) 37 randomi?ed.mp. (1099661) 38 placebo.mp. (252799) 39 or/36-38 (1166623) 40 (MEDLINE or pubmed).tw. (344612) 41 systematic review.tw. (287748) 42 systematic review.pt. (249879) 43 meta-analysis.pt. (193317) 44 intervention$.ti. (208375) 45 or/40-44 (719849) 46 Epidemiologic studies/ (9465) 47 exp case control studies/ (1474038)

Searches
48 exp cohort studies/ (2562056)
49 Case control.tw. (159034)
50 (cohort adj (study or studies)).tw. (337093)
51 Cohort analy$.tw. (12565)
52 (Follow up adj (study or studies)).tw. (57443)
53 (observational adj (study or studies)).tw. (171478)
54 Longitudinal.tw. (336148)
55 Retrospective.tw. (784597)
56 Cross sectional.tw. (542555)
57 Cross-sectional studies/ (489693)
58 or/46-57 (3917614)
59 39 or 45 or 58 (5240090)
60 35 and 59 (10204)
61 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1322150)
62 "organisation for economic co-operation and development"/ (581)
63 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or

Searches
ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3526314) 64 european union/ (17879) 65 developed countries/ (21470) 66 or/62-65 (3542495) 67 61 not 66 (1231834) 68 60 not 67 (9991)

Database name: Embase

Searches
1 exp kidney tumor/ (169289) 2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (25843) 3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (738) 4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (105763) 5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1179) 6 or/1-5 (199212) 7 exp nephrectomy/ (79135) 8 (nephrectom* or lymphadenectom*).ti,ab,kw. (95869) 9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (296316) 10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (84073) 11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (1172497)

Searches
12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (39682) 13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4849) 14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (923) 15 radiotherapy/ or cancer radiotherapy/ or adjuvant radiotherapy/ or exp radiosurgery/ or radiotherapy dosage/ or megavoltage radiotherapy/ or re-irradiation/ or cytoreductive surgery/ or ablation therapy/ or radiofrequency ablation/ or robot assisted surgery/ or minimally invasive surgery/ or metastasis resection/ or lymph node dissection/ or cryotherapy/ or stereotactic body radiation therapy/ or active surveillance/ or watchful waiting/ (700411) 16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (1245790) 17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (3847) 18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (21) 19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (58741) 20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (8) 21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (642) 22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (36) 23 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (56960) 24 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (432) 25 (delay* adj2 treat*).ti,ab. (32640) 26 (delay* and treat*).kw. (278) 27 (watchful* adj1 wait*).ti,ab. (4967) 28 (watchful* and wait*).kw. (8) 29 or/7-28 (3008790) 30 6 and 29 (72417) 31 nonhuman/ not human/ (5369703) 32 30 not 31 (70586) 33 limit 32 to english language (63135) 34 33 not (letter or editorial).pt. (61048) 35 34 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (41463) 36 random:.tw. (2023923) 37 placebo:.mp. (532136) 38 double-blind:.tw. (248720) 39 or/36-38 (2304835) 40 (MEDLINE or pubmed).tw. (428718) 41 exp systematic review/ or systematic review.tw. (533296) 42 meta-analysis/ (304008)

Searches
43 intervention$.ti. (274290)
44 or/40-43 (1007209)
45 Clinical study/ (165319)
46 Case control study/ (212430)
47 Family study/ (25771)
48 Longitudinal study/ (205110)
49 Retrospective study/ (1556506)
50 comparative study/ (1042643)
51 Prospective study/ (902470)
52 Randomized controlled trials/ (268035)
53 51 not 52 (891477)
54 Cohort analysis/ (1106561)
55 cohort analy$.tw. (20347)
56 (Cohort adj (study or studies)).tw. (487394)
57 (Case control$ adj (study or studies)).tw. (176315)
58 (follow up adj (study or studies)).tw. (75066)
59 (observational adj (study or studies)).tw. (266587)
60 (epidemiologic$ adj (study or studies)).tw. (124259)
61 (cross sectional adj (study or studies)).tw. (359262)
62 case series.tw. (152596)
63 prospective.tw. (1133006)
64 retrospective.tw. (1304827)
65 or/45-50,53-64 (5603678)
66 39 or 44 or 65 (7885322)
67 35 and 66 (13670)
68 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or

Searches
peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1736652) 69 exp "organisation for economic co-operation and development"/ (2827) 70 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3832351) 71 european union/ (31891) 72 developed country/ (35945) 73 or/69-72 (3866518) 74 68 not 73 (1580645) 75 67 not 74 (13394)

Database name: Cochrane CDSR & CENTRAL

Searches
#1 MeSH descriptor: [Kidney Neoplasms] explode all trees 1694 #2 (Kidney* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)):ti,ab 1332 #3 (collecting-duct* NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)):ti,ab 14 #4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*):ti,ab 3747 #5 (Kidney* NEAR/2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR/2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)):ti,ab 69

Searches
#6 {or #1-#5} 5140 #7 MeSH descriptor: [Nephrectomy] explode all trees 594 #8 (nephrectom* or lymphadenectom*):ti,ab 3676 #9 MeSH descriptor: [Radiotherapy] this term only 2824 #10 MeSH descriptor: [Lymphatic Irradiation] this term only 76 #11 MeSH descriptor: [Radiosurgery] this term only 485 #12 MeSH descriptor: [Radiotherapy, Adjuvant] this term only 1427 #13 MeSH descriptor: [Radiotherapy Dosage] this term only 2429 #14 MeSH descriptor: [Radiotherapy, High-Energy] this term only 320 #15 MeSH descriptor: [Re-Irradiation] this term only 37 #16 MeSH descriptor: [Cytoreduction Surgical Procedures] this term only 232 #17 MeSH descriptor: [Ablation Techniques] this term only 127 #18 MeSH descriptor: [Radiofrequency Ablation] this term only 342 #19 MeSH descriptor: [Robotic Surgical Procedures] this term only 716 #20 MeSH descriptor: [Minimally Invasive Surgical Procedures] this term only 1280 #21 MeSH descriptor: [Metastasectomy] this term only 43 #22 MeSH descriptor: [Lymph Node Excision] this term only 1540 #23 MeSH descriptor: [Watchful Waiting] this term only 469 #24 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) NEAR/3 (remov* or surg* or extract* or extirpat* or operat*)):ti,ab 18334 #25 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) NEAR/3 (surg* or remov* or partial* or procedur* or treat* or operat*)):ti,ab 63782 #26 (nephron* NEAR/2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)):ti,ab 123 #27 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR):ti,ab 63947 #28 ((RAS or (robotic* NEAR/1 assist*)) NEAR/1 (surg* or remov* or partial* or procedur* or treat* or operat*)):ti,ab 256 #29 (minimal* NEAR/2 invas* NEAR/2 (surg* or procedur* or treat*)):ti,ab 3606 #30 ((inferior-vena-cava or IVC) NEAR/2 thrombectom*):ti,ab 2 #31 ((activ* or tumor* or tumour* or delay*) NEAR/2 (surveil* or monitor*)):ti,ab 4050 #32 (delay* NEAR/2 treat*):ti,ab 2913 #33 (watchful* NEAR/1 wait*):ti,ab 668 #34 {or #7-#33} 150254 #35 #6 AND #34 1693 #36 "conference":pt or (clinicaltrials or trialsearch):so 725938 #37 #35 NOT #36 776

Database name: Epistemonikos

Searches
(kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR (collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR ((collecting duct*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4 or (stage 1) or (stage 2) or (stage 3) or (stage 4))) OR (renal-cell* or (renal cell*) or rcc or ccrcc or renal-mass* or (renal mass*) or renal-tumor* or (renal tumor*) or renal-tumour* or (renal tumour*) or grawitz-tumor* or (grawitz tumor*) or grawitz-tumour* or (grawitz tumour*) or hypernephroma* or nephrocarcinoma*) OR (kidney* AND (transitional-cell* or (transitional cell*) or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)) AND (nephrectom* or lymphadenectom*) OR ((kidney* or renal* or rcc or ccrcc or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*)) OR ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) OR (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) OR (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or sabr) OR ((ras or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) OR (minimal* AND invas* AND (surg* or procedur* or treat*)) OR ((inferior-vena-cava or ivc or (inferior vena cava)) AND thrombectom*) OR ((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*)) OR (delay* AND treat*) OR (watchful* AND wait*)

Database name: INAHTA

Searches
#1 "Kidney Neoplasms"[mhe] 111
#2 ((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or

Searches
tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) 105
#3 (((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*)))) OR ("Kidney Neoplasms"[mhe]) 155
#4 "Nephrectomy"[mhe] 12
#5 ((nephrectom* or lymphadenectom*)) 31
#6 "Radiotherapy"[mh] 220
#7 "Lymphatic Irradiation"[mh] 0
#8 "Radiosurgery"[mh] 71
#9 "Radiotherapy Adjuvant"[mh] 27
#10 "Radiotherapy Dosage"[mh] 27
#11 "Radiotherapy High-Energy"[mh] 9
#12 "Re-Irradiation"[mh] 2
#13 "Cytoreduction Surgical Procedures"[mh] 2
#14 "Ablation Techniques"[mh] 35
#15 "Radiofrequency Ablation"[mh] 29
#16 "Robotic Surgical Procedures"[mh] 22
#17 "Minimally Invasive Surgical Procedures"[mh] 109
#18 "Metastasectomy"[mh] 1
#19 "Lymph Node Excision"[mh] 9
#20 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*)) 878
#21 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) 756
#22 (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) 2
#23 radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR) 1000
#24 ((RAS or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) 73
#25 (minimal* AND invas* AND (surg* or procedur* or treat*))246
#26 ((inferior-vena-cava or IVC) AND thrombectom*) 0
#27 ((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*)) 318
#28 (delay* AND treat*) 201

Searches		
#29	(watchful* AND wait*)	45
#29	#28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4	2796
#30	#29 AND #3	155
Limit	English language	97

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	05/02/2024	OVID	1886 to January 25, 2024	1
EED	07/02/2024	CRD	n/a	23
Embase	05/02/2024	Ovid	1974 to 2024 February 02	65
HTA	07/02/2024	CRD	n/a	27
INAHTA	05/02/2024	INAHTA	n/a	155
MEDLINE ALL	05/02/2024	Ovid	1946 to February 02, 2024	62

Rerun search database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	06/05/2025	OVID	1886 to May 01, 2025	1
Embase	06/05/2025	Ovid	1974 to 2025 May 05	73
INAHTA	06/05/2025	INAHTA	n/a	177
MEDLINE ALL	06/05/2025	Ovid	1946 to May 05, 2025	68

Search strategy history

Database name: Econlit

Searches
1 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (8) 2 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (0) 3 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (22)

Searches
4 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (0) 5 or/1-4 (30) 6 (nephrectom* or lymphadenectom*).ti,ab,kw. (0) 7 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (80) 8 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (25798) 9 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (0) 10 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (599) 11 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (10) 12 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (0) 13 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (7) 14 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (0) 15 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (0) 16 ((inferior-vena-cava or IVC) and thrombectom*).kw. (0) 17 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (388) 18 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (4) 19 (delay* adj2 treat*).ti,ab. (48) 20 (delay* and treat*).kw. (0) 21 (watchful* adj1 wait*).ti,ab. (10) 22 (watchful* and wait*).kw. (0) 23 or/6-22 (26909) 24 5 and 23 (1)

Database name: CRD EED & HTA

Searches

Line	Search	Hits
1	MESH DESCRIPTOR Kidney Neoplasms EXPLODE ALL TREES	201
2	(Kidney* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))	194
3	(collecting-duct* NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4))	1
4	(renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)	204
5	(Kidney* NEAR2 (Transitional-cell* or cell or urothelial* or duct or advanc*) NEAR2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))	3
6	#1 OR #2 OR #3 OR #4 OR #5	262
7	MESH DESCRIPTOR Nephrectomy EXPLODE ALL TREES	95
8	(nephrectom* or lymphadenectom*)	235
9	MESH DESCRIPTOR Radiotherapy	247
10	MESH DESCRIPTOR Lymphatic Irradiation	1
11	MESH DESCRIPTOR Radiosurgery	125
12	MESH DESCRIPTOR Radiotherapy, Adjuvant	176
13	MESH DESCRIPTOR Radiotherapy Dosage	112
14	MESH DESCRIPTOR Radiotherapy, High-Energy	15
15	MESH DESCRIPTOR Re-Irradiation	0
16	MESH DESCRIPTOR Cytoreduction Surgical Procedures	4
17	MESH DESCRIPTOR Ablation Techniques	29
18	MESH DESCRIPTOR Radiofrequency Ablation	0
19	MESH DESCRIPTOR Robotic Surgical Procedures	23
20	MESH DESCRIPTOR Minimally Invasive Surgical Procedures	260
21	MESH DESCRIPTOR Metastasectomy	5
22	MESH DESCRIPTOR Lymph Node Excision	171
23	((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) NEAR3 (remov* or surg* or extract* or extirpat* or operat*))	2281
24	((laproscop* or open or partial* or radical or transperiton* or retroperiton*) NEAR3 (surg* or remov* or partial* or procedur* or treat* or operat*))	1045
25	(nephron* NEAR2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*))	9
26	(radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR)	3151
27	((RAS or (robotic* NEAR1 assist*)) NEAR1 (surg* or remov* or partial* or procedur* or treat* or operat*))	28
28	(minimal* NEAR2 invas* NEAR2 (surg* or procedur* or treat*))	425
29	((inferior-vena-cava or IVC) NEAR2 thrombectom*)	0
30	((activ* or tumor* or tumour* or delay*) NEAR2 (surveil* or monitor*))	119
31	(delay* NEAR2 treat*)	119
32	MESH DESCRIPTOR Watchful Waiting	38
33	(watchful* NEAR1 wait*)	137
34	#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33	6388
35	#6 AND #34	97
36	(#35) IN NHSEED	23
37	(#35) IN HTA	27

Database name: Embase

Searches
1 exp kidney tumor/ (169657) 2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (25905) 3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (739) 4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (105980) 5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (1182) 6 or/1-5 (199645) 7 exp nephrectomy/ (79289) 8 (nephrectom* or lymphadenectom*).ti,ab,kw. (96024) 9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (296981) 10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (84341) 11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (1174471) 12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (39794) 13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (4849) 14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (927) 15 radiotherapy/ or cancer radiotherapy/ or adjuvant radiotherapy/ or exp radiosurgery/ or radiotherapy dosage/ or megavoltage radiotherapy/ or re-irradiation/ or cytoreductive surgery/ or ablation therapy/ or radiofrequency ablation/ or robot assisted surgery/ or minimally invasive surgery/ or metastasis resection/ or lymph node dissection/ or cryotherapy/ or stereotactic body radiation therapy/ or active surveillance/ or watchful waiting/ (702412)

Searches
16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (1248256)
17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (3873)
18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (21)
19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (58898)
20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (8)
21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (647)
22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (36)
23 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (57069)
24 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (432)
25 (delay* adj2 treat*).ti,ab. (32723)
26 (delay* and treat*).kw. (281)
27 (watchful* adj1 wait*).ti,ab. (4971)
28 (watchful* and wait*).kw. (8)
29 or/7-28 (3014855)
30 6 and 29 (72543)
31 nonhuman/ not human/ (5377221)
32 30 not 31 (70709)
33 limit 32 to english language (63258)
34 33 not (letter or editorial).pt. (61164)
35 34 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. (41542)
36 afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or cote d'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or

Searches
peru/ or philippines/ or polynesia/ or qatar/ or "republic of north macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/ (1740991) 37 exp "organisation for economic co-operation and development"/ (2851) 38 exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or "Turkey (republic)"/ or exp united kingdom/ or exp united states/ or western europe/ (3835523) 39 european union/ (31807) 40 developed country/ (35992) 41 or/37-40 (3869712) 42 36 not 41 (1584824) 43 35 not 42 (41050) 44 cost utility analysis/ (12696) 45 (cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. (30947) 46 ((incremental* adj2 cost*) or ICER).tw. (31650) 47 (cost adj2 utilit*).tw. (11338) 48 (cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. (3393) 49 ((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. (37671) 50 (cost and (effect* or utilit*)).ti. (58589) 51 or/44-50 (92726) 52 43 and 51 (65)

Database name: Medline ALL

Searches
1 exp Kidney Neoplasms/ (85968) 2 (Kidney* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4)).ti,ab. (17223)

Searches
3 (collecting-duct* adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)).ti,ab. (491)
4 (renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumo?r* or grawitz-tumo?r* or hypernephroma* or nephrocarcinoma*).ti,ab. (70816)
5 (Kidney* adj2 (Transitional-cell* or cell or urothelial* or duct or advanc*) adj2 (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma*)).ti,ab. (817)
6 or/1-5 (118910)
7 exp nephrectomy/ (37965)
8 (nephrectom* or lymphadenectom*).ti,ab,kw. (62344)
9 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) adj3 (remov* or surg* or extract* or extirpat* or operat*)).ti,ab. (205263)
10 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) and (remov* or surg* or extract* or extirpat* or operat*)).kf. (60200)
11 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) adj3 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (920508)
12 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kf. (22001)
13 (nephron* adj2 (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).ti,ab. (2662)
14 (nephron* and (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)).kf. (447)
15 radiotherapy/ or lymphatic irradiation/ or radiosurgery/ or radiotherapy, adjuvant/ or radiotherapy dosage/ or radiotherapy, high-energy/ or re-irradiation/ or Cytoreduction Surgical Procedures/ or Ablation Techniques/ or Radiofrequency Ablation/ or Robotic Surgical Procedures/ or Minimally Invasive Surgical Procedures/ or Metastasectomy/ or Lymph Node Excision/ or Watchful Waiting/ (240052)
16 (radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR).ti,ab,kw. (936452)
17 ((RAS or (robotic* adj1 assist*)) adj1 (surg* or remov* or partial* or procedur* or treat* or operat*)).ti,ab. (2212)
18 ((RAS or (robotic* adj1 assist*)) and (surg* or remov* or partial* or procedur* or treat* or operat*)).kw. (11)
19 (minimal* adj2 invas* adj2 (surg* or procedur* or treat*)).ti,ab. (38673)
20 (minimal* and invas* and (surg* or procedur* or treat*)).kw. (5)
21 ((inferior-vena-cava or IVC) adj2 thrombectom*).ti,ab. (279)
22 ((inferior-vena-cava or IVC) and thrombectom*).kw. (26)
23 ((activ* or tumo?r* or delay*) adj2 (surveil* or monitor*)).ti,ab. (38554)

Searches
24 ((activ* or tumo?r* or delay*) and (surveil* or monitor*)).kw. (268) 25 (delay* adj2 treat*).ti,ab. (20957) 26 (delay* and treat*).kw. (163) 27 (watchful* adj1 wait*).ti,ab. (3243) 28 (watchful* and wait*).kw. (4) 29 or/7-28 (2207356) 30 6 and 29 (38664) 31 animals/ not humans/ (5159676) 32 30 not 31 (36990) 33 limit 32 to english language (30881) 34 limit 33 to (letter or historical article or comment or editorial or news or case reports) (9092) 35 33 not 34 (21789) 36 afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/ (1325188) 37 "organisation for economic co-operation and development"/ (587) 38 australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or

Searches
ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ (3530229) 39 european union/ (17894) 40 developed countries/ (21491) 41 or/37-40 (3546443) 42 36 not 41 (1234802) 43 35 not 42 (21490) 44 Cost-Benefit Analysis/ (93959) 45 (cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. (18159) 46 ((incremental* adj2 cost*) or ICER).tw. (18654) 47 (cost adj2 utilit*).tw. (7142) 48 (cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. (2429) 49 ((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. (24749) 50 (cost and (effect* or utilit*)).ti. (39941) 51 or/44-50 (116479) 52 43 and 51 (62)

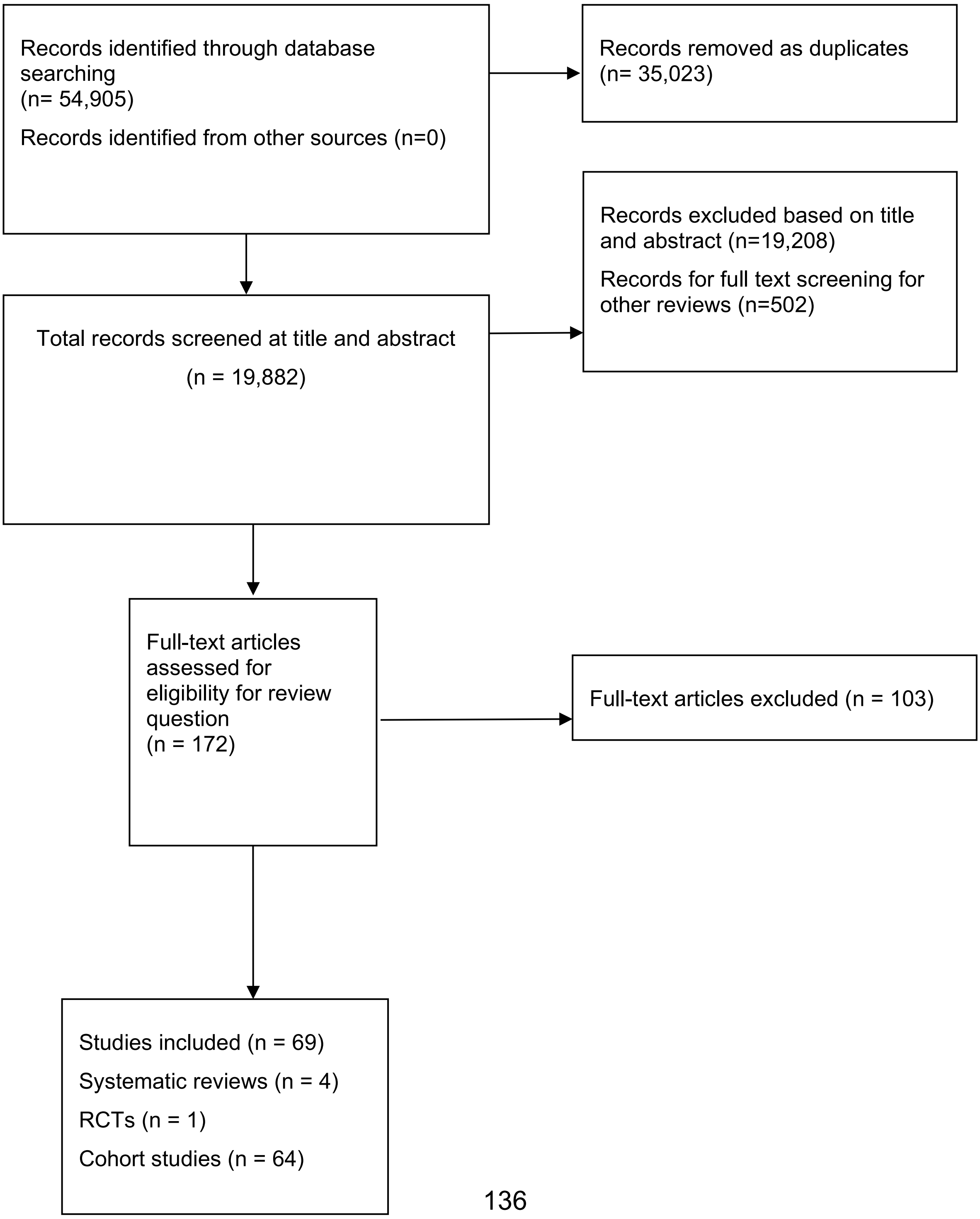
Database name: INAHTA

Searches
#1 "Kidney Neoplasms"[mhe] 111
#2 ((Kidney* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumo?r* or mass or metastat* or malignan* or sarcoma* or parenchyma* or t1 or t1a or t1b or tb or t2a or t2b or t3 or t3a or t3b or t3c or stage-1 or stage-2 or stage-3 or stage-4))) OR ((collecting-duct* AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma* or stage-4)) OR ((renal-cell* or RCC or ccRCC or Renal-mass* or renal-tumor* or renal-tumour* or grawitz-tumor* or grawitz-tumour* or hypernephroma* or nephrocarcinoma*)) OR ((Kidney* AND (Transitional-cell* or cell or urothelial* or duct or advanc*) AND (cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or parenchyma*))) 105
#3 #1 or #2 155
#4 "Nephrectomy"[mhe] 12
#5 ((nephrectom* or lymphadenectom*)) 31
#6 "Radiotherapy"[mh] 220
#7 "Lymphatic Irradiation"[mh] 0
#8 "Radiosurgery"[mh] 71
#9 "Radiotherapy Adjuvant"[mh] 27

Searches
#10 "Radiotherapy Dosage"[mh] 27
#11 "Radiotherapy High-Energy"[mh] 9
#12 "Re-Irradiation"[mh] 2
#13 "Cytoreduction Surgical Procedures"[mh] 2
#14 "Ablation Techniques"[mh] 35
#15 "Radiofrequency Ablation"[mh] 29
#16 "Robotic Surgical Procedures"[mh] 22
#17 "Minimally Invasive Surgical Procedures"[mh] 109
#18 "Metastasectomy"[mh] 1
#19 "Lymph Node Excision"[mh] 9
#20 ((kidney* or renal* or RCC or ccRCC or lymph* or adrenal* or cancer* or carcinoma* or carcinosarcoma* or adenocarcino* or neoplas* or tumor* or tumour* or mass or metastat* or malignan* or sarcoma* or hypernephroma* or nephrocarcinoma*) AND (remov* or surg* or extract* or extirpat* or operat*)) 878
#21 ((laproscop* or open or partial* or radical or transperiton* or retroperiton*) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) 756
#22 (nephron* AND (surg* or remov* or partial* or procedur* or treat* or operat* or spar* or preserv*)) 2
#23 radiotherap* or radiation* or radiosurg* or cyberknife* or irradiat* or thermoablat* or ablat* or cyrotherap* or cytoreduct* or cyroablat* or stereostat* or SABR) 1000
#24 ((RAS or (robotic* AND assist*)) AND (surg* or remov* or partial* or procedur* or treat* or operat*)) 73
#25 (minimal* AND invas* AND (surg* or procedur* or treat*))246
#26 ((inferior-vena-cava or IVC) AND thrombectom*) 0
#27 ((activ* or tumor* or tumour* or delay*) AND (surveil* or monitor*)) 318
#28 (delay* AND treat*) 201
#29 (watchful* AND wait*) 45
#30 "Watchful Waiting"[mh] 17
#31 #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18 OR #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6 OR #5 OR #4 2803
#32 #31 AND #3 155

Appendix C – Effectiveness evidence study selection

Figure 1: PRISMA diagram



Appendix D – Effectiveness evidence

Evidence tables are presented for studies data extracted by the NICE team. Studies and data taken directly from systematic reviews (SRs) are not included in these evidence tables. Some studies were included in SRs but contained additional relevant outcomes that were not reported in the SR – these studies were data extracted by the NICE team with only the additional outcomes extracted and assessed for risk of bias, and are included in this appendix.

All critical appraisals in appendix D are those conducted by the NICE team.

Table 21 shows primary studies for which outcomes were taken directly from systematic reviews and which systematic reviews these were extracted from. The table also records the original risk of bias as reported in the systematic review, and the risk of bias once modified by the NICE team (see section 1.1.3 on Methods and Process).

Table 21: Outcomes extracted directly from systematic reviews (SRs)

Primary study	Source SR	Outcomes taken from SR	Risk bias checklist used in SR	Original risk of bias	Modified risk of bias
Acosta Ruiz 2019	Yanagisawa 2022	Complications (all) TA versus PN	ROBINS-I	Serious	No modification made
Alam 2019	Xu 2019	Overall survival ≤5 years TA versus PN, Cancer-specific survival ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Alam 2019	Guo 2019	Cancer-specific survival ≤5 years AS versus PN, Cancer-specific survival ≤5 years AS versus TA, Overall survival ≤5 years AS versus PN, Overall survival ≤5 years AS versus TA	Newcastle-Ottawa	Low	Serious
Anglickis 2019	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN	ROBINS-I	Serious	No modification made

Caputo 2017	Yanagisawa 2022	Complications (all) TA versus PN, Major complications (Clavien-Dindo 3-5) TA versus PN	ROBINS-I	Low	No modification made
Cooper 2015	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Danzig 2015	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Deklaj 2010	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Desai 2005	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN, Duration of stay TA versus PN	ROBINS-I	Serious	No modification made
Desai 2005	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Emara 2014	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Faddegon 2013	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made

Fosatti 2015	Yanagisawa 2022	Complications (all) TA versus PN, Duration of stay TA versus PN, Major complications (Clavien-Dindo 3-5) TA versus PN	ROBINS-I	Serious	No modification made
Fosati 2015	Xu 2019	Local recurrence ≤5 years TA versus PN, Disease-free survival ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Foyil 2008	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Garcia 2021	Yanagisawa 2022	Complications (all) TA versus PN, Duration of stay TA versus PN, Major complications (Clavien-Dindo 3-5) TA versus PN	ROBINS-I	Serious	No modification made
Guillotreau 2012	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	Serious	No modification made
Guillotreau 2012	Patel 2017	Change in eGFR ≤5 years TA versus PN, New onset eGFR <15 ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Guillotreau 2012	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Haramis 2012	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	Serious	No modification made

Kim 2015	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Duration of stay TA versus PN	ROBINS-I	low	No modification made
Kiriluk 2011	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Klatte 2011	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	low	No modification made
Klatte 2011	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Klatte 2011	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Ko 2008	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN, Duration of stay TA versus PN	ROBINS-I	low	No modification made
Larcher 2015	Guo 2019	Cancer-specific survival ≤5 years AS versus TA	Newcastle-Ottawa	Low	Serious
Lucas 2008	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Lucas 2008	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN, New	Cochrane Risk of Bias Assessment Tool for Non-Randomized	Moderate	No modification made

		onset eGFR <15 ≤5 years TA versus PN	Studies of Interventions		
Miller 2018	Guo 2019	Cancer-specific survival ≤5 years AS versus PN, Cancer-specific survival ≤5 years AS versus TA, Overall survival ≤5 years AS versus PN, Overall survival ≤5 years AS versus TA	Newcastle-Ottawa	Low	Serious
Mitchell 2011	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Mues 2012	Patel 2017	Change in eGFR ≤5 years TA versus PN, New onset eGFR <15 ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Olweny 2012	Xu 2019	Local recurrence >5 years TA versus PN, Overall Survival >5 years TA versus PN, Cancer-specific survival >5 years TA versus PN, Disease-free survival >5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Park 2018	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Duration of stay TA versus PN	ROBINS-I	low	No modification made
Park 2019	Yanagisawa 2022	Major complications	ROBINS-I	Serious	No modification made

		(Clavien-Dindo 3-5) TA versus PN			
Park 2018	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Pascal 2011	Patel 2017	Change in eGFR ≤5 years TA versus PN, New onset eGFR <15 ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Patel 2015	Guo 2019	Cancer-specific survival ≤5 years AS versus PN, Overall survival ≤5 years AS versus PN	Newcastle-Ottawa	Low	Serious
Patel 2012	Guo 2019	Cancer-specific survival ≤5 years AS versus PN, Overall survival ≤5 years AS versus PN	Newcastle-Ottawa	Low	Serious
Rembeyo 2019	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	Serious	No modification made
Shapiro 2020	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	Serious	No modification made
Stern 2007	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5) TA versus PN, Complications (all) TA versus PN	ROBINS-I	Serious	No modification made
Stern 2007	Xu 2019	Local recurrence ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Takaki 2012	Xu 2019	Overall survival ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious

Takaki 2010	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Takaki 2014	Patel 2017	Change in eGFR ≤5 years TA versus RN, Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Tanagho 2013	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Tang 2017	Guo 2019	Cancer-specific survival ≤5 years AS versus PN, Overall survival ≤5 years AS versus PN	Newcastle-Ottawa	Low	Serious
Thompson 2015	Xu 2019	Local recurrence ≤5 years TA versus PN, Local recurrence ≤5 years TA versus PN, Overall survival ≤5 years TA versus PN, Overall survival ≤5 years TA versus PN	Newcastle-Ottawa	Low	Serious
Turna 2009	Patel 2017	Change in eGFR ≤5 years TA versus PN, New onset eGFR <15 ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made
Yanagisawa 2018	Yanagisawa 2022	Major complications (Clavien-Dindo 3-5)	ROBINS-I	Serious	No modification made

		TA versus PN, Complications (all) TA versus PN, Duration of stay TA versus PN			
Youn 2013	Patel 2017	Change in eGFR ≤5 years TA versus PN	Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions	Moderate	No modification made

TA: thermal ablation; PN: partial nephrectomy; AS: active surveillance; RN radical nephrectomy

Systematic review evidence

Guo, 2019

Bibliographic Reference	Guo, Run-Qi; Li, Xiao-Guang; Comparison of survival benefits of nephron-sparing intervention or active surveillance for patients with localized renal masses: a systematic review and meta-analysis.; BMC urology; 2019; vol. 19 (no. 1); 74

Study Characteristics

Study design	Systematic review
Study details	Dates searched January 2000 to September 2018 Databases searched PubMed, EMBASE and Web of Science Sources of funding No funding received.
Inclusion criteria	(1) studies comparing the effectiveness or survival between 'nephron sparing intervention' (enucleation, PN, and TA, like radiofrequency ablation, cryoablation, microwave ablation, etc.) and Active Surveillance (AS) (2) studies that clearly described outcome assessment by representing it in overall survival or cancer-specific survival or cardiovascular-specific survival (3) survival outcome further demonstrated hazard ratio (HR) and corresponding 95% confidence interval (CI) or adequate data to achieve an estimated HR and 95% CI by using the methods reported by Tierney et al (4) prospective cohort or retrospective study (5) median follow-up of at least 12 months.

Exclusion criteria	(1) The literature was review, letter, case reports and meta-analysis (2) The data were not available (3) The literature deals with recurrent RCC, metastatic carcinoma, or urothelial carcinoma (4) Duplicate publication.
Intervention(s)	Partial nephrectomy Thermal ablation Active surveillance
Outcome(s)	Overall survival Cancer-specific survival Not extracted as not an included outcome Cardiovascular specific survival Not extracted as not an included outcome
Number of studies included in the systematic review	7 studies: 1 prospective cohort, 6 retrospective cohorts.
Studies from the systematic review that are relevant for use in the current review	Alam 2018 Larcher 2015 Miller 2018 Patel 2012 Tang 2017 Patel 2015
Studies from the systematic review that are not relevant for use in the current review	Larcher 2015 (thermal ablation and partial nephrectomy presented as a single intervention compared with active surveillance. Cannot be disaggregated).
Additional comments	Log HR and the variance were utilized as the summary outcome measure from all studies in the meta-analysis. For each study, HR with the 95%CI of the survival rate was derived to compare the effectiveness between NSI and AS for patients with renal masses. Fixed effects model applied when I 2 < 50% and P value < 0.1. The funnel plot was constructed for each meta-analysis to detect the publication bias, and the Egger's test was utilized to assess publication bias statistically

	Quality assessment: Newcastle-Ottawa scale for nRCTs. Studies with scores less than 4 were considered to have a high risk of bias, scores of 4–6 to have a moderate risk of bias, and scores over 6 to have a low risk of bias. All included studies had results from 7-9. Study aims to compare active surveillance with nephron-sparing intervention (NSI). NSI includes enucleation but all included studies consider partial nephrectomy or thermal ablation only. SR categorises these as NSI. NICE will separate out these two interventions in the analysis. 2 studies draw on the SEER database (Larcher 2015 and Patel 2015) but one (Larcher 2015) is not included in the overall survival outcome.

Study arms

Nephron sparing intervention (N = 2559)

Partial nephrectomy and thermal ablation

Active surveillance (N = 1372)

Critical appraisal - Critical Appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(There was no reference of a review protocol and it was unclear whether criteria were pre-specified or adapted post-hoc. English language studies only.)*
Overall study ratings	Applicability as a source of data	Partially applicable *(did not include all relevant interventions in the protocol)*

Hu, 2019

Bibliographic Reference	Hu, Xu; Shao, Yan-Xiang; Wang, Yan; Yang, Zhi-Qiang; Yang, Wei-Xiao; Li, Xiang; Partial nephrectomy versus ablative therapies for cT1a renal masses: A Systematic Review and meta-analysis.; European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology; 2019; vol. 45 (no. 9); 1527-1535

Study Characteristics

Study design	Systematic review
Study details	Dates searched Up to November 2018 Databases searched Pubmed, Embase, Cochrane central register of controlled trials Sources of funding No funding received.
Inclusion criteria	(1) randomized controlled trials (RCTs) or observational studies (2) involved renal masses patients treated with PN or ablation (3) comparison of PN versus ablation (4) reported the outcome such as cancer-specific survival (CSS), overall survival (OS), disease-free survival (DFS), local recurrence, complications or change in renal function.
Exclusion criteria	(1) fewer than 20 patients (2) non-English language (3) animal-based studies (4) renal masses larger than 4 cm (5) did not report the clinical outcomes (6) conference literature and studies based on national database because of no detailed information. If reported data duplicated, only the latest report was included.
Intervention(s)	Partial nephrectomy Thermal ablation
Outcome(s)	Overall survival Disease-free survival Recurrence Renal functional outcomes - Not extracted as a more applicable systematic review (Patel 2017) is used. Postoperative complications - Not extracted as does not use Clavien-Dindo. Cancer-specific survival - Not extracted as not an included outcome
Number of studies included in the systematic review	20 studies: 1 RCT, 5 prospective cohort studies, 14 retrospective cohort studies.
Studies from the systematic review that	Alam 2018 Park 2018 Ji 2016 Chang 2015

are relevant for use in the current review	Fossati 2015 Thompson 2015 Emara 2014 Youn 2013 Guan 2012 Guillotreau 2012 Olweny 2012 Klatte 2011 Takaki 2010 Ko 2008 Lucas 2008 Stern 2007 Desai 2005
Studies from the systematic review that are not relevant for use in the current review	Mason 2017 (only renal functional outcomes) Liu 2017 (not included in any data presented in this SR). Arm totals do not include these studies.
Additional comments	Systematic review methods: • HRs and 95% CI were generally obtained directly from each eligible study. If not, based on the method by Tierney, they were estimated indirectly according to Kaplan-Meier curve. Local recurrence was evaluated using odds ratios (OR). • Quality assessment used by the SR: Cochrane Risk of Bias tool for RCTs; Newcastle-Ottawa scale for nRCTs. OS: time between the initial diagnosis and the death from all causes DFS: the length of time after primary treatment for renal cancer ends that the patient survives without any signs or symptoms of renal cancer Local recurrence: Local recurrence following ablation was defined as new focal enhancement in the ablation bed or enlargement of the ablation defect on follow-up imaging. Local recurrence following PN was defined as a mass in the ipsilateral kidney

Study arms

Partial nephrectomy (N = 2991)

Open, laparoscopic or robotic.

Thermal ablation (N = 1516)

Radiofrequency ablation, microwave ablation, cryoablation.

Critical appraisal - Critical Appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(There was no reference of a review protocol and it was unclear whether criteria were pre-specified or adapted post-hoc. English language studies only.)*
Overall study ratings	Applicability as a source of data	Partially applicable *(T1a only - T1b and T2 studies will be added by NICE)*

Patel, 2017

Bibliographic Reference	Patel, Hiten D; Pierorazio, Phillip M; Johnson, Michael H; Sharma, Ritu; Iyoha, Emmanuel; Allaf, Mohamad E; Bass, Eric B; Sozio, Stephen M; Renal Functional Outcomes after Surgery, Ablation, and Active Surveillance of Localized Renal Tumors: A Systematic Review and Meta-Analysis.; Clinical journal of the American Society of Nephrology : CJASN; 2017; vol. 12 (no. 7); 1057-1069

Study Characteristics

Study design	Systematic review
Study details	Dates searched Jan 1997 (when TNM was modified to include T1a T1b T2a T2b distinctions) to May 2015. Databases searched MEDLINE, Embase, Cochrane central register of controlled trials. Clinicaltrials.gov (US) Sources of funding Funded under contract HHSA290201200007I from the AHRQ, US Department of Health and Human Services.
Inclusion criteria	Comparative studies of the management options or single cohort studies of AS (given the expectation that comparative studies of AS would be sparse). The key questions included determining the comparative renal functional outcomes of different interventions for the management of a renal mass suspicious for localized renal cell carcinoma.

Exclusion criteria	Not reported.
Intervention(s)	Partial nephrectomy Radical nephrectomy Thermal ablation Active surveillance
Outcome(s)	Renal functional outcomes
Number of studies included in the systematic review	53 studies (17,784 patients) related to primary renal functional outcomes and 17 related to AKI ultimately included in this systematic review (58 total unique articles). All relevant studies to this review (n=20) are cohort studies.
Studies from the systematic review that are relevant for use in the current review	20 relevant studies. Chang 2015 Guillotreau 2012 Klatte 2011 Takaki 2010 Cooper 2015 Danzig 2015 Deklaj 2010 Foyil 2008 Lucas 2007 Takaki 2014 Faddegon 2013 Kiriluk 2011 Mitchell 2011 Mues 2012 Pascal 2011 Tanagho 2013 Turna 2009 Youn 2013
Studies from the systematic review that are not relevant for use in the current review	38 studies not relevant: Compared only partial and radical nephrectomy: Antoniewicz 2012 Barbalias 1999 Brewer 2012 Chung 2014 Iizuka 2012 Jeon 2009 Kim 2010 Kim 2014 Kyung 2014 Lane 2010 Mariusdottir 2013 Medina-Polo 2011

	Miyamoto 2012 Roos 2010 Roos 2012 Scosyrev 2014 Snow 2008 Woldu 2014 Yasuda 2012 Zorn 2007 Huang 2006 McKiernan 2002 Sun 2012 Deklaj 2010b Dash 2006 Matin 2002 Takagi 2011 Reports on irrelevant outcomes only: Shinohara 2001 Gratzke 2009 Kim 2003 Tomaszewski 2014 Xu 2014 Van Poppel 2011 Li 2007 Cooper 2015 Haramis 2012 Haber 2012 Non-OECD study: Huang 2006
Additional comments	Systematic review methods: • Renal functional outcomes were categorized into continuous (changes in eGFR largely on the basis of the Modification of Diet in Renal Disease Study equation when specified) and categorical (incidence of CKD stages ≥3, ≥3b, and ≥4 and end stage renal disease (ESRD)) outcomes. • When possible, authors used outcomes assessed via tabulated data or Kaplan–Meier curves closest to 1 year to avoid including competing causes of CKD other than the management strategy. • Risk of bias: RCTs - Cochrane Collaboration's tool. nRCTs - Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions. Outcomes for comparisons with active surveillance are not meta-analysed. 2 studies are included (Danzig 2015; Lane 2010). These will be evaluated and data added by the NICE team.

Study arms

Radical nephrectomy (N = 819)

Partial nephrectomy (N = 978)

Thermal ablation (N = 721)

Critical appraisal - Critical Appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(Search strategy and terms not presented, study characteristics not presented.)*
Overall study ratings	Applicability as a source of data	Partially applicable *(review did not include all relevant interventions)*

Yanagisawa, 2022

Bibliographic Reference	Yanagisawa, Takafumi; Mori, Keiichiro; Kawada, Tatsushi; Motlagh, Reza Sari; Mostafaei, Hadi; Quhal, Fahad; Laukhtina, Ekaterina; Rajwa, Pawel; Aydh, Abdulmajeed; Konig, Frederik; Pallauf, Maximilian; Pradere, Benjamin; Miki, Jun; Kimura, Takahiro; Egawa, Shin; Shariat, Shahrokh F; Differential efficacy of ablation therapy versus partial nephrectomy between clinical T1a and T1b renal tumors: A systematic review and meta-analysis.; Urologic oncology; 2022; vol. 40 (no. 7); 315-330

Study Characteristics

Study design	Systematic review
Study details	Dates searched To August 2021 Databases searched PUBMED, Web of Science, Scopus Sources of funding No funding provided.
Inclusion criteria	People with cT1a or cT1b renal tumours who underwent partial nephrectomy compared to ablation therapy. Studies reporting a relevant outcome RCTs, non-randomised, observational or cohort studies (Data from conference proceedings from the annual meeting of the American

	Urological Association (AUA) or the European Association of Urology (EAU) were included in the results to reduce the risk of publication bias)
Exclusion criteria	Meta-analyses, reviews, letters, editorial comments, replies from authors, case reports, and non-English articles. Studies not reporting results for cT1a and cT1b tumours separately
Intervention(s)	Partial nephrectomy Thermal ablation (Radiofrequency ablation, cryoablation, microwave ablation)
Outcome(s)	Recurrence Not taken from this SR Renal functional outcomes Not taken from this SR Postoperative complications Duration of hospital stay
Number of studies included in the systematic review	27 (26 cohort studies, 1 RCT)
Studies from the systematic review that are relevant for use in the current review	Park 2018 Chang 2015 Fossati 2015 Guan 2012 Guillotreau 2012 Klatte 2011 Ko 2008 Stern 2007 Desai 2005 Liu 2017 Garcia 2021 Haramis 2012 Yanagisawa 2018 Rembeyo 2019 Shapiro 2019 Acosta Ruiz 2019 Caputo 2017 Kim 2015 Anglickis 2019 Yu 2020 Park 2019 Liu 2021
Studies from the systematic	Complications and duration of hospital stay outcomes extracted from this SR. The following studies only reported other outcomes: Olweny 2012

review that are not relevant for use in the current review	Whitson 2012 Andrews 2019
Additional comments	SR did not include studies reporting cT1a and cT1b results together as one group. These studies were therefore identified from the searches conducted by NICE and added to the review, along with T2 studies. Complications and duration of hospital stay extracted for this systematic review. Other reported outcomes covered in other included SRs. For outcomes of continuous outcomes such as hospitalization period, the weighted mean difference (WMD) was used to measure the difference. To minimize the procedural heterogeneity, subgroup analyses were performed by differential approach of AT, percutaneous or others. Heterogeneity among each outcome of analysed studies was assessed by Cochrane's Q test and the I^2 statistic. Significant heterogeneity was identified in case of P < 0.05 in the Cochrane Q test and a ratio > 50% in I^2 statistics. Random effects models and Fixed-effect models were applied for the calculation of pooled HRs for heterogenous and non-heterogeneous results.

Study arms

Partial nephrectomy (N = 932)

Thermal ablation (N = 590)

Critical appraisal - Critical Appraisal - ROBIS checklist

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low *(Protocol identified and matches report. Identification of studies, data collection and data synthesis appears robust.)*
Overall study ratings	Applicability as a source of data	Partially applicable *(Fully applicable for most outcomes. For overall complications, it is unclear whether intraoperative complications are included, so this outcome is partially indirect.)*

RCT evidence

Neves, 2023

Bibliographic Reference	Neves, Joana B; Warren, Hannah; Santiapillai, Joseph; Rode, Nicola; Cullen, David; Pavlou, Menelaos; Walkden, Miles; Patki, Prasad; Barod, Ravi; Mumtaz, Faiz; Aitchison, Michael; Bandula, Steven; Pizzo, Elena; Ranieri, Veronica; Williams, Norman; Wildgoose, William; Gurusamy, Kurinchi; Emberton, Mark; Bex, Axel; Tran, Maxine G B; Nephron Sparing Treatment (NEST) for Small Renal Masses: A Feasibility Cohort-embedded Randomised Controlled Trial Comparing Percutaneous Cryoablation and Robot-assisted Partial Nephrectomy.; European urology; 2023

Study details

Trial registration number and/or trial name	ISRCTN18156881
Study type	Randomised controlled trial (RCT)
Study location	UK
Study setting	Hospital. Single-centre, high volume tertiary referral centre for kidney cancer.
Study dates	Recruitment: May 2019 to July 2021
Sources of funding	NIHR Research for Patient Benefit Programme (PB-PG-0817-20013). The Royal Free Hospital was the sponsor.
Inclusion criteria	Age 18 and over Any gender Ability to provide informed consent Diagnosis of small renal mass (SRM) - tumours <4 cm with an imaging appearance consistent with stage T1a Biopsy-diagnosed RCC Technical feasibility of treatment with either percutaneous cryoablation or robot-assisted partial nephrectomy

Exclusion criteria	Advanced disease (N1 or M1 on TNM staging) A concurrent medical or surgical condition or indication that meant that the tumour board/multidisciplinary team recommended one treatment modality over another.
Intervention(s)	Robot-assisted partial nephrectomy (RPN)
Comparator	Percutaneous cryoablation (CRA)
Outcome measures	Postoperative complications Renal functional impairment
Number of participants	N=50 RPN: 25 CRA: 25
Duration of follow-up	6 months
Loss to follow-up	10% (n=5) at 6 months were not retained (2 from CRA arm, 3 from RPN arm). Reasons were follow up at local hospital, withdrawing from study or data not available). Of 25 participants randomised to consider CRA, 21 consented and 19 of these completed treatment (2 patients were deemed unsuitable on positioning - one of these underwent RPN and the other underwent active surveillance). Of the 4 randomised who declined CRA, all were treated with RPN and are included in the analysis in the CRA arm. Of 25 participants randomised to RPN, all consented. There were 2 intraoperative conversions to radical nephrectomy (one for bleeding, one for tumour extension to the renal sinus fat and segmental renal vein).
Methods of analysis	Analysis was on an intention-to-treat basis. Continuous variables are summarised using the mean and SD if approximately normally distributed, and otherwise using the median and interquartile range. Continuous variables were compared across the randomised groups in intention-to-treat analysis (CRA v RPN) for equality of means using the t test if normality assumptions are met, and otherwise using the Wilcoxon test. Categorical variables were compared using a chi squared test or Fisher's exact test when frequencies in the corresponding 2 by 2 table were small. The change in renal function between the two groups at 6 mo was assessed by fitting a regression model for the estimated glomerular

	filtration rate (eGFR) at 6 mo in terms of the randomised group indicator variable, adjusting for the eGFR at baseline.
Additional comments	RCT is embedded in the NEST cohort study. Complications were measured at 30 days after treatment. eGFR change was measured at baseline and at 6 months. Blinding and randomisation: Randomisation was performed in blocks of ten via the Sealed Envelope online system (www.sealedenvelope.com) to allocate enrolled participants to CRA or RPN and to ensure allocation concealment. The trial was open label, with unblinded assessment of clinical outcomes. Limitations: RCT is designed to assess the feasibility of recruitment to a cohort-embedded RCT, not to assess effectiveness of the treatments. The single-site recruitment at an academic institution may not be generalisable. Only 25% of patients presenting with a small renal mass were eligible for the RCT (due to requirement for equipoise in selecting treatment arms). Baseline characteristics not statistically compared between arms. RPN arm has fewer smokers and more moderate (rather than low) RENAL score for the index tumour.

Study arms

Cryoablation (N = 25)

Percutaneous

Partial nephrectomy (N = 25)

Robot-assisted

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 25)	Partial nephrectomy (N = 25)
% Female No of events	n = 8 ; % = 32	n = 11 ; % = 44
Age	58.8 (10.8)	57.2 (8.8)

Characteristic	Cryoablation (N = 25)	Partial nephrectomy (N = 25)
Mean (SD)		
Tumour size mm Mean (SD)	29 (5)	27 (6)
Baseline eGFR ml/min/1.73 m2 Mean (SD)	84.7 (15.9)	83.7 (18.1)
History of smoking (yes) No of events	n = 14 ; % = 56	n = 7 ; % = 28
RENAL score for index tumour - low No of events	n = 5 ; % = 20	n = 11 ; % = 44
RENAL score for index tumour - moderate No of events	n = 19 ; % = 76	n = 12 ; % = 48
RENAL score for index tumour - high No of events	n = 1 ; % = 4	n = 2 ; % = 8

Outcomes

Complications

Outcome	Cryoablation, , N = 25	Partial nephrectomy, , N = 25
Clavien-Dindo grade 1 No of events	n = 2 ; % = 8	n = 3 ; % = 12
Clavien-Dindo grade 2 No of events	n = 1 ; % = 4	n = 4 ; % = 17
Clavien-Dindo grade 3 No of events	n = 0 ; % = 0	n = 0 ; % = 0
Clavien-Dindo grade 4	n = 0 ; % = 0	n = 0 ; % = 0

Outcome	Cryoablation, , N = 25	Partial nephrectomy, , N = 25
No of events		

Clavien-Dindo grade 1 - Polarity - Lower values are better

Renal functional impairment

Outcome	Cryoablation, , N = 25	Partial nephrectomy, , N = 25
Change in eGFR at 6 months Mean (SD)	-5 (10.3)	-5.8 (15.4)

Critical appraisal - Critical Appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Complications

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(4/25 patients in CRA arm sought out and were treated with RPN (a further 1 in CRA arm was treated with RPN based on additional medical evidence). This is a meaningful proportion of the whole, and could affect the results, making the groups artificially similar. Unblinded assessors but objective outcome unlikely to be influenced.)*
Overall bias and Directness	Overall Directness	Partially applicable *(Feasibility study)*

Change in eGFR2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(4/25 patients in CRA arm sought out and were treated with RPN (a further 1 in CRA arm was treated with RPN based on additional medical evidence). This is a meaningful proportion of the whole, and could affect the results, making the groups artificially similar. eGFR not listed in protocol as outcomes that would be investigated. No information on method of measurement of eGFR or whether this differed between groups.*

Section	Question	Answer
		Unblinded assessors but objective outcome unlikely to be influenced.)
Overall bias and Directness	Overall Directness	Partially applicable *(Feasibility study)*

Non-randomised studies evidence

Acosta Ruiz, 2021

Bibliographic Reference	Acosta Ruiz, Vanessa; Batelsson, Sarah; Onkamo, Elina; Wernroth, Lisa; Nilsson, Thomas; Lonnemark, Maria; Dahlman, Par; Magnusson, Anders; Split renal function after treatment of small renal masses: comparison between radiofrequency ablation and laparoscopic partial nephrectomy.; Acta radiologica (Stockholm, Sweden: 1987); 2021; vol. 62 (no. 9); 1248-1256

Study details

Study type	Retrospective cohort study
Study location	Sweden
Study setting	Hospital setting.
Study dates	October 2007 and December 2016
Sources of funding	The author(s) disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This work was supported by The Japanese-Swedish Research Foundation.
Inclusion criteria	Patients with T1a Patients aged ≤75 years Pre-treatment CE-CT images within one year previously and after treatment Patients needed to have two kidneys Non-hereditary renal tumours originating from the renal parenchyma
Exclusion criteria	Tumours treated by multiple treatment methods
Intervention(s)	Radiofrequency ablation (RFA), percutaneous
Comparator	Laparoscopic partial nephrectomy (LPN)
Outcome measures	Renal functional impairment

Number of participants	Total number of participants: N = 91 Radiofrequency ablation (RFA) = 60 Laparoscopic partial nephrectomy (LPN) = 31
Duration of follow-up	Median = 38 months; range = 2.5–99 months
Loss to follow-up	Not reported
Methods of analysis	Treatment effects were compared with Student's t-test and multivariable linear regression models, and both crude and adjusted mean differences with 95% CI are reported. Three separate regression models were fitted with the change (post-value – pre-value) in SRF, eGFR, and creatinine as the response variables. Treatment (LPN/RFA), the pre-value of the response variables, and confounders (pre-treatment eGFR, BMI, age, tumour size, tumour nearness [distance to the collecting system or sinus] and Charlson Comorbidity Index) were included in the models as explanatory variables.

Study arms

Radiofrequency ablation (N = 60)

Laparoscopic partial nephrectomy (N = 31)

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 60)	Laparoscopic partial nephrectomy (N = 31)
% Female No of events	n = 23 ; % = 38.3	n = 10 ; % = 32.3
Age Mean (SD)	65 (9.8)	57.8 (12.4)
Oncocytoma No of events	n = 6 ; % = 10	n = 5 ; % = 16.1
Clear cell RCC No of events	n = 27 ; % = 45	n = 20 ; % = 64.5
Papillary RCC No of events	n = 7 ; % = 11.6	n = 4 ; % = 13
Chromophobe RCC No of events	n = 8 ; % = 13.4	n = 1 ; % = 3.2
Other cancer No of events	n = 4 ; % = 6.7	n = 1 ; % = 3.2

Characteristic	Radiofrequency ablation (N = 60)	Laparoscopic partial nephrectomy (N = 31)
Non-diagnostic biopsies No of events	n = 8 ; % = 13.3	n = 0 ; % = 0
Tumour size, mm Standardised Mean (SD)	27.1 (6.6)	28.6 (6.9)

Outcomes

Renal functional impairment

Outcome	Radiofrequency ablation versus Laparoscopic partial nephrectomy, , N2 = 31, N1 = 60
eGFR change post–pre (mL/min/1.73 m2) Mean (95% CI)	-0.01 (-3.3 to 3.3)

eGFR change post–pre (mL/min/1.73 m2) - Polarity - Higher values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Aikawa, 2023

Bibliographic Reference	Aikawa, Koichi; Yanagisawa, Takafumi; Fukuokaya, Wataru; Shimizu, Kanichiro; Miyajima, Keiichiro; Nakazono, Minoru; Iwatani, Kosuke; Matsukawa, Akihiro; Obayashi, Koki; Kimura, Shoji; Tsuzuki, Shunsuke; Sasaki, Hiroshi; Abe, Hirokazu; Sadaoka, Shunichi; Miki, Jun; Kimura, Takahiro; Percutaneous cryoablation versus partial nephrectomy

for cT1b renal tumors: An inverse probability weight analysis.; Urologic oncology; 2023; vol. 41 (no. 3); 150e11-150e19

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital setting. Data obtained from three affiliated hospitals.
Study dates	January 2011 to November 2021
Sources of funding	No external funding was provided for this research.
Inclusion criteria	Had undergone either partial nephrectomy or percutaneous cryoablation for de novo cT1b renal tumour
Exclusion criteria	Missing data on long-term survival or renal function Synchronous metastasis or renal tumour accompanied by The Von Hippel-Lindau (VHL) disease
Intervention(s)	Percutaneous cryoablation was performed under CT or MRI guidance with local anaesthesia, using cryoablation with 17-gauge cryoneedles placed percutaneously. Transcatheter arterial embolisation using iodised oil was routinely performed 2 or 3 days prior to percutaneous cryoablation.
Comparator	Partial nephrectomy was performed by open or laparoscopic surgery, using either a transperitoneal or retroperitoneal approach, as determined by tumour location, size, and the patient's physical characteristics. Tumours were generally excised by clamping only the main renal artery under cold ischaemia in open surgery or warm ischaemia in laparoscopic surgery. Parenchymal sutures were used in all patients.
Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants: N = 119 Percutaneous cryoablation: 29 (24.4%) Partial nephrectomy: 90 (75.6%)
Duration of follow-up	Median follow-up was 43 months (IQR: 29-59) in the percutaneous cryoablation group and 36.5 months (IQR: 18-59) in the partial nephrectomy group.
Loss to follow-up	Not reported
Methods of analysis	Inverse probability weighting was used for balancing patient demographics, including renal function and tumour complexity. Perioperative complications, renal function preservation rates, and oncological outcomes

	such as local recurrence-free, metastasis-free, cancer-specific, and overall survival were compared using inverse probability weighting-adjusted restricted mean survival times.
Additional comments	The authors noted several limitations of their study. Even though they used inverse probability weighting-adjusted analysis to reduce selection bias, the study had a rather low number of patients and fatalities due to the relatively favourable prognosis of localised renal cancer with shorter follow-up. Despite the inverse probability weighting-adjusted analysis, the weighted population of the two groups was not entirely equal, and the approach did not adjust for unmeasured confounders which may affect the selection of treatment methods. Only a prospective randomised controlled trial would clarify the robust oncologic outcomes. Another limitation was procedural heterogeneity in the partial nephrectomy group, despite only offering a percutaneous approach for cryoablation. The absence of clearly defined primary outcome measures when comparing percutaneous cryoablation and partial nephrectomy, specifically in recurrence and primary/secondary efficacy after salvage cryoablation, was also a limitation. Follow-up duration and methods differed between partial nephrectomy and percutaneous cryoablation, requiring meticulous follow-up with contrast-enhanced CT for patients who underwent percutaneous cryoablation. Although the authors have performed routine renal tumour biopsy since 2018, 11 of 29 patients in the percutaneous cryoablation group did not undergo renal tumour biopsy. In the partial nephrectomy group, all patients underwent surgery with radiographical clinical diagnosis only; nevertheless, all patients were diagnosed with renal cell carcinoma. Possible contamination with benign tumours might have overestimated oncologic outcomes in the percutaneous cryoablation group. The authors routinely adopted arterial embolisation 2 or 3 days prior to percutaneous cryoablation in all patients to obtain better visualisation despite plain CT. Although a recent publication showed technical feasibility and better oncologic outcomes of percutaneous cryoablation in combination with embolisation for large renal tumours, the direct impact of embolisation on oncologic outcomes is not still investigated. The results should be interpreted with care regarding these limitations, which might affect the oncologic outcomes. Further investigation with more patients (i.e., multicentre study) and longer follow-up are needed to establish more robust evidence. Note: Ethnicity, preoperative CKD stage, and preoperative eGFR were not reported in the study.

Study arms

Percutaneous cryoablation (N = 29)

Partial nephrectomy (N = 90)

Characteristics

Arm-level characteristics

Characteristic	Percutaneous cryoablation (N = 29)	Partial nephrectomy (N = 90)
% Female No of events	n = 7 ; % = 24.1	n = 26 ; % = 28.9
Age: 80 years or under No of events	n = 17 ; % = 58.6	n = 85 ; % = 94.4
80 years or over No of events	n = 12 ; % = 41.4	n = 5 ; % = 5.6
Treatment/surgery technique used: Open surgery Nominal	NA	22
Treatment/surgery technique used: Laparoscopic surgery Nominal	NA	68
R.E.N.A.L nephrometry score less than or equal to 9 No of events	n = 22 ; % = 75.9	n = 77 ; % = 85.6
R.E.N.A.L nephrometry score greater than 9 No of events	n = 7 ; % = 24.1	n = 13 ; % = 14.4
Tumour size, mm Mean (SD)	45.3 (4.7)	46.1 (7)
Primary RCC type: Clear cell No of events	n = 13 ; % = 93	n = 70 ; % = 78
Primary RCC type: Clear cell with sarcomatoid No of events	n = 0 ; % = 0	n = 1 ; % = 1.1
Primary RCC type: Papillary No of events	n = 1 ; % = 7.1	n = 7 ; % = 7.8

Characteristic	Percutaneous cryoablation (N = 29)	Partial nephrectomy (N = 90)
Primary RCC type: Chromophobe No of events	n = 0 ; % = 0	n = 9 ; % = 10
Primary RCC type: Translocation No of events	n = 0 ; % = 0	n = 1 ; % = 1.1
Primary RCC type: Unclassified No of events	n = 0 ; % = 0	n = 2 ; % = 2.2
Baseline renal function (eGFR, ml/min/1.73 m2) less than or equal to 30 No of events	n = 3 ; % = 10.3	n = 5 ; % = 5.6
Baseline renal function (eGFR, ml/min/1.73 m2) greater than 30 No of events	n = 26 ; % = 89.7	n = 85 ; % = 94.4
Charlson comorbidity index: Less than or equal to 3 No of events	n = 21 ; % = 72.4	n = 79 ; % = 87.8
Charlson comorbidity index: Greater than 3 No of events	n = 8 ; % = 27.6	n = 11 ; % = 12.2

Outcomes

Study timepoints

- See below (The study reported the following timepoints for data extraction: Residual unablated tumor, local tumor recurrence, and metastasis were assessed by plain CT following partial nephrectomy or contrast-enhanced CT following percutaneous cryoablation at 1, 3, 6, and 12 months after treatment during the first year and every 6 months thereafter. Renal function was postoperatively assessed by estimated glomerular filtration rate (eGFR) postoperative months 6-12. Perioperative complications were evaluated using the Clavien-Dindo classification, but the specific timepoints were not mentioned. The study did not report any outcomes between 5-10 years of follow-up.)

Outcomes

Outcome	Percutaneous cryoablation, See below, N = 29	Partial nephrectomy, See below, N = 90
Overall complications (Clavien-Dindo classification; specific timepoints not reported) No of events	n = 3 ; % = 10	n = 13 ; % = 14
Severe complications (Clavien-Dindo classification grade greater than or equal to III; specific timepoints not reported) No of events	n = 1 ; % = 3.4	n = 7 ; % = 7.8

Summary statistic outcomes

Outcome

Summary statistic outcomes

Outcome	Partial nephrectomy versus Percutaneous cryoablation, See below, N2 = 90, N1 = 29
Overall mortality (median follow-up: 43 months for percutaneous cryoablation, 36.5 months for partial nephrectomy) Hazard ratio/95% CI	0.17 (0.03 to 1.06)
Overall complications (Clavien-Dindo classification; specific timepoints not reported) Odds ratio/95% CI	1.27 (0.57 to 2.93)
Severe complications (Clavien-Dindo classification grade greater than or equal to III; specific timepoints not reported) Odds ratio/95% CI	0.95 (0.35 to 2.64)
Cancer-specific survival Hazard ratio/95% CI	0.46 (0.04 to 5.2)
Local recurrence free survival Hazard ratio/95% CI	0.2 (0.05 to 0.87)
Metastasis-free survival Hazard ratio/95% CI	0.37 (0.1 to 1.39)

Cancer-specific survival - Polarity - Lower values are better
Local recurrence free survival - Polarity - Lower values are better
Metastasis-free survival - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(While the study has a low risk of bias in several domains, including the classification of interventions and the selection of the reported results, there are concerns regarding confounding, missing data, and the measurement of outcomes. The use of inverse probability weighting helps to mitigate some confounding, but residual confounding may remain. The exclusion of participants due to missing data and the potential influence of outcome assessors' knowledge of the intervention on outcome assessment also contribute to the overall serious risk of bias.)*
Overall bias	Directness	Directly applicable

All hazard ratios

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(While the study has a low risk of bias in several domains, including the classification of interventions and the selection of the reported results, there are concerns regarding confounding, missing data, and the measurement of outcomes. The use of inverse probability weighting helps to mitigate some confounding, but residual confounding may remain. The exclusion of participants due to missing data and the potential influence of outcome assessors' knowledge of the intervention on outcome assessment also contribute to the overall moderate risk of bias.)*
Overall bias	Directness	Directly applicable

Complications - odds ratios

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(While the study has a low risk of bias in several domains, including the classification of interventions and the selection of the reported*

Section	Question	Answer
		results, there are concerns regarding confounding, missing data, and the measurement of outcomes. The use of inverse probability weighting helps to mitigate some confounding, but residual confounding may remain. The exclusion of participants due to missing data and the potential influence of outcome assessors' knowledge of the intervention on outcome assessment also contribute to the overall moderate risk of bias.)
Overall bias	Directness	Directly applicable

Alam, 2019

Bibliographic Reference	Alam, Ridwan; Patel, Hiten D; Osumah, Tijani; Srivastava, Arnav; Gorin, Michael A; Johnson, Michael H; Trock, Bruce J; Chang, Peter; Wagner, Andrew A; McKiernan, James M; Allaf, Mohamad E; Pierorazio, Phillip M; Comparative effectiveness of management options for patients with small renal masses: a prospective cohort study.; BJU international; 2019; vol. 123 (no. 1); 42-50

Study details

Study type	Prospective cohort study
Study location	US
Study setting	Hospital setting, DISSRM registry.
Study dates	Since January 1, 2009
Sources of funding	Not reported
Inclusion criteria	Patients aged ≥18 years Patients with T1a Contrast-enhancing renal mass ≤4.0 cm in diameter on axial imaging
Exclusion criteria	Not reported
Intervention(s)	Partial nephrectomy (PN)
Comparator	Ablation, or active surveillance
Outcome measures	Renal functional impairment
Number of participants	Total number of patients: 597 PN: 231 Ablation: 27 AS: 339

Duration of follow-up	The median follow-up time was 3.0 years [IQR 1.6-5.0], and 158 patients (24.7%) were followed for ≥5 years.
Loss to follow-up	Not reported
Methods of analysis	Survival outcomes were estimated using the Kaplan-Meier approach and compared using the log-rank test. The Cox proportional hazards regression was used to identify variables associated with survival. The mixed effects model was used for eGFR analysis, where linear regression was performed for continuous outcomes and logistic regression was performed for binary outcomes. Analysis controlled for age, sex and comorbidity index
Additional comments	Survival outcomes not extracted as included in an included systematic review (Guo 2019)

Study arms

Partial nephrectomy (N = 231)

Ablation (N = 27)

Active surveillance (N = 339)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 231)	Ablation (N = 27)	Active surveillance (N = 339)
% Female No of events	n = 86 ; % = 37.2	n = 14 ; % = 51.9	n = 149 ; % = 44
Age Median (IQR)	61.3 (52.9 to 67.3)	71.8 (62 to 74.8)	70.6 (63.2 to 78.2)
Median Tumor Diameter (cm) Median (IQR)	2.4 (1.8 to 3.2)	2.1 (1.7 to 2.5)	1.8 (1.3 to 2.4)

Outcomes

Survival

Outcome	Ablation versus Partial nephrectomy, , N2 = 27, N1 = 231	Active surveillance versus Partial nephrectomy, , N2 = 339, N1 = 231

Renal functional impairment

Outcome	Ablation versus Partial nephrectomy, , N2 = 27, N1 = 231	Active surveillance versus Partial nephrectomy, , N2 = 339, N1 = 231
eGFR <45 mL/min/1.73m2 (CKD stage ≥3B) Odds ratio/95% CI	1.72 (0.39 to 7.53)	0.97 (0.37 to 2.51)

eGFR <45 mL/min/1.73m2 (CKD stage ≥3B) - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Almadalal, 2022

Bibliographic Reference	Almadalal, T.; Sundqvist, P.; Harmenberg, U.; Hellstrom, M.; Lindskog, M.; Lindblad, P.; Lundstam, S.; Ljungberg, B.; Clinical T1a Renal Cell Carcinoma, Not Always a Harmless Disease-A National Register Study; European Urology Open Science; 2022; vol. 39; 22-28

Study details

Study type	Retrospective cohort study
Study location	Sweden
Study setting	Hospital setting. Data obtained from the National Swedish Kidney Cancer Register.
Study dates	January 2005 to December 2012

Sources of funding	The Swedish Association of Local Authorities and Regions (SALAR) and the Clinical Research Center in the county of Sörmland, Sweden
Inclusion criteria	Patients with clinical T1aM0 renal cell carcinoma registered in the National Swedish Kidney Cancer Register from January 2005 to December 2012
Exclusion criteria	Metastatic disease at diagnosis
Intervention(s)	Radical nephrectomy, partial nephrectomy, ablative treatments (radiofrequency ablation, cryoablation, high-intensity focused ultrasound), other. The 'Other' category included eight patients who underwent other surgeries and 82 patients who did not have surgery. The study does not explicitly state that the 82 patients who did not have surgery were under "active surveillance". They are simply described as being treated non-surgically, without further details provided about the nature of their non-surgical management.
Comparator	The different interventions were compared to each other
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: N = 1935 Radical nephrectomy: 938 (48.5%) Partial nephrectomy: 738 (38.1%) Ablative treatments: 169 (8.7%) Other: 90 (4.7%)
Duration of follow-up	At least 5 years for disease recurrence. Overall survival data available until December 2019.
Loss to follow-up	Not reported
Methods of analysis	Univariable and multivariable logistic regression analyses to identify factors associated with disease recurrence. Kaplan-Meier method and log-rank test for overall survival. Cox regression models to identify independent prognostic variables for overall survival. Factors adjusted for in the model not specified. No propensity score matching reported.
Additional comments	The authors acknowledged several limitations of this register-based study. Clinical, radiological, and histopathological information was gathered from all Swedish hospitals, and chart data can be subject to reporting errors. The National Swedish Kidney Cancer Register did not contain information on performance status, comorbidities, pre- and postoperative complications, and cancer-specific survival. Treatment allocation was based on patients' and surgeons' preferences, which may introduce selection bias. However, the strength of this study is that it represents real-world data of an unselected nationwide patient population with a 99% inclusion rate of newly diagnosed renal cell carcinoma in Sweden, which minimises selection bias found in most other studies. The long-term follow-

	up data and the highly valid data on overall survival strengthen the results obtained. The study did not report on several important outcomes such as adverse events, renal function, cardiovascular events, duration of hospital stay, and quality of life. The lack of these outcomes may warrant downgrading the quality of evidence for certain comparisons. Additionally, the 'Other' category, which included patients who underwent other surgeries or no surgery, was not well defined, limiting the interpretability of results for this group.

Study arms

Radical nephrectomy (N = 938)

Partial nephrectomy (N = 738)

Ablative treatments (N = 169)

Other (other surgeries and patients who did not have surgery) (N = 90)

Characteristics

Arm-level characteristics

Characteristic	Radical nephrectomy (N = 938)	Partial nephrectomy (N = 738)	Ablative treatments (N = 169)	Other (other surgeries and patients who did not have surgery) (N = 90)
% Female No of events	n = 366 ; % = 39	n = 278 ; % = 37.7	n = 63 ; % = 37.3	n = 36 ; % = 40
Age (years) Mean Custom value	65.7	60.6	67.3	73.6
TNM staging: pT1a No of events	n = 872 ; % = 93	n = 727 ; % = 98.5	n = 169 ; % = 100	n = 89 ; % = 98.9
TNM staging: pT3a No of events	n = 66 ; % = 7	n = 11 ; % = 1.5	n = 0 ; % = 0	n = 1 ; % = 1.1
RCC type: Clear cell RCC No of events	n = 746 ; % = 79.5	n = 525 ; % = 71.1	n = 114 ; % = 67.5	n = 34 ; % = 37.8

Characteristic	Radical nephrectomy (N = 938)	Partial nephrectomy (N = 738)	Ablative treatments (N = 169)	Other (other surgeries and patients who did not have surgery) (N = 90)
RCC type: Papillary RCC No of events	n = 124 ; % = 13.2	n = 155 ; % = 21	n = 29 ; % = 17.2	n = 10 ; % = 11.1
RCC type: Chromophobe RCC No of events	n = 54 ; % = 5.8	n = 50 ; % = 6.8	n = 9 ; % = 5.3	n = 2 ; % = 2.2
RCC type: Other/unknown No of events	n = 14 ; % = 1.5	n = 8 ; % = 1.1	n = 17 ; % = 10.1	n = 44 ; % = 48.9

Outcomes

Study timepoints

- See below (The study provided the following information regarding the timepoints for data extraction: All patients had potentially at least a 5-year follow-up time for disease recurrence. Follow-up overall survival data were available for all 1935 patients until December 2019. At that time, 1429 (73.9%) patients were alive and 506 (26.1%) had died of any cause. Based on this information, the timepoints for data extraction can be summarised as: 0 to 5 years: At least 5 years of follow-up for disease recurrence; 5 to 10 years: Not explicitly reported; Beyond 10 years: Overall survival data available until December 2019, which is approximately 7 to 14 years after the initial diagnosis (January 2005 to December 2012).)

Survival

Outcome	Radical nephrectomy, See below, N = 938	Partial nephrectomy, See below, N = 738	Ablative treatments, See below, N = 169	Other (other surgeries and patients who did not have surgery), See below, N = 90
Overall mortality: All-cause	301	109	42	54

Outcome	Radical nephrectomy, See below, N = 938	Partial nephrectomy, See below, N = 738	Ablative treatments, See below, N = 169	Other (other surgeries and patients who did not have surgery), See below, N = 90
mortality, until December 2019 Nominal				

Recurrence

Outcome	Radical nephrectomy, See below, N = 938	Partial nephrectomy, See below, N = 738	Ablative treatments, See below, N = 169	Other (other surgeries and patients who did not have surgery), See below, N = 90
Recurrence: Local recurrence in the treated kidney only, at least 5 years of follow-up No of events	*empty data*	n = 12 ; % = 1.6	n = 22 ; % = 13	*empty data*
Recurrence: Overall recurrence, at least 5 years of follow-up No of events	n = 64 ; % = 6.8	n = 44 ; % = 6	n = 30 ; % = 17.8	n = 7 ; % = 7.8

Survival

Outcome	Ablative treatments versus Radical nephrectomy, See below, N2 = 169, N1 = 938
Overall survival Multivariate analysis Hazard ratio/95% CI	0.73 (0.5 to 1.07)
Disease free survival Multivariate analysis	5.67 (3.23 to 9.95)

Outcome	Ablative treatments versus Radical nephrectomy, See below, N2 = 169, N1 = 938
Hazard ratio/95% CI	

Overall survival - Polarity - Lower values are better
Disease free survival - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Overall recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The main concerns arise from the potential for confounding due to the lack of propensity score matching and the possibility of missing important confounding variables in the multivariable analyses. Additionally, there is insufficient information about deviations from intended interventions, co-interventions, and adherence to the assigned intervention regimen. However, the risk of bias is low for the selection of participants into the study, classification of interventions, missing data, measurement of outcomes, and selection of the reported results.)*
Overall bias	Directness	Directly applicable *(Despite the assumption of directness based on the study meeting the predefined PICO criteria, it is important to note that the retrospective nature of the study and the potential differences in the Swedish healthcare system compared to the UK NHS may impact the directness of the evidence provided.)*

Local recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The main concerns arise from the potential for confounding due to the lack of propensity score matching and the possibility of missing important confounding variables in the multivariable analyses. Additionally, there is insufficient information about deviations from intended interventions, co-interventions, and adherence to the assigned intervention regimen. However, the risk of bias is low for the selection of participants into the study, classification of*

Section	Question	Answer
		interventions, missing data, measurement of outcomes, and selection of the reported results.)
Overall bias	Directness	Directly applicable *(Despite the assumption of directness based on the study meeting the predefined PICO criteria, it is important to note that the retrospective nature of the study and the potential differences in the Swedish healthcare system compared to the UK NHS may impact the directness of the evidence provided.)*

Overall mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The main concerns arise from the potential for confounding due to the lack of propensity score matching and the possibility of missing important confounding variables in the multivariable analyses. Additionally, there is insufficient information about deviations from intended interventions, co-interventions, and adherence to the assigned intervention regimen. However, the risk of bias is low for the selection of participants into the study, classification of interventions, missing data, measurement of outcomes, and selection of the reported results.)*
Overall bias	Directness	Directly applicable *(Despite the assumption of directness based on the study meeting the predefined PICO criteria, it is important to note that the retrospective nature of the study and the potential differences in the Swedish healthcare system compared to the UK NHS may impact the directness of the evidence provided.)*

Overall survival (HR)

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The main concerns arise from the potential for confounding due to the lack of propensity score matching and the possibility of missing important confounding variables in the multivariable analyses. Additionally, there is insufficient information about deviations from intended interventions, co-interventions, and adherence to the assigned intervention regimen. However, the risk of bias is low for the selection of participants into the study, classification of interventions, missing data, measurement of outcomes, and selection of the reported results.)*

Section	Question	Answer
Overall bias	Directness	Directly applicable *(Despite the assumption of directness based on the study meeting the predefined PICO criteria, it is important to note that the retrospective nature of the study and the potential differences in the Swedish healthcare system compared to the UK NHS may impact the directness of the evidence provided.)*

Disease-free survival (HR)

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The main concerns arise from the potential for confounding due to the lack of propensity score matching and the possibility of missing important confounding variables in the multivariable analyses. Additionally, there is insufficient information about deviations from intended interventions, co-interventions, and adherence to the assigned intervention regimen. However, the risk of bias is low for the selection of participants into the study, classification of interventions, missing data, measurement of outcomes, and selection of the reported results.)*
Overall bias	Directness	Directly applicable *(Despite the assumption of directness based on the study meeting the predefined PICO criteria, it is important to note that the retrospective nature of the study and the potential differences in the Swedish healthcare system compared to the UK NHS may impact the directness of the evidence provided.)*

Andrews, 2019

Bibliographic Reference	Andrews, Jack R; Atwell, Thomas; Schmit, Grant; Lohse, Christine M; Kurup, A Nicholas; Weisbrod, Adam; Callstrom, Matthew R; Cheville, John C; Boorjian, Stephen A; Leibovich, Bradley C; Thompson, R Houston; Oncologic Outcomes Following Partial Nephrectomy and Percutaneous Ablation for cT1 Renal Masses.; European urology; 2019; vol. 76 (no. 2); 244-251

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting

Study dates	Between 2000 and 2011
Sources of funding	R. Houston Thompson certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None. Funding/Support and role of the sponsor: None
Inclusion criteria	Localised renal tumour Patients with cT1 renal tumour
Exclusion criteria	Renal masses with radiographic evidence of extension beyond the kidney or extension into the renal or segmental veins Patients with a history of prior RCC Patients with genetic syndromes
Intervention(s)	Partial nephrectomy (PN)
Comparator	Radiofrequency ablation (RFA) and cryoablation (CA)
Outcome measures	Recurrence Survival
Number of participants	Total number of patients (cT1a): 1422 PN: 1055 RFA: 180 CA: 187 Total number of patients (cT1b): 376 PN: 324 CA: 52
Duration of follow-up	Among cT1a patients, the median clinical follow-up was 9.4, 7.5, and 6.3 yr, respectively. Among cT1b patients, the clinical follow-up was 8.7 and 6.0 yr, respectively.
Loss to follow-up	Not reported
Methods of analysis	Local recurrence-free, local or ipsilateral recurrence-free, distant metastases-free, overall, and cancer-specific survival were estimated using the Kaplan-Meier method. Duration of follow-up for recurrence-free survival was calculated from the treatment to recurrence, last follow-up for patients treated with PN, or last imaging for patients treated with ablation. Duration of follow-up for distant metastases-free survival was calculated from treatment to distant metastases or last follow-up. Duration of follow-up for overall and cancer-specific survival was calculated from treatment to last follow-up; deaths from non-RCC causes were censored for the assessment of cancer-specific survival. The effects of treatment on outcomes were evaluated using Cox proportional hazards regression models and summarised with hazard ratios (HRs) and 95% confidence intervals (CIs). Propensity score adjusted results used.

Study arms

Partial nephrectomy (cT1a) (N = 1055)

Radiofrequency ablation (cT1a) (N = 180)

Cryoablation (cT1a) (N = 187)

Partial nephrectomy (cT1b) (N = 324)

Cryoablation (cT1b) (N = 52)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (cT1a) (N = 1055)	Radiofrequency ablation (cT1a) (N = 180)	Cryoablation (cT1a) (N = 187)	Partial nephrectomy (cT1b) (N = 324)	Cryoablation (cT1b) (N = 52)
% Female No of events	n = 409 ; % = 39	n = 66 ; % = 37	n = 64 ; % = 34	n = 102 ; % = 32	n = 13 ; % = 25
Age Median (IQR)	62 (52 to 69)	72 (64 to 78)	72 (65 to 79)	61 (52 to 70)	77 (69.5 to 83)
Clear cell No of events	n = 559 ; % = 67	n = 38 ; % = 52	n = 73 ; % = 68	n = 181 ; % = 67	n = 24 ; % = 69
Papillary No of events	n = 153 ; % = 18	n = 20 ; % = 27	n = 20 ; % = 19	n = 59 ; % = 22	n = 4 ; % = 11
Chromophobe No of events	n = 55 ; % = 7	n = 3 ; % = 4	n = 1 ; % = 1	n = 18 ; % = 7	n = 0 ; % = 0
Collecting duct No of events	n = 1 ; % = 1	n = 0 ; % = 0	n = 0 ; % = 0	*empty data*	*empty data*
Not indicated No of events	n = 67 ; % = 8	n = 12 ; % = 16	n = 14 ; % = 13	n = 14 ; % = 5	n = 7 ; % = 20
Tumor size (cm) Median (IQR)	2.4 (1.8 to 3.1)	1.9 (1.5 to 2.5)	2.8 (2.4 to 3.4)	5 (4.5 to 5.5)	4.8 (4.4 to 5.6)

Outcomes

Survival

Outcome	Radiofrequency ablation (cT1a) versus Partial nephrectomy (cT1a), , N2 = 175, N1 = 1055	Cryoablation (cT1a) versus Partial nephrectomy (cT1a), , N2 = 178, N1 = 1055	Cryoablation (cT1b) versus Partial nephrectomy (cT1b), , N2 = 48, N1 = 324
Local recurrence-free survival Hazard ratio/95% CI	1.49 (0.55 to 4.04)	1.88 (0.76 to 4.66)	1.22 (0.33 to 4.48)
Metastases-free survival Hazard ratio/95% CI	1.46 (0.41 to 5.19)	0.23 (0.03 to 1.72)	0.95 (0.21 to 4.38)
Cancer-specific survival Hazard ratio/95% CI	1.99 (0.29 to 13.56)	0.29 (0.01 to 6.11)	1.94 (0.42 to 8.96)
Overall survival Hazard ratio/95% CI	1.81 (1.35 to 2.44)	2.03 (1.51 to 2.74)	2.74 (1.61 to 4.66)

Local recurrence-free survival - Polarity - Lower values are better
Metastases-free survival - Polarity - Lower values are better
Cancer-specific survival - Polarity - Lower values are better
Overall survival - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study presents a serious risk of bias due to confounding, as the study did not control the analysis for all important confounding domains. Furthermore, there is a bias due to missing data. Patients treated with RFA or cryoablation were excluded from analyses of local recurrence-free survival due to a lack of imaging follow-up.)*

Section	Question	Answer
Overall bias	Directness	Directly applicable

Anglickis, 2019

Bibliographic Reference	Anglickis, Marius; Anglickiene, Giedre; Andreikaite, Gintare; Skrebunas, Arminas; Microwave Thermal Ablation versus Open Partial Nephrectomy for the Treatment of Small Renal Tumors in Patients Over 70 Years Old.; Medicina (Kaunas, Lithuania); 2019; vol. 55 (no. 10)

Study details

Study type	Retrospective cohort study
Study location	
Study setting	Lithuania
Study dates	January 2012 to January 2019
Sources of funding	This research received no external funding.
Inclusion criteria	Patients aged ≥70 years Patients with T1a exophytic solitary small (<4 cm) renal mass
Exclusion criteria	Uninformative or benign biopsy result
Intervention(s)	Microwave Thermal Ablation (MWT) • All the cases in the MWT group had previously undergone kidney biopsy. MWT was done following a histological answer and during second hospitalisation. • MWT was performed for patients who did not want to have OPN or for patients with serious comorbidities in those cases where the urine collecting system, renal calyx, and great vessels were free from tumour margins of more than 1 cm. • Other indications for ablative therapy included a solitary kidney and possible kidney disfunction following the resection. • MWT was performed with a 915 MHz MicroThermXTM Microwave Ablation System generator and a single (with one 2.0 cm short tip or 4.1 cm long tip) internally cooled electrode.
Comparator	Open partial nephrectomy (OPN) OPN was recommended for patients without serious comorbidities and when general anaesthesia was possible. Off-clamp OPN was performed in a retroperitoneal approach.

Outcome measures	Recurrence Postoperative severe adverse events
Number of participants	33
Duration of follow-up	A follow-up CT was performed 1, 3 and 6 months after MWT or OPN and then every 6 months over the years of the study In order to determine whether there was any remnant or residual enhancement of the ablation lesion, a follow-up CT was performed after one month. The treatment was considered to be successful when no enhancement was seen on the CT. The technical success rate for surgery was defined as complete tumour ablation after the initial procedure and additional sessions within one month Median follow up was 40 months. MWT 40 (IQR: 34–47) OPN 40.10 (IQR: 38–43)
Loss to follow-up	None
Methods of analysis	All the ordinal data was presented as an absolute number and percentage prevalence in the study population. Comparisons among the categorical variables were performed using the chi-square test. A p value <0.05 was considered statistically significant.
Additional comments	Overall survival rate was 100% (across both arms) Authors note that there are different MWT devices used by hospitals so results may not be applicable to other settings.

Study arms

Microwave Thermal Ablation (N = 15)

Open partial nephrectomy (N = 18)

Characteristics

Arm-level characteristics

Characteristic	Microwave Thermal Ablation (N = 15)	Open partial nephrectomy (N = 18)
% Female No of events	n = 6 ; % = 40	n = 8 ; % = 44
Age Median (IQR)	75 (71 to 79)	71.5 (70 to 75)
RCC type: Renal cell carcinoma No of events	n = 12 ; % = 80	n = 15 ; % = 83.3

Characteristic	Microwave Thermal Ablation (N = 15)	Open partial nephrectomy (N = 18)
RCC type: papillary renal cell carcinoma No of events	n = 1 ; % = 6.67	n = 2 ; % = 11.1
RCC type: Chromophobe renal cell carcinoma No of events	n = 2 ; % = 13.3	n = 1 ; % = 5.56
Baseline renal function (glomerular filtration rate (mL/min/1.73 m2)) Median (IQR)	59.9 (49.5 to 73.8)	46.2 (42.7 to 65.8)
ASA score: 1 No of events	n = 1 ; % = 6.67	n = 4 ; % = 22.2
ASA score: 2 No of events	n = 9 ; % = 60	n = 13 ; % = 86.7
ASA score ≥3 No of events	n = 5 ; % = 33.3	n = 1 ; % = 5.56

Outcomes

Recurrence

Outcome	Microwave Thermal Ablation, , N = 15	Open partial nephrectomy, , N = 18
Recurrence of tumour No of events	n = 0 ; % = 0	n = 0 ; % = 0

Recurrence of tumour - Polarity - Lower values are better

Complications

Outcome	Microwave Thermal Ablation, , N = 15	Open partial nephrectomy, , N = 18
Complications (major) No of events	n = 0 ; % = 0	n = 0 ; % = 0

Complications (major) - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders. Event data only. Those with TA were more likely to be at risk of complications)*
Overall bias	Directness	Directly applicable

Attawettayanon, 2023

Bibliographic Reference	Attawettayanon, Worapat; Kazama, Akira; Yasuda, Yosuke; Zhang, J J H; Shah, Snehi; Rathi, Nityam; Munoz-Lopez, Carlos; Lewis, Kieran; Li, Jianbo; Beksac, Alp T; Campbell, Rebecca A; Kaouk, Jihad; Haber, Georges-Pascal; Weight, Christopher; Martin, Charles 3rd; Campbell, Steven C; Thermal Ablation Versus Partial Nephrectomy for cT1 Renal Mass in a Solitary Kidney: A Matched Cohort Comparative Analysis.; Annals of surgical oncology; 2023

Study details

Study type	Retrospective cohort study
Study location	USA
Study setting	Hospital setting. Data obtained from the Cleveland Clinic kidney cancer database, which identified 504 patients with renal mass in a solitary kidney treated at a single institution.
Study dates	1975 to 2022
Sources of funding	Not reported
Inclusion criteria	Patients with clinical stage T1 renal mass in a solitary kidney Necessary data available for analysis
Exclusion criteria	Patients with familial disease
Intervention(s)	Thermal ablation, performed using either a percutaneous (45%) or laparoscopic (55%) approach.
Comparator	Partial nephrectomy, performed using either a minimally invasive (30%) or open (70%) approach.

Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment
Number of participants	Total number of participants: N = 132 Thermal ablation: 66 (50%) Partial nephrectomy: 66 (50%)
Duration of follow-up	Median overall follow-up was 59 months in the thermal ablation cohort and 41 months in the partial nephrectomy cohort.
Loss to follow-up	Not reported
Methods of analysis	Propensity score matching was used to balance differences in relevant baseline characteristics (age, sex, preoperative glomerular filtration rate, body mass index, diabetes, hypertension, cardiovascular disease, R.E.N.A.L. nephrometry score, and tumour diameter) between the thermal ablation and partial nephrectomy cohorts. Kaplan-Meier analysis was used to assess survival outcomes. Continuous variables were compared using the Wilcoxon signed-rank test, and categorical variables were compared using the Chi-square or Fisher tests.
Additional comments	The authors acknowledged several limitations of this study, including its retrospective and single-institution design. Although propensity score matching was used to balance the thermal ablation and partial nephrectomy cohorts, there remains a possibility that patients and tumours in the thermal ablation cohort may have been less favourable than those in the partial nephrectomy cohort, as randomisation was not performed. Long-term follow-up is needed to more fully evaluate oncology outcomes. The study also spanned over four decades, during which techniques for partial nephrectomy and thermal ablation evolved, likely influencing outcomes. Thermal ablation appeared to provide better outcomes after substantial experience was gained, whereas partial nephrectomy tended to provide strong outcomes throughout, reflecting its more established status. Another limitation relates to the differing surveillance recommendations after partial nephrectomy or thermal ablation, which could have affected the results to some degree. Local recurrence after thermal ablation is more common than after partial nephrectomy, so guidelines recommend an early cross-sectional imaging study at 6 months after thermal ablation. This more intensive follow-up in the first year after thermal ablation, especially for low-risk patients, might lead to earlier detection of recurrences in the thermal ablation cohort, potentially affecting the recurrence-free survival analysis. However, given the magnitude of differences observed, it is unlikely that this would have changed the main findings. Strengths of this study include a robust number of patients with renal mass in a solitary kidney managed with thermal ablation and partial nephrectomy, as well as the use of propensity matching to balance the most relevant variables between the cohorts. The study also evaluated treatment sequelae after local recurrence and patient characteristics

	associated with failure of local control in the thermal ablation cohort, which can help inform patient selection and management for clinical stage T1 tumours in patients with renal mass in a solitary kidney moving forward. The sources of funding were not reported, which is a potential weakness. Additionally, information on loss to follow-up was not provided, which could introduce bias if differential between the study arms. The study did not report on certain outcomes, such as intraoperative severe adverse events, cardiovascular events, duration of hospital stay, and quality of life, which may be important to patients and clinicians when deciding between treatment options. Median overall follow-up was 59 months (4.9 years) in the thermal ablation cohort and 41 months (3.4 years) in the partial nephrectomy cohort. Five-year recurrence-free survival, local recurrence-free survival, metastasis-free survival, overall survival, cancer-specific survival, and dialysis-free survival were reported. Renal function outcomes were reported preoperatively, 1-12 months postoperatively (defined as new baseline glomerular filtration rate), and at 3 and 5 years after the intervention.

Study arms

Thermal ablation (N = 66)

Partial nephrectomy (N = 66)

Characteristics

Arm-level characteristics

Characteristic	Thermal ablation (N = 66)	Partial nephrectomy (N = 66)
% Female No of events	n = 19 ; % = 29	n = 22 ; % = 33
Age Median (IQR)	67.8 (60.2 to 73.6)	67.3 (57.6 to 73.8)
Race: African American No of events	n = 9 ; % = 14	n = 6 ; % = 9
Race: Caucasian/others No of events	n = 57 ; % = 86	n = 60 ; % = 91
Surgical approach: Percutaneous No of events	n = 30 ; % = 45	n = NA
Surgical approach: Laparoscopic	n = 36 ; % = 55	n = NA

Characteristic	Thermal ablation (N = 66)	Partial nephrectomy (N = 66)
No of events		
Surgical approach: Minimally invasive surgery No of events	n = NA	n = 20 ; % = 30
Surgical approach: Open No of events	n = NA	n = 46 ; % = 70
Clinical staging: cT1a, M0 No of events	n = 58 ; % = 88	n = 61 ; % = 92
Clinical staging: cT1b, M0 No of events	n = 8 ; % = 12	n = 5 ; % = 8
Tumour size (cm) Median (IQR)	2.3 (1.7 to 3)	2.4 (1.7 to 3)
Histology: Clear cell No of events	n = 36 ; % = 55	n = 41 ; % = 62
Histology: Non-clear cell No of events	n = 11 ; % = 17	n = 19 ; % = 29
Histology: Benign No of events	n = 14 ; % = 21	n = 6 ; % = 9
Histology: N/A No of events	n = 5 ; % = 7	n = 0 ; % = 0
Preoperative glomerular filtration rate (mL/min/1.73 m2) Median (IQR)	50.9 (40.4 to 63)	51.8 (42.5 to 64.3)
Hypertension No of events	n = 16 ; % = 24	n = 13 ; % = 20
Diabetes No of events	n = 4 ; % = 6	n = 6 ; % = 9
Cardiovascular disease No of events	n = 16 ; % = 24	n = 13 ; % = 20
R.E.N.A.L. nephrometry score Median (IQR)	6 (5 to 8)	6 (5 to 8)
R.E.N.A.L. nephrometry score: Low (4-6) No of events	n = 38 ; % = 58	n = 41 ; % = 62
R.E.N.A.L. nephrometry score: Intermediate (7-9) No of events	n = 24 ; % = 36	n = 20 ; % = 30
R.E.N.A.L. nephrometry score: High (10-12) No of events	n = 4 ; % = 6	n = 5 ; % = 8

Outcomes

Study timepoints

- **NA**

Local recurrence and metastasis

Outcome	Thermal ablation, NA, N = 66	Partial nephrectomy, NA, N = 66
Local recurrence, 5 years (Events) Nominal	14	2
Metastasis, 5 years (Events) Nominal	4	2

Adverse events

Outcome	Thermal ablation, NA, N = 66	Partial nephrectomy, NA, N = 66
Postoperative severe adverse events: Clavien-Dindo grade 3-5, 90 days No of events	n = 5 ; % = 7	n = 7 ; % = 11

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Recurrence and metastasis

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(The study has a moderate risk of bias due to potential confounding, as there is no information on whether the authors controlled for any post-intervention variables that could have been affected by the intervention. There is also a moderate risk of bias due to deviations from intended interventions, as there is no information on whether there were deviations from the intended intervention beyond what would be expected in usual practice or if important co-interventions were balanced across intervention groups. Additionally, there is a moderate risk of bias in measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study*

Section	Question	Answer
		participants. However, the risk of bias is low for the selection of participants into the study, classification of interventions, and selection of the reported result. There is no information to assess the risk of bias due to missing data.)
Overall bias	Directness	Directly applicable

Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(The study has a moderate risk of bias due to potential confounding, as there is no information on whether the authors controlled for any post-intervention variables that could have been affected by the intervention. There is also a moderate risk of bias due to deviations from intended interventions, as there is no information on whether there were deviations from the intended intervention beyond what would be expected in usual practice or if important co-interventions were balanced across intervention groups. Additionally, there is a moderate risk of bias in measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study participants. However, the risk of bias is low for the selection of participants into the study, classification of interventions, and selection of the reported result. There is no information to assess the risk of bias due to missing data.)*
Overall bias	Directness	Directly applicable

Beksac, 2022

Bibliographic Reference	Beksac, Alp T; Corrigan, Dillon; Abou Zeinab, Mahmoud; Ferguson, Ethan; Kaviani, Aaron; Schwen, Zeyad R; Kaouk, Jihad H; Long-term comparative outcomes of partial nephrectomy and cryoablation in patients with solitary kidneys: a single-center analysis.; Minerva urology and nephrology; 2022; vol. 74 (no. 6); 722-729

Study details

Study type	Retrospective cohort study
Study location	USA

Study setting	Hospital setting. Retrospective analysis of a single-institution series. One hospital involved (Cleveland Clinic Foundation).
Study dates	February 1998 to March 2020
Sources of funding	Not provided
Inclusion criteria	Patients with a solitary kidney who underwent treatment for a cT1a renal mass
Exclusion criteria	Multiple tumours Tumours larger than 4 cm Von Hippel Lindau disease Previous ipsilateral partial nephrectomy Previous ipsilateral thermal ablation Previous kidney transplantation
Intervention(s)	Partial nephrectomy (open or robotic)
Comparator	Cryoablation (laparoscopic or percutaneous)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: N = 74 Partial nephrectomy: 31 (41.9%) Cryoablation: 43 (58.1%)
Duration of follow-up	Median follow-up was 59.4 months
Loss to follow-up	Not provided
Methods of analysis	Univariate analysis using χ2 test or Fischer's exact test for categorical variables and Mann Whitney-U test for continuous variables. Linear mixed-effects models used to assess association between treatment type and eGFR preservation while adjusting for confounders. Survival outcomes analysed using Kaplan-Meier method and log-rank tests. No propensity score matching was described.
Additional comments	Additional comments: The study is limited by its retrospective design and the inherent selection bias. The baseline cohorts were different, with the cryoablation group having older patients and smaller tumour sizes. Although the authors adjusted for these differences for some outcomes, there is the possibility of unaccounted confounders. Furthermore, the study consists of a small sample size and a high censoring rate. The authors were unable to perform Cox regression analyses due to the small rate of events. A strength of the study is that it has a larger sample size than many predecessor studies. Moreover, the cohort has a substantial median follow-up period, which strengthens the recurrence-free survival and overall survival analyses. Some information that is missing includes the loss to follow-up rate and the sources of funding for the study.

	The oncological outcomes may need more downgrading due to the high risk of selection bias. The decision between partial nephrectomy and cryoablation was made by the patient after discussing the pros and cons of each approach. This could introduce significant bias, as evidenced by the baseline differences between the two groups. The cryoablation cohort was much older with an approximate 8-year mean age difference and had smaller tumours. It is likely that patient age, comorbidity, and other possible tumour-related variables, which could not be captured, affected the decision-making process. The study did not assess some important outcomes such as intraoperative severe adverse events, cardiovascular events, duration of hospital stay, or quality of life. The inclusion of these outcomes could have provided a more comprehensive comparison between the two treatment modalities.

Study arms

Partial nephrectomy (N = 31)

Cryoablation (N = 43)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 31)	Cryoablation (N = 43)
% Female Custom value	Not provided	Not provided
Age (years) Median Custom value	59	68
Baseline chronic kidney disease (CKD) No of events	n = 16 ; % = 52	n = 30 ; % = 70
Tumour size (cm) median Nominal	2.8	2

Outcomes

Study timepoints

- See below (The study reported outcomes at the following timepoints: postoperative day 1, discharge, 3 months, and 12 months for functional outcomes such as acute kidney injury (AKI) and estimated glomerular filtration rate (eGFR) preservation. Oncological outcomes, including local recurrence, distant metastasis, and death, were reported at a median follow-up of 59.4 months (approximately 5 years). The study did not provide data extraction timepoints beyond 5 years.)

Recurrence

Outcome	Partial nephrectomy, See below, N = 31	Cryoablation, See below, N = 43
Recurrence-free survival: Local recurrence, follow-up timepoint is not specified No of events	n = 1 ; % = 3.2	n = 11 ; % = 29

Renal functional impairment

Outcome	Partial nephrectomy, See below, N = 31	Cryoablation, See below, N = 43
New onset CKD No of events	n = 6 ; % = 19	n = 4 ; % = 9.3
End stage renal disease (CKD stage 5) No of events	n = 3 ; % = 9.7	n = 5 ; % = 12

New onset CKD - Polarity - Lower values are better
End stage renal disease (CKD stage 5) - Polarity - Lower values are better

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Recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding factors related to the retrospective design and lack of propensity*

Section	Question	Answer
		score matching, which is considered important by the NICE committee. The risk of bias in other domains is generally low, except for the missing data domain, where no information was provided. The study directly addresses the research question without significant indirectness in terms of population, interventions, comparisons, or outcomes measured, assuming it meets the predefined inclusion criteria for the PICO.)
Overall bias	Directness	Directly applicable

Renal functional impairment outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding factors related to the retrospective design and lack of propensity score matching, which is considered important by the NICE committee. The risk of bias in other domains is generally low, except for the missing data domain, where no information was provided. The study directly addresses the research question without significant indirectness in terms of population, interventions, comparisons, or outcomes measured, assuming it meets the predefined inclusion criteria for the PICO.)*
Overall bias	Directness	Directly applicable *(For the purpose of this systematic review, we are assuming that all studies meeting the predefined inclusion criteria for the PICO will be graded as 'direct' in terms of their evidence. This assumption is based on the notion that studies satisfying the PICO criteria will directly address the research question at hand, without significant indirectness in terms of population, interventions, comparisons, or outcomes measured. However, it is important to note that this study was conducted in the USA, and the patient population and healthcare system may differ from those in the UK NHS. Factors such as differences in patient demographics, comorbidities, and access to healthcare could potentially impact the applicability of the findings to the UK setting. Additionally, the specific techniques and protocols used for partial nephrectomy and cryoablation may vary between the USA and the UK. Despite these potential sources of indirectness, the study does not appear to have any major issues that would significantly limit its applicability to the UK NHS. The interventions and comparisons are broadly similar to those used in the UK, and the outcomes measured are clinically relevant and important for decision-making.)*

Bertolo, 2019

Bibliographic Reference	Bertolo, Riccardo; Garisto, Juan; Armanyous, Sherif; Agudelo, Jose; Lioudis, Michael; Kaouk, Jihad; Perioperative, oncological and functional outcomes after robotic partial nephrectomy versus. cryoablation in the elderly: A propensity score matched analysis.; Urologic oncology; 2019; vol. 37 (no. 4); 294e9-294e15

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	June 2006−December 2016
Sources of funding	Jihad H. Kaouk certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (e.g. Employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patent filed, received or pending) are the following: Endocare, Inc, Intuitive Nothing to disclose: Riccardo Bertolo, Juan Garisto, Sherif Armanyous, Jose Agudelo, and Michael Lioudis.
Inclusion criteria	Patients older than 75 years People who who underwent robotic PN or cryoablation (either laparoscopic or CT-scan guided percutaneous) for renal tumour
Exclusion criteria	Not reported
Intervention(s)	Robotic partial nephrectomy
Comparator	Cryoablation
Outcome measures	Renal functional impairment
Number of participants	Total number of participants: 130 Robotic partial nephrectomy: 65 Cryoablation: 65
Duration of follow-up	Median follow-up of 37 (29−44) and 46 (38−53) months for robotic partial nephrectomy and cryoablation, respectively
Loss to follow-up	Not reported
Methods of analysis	Overall (OS), recurrence-free (RFS), and cancer-specific survival (CSS) were analysed using the Kaplan-Meier method. Comparisons by treatment groups were performed by log-rank test. The propensity scores of the 2 treatment groups were then matched from the nearest neighbour (greedy

	matching algorithm) in a ratio of 1:1 with no replacement. Patients were matched according to age, sex, race, BMI, ASA score, diabetes, hypertension, pre-existing CKD, Charlson's Comorbidity Index, clinical tumour size, R.E.N.A.L. score and preoperative serum creatinine.

Study arms

Robotic partial nephrectomy (N = 65)

Cryoablation (N = 65)

Characteristics

Arm-level characteristics

Characteristic	Robotic partial nephrectomy (N = 65)	Cryoablation (N = 65)
% Female No of events	n = 45 ; % = 66	n = 38 ; % = 60
Age Mean (SD)	79.3 (3.3)	79.3 (4.1)
cT1a No of events	n = 55 ; % = 85	n = 54 ; % = 83
cT1b No of events	n = 10 ; % = 15	n = 11 ; % = 17
Clinical tumor size, cm Mean (SD)	2.9 (1)	3 (1)

Outcomes

Renal function impairment

Outcome	Cryoablation versus Robotic partial nephrectomy, , N2 = 65, N1 = 65
Estimated glomerular filtration rate (eGFR) differences Mean (95% CI)	1.2 (-6.5 to 8.9)

Estimated glomerular filtration rate (eGFR) differences - Polarity - Higher values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Bhindi, 2018

Bibliographic Reference	Bhindi, B.; Mason, R.J.; Haddad, M.M.; Boorjian, S.A.; Leibovich, B.C.; Atwell, T.D.; Weisbrod, A.J.; Schmit, G.D.; Thompson, R.H.; Outcomes After Cryoablation Versus Partial Nephrectomy for Sporadic Renal Tumors in a Solitary Kidney: A Propensity Score Analysis; European Urology; 2018; vol. 73 (no. 2); 254-259

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Mayo clinic registries used as data source.
Study dates	2005 to 2015
Sources of funding	No funding obtained
Inclusion criteria	Solitary kidney Single localised noncystic primary renal tumour Node-negative, non-metastatic
Exclusion criteria	Multiple tumours Salvage procedures Inherited tumour syndromes Tumour in a transplanted kidney
Intervention(s)	Cryoablation (CRA) Percutaneous. Performed under CT and/or ultrasound guidance. Follow-up: Patients were generally assessed at 3, 6, 12, 18, 24, and 36 mo, with annual follow-up thereafter. Patients were recommended to undergo renal function assessment and cross-sectional imaging at 3 mo and at each visit thereafter.

Comparator	Partial nephrectomy (PN) Follow-up: As for CRA arm.
Outcome measures	Recurrence Survival Postoperative severe adverse events
Number of participants	N=118 PN: 64 CRA: 54
Duration of follow-up	Months, median (IQR) Whole cohort: 47 (18, 74). Not reported at arm level.
Loss to follow-up	Not reported.
Methods of analysis	Inverse probability treatment weighting (IPTW) was used to adjust the cohort for confounders. The propensity to undergo CRA versus PN was estimated using a logistic regression model based on age, sex, Charlson comorbidity index, treatment year, RENAL nephrometry score, tumour size (maximum tumour diameter in centimetres), baseline eGFR, renal cell carcinoma (RCC) tumour histology, and history of prior contralateral nephrectomy for RCC. Patient and tumour characteristics were compared between groups pre- and post-weighting using standardized differences. The probability of overall survival (OS) was compared between groups using Cox proportional hazards regression. The risk of local failure, distant metastasis, and cancer-specific mortality was compared between groups using Fine-and-Grey competing risk models, with death from non-RCC causes considered a competing event. Sensitivity analyses carried out (OPTW with truncating nonoverlapping tails of the PS distribution and stabilising weights; IPTW model without tumour histology adjusted for; propensity score matching and propensity score regression adjustment).
Additional comments	Results from the IPTW analysis are extracted as they adjust for confounding. Limitations: unmeasured confounding, relatively small sample size, long-term renal function could not be assessed due to patients being followed up by outside institutions and because CRA patients were more likely to die from competing causes and therefore not have long term follow-up data.

Study arms

Cryoablation (N = 54)

Percutaneous

Partial nephrectomy (N = 64)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 54)	Partial nephrectomy (N = 64)
Age Median (IQR)	65 (54 to 75)	63 (58 to 67)
Tumour size cm Median (IQR)	3.5 (2.3 to 6.5)	3.7 (2 to 5)
Histologically confirmed RCC No of events	n = NR ; % = 78	n = NR ; % = 74
Baseline eGFR ml/min/1.73 m2 Median (IQR)	56 (48 to 69)	56 (47 to 77)
R.E.N.A.L. nephrometry score Median (IQR)	7 (6 to 9)	8 (5 to 9)

Outcomes

Survival and recurrence

Outcome	Cryoablation versus Partial nephrectomy , , N2 = 54, N1 = 64
Distant metastasis IPTW results Hazard ratio/95% CI	0.6 (0.3 to 1.2)
RCC death IPTW results Hazard ratio/95% CI	1.13 (0.32 to 3.98)
Death from any cause IPTW results, additional adjustments for age Hazard ratio/95% CI	2.6 (1.42 to 4.76)

Distant metastasis - Polarity - Lower values are better
RCC death - Polarity - Lower values are better

Death from any cause - Polarity - Lower values are better

Complications

Outcome	Cryoablation versus Partial nephrectomy , , N2 = 54, N1 = 64
Any complications (Clavien-Dindo 1-5) Odds ratio/95% CI	0.95 (0.53 to 1.69)

Any complications (Clavien-Dindo 1-5) - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Possible residual confounding (although IPTW analysis and additional adjustment for age for the OS outcome likely to reduce effect of confounders). Protocol not identified but results clearly presented. Missing data not reported.)*
Overall bias	Directness	Directly applicable

Bianchi, 2021

Bibliographic Reference	Bianchi, Lorenzo; Mineo Bianchi, Federico; Chessa, Francesco; Barbaresi, Umberto; Casablanca, Carlo; Piazza, Pietro; Mottaran, Angelo; Droghetti, Matteo; Roveroni, Carlo; Balestrazzi, Eleonora; Gentile, Giorgio; Gaudiano, Caterina; Bertaccini, Alessandro; Marcelli, Emanuela; Porreca, Angelo; DE Concilio, Bernardino; Serra, Carla; Celia, Antonio; Brunocilla, Eugenio; Schiavina, Riccardo; Percutaneous tumor ablation versus partial nephrectomy for small renal mass: the impact of histologic variant and tumor size.; Minerva urology and nephrology; 2021; vol. 73 (no. 5); 581-590

Study details

Study type	Retrospective cohort study
Study location	Italy

Study setting	Hospital setting. Two tertiary centres (Sant' Orsola-Malpighi Hospital in Bologna and San Bassiano Hospital in Bassano del Grappa, Italy)
Study dates	Between January 2007 and July 2019
Sources of funding	Not reported
Inclusion criteria	Patients with cT1aN0M0 renal masses
Intervention(s)	Partial nephrectomy (PN)
Comparator	Radiofrequency ablation (RFA) and cryoablation (CA)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: 816 PN: 665 RFA: 68 CA: 83
Duration of follow-up	Median (IQR) Overall: 61 (33-93) PN: 63 (32-100) RFA: 48 (35-66) CA: 63 (44-85)
Loss to follow-up	Not reported
Methods of analysis	Uni- and multivariate Cox regression models were used to assess predictors of cancer recurrence. Covariates consisted of patient's characteristics (age, CCI and gender), preoperative tumour's features (PADUA score, size, side, local stage and number of synchronous renal masses), histologic data (non-clear cell RCC versus. clear cell RCC) and type of procedure (PN versus RFA versus. CA).

Study arms

Partial nephrectomy (N = 816)

Radiofrequency ablation (N = 68)

Cryoablation (N = 83)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 816)	Radiofrequency ablation (N = 68)	Cryoablation (N = 83)
% Female No of events	n = 227 ; % = 34.1	n = 26 ; % = 38.2	n = 24 ; % = 28.9
Age Median (IQR)	63 (53 to 71)	77 (65 to 82)	71 (65 to 77)
T1a No of events	n = 537 ; % = 80.8	n = 61 ; % = 89.7	n = 76 ; % = 91.6
T1b No of events	n = 129 ; % = 19.2	n = 7 ; % = 10.3	n = 7 ; % = 8.4
Benign No of events	n = 174 ; % = 26.2	n = 22 ; % = 32.4	n = 12 ; % = 14.5
Clear cell No of events	n = 293 ; % = 44.1	n = 21 ; % = 30.9	n = 46 ; % = 55.4
Papillary No of events	n = 110 ; % = 16.5	n = 16 ; % = 23.5	n = 14 ; % = 16.9
Chromophobe No of events	n = 45 ; % = 6.8	n = 3 ; % = 4.4	n = 5 ; % = 6
Others No of events	n = 43 ; % = 6.5	n = 0 ; % = 0	n = 0 ; % = 0
Non-diagnostic No of events	n = 0 ; % = 0	n = 6 ; % = 8.8	n = 6 ; % = 7.2
Tumor size (cm) Median (IQR)	3 (2.1 to 4)	2.5 (1.8 to 3.5)	2.2 (1.7 to 2.7)

Outcomes

Survival

Outcome	Partial nephrectomy, , N = 665	Radiofrequency ablation, , N = 68	Cryoablation, , N = 83
Cancer specific mortality No of events	n = 4 ; % = 0.8	n = 2 ; % = 4.3	n = 2 ; % = 2.8
recurrence-free survival No of events	n = 641 ; % = 96.4	n = 54 ; % = 79.4	n = 73 ; % = 87.8
local recurrence No of events	n = 17 ; % = 3.5	n = 11 ; % = 23.9	n = 12 ; % = 16.9
Systemic recurrence No of events	n = 15 ; % = 3.1	n = 3 ; % = 6.5	n = 1 ; % = 1.4

Cancer specific mortality - Polarity - Lower values are better
recurrence-free survival - Polarity - Lower values are better
local recurrence - Polarity - Lower values are better
Systemic recurrence - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Furthermore, there is a statistical difference in the mean age at the baseline characteristics, which may have affected the outcome, favouring the PN. arm)*
Overall bias	Directness	Directly applicable

Bird, 2009

Bibliographic Reference	Bird, Vincent G; Carey, Robert I; Ayyathurai, Rajinikanth; Bird, Victoria Y; Management of renal masses with laparoscopic-guided radiofrequency ablation versus laparoscopic partial nephrectomy.; Journal of endourology; 2009; vol. 23 (no. 1); 81-8

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Databases of two surgeons (authors) from two different institutions were extracted.
Study dates	2002 to 2007
Sources of funding	Study reports that no competing financial interests exist.
Inclusion criteria	Solitary enhancing renal mass noted either on CT or MRI Localised renal tumour
Exclusion criteria	Not reported
Intervention(s)	Radiofrequency ablation (RFA) Performed by transperitoneal laparoscopy. The radiofrequency probe was then placed, and its position within the tumour was confirmed by laparoscopic ultrasonography. Immediately before LRFA, through a percutaneous sheath, multiple biopsy samples of the tumour were obtained. Under ultrasonographic guidance, the probe was passed into the tumour to a point so as to create a zone of ablation 1 cm beyond the tumour margin
Comparator	Partial nephrectomy (PN) Transperitoneal laparoscopy. All patients underwent biopsy of the resection bed.
Outcome measures	Recurrence Duration of hospital stay
Number of participants	N:69 RFA: 36 PN: 33
Duration of follow-up	RFA: mean 12 months, range 6 to 23 months PN: mean 27 months, range 6 to 58 months
Loss to follow-up	Not reported
Methods of analysis	Statistical analysis was performed using the Student t test and chi-square analysis. No further information reported.
Additional comments	Limitations: small sample size, no adjustments for confounding (RFA group older, with higher ASA score and lower preoperative GFR than PN group), no indication of spread of treatments across the two study sites.

Study arms

Radiofrequency ablation (N = 36)

Laparoscopic-guided

Partial nephrectomy (N = 33)

Laparoscopic

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 36)	Partial nephrectomy (N = 33)
% Female No of events	n = 14 ; % = 38.89	n = 15 ; % = 45.45
Age Custom value	mean 75.2, range 56-86	mean 57.8, range 27-77
Preoperative GFR ml/min/1.73m2) Mean (SD)	59.69 (NR)	82.58 (NR)
Tumour size (cm) Mean (SD)	2.8 (NR)	3.1 (NR)
Total RCC (not benign) Custom value	72.3%	60.6%

Outcomes

Duration of hospital stay

Outcome	Radiofrequency ablation, , N = 36	Partial nephrectomy, , N = 33
Duration of hospital stay Mean (SD)	1 (0.72)	3 (1.19)

Duration of hospital stay - Polarity - Lower values are better

Recurrence

Outcome	Radiofrequency ablation, , N = 36	Partial nephrectomy, , N = 33
Recurrence at longest follow up (RFA 12 mean 12 months, PN mean 27 months) No of events	n = 0 ; % = 0	n = 0 ; % = 0

Recurrence - Polarity - Lower values are better

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Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, unblinded staff with responsibility for discharge decisions, and protocol not identified)*
Overall bias	Directness	Directly applicable

Recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, and protocol not identified)*
Overall bias	Directness	Directly applicable

Caputo, 2017

Bibliographic Reference	Caputo, Peter A; Zargar, Homayoun; Ramirez, Daniel; Andrade, Hiury S; Akca, Oktay; Gao, Tianming; Kaouk, Jihad H; Cryoablation versus Partial Nephrectomy for Clinical T1b Renal Tumors: A Matched Group Comparative Analysis.; European urology; 2017; vol. 71 (no. 1); 111-117

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Review of data from a single institution.
Study dates	1999 to 2014
Sources of funding	No funding received for this paper. One author has received consultancy fees from Endocare.
Inclusion criteria	cT1b renal mass (between 4 and 7cm) No imaging concerns regarding more advanced disease
Exclusion criteria	Not reported
Intervention(s)	Cryoablation Laparoscopic and percutaneous techniques. Biopsy taken for all procedures. Contrast-enhanced imaging performed at 3, 6 and 12 months and then annually.
Comparator	Partial nephrectomy (PN). Robot-assisted. Contrast-enhanced imaging performed within 3-12 months of surgery and then annually.
Outcome measures	Recurrence
Number of participants	N=192 Cryoablation: 31 PN: 161
Duration of follow-up	Median months (IQR) Cryoablation: 30.1 (13.2-64) PN: 13 (3.19-19.2)
Loss to follow-up	Not reported
Methods of analysis	Matching was used to reduce the effect of confounders between the groups. Matching was based on key baseline variables (tumour size, Charlson comorbidity index, age, BMI, ASA score, preoperative serum creatinine, preoperative eGFR, gender and solitary kidney). RENAL scores were not included in the matching algorithm. The matching algorithm was 1:1 genetic matching with no replacement, which automatically finds a balance using a genetic search algorithm to determine the optimal weight for each covariate within the matching algorithm. Genetic matching maximizes the balance of observed covariates between groups. Recurrence-free survival, overall survival, and cancer-specific survival were analysed using Kaplan-Meier survival curves but data was not extractable.

Additional comments	Cryoablation was used for patients with comorbid medical conditions for whom, at the discretion of the physician, the risk of surgery outweighed the benefit of PN. Cryoablation was also used for patients unwilling to accept the risks for PN. Tumour recurrence in the PN group was defined as a new contrast-enhancing lesion found within or abutting the surgical resection bed for the ipsilateral kidney. Tumour recurrence in the cryoablation group was defined as an area of new contrast enhancement within a previous completely treated ablation site appearing >3 mo after treatment. Limitations: small sample size. The median follow-up was significantly shorter for the PN group (13.0 mo) than for the CA group (30.1 mo). Authors state that percutaneous cryoablation has largely replaced laparoscopic techniques, so the results of the study should be interpreted with caution as they include laparoscopic procedures. The study also reports postoperative complications but these are not extracted as they are reported in an included systematic review (Yanagisawa 2022).

Study arms

Cryoablation (N = 31)

Laparoscopic and percutaneous

Partial nephrectomy (N = 31)

Robot-assisted

Characteristics

Arm-level characteristics

Characteristic	Cryoablatio (N = 31)	Partial nephrectomy (N = 31)
% Female No of events	n = 6 ; % = 19	n = 7 ; % = 23
Age Median (IQR)	68 (64 to 76)	68 (64 to 76)
Tumour size cm Median (IQR)	4.3 (4.2 to 4.7)	4.6 (4.3 to 4.9)
Benign tumour	n = 9 ; % = 29	n = 3 ; % = 10

Characteristic	Cryoablatio (N = 31)	Partial nephrectomy (N = 31)
No of events		
RENAL score Median (IQR)	8 (6 to 9)	9 (7 to 10)
Preoperative eGFR ml/min/1.73 m2) Median (IQR)	53.4 (39.6 to 72.6)	62.6 (52.1 to 72.4)
Solitary kidney No of events	n = 10 ; % = 32	n = 6 ; % = 19

Outcomes

Recurrence

Outcome	Cryoablatio, , N = 22	Partial nephrectomy, , N = 28
Recurrence No of events	n = 5 ; % = 16	n = 0 ; % = 0

Recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Matching undertaken but RENAL score not matched for, differences in numbers of benign masses between groups. Follow-up longer for cryoablation arm. No protocol identified.)*
Overall bias	Directness	Directly applicable

Cazalas, 2023

Bibliographic Reference	Cazalas, Gregoire; Klein, Clement; Piana, Gilles; De Kerviler, Eric; Gangi, Afshin; Puech, Philippe; Nedelcu, Cosmina; Grange, Remi; Buy, Xavier; Jegonday, Marc-Antoine; Bigot, Pierre; Bensalah, Charles Karim; Gaillard, Victor; Pignot, Geraldine; Paparel, Philippe; Badet, Lionel; Michiels, Clement; Bernhard, Jean Christophe; Rouviere, Olivier; Grenier, Nicolas; Marcelin, Clement; A multicenter comparative matched-pair

analysis of percutaneous tumor ablation and robotic-assisted partial nephrectomy of T1b renal cell carcinoma (AblatT1b study-UroCCR 80).; European radiology; 2023; vol. 33 (no. 9); 6513-6521

Study details

Trial registration number and/or trial name	NCT03293563/CNIL agreement DR-2013-206 (UroCCR database)
Study type	Retrospective cohort study
Study location	France
Study setting	Hospital setting. Data obtained from 11 centres participating in the national prospective UroCCR database.
Study dates	2010 to 2020
Sources of funding	The authors state that this work has not received any funding.
Inclusion criteria	Sporadic, biopsy-proven, stage cT1b renal cell carcinoma treated with percutaneous thermal ablation or robotic-assisted partial nephrectomy
Exclusion criteria	Benign renal tumour on histology Presence of metastases Patients with a genetic predisposition to cancer (Von Hippel-Lindau syndrome)
Intervention(s)	Percutaneous thermal ablation, including cryoablation, radiofrequency ablation, and microwave ablation, performed by trained interventional radiologists.
Comparator	Robotic-assisted partial nephrectomy via a transperitoneal approach using the da Vinci Si Surgical System.
Outcome measures	Recurrence Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	N = 150 Thermal ablation: 75 (50%) Robotic-assisted partial nephrectomy: 75 (50%)
Duration of follow-up	Mean follow-up was 28.8 ± 17.4 months for the RAPN patients and 31.4 ± 28.8 months for the TA patients.
Loss to follow-up	Not reported.

Methods of analysis	Retrospective 1:1 propensity-score matched analysis adjusting for tumour size, histology results, and RENAL score. Univariable, multivariable, and logistic regression analyses were conducted to identify factors predictive of cancer local recurrence.
Additional comments	This retrospective cohort study compared the outcomes of percutaneous thermal ablation and robotic-assisted partial nephrectomy for the treatment of T1b renal cell carcinoma. The study used a propensity-score matched analysis to adjust for potential selection biases arising from the non-random allocation of patients to the different treatment groups. The authors acknowledged several limitations of the study. Firstly, it was a retrospective study with a relatively short follow-up period (< 5 years) and inhomogeneous patient backgrounds. Secondly, there was an absence of description of the ablation procedures, with different operators of varying experience levels and a lack of randomisation. Additionally, the International Society of Urological Pathology (ISUP) classification was not commonly used for grading the tumours. One strength of the study is the use of propensity-score matching to minimise selection bias. However, the study's retrospective nature and the potential for unmeasured confounders may still limit the comparability of the treatment groups. The small sample size (75 patients in each group) may also limit the statistical power to detect differences in outcomes between the two treatments. The study did not report on several important outcomes, such as overall survival, intraoperative severe adverse events, cardiovascular events, and quality of life. The inclusion of these outcomes would have provided a more comprehensive assessment of the comparative effectiveness and safety of the two treatments. **Follow-up time points:** The mean follow-up duration was 28.8 ± 17.4 months for the robotic-assisted partial nephrectomy patients and 31.4 ± 28.8 months for the thermal ablation patients (not statistically different). The mean follow-up for all patients was 30.1 (± 20.4) months.

Study arms

Thermal ablation (N = 75)

Robotic-assisted partial nephrectomy (N = 75)

Characteristics

Arm-level characteristics

Characteristic	Thermal ablation (N = 75)	Robotic-assisted partial nephrectomy (N = 75)
% Female No of events	n = 23 ; % = 30.7	n = 18 ; % = 24
Age Mean (SD)	76.9 (9.1)	61.1 (12)
ASA score: 1 No of events	n = 4 ; % = 6.3	n = 15 ; % = 20
ASA score: 2 No of events	n = 23 ; % = 34.3	n = 45 ; % = 60
ASA score 3 (three) No of events	n = 36 ; % = 56.3	n = 14 ; % = 18.7
ASA score: 4 No of events	n = 2 ; % = 3.1	n = 1 ; % = 1.3
Treatment technique used: Cryoablation No of events	n = 61 ; % = 81.3	n = NA
Treatment technique used: Radiofrequency ablation No of events	n = 9 ; % = 12	n = NA
Treatment technique used: Microwave ablation No of events	n = 5 ; % = 6.7	n = NA
RENAL score: 1 (5-6) No of events	n = 13 ; % = 17.3	n = 12 ; % = 16
RENAL score: 2 (7-9) No of events	n = 44 ; % = 58.7	n = 51 ; % = 68
RENAL score: 3 (10-12) No of events	n = 18 ; % = 24	n = 12 ; % = 16
Preoperative tumour size (cm) Mean (SD)	4.6 (0.57)	4.7 (0.56)

Characteristic	Thermal ablation (N = 75)	Robotic-assisted partial nephrectomy (N = 75)
Primary RCC type: Clear cell renal carcinoma No of events	n = 61 ; % = 81.3	n = 55 ; % = 72
Primary RCC type: Papillary renal cell carcinoma No of events	n = 11 ; % = 14.7	n = 15 ; % = 20
Primary RCC type: Chromophobe renal cell carcinoma No of events	n = 3 ; % = 4	n = 6 ; % = 8
Preoperative GFR-MDRD (mL/min/1.73 m2) Mean (SD)	64.1 (23.2)	89.6 (25.1)
Fuhrman grade: Low (1-2) No of events	n = 50 ; % = 94.4	n = 44 ; % = 62.8
Fuhrman grade: High (3-4) No of events	n = 3 ; % = 5.6	n = 26 ; % = 37.1

Outcomes

Local recurrence and metastases

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Local recurrence; follow-up timepoint is not specified No of events	n = 11 ; % = 14.6	n = 3 ; % = 4
Metastases; follow-up timepoint is not specified No of events	n = 1 ; % = 1.3	n = 2 ; % = 2.6

Adverse events

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Major complications (Clavien-Dindo Classification ≥ 3); follow-up timepoint is not specified No of events	n = 0 ; % = 0	n = 4 ; % = 5.3

Kidney function

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Postoperative GFR-MDRD (mL/min/1.73 m2); follow-up timepoint is not specified Mean (SD)	60.3 (21.6)	94.6 (102.7)
eGFR decrease (mL/min/1.73 m2); follow-up timepoint is not specified Mean (SD)	7.1 (20.3)	4.6 (104.4)

Transform

Local recurrence and metastases

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Local recurrence; follow-up timepoint is not specified No of events	n = 11 ; % = 14.6	n = 3 ; % = 4
Metastases; follow-up timepoint is not specified No of events	n = 1 ; % = 1.3	n = 2 ; % = 2.6

Arm based : Data distribution : Not set

Adverse events

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Major complications (Clavien-Dindo Classification ≥ 3); follow-up timepoint is not specified	n = 0 ; % = 0	n = 4 ; % = 5.3

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
No of events		

Arm based : Data distribution : Not set

Kidney function

Outcome	Thermal ablation, , N = 75	Robotic-assisted partial nephrectomy , , N = 75
Postoperative GFR-MDRD (mL/min/1.73 m2); follow-up timepoint is not specified Mean (SD)	60.3 (21.6)	94.6 (102.7)
eGFR decrease (mL/min/1.73 m2); follow-up timepoint is not specified Mean (SD)	7.1 (20.3)	4.6 (104.4)

Arm based : Data distribution : Not set

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Recurrence and metastasis outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as there may be residual confounding from unmeasured or inadequately measured confounders despite the use of propensity score matching. There is also a moderate risk of bias in the measurement of outcomes, as outcome assessors were likely aware of the intervention received by study participants. However, the risk of bias is low for the selection of participants into the study, classification of interventions, and selection of the reported result. There is no clear information on the risk of bias due to deviations from intended interventions or missing data.)*
Overall bias	Directness	Directly applicable

Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as there may be residual confounding from unmeasured or inadequately measured confounders despite the use of propensity score matching. There is also a moderate risk of bias in the measurement of outcomes, as outcome assessors were likely aware of the intervention received by study participants. However, the risk of bias is low for the selection of participants into the study, classification of interventions, and selection of the reported result. There is no clear information on the risk of bias due to deviations from intended interventions or missing data.)*
Overall bias	Directness	Directly applicable

Kidney function outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as there may be residual confounding from unmeasured or inadequately measured confounders despite the use of propensity score matching. There is also a moderate risk of bias in the measurement of outcomes, as outcome assessors were likely aware of the intervention received by study participants. However, the risk of bias is low for the selection of participants into the study, classification of interventions, and selection of the reported result. There is no clear information on the risk of bias due to deviations from intended interventions or missing data.)*
Overall bias	Directness	Directly applicable

Chan, 2022

Bibliographic Reference	Chan, Vinson Wai-Shun; Osman, Filzah Hanis; Cartledge, Jon; Gregory, Walter; Kimuli, Michael; Vasudev, Naveen S; Ralph, Christy; Jagdev, Satinder; Bhattarai, Selina; Smith, Jonathan; Lenton, James; Wah, Tze Min; Long-term outcomes of image-guided ablation and laparoscopic

partial nephrectomy for T1 renal cell carcinoma.; European radiology; 2022; vol. 32 (no. 9); 5811-5820

Study details

Study type	Retrospective cohort study
Study location	UK
Study setting	Hospital setting
Study dates	From 2003 to 2016
Sources of funding	Not reported
Inclusion criteria	Patients with cT1N0M0 histology-confirmed RCC
Exclusion criteria	Multiple tumours Inherited tumour syndromes Patients with tumour recurrence Patients with solitary kidney Patients with a history of LPN, CRYO, or RFA of the same kidney
Intervention(s)	Cryoablation and radio-frequency ablation
Comparator	Laparoscopic partial nephrectomy
Outcome measures	Recurrence Survival Postoperative severe adverse events
Number of participants	Total number of participants: N = 238 Cryoablation (CRYO) N = 72 Radio-frequency ablation (RFA) N = 87 Laparoscopic partial nephrectomy (LPN) N = 79
Duration of follow-up	The median (IQR) follow-up duration is 72.5 (42.0– 100.9) months, 59.5 (27.5–99.39) months, and 67.9 (50.8– 91.3) months for CRYO, RFA, and LPN, respectively.
Loss to follow-up	Not reported
Methods of analysis	Outcomes were evaluated from the time of treatment to the time of event using the Kaplan-Meier method. Ten-year survival rates and corresponding 95% confidence intervals (95% CI) were reported. The Cox proportional hazard regression model was utilised to evaluate survival in CRYO, RFA, and LPN patients, reporting as hazard ratios (HRs), 95% CI, and p-values. Cox multivariable model adjusted for age, sex, R.E.N.A.L nephrometry score, lesion size, RCC type, grade and t-stage. Complication rates and severity were evaluated using the chi-squared test and logistic regression. Changes in peri-operative renal function were

	evaluated using the Kruskal-Wallis test and the Wilcoxon matched pairs signed rank sum test. Amongst 10 patients with missing Charlson Comorbidity Index (CCI) or R.E.N.A.L. nephrometry score, median CCI or nephrometry score was imputed. Sensitivity analyses have shown identical results and hence all patients were included in the final analyses.
Additional comments	Complication events calculated from percentages provided in the paper.

Study arms

Cryoablation (N = 72)

Radio-frequency ablation (N = 87)

Laparoscopic partial nephrectomy (N = 79)

Cryo/RF combined (N = 151)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 72)	Radio-frequency ablation (N = 87)	Laparoscopic partial nephrectomy (N = 79)	Cryo/RF combined (N = 151)
T1a No of events	n = 30 ; % = 41.7	n = 28 ; % = 32.2	n = 27 ; % = 34.2	*empty data*
T1b No of events	n = 9 ; % = 29	n = 7 ; % = 53.8	n = 8 ; % = 57.1	*empty data*
T1a Median (IQR)	72 (62 to 76)	73 (66 to 78)	59 (49 to 67)	*empty data* (*empty data* to *empty data*)
T1b Median (IQR)	77 (65 to 80)	78 (65 to 79)	57 (44 to 67)	*empty data* (*empty data* to *empty data*)
T1a No of events	n = 72 ; % = 69.9	n = 87 ; % = 87	n = 79 ; % = 84.9	*empty data*
T1b No of events	n = 31 ; % = 30.1	n = 13 ; % = 13	n = 14 ; % = 15.1	*empty data*

Characteristic	Cryoablation (N = 72)	Radio-frequency ablation (N = 87)	Laparoscopic partial nephrectomy (N = 79)	Cryo/RF combined (N = 151)
T1a - Conventional No of events	n = 45 ; % = 62.5	n = 71 ; % = 81.6	n = 49 ; % = 62	*empty data*
T1b - Conventional No of events	n = 24 ; % = 77.4	n = 12 ; % = 100	n = 12 ; % = 85.7	*empty data*
T1a - Papillary No of events	n = 6 ; % = 8.3	n = 5 ; % = 5.7	n = 17 ; % = 21.5	*empty data*
T1b - Papillary No of events	n = 2 ; % = 6.5	n = 0 ; % = 0	n = 1 ; % = 7.1	*empty data*
T1a - Oesinophil No of events	n = 2 ; % = 2.8	n = 6 ; % = 6.9	n = 1 ; % = 1.3	*empty data*
T1b - Oesinophil No of events	n = 0 ; % = 0	n = 0 ; % = 0	n = 1 ; % = 1.7	*empty data*
T1a - Chromophobe No of events	n = 19 ; % = 26.4	n = 5 ; % = 5.7	n = 12 ; % = 15.2	*empty data*
T1b - Chromophobe No of events	n = 5 ; % = 16.1	n = 0 ; % = 0	n = 0 ; % = 0	*empty data*
T1a Median (IQR)	77.88 (60.9 to 87.8)	89.02 (71.2 to 104.4)	91.31 (75.3 to 101.9)	*empty data* (*empty data* to *empty data*)
T1b Median (IQR)	57.6 (42.8 to 79.2)	37.3 (30.5 to 43.4)	84.8 (73.3 to 97.1)	*empty data* (*empty data* to *empty data*)
T1a Median (IQR)	4.5 (4.1 to 5.1)	4.5 (4.5 to 4.8)	4.45 (4.2 to 5.3)	*empty data* (*empty data* to *empty data*)

Outcomes

Complications

Outcome	Cryoablation versus Laparoscopic partial nephrectomy, , N2 = 93, N1 = 103	Radio-frequency ablation versus Laparoscopic partial nephrectomy, , N2 = 93, N1 = 100	Cryoablation versus Laparoscopic partial nephrectomy, , N2 = , N1 =
CD-I Relative risk/95% CI	1.43 (0.38 to 5.31)	1.29 (0.35 to 4.78)	*empty data* (*empty data* to *empty data*)
CD-II Relative risk/95% CI	0.24 (0.03 to 2.19)	1.29 (0.35 to 4.78)	*empty data* (*empty data* to *empty data*)
CD-III Relative risk/95% CI	0.48 (0.04 to 5.39)	1.29 (0.21 to 7.97)	*empty data* (*empty data* to *empty data*)

CD-I - Polarity - Lower values are better
CD-II - Polarity - Lower values are better
CD-III - Polarity - Lower values are better

Survival

Outcome	Cryoablation versus Laparoscopic partial nephrectomy, , N2 = 93, N1 = 103	Radio-frequency ablation versus Laparoscopic partial nephrectomy, , N2 = 93, N1 = 100	Cryo/RF combined versus Laparoscopic partial nephrectomy, , N2 = 93, N1 = 151
Overall survival Hazard ratio/95% CI	1.2 (0.47 to 3.59)	0.62 (0.19 to 2.03)	0.73 (0.3 to 1.77)
Local recurrence-free survival Hazard ratio/95% CI	0.07 (0.01 to 0.73)	0.04 (0.03 to 0.48)	0.08 (0.01 to 0.44)
Metastasis-free survival Hazard ratio/95% CI	*empty data* (*empty data* to *empty data*)	0.19 (0.01 to 3.1)	0.13 (0.01 to 2.22)

Overall survival - Polarity - Lower values are better

Local recurrence-free survival - Polarity - Lower values are better
Metastasis-free survival - Polarity - Lower values are better

Complications

Outcome	Cryoablation, , N =	Radio-frequency ablation, , N =	Laparoscopic partial nephrectomy, , N = 93	Cryo/RF combined, , N = 203
Any complication (Clavien-Dindo 1-5) T1a No of events	*empty data*	*empty data*	n = 11 ; % = 14	n = 24 ; % = 16
Any complication (Clavien-Dindo 1-5) T1b No of events	*empty data*	*empty data*	n = 1 ; % = 7.7	n = 8 ; % = 18.2

Any complication (Clavien-Dindo 1-5) - Polarity - Lower values are better
Any complication (Clavien-Dindo 1-5) - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains. Authors have imputed data and there is no information on the proportion of participants in each assessed group with missing data and their reason for missing data. Furthermore, there is no information on the method used to input data.)*
Overall bias	Directness	Directly applicable *(The study was conducted in the UK NHS. The interventions (cryoablation, radiofrequency ablation, and laparoscopic partial nephrectomy) and the patient population (T1a and T1b) are relevant to the UK NHS setting. The outcomes assessed in the study, such as OS, DFS, and complications are important for decision-making in the UK NHS context.)*

Cheung, 2023

Bibliographic Reference	Cheung, D.C.; Martin, L.J.; Komisarenko, M.; McAlpine, K.; Alibhai, S.M.H.; Finelli, A.; A Matched Analysis of Active Surveillance Versus Nephrectomy for T1a Small Renal Masses; European Urology Oncology; 2023; vol. 6 (no. 5); 535-539

Study details

Study type	Retrospective cohort study
Study location	Canada
Study setting	Hospital setting. Data obtained from an institutional database (Princess Margaret Cancer Centre, Toronto, Canada). Single institution.
Study dates	2000 to 2020
Sources of funding	None
Inclusion criteria	Patients with a small renal mass (≤4 cm, T1a solid renal mass) Aged 55-75 years
Exclusion criteria	Symptomatic lesions Personal history of cancer Family history of renal cancer Undergoing radiofrequency ablation
Intervention(s)	Active surveillance
Comparator	Nephrectomy (135 partial and 37 radical nephrectomy)
Outcome measures	Survival
Number of participants	N = 377 Active surveillance: 205 (54.4%) Nephrectomy: 172 (45.6%) After exact matching: N = 110 Active surveillance: 53 (48.2%) Nephrectomy: 57 (51.8%)
Duration of follow-up	Median follow-up for patients alive at the end of follow-up was 4.6 years in the active surveillance group and 4.9 years in the nephrectomy group.
Loss to follow-up	Not reported
Methods of analysis	Patients undergoing active surveillance or nephrectomy were exactly matched for age, sex, Eastern Cooperative Oncology Group (ECOG) performance status score, biopsy status, and histology. The average

	treatment effect for the treated (ATT) was estimated via Cox proportional-hazards models using matching weights and robust standard errors.
Additional comments	Additional comments: The authors acknowledged several limitations of their study. Firstly, it was a retrospective study with a small sample size, which may introduce selection bias despite the matching process. While matching aimed to address important confounders, it cannot completely account for unmeasured and unknown confounders. Secondly, due to the low number of events, the authors could not use tumour size as a matching parameter in their model. However, they noted that size was not significantly associated with mortality or event-free survival on univariable analyses and did not change the estimates for these outcomes between active surveillance and nephrectomy groups. Thirdly, the authors were limited to matching on the clinically available ECOG score for comorbidity. Nevertheless, based on data from clinical notes, the two groups were generally similar regarding the most relevant comorbidities (hypertension, diabetes, and heart disease). The study excluded patients with a family history of renal cell carcinoma or a personal history of cancer; therefore, caution must be used in extrapolating the results to these patients. The group after exact matching was notably different from the original cohort, representing a subset of selected patients. However, the authors believe that the selection obtained via matching is appropriate as it excludes patients who are unlikely to be equally eligible for both management strategies, and the resulting matched set is probably less biased than the full cohort. A strength of the study is that the characteristics of the matched cohort closely approximate the treatment arms in contemporary studies, suggesting that active surveillance is a suitable management strategy in routine clinical practice for the younger, healthier patient population equally eligible for active surveillance or primary intervention. The study did not report on several important outcomes, such as recurrence, intraoperative and postoperative severe adverse events, renal functional impairment, cardiovascular events, duration of hospital stay, and quality of life. Inclusion of these outcomes would have provided a more comprehensive assessment of the comparative effectiveness and safety of active surveillance versus nephrectomy. In conclusion, while this study provides valuable insights into the comparative outcomes of active surveillance and nephrectomy in a well-matched cohort of patients with small renal masses, larger prospective studies with longer follow-up are needed to obtain more precise estimates of the outcomes and to confirm these findings. The study reported 5-year overall survival and event-free survival probabilities for both groups. No other follow-up timepoints were specified for the reported outcomes.

Study arms

Active surveillance (N = 53)

Nephrectomy (N = 57)

Characteristics

Arm-level characteristics

Characteristic	Active surveillance (N = 53)	Nephrectomy (N = 57)
% Female No of events	n = 12 ; % = 23	n = 13 ; % = 23
Age Mean (SD)	64.3 (5.4)	64.3 (5.3)
Treatment/surgery technique used: Partial nephrectomy Nominal	NA	135
Treatment/surgery technique used: Radical nephrectomy Nominal	NA	37
Primary RCC type: clear cell No of events	n = 21 ; % = 39	n = 22 ; % = 39
Primary RCC type: papillary No of events	n = 3 ; % = 5.3	n = 3 ; % = 5.3
Primary RCC type: No histology No of events	n = 30 ; % = 56	n = 32 ; % = 56
Performance status at baseline: Eastern Cooperative Oncology Group (ECOG) performance status score 0 No of events	n = 40 ; % = 75	n = 43 ; % = 75
Performance status at baseline: Eastern Cooperative Oncology Group (ECOG) performance status score 1 No of events	n = 2 ; % = 3.5	n = 2 ; % = 3.5
Performance status at baseline: Eastern Cooperative Oncology Group (ECOG) performance status score Unknown/missing No of events	n = 11 ; % = 21	n = 12 ; % = 21

Outcomes

Study timepoints

- See below (The study reported a median follow-up of 4.6 years in the active surveillance group and 4.9 years in the nephrectomy group for patients alive at the end of follow-up. The authors did not specify the exact timepoints for data extraction. However, they reported 5-year overall survival and event-free survival probabilities for both groups. No outcomes were reported for follow-up periods between 0-5 years or 5-10 years.)

Survival outcomes

Outcome	Active surveillance versus Nephrectomy, See below, N2 = 53, N1 = 57
Overall mortality, follow-up timepoint is not specified Hazard ratio/95% CI	0.83 (0.13 to 5.32)

Overall mortality, follow-up timepoint is not specified - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Survival outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(The study has a moderate risk of bias due to potential residual confounding, lack of information on important co-interventions, and the retrospective nature of the study. The risk of bias due to selection of participants, classification of interventions, and selection of the reported result is low. However, there is insufficient information to assess the risk of bias due to missing data.)*
Overall bias	Directness	Directly applicable

de Angelis, 2024

Bibliographic Reference	de Angelis, M.; Morra, S.; Scheipner, L.; Siech, C.; Jannello, L.M.I.; Baudo, A.; Goyal, J.A.; Tian, Z.; Longo, N.; Ahyai, S.; de Cobelli, O.; Chun, F.K.H.; Saad, F.; Shariat, S.F.; Carmignani, L.; Montorsi, F.; Briganti, A.; Karakiewicz, P.I.; Cancer-specific mortality in non-metastatic T1a renal cell carcinoma treated with radiotherapy versus partial nephrectomy; World journal of urology; 2024; vol. 42 (no. 1); 193

Study details

Study type	Retrospective cohort study
Study location	United States of America
Study setting	Data were examined from the Surveillance, Epidemiology, and End Results database (SEER)
Study dates	2004 – 2020
Sources of funding	This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors
Inclusion criteria	Patients older than 18 years, with T1aN0M0 renal cell carcinoma who underwent either partial nephrectomy or exclusive radiotherapy (external beam radiotherapy)
Exclusion criteria	Patients with metastatic disease Patients with unknown histological subtype Patients with unknown vital status information Patients with unknown and other treatment Patients with unknown tumour size as well as all autopsy or death certificate cases
Intervention(s)	Radiotherapy
Comparator	Partial nephrectomy
Outcome measures	Survival
Number of participants	N = 184 Radiotherapy = 92 Partial nephrectomy = 92
Duration of follow-up	Not reported

Loss to follow-up	Not reported
Methods of analysis	To optimise the comparison between radiotherapy and partial nephrectomy it relied on 1:1 propensity score matching, according to the nearest neighbour. Specifically, propensity score matching applied to age, tumour size, and histology. Furthermore, multivariable competing risks regression (CRR) models to test the effect of radiotherapy versus partial nephrectomy on cancer-specific mortality.

Study arms

Radiotherapy (N = 92)

Partial nephrectomy (N = 92)

Characteristics

Arm-level characteristics

Characteristic	Radiotherapy (N = 92)	Partial nephrectomy (N = 92)
Age Median (IQR)	72 (66 to 79)	72 (66 to 79)
Primary RCC type - Clear-cell No of events	n = 47 ; % = 51	n = 47 ; % = 51
Primary RCC type - Non clear-cell No of events	n = 45 ; % = 49	n = 45 ; % = 49
Tumour size Median (IQR)	28 (24 to 35)	28 (24 to 35)

Outcomes

Survival

Outcome	Radiotherapy versus Partial nephrectomy, , N2 = 92, N1 = 92
Cancer-specific mortality Hazard ratio/95% CI	4.3 (1.7 to 10.5)

Cancer-specific mortality - Polarity - Lower values are better

Critical appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The outcomes were not adjusted for all important confounder factors)*
Overall bias	Directness	Directly applicable

Duus, 2023

Bibliographic Reference	Duus, L.A.; Junker, T.; Brandt Rasmussen, B.S.; Vilstrup, M.H.; Lund, L.; Pedersen, M.; Graumann, O.; Renal functional outcomes after robot-assisted partial nephrectomy and percutaneous cryoablation of clinical T1 renal cell carcinoma - A prospective study; Journal of Clinical Imaging Science; 2023; vol. 13 (no. 1)

Study details

Study type	Prospective cohort study
Study location	Denmark
Study setting	Hospital setting. Single-centre study at Odense University Hospital. Data obtained from picture archiving and communication systems (PACS) and electronic patient records.
Study dates	June 2019 to January 2021

Sources of funding	Duus LA: Grant for participation in international conference: Boehringer-Ingelheim. Graumann, O: Speaker honoraria, Advisory Board member, and Research grant: Boston Scientific. Junker T: Research grant: Boston Scientific.
Inclusion criteria	Patients with clinical stage T1 (cT1) renal cell carcinoma (RCC) treated with RAPN or PCA at Odense University Hospital Patients from the Region of Southern Denmark
Exclusion criteria	Under 18 years old at the time of treatment Presence of a benign tumour Conversion of robot-assisted partial nephrectomy (RAPN) to open surgery Conversion of RAPN to radical nephrectomy Salvage treatment within 6 months after primary treatment Missing baseline examinations Multiple treatments in cases of multiple tumours
Intervention(s)	Robot-assisted partial nephrectomy (RAPN) performed under general anaesthesia using the four-armed Da Vinci Si robotic surgical system. The renal artery was clamped, and warm ischaemia time was registered. The tumour was excised with cold scissors leaving a healthy tissue margin.
Comparator	Percutaneous cryoablation (PCA) performed under CT-fluoroscopy guidance using an argon-based cryoablation system with a double-freeze-thaw cycle of 10 min freeze and 8 min thaw. Patients were sedated using intravenous dexmedetomidine and remifentanil and local anaesthesia with lidocaine and bupivacaine.
Outcome measures	Renal functional impairment
Number of participants	Total number of participants: N = 56 Robot-assisted partial nephrectomy (RAPN): 18 (32.1%) Percutaneous cryoablation (PCA): 38 (67.9%)
Duration of follow-up	6 months
Loss to follow-up	Not reported
Methods of analysis	Continuous variables were described as median with interquartile range and categorical variables as frequencies. Renal functional outcome was calculated with a paired t-test to evaluate mean differences between baseline and 6 months post-treatment for normally distributed continuous variables. The Wilcoxon signed-rank test was used for categorical and ordinal variables and non-normal continuous variables. The primary outcome was assessed with a linear mixed effect model with patients as random effects and renal volume, eGFR or DTPA-GFR, and visits (baseline and 6 months) as fixed effects. No propensity score matching was reported.
Additional comments	The authors acknowledged several limitations of this study. As a single-centre study with no randomisation, it is sensitive to selection bias in the

	recruitment process. The majority of patients did not wish to participate in the study, which could be explained by the fact that treatment was performed in a fast-track setting at a highly specialised hospital with a large uptake area. Patients had to attend the hospital for baseline diethylenetriamine pentaacetic acid (DTPA) examination in the short time frame from diagnosis to treatment. Furthermore, the inclusion period of the study was during the COVID-19 pandemic, and research examinations were temporarily shut down. The small sample size introduces a degree of uncertainty to its statistical findings and the conclusions based on them. Moreover, because patients were recruited from a large geographical area, many refused to participate due to supplementary examinations requiring an additional hospital visit within the short period between diagnosis and treatment. Finally, its use of a single post-treatment renal function measurement will miss longitudinal fluctuations in changes in renal function. The study has some strengths, including its prospective design and the use of multiple renal function parameters to assess outcomes. However, the lack of randomisation, small sample size, and potential for selection bias are significant limitations that may impact the generalisability of the findings. The study also did not report on several important outcomes, such as recurrence, survival, adverse events, cardiovascular events, duration of hospital stay, and quality of life. The absence of these outcomes limits the comprehensive evaluation of the two treatment approaches. Additionally, the study only had a 6-month follow-up period, which may not be sufficient to capture long-term changes in renal function or other potential complications. Given these limitations, the findings of this study should be interpreted with caution, and further research with larger, randomised cohorts and longer follow-up periods may be necessary to confirm the results and provide more robust evidence.

Study arms

Robot-assisted partial nephrectomy (N = 18)

Percutaneous cryoablation (N = 38)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 18)	Percutaneous cryoablation (N = 38)
% Female No of events	n = 5 ; % = 27.8	n = 11 ; % = 29
Age Median (IQR)	57.5 (53 to 69)	68.5 (61 to 76)
Treatment/surgery technique used: Force cryoprobes No of events	n = NA	n = 26 ; % = 68.4
Treatment/surgery technique used: Rod cryoprobes No of events	n = NA	n = 2 ; % = 5.3
Treatment/surgery technique used: Pearl cryoprobes No of events	n = NA	n = 9 ; % = 23.7
Treatment/surgery technique used: Mix cryoprobes No of events	n = NA	n = 1 ; % = 2.6
Clinical tumour stage: cT1a No of events	n = 12 ; % = 66.7	n = 34 ; % = 87.2
Clinical tumour stage: cT1b No of events	n = 6 ; % = 33.3	n = 5 ; % = 12.8
Pathological tumour stage: pT1a No of events	n = 16 ; % = 88.9	n = NA
Pathological tumour stage: pT1b No of events	n = 1 ; % = 5.6	n = NA
Pathological tumour stage: pT2a No of events	n = 1 ; % = 5.6	n = NA
Tumour size (cm) Median (IQR)	3.6 (2.5 to 4.3)	3 (2.5 to 3.9)

Characteristic	Robot-assisted partial nephrectomy (N = 18)	Percutaneous cryoablation (N = 38)
Primary RCC type: Unclassified RCC No of events	n = 0 ; % = 0	n = 2 ; % = 5.1
Primary RCC type: clear cell No of events	n = 12 ; % = 66.7	n = 25 ; % = 64.1
Primary RCC type: papillary No of events	n = 4 ; % = 22.2	n = 10 ; % = 25.6
Primary RCC type: chromophobe No of events	n = 1 ; % = 5.6	n = 1 ; % = 2.6
Primary RCC type: Multilocular cystic clear cell neoplasm No of events	n = 0 ; % = 0	n = 1 ; % = 2.6
Primary RCC type: Epithelioid angiomyolipoma No of events	n = 1 ; % = 5.6	n = 0 ; % = 0
Baseline renal function: eGFR CKD I No of events	n = 10 ; % = 55.6	n = 13 ; % = 34.2
Baseline renal function: eGFR CKD II No of events	n = 8 ; % = 44.4	n = 18 ; % = 47.4
Baseline renal function: eGFR CKD IIIa No of events	n = 0 ; % = 0	n = 2 ; % = 5.3
Baseline renal function: eGFR CKD IIIb No of events	n = 0 ; % = 0	n = 2 ; % = 5.3
Baseline renal function: eGFR CKD IV No of events	n = 0 ; % = 0	n = 3 ; % = 7.9
Baseline renal function: DTPA-GFR CKD I No of events	n = 9 ; % = 64.3	n = 8 ; % = 29.6
Baseline renal function: DTPA-GFR CKD II No of events	n = 5 ; % = 35.7	n = 12 ; % = 44.4
Baseline renal function: DTPA-GFR CKD IIIa No of events	n = 0 ; % = 0	n = 4 ; % = 14.8
Baseline renal function: DTPA-GFR CKD IIIb No of events	n = 0 ; % = 0	n = 2 ; % = 7.4
Baseline renal function: DTPA-GFR CKD IV No of events	n = 0 ; % = 0	n = 1 ; % = 3.7
Performance status at baseline: American Society of Anesthesiologists physical status classification system 1	n = 2 ; % = 11.1	n = 1 ; % = 2.6

Characteristic	Robot-assisted partial nephrectomy (N = 18)	Percutaneous cryoablation (N = 38)
No of events		
Performance status at baseline: American Society of Anesthesiologists physical status classification system 2 No of events	n = 10 ; % = 55.6	n = 18 ; % = 47.4
Performance status at baseline: American Society of Anesthesiologists physical status classification system 3 No of events	n = 6 ; % = 33.3	n = 19 ; % = 50
Performance status at baseline: American Society of Anesthesiologists physical status classification system 4 No of events	n = 0 ; % = 0	n = 0 ; % = 0

Outcomes

Study timepoints

- 6 month

Kidney function

Outcome	Robot-assisted partial nephrectomy, 6 month, N = 18	Percutaneous cryoablation, 6 month, N = 38
Change in eGFR, mL/min/1.73 m², 6 months Mean (95% CI)	-6.5 (-10.5 to -2.4)	-5.5 (-8.7 to -2.3)

Change in eGFR, mL/min/1.73 m², 6 months - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Change in eGFR

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as it is a non-randomised study with potential differences in baseline characteristics between the intervention groups. The authors did not use an appropriate analysis method to control for all important confounding domains. There is also a serious risk of bias due to missing data, as the study had missing data for some outcomes, and participants were likely excluded due to missing data on other variables needed for the analysis. The risk of bias in the selection of participants into the study and measurement of outcomes is moderate, while there is no information to assess the risk of bias due to deviations from intended interventions and selection of the reported result.)*
Overall bias	Directness	Directly applicable

Emara, 2014

Bibliographic Reference	Emara, Amr M; Kommu, Sashi S; Hindley, Richard G; Barber, Neil J; Robot-assisted partial nephrectomy versus laparoscopic cryoablation for the small renal mass: redefining the minimally invasive 'gold standard'.; BJU international; 2014; vol. 113 (no. 1); 92-9

Study details

Study type	Retrospective cohort study
Study location	UK
Study setting	Hospital. Single institution.
Study dates	2008 to 2012 (cryoablation arm recruited between 2008 and 2012; partial nephrectomy arm recruited between 2010 and 2012)
Sources of funding	Not reported. No conflicts of interest declared.
Inclusion criteria	Patients diagnosed with small renal masses (T1) and treated using the relevant interventions.
Exclusion criteria	Not reported

Intervention(s)	Cryoablation. Laparoscopic. All patients (except those with cystic lesions) had pretreatment, intra-operative, needle core biopsies taken through one of the laparoscopic ports. Thermal sensors were usually carefully positioned after the cryoneedles, one at the centre of the tumour and the other at the periphery; thereafter, two freeze–thaw cycles were applied using argon-helium gases with each cycle lasting 20 min.
Comparator	Partial nephrectomy (PN) Robbot-assisted.
Outcome measures	Postoperative severe adverse events Duration of hospital stay
Number of participants	N=104 Cryoablation: 56 PN: 47
Duration of follow-up	Months: mean, standard error Cryoablation: 25.59 (0.958) PN: 32.78 (1.787)
Loss to follow-up	Not reported
Methods of analysis	An unpaired t-test was used for comparing the data on patients' age, tumour size, R.E.N.A.L nephrometry score and follow-up times, intra-operative time, intra-operative bleeding, and postoperative hospital stay. No adjustment for confounders or matching undertaken.
Additional comments	Renal functional outcomes and recurrence not extracted as these outcomes are reported in included systematic reviews (Patel 2017 and Xu 2019). Patients were not recruited at the same time (see study dates), as robot-assisted partial nephrectomy only became part of practice in 2010. Follow-up is significantly longer for the PN group. The longer mean hospital stay in the cryoablation group was affected by the long hospital stay of one patient who had postoperative pneumonia. Complications outcomes cover all complications - there were no complications at grade 3a, 4 or 5.

Study arms

Cryoablation (N = 56)

Laparoscopic

Partial nephrectomy (N = 47)

Robot-assisted

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 56)	Partial nephrectomy (N = 47)
% Female No of events	n = 11 ; % = 19.6	n = 16 ; % = 34
Age Custom value	mean 69.75, range 42-90	mean 60.5, range 38-80
Tumour size mm Mean (SE)	25.59 (0.96)	32.78 (1.79)
Benign tumours No of events	n = 9 ; % = 16	n = 14 ; % = 30
Primary RCC type - Clear cell No of events	n = 27 ; % = 48	n = 19 ; % = 40
Primary RCC type - Papillary No of events	n = 7 ; % = 13	n = 9 ; % = 19
Primary RCC type - Chromophobe No of events	n = 5 ; % = 9	n = 3 ; % = 6
Primary RCC type - other/inconclusive/no results No of events	n = 17 ; % = 30	n = 16 ; % = 34

Outcomes

Complications

Outcome	Cryoablation, , N = 56	Partial nephrectomy, , N = 47
Clavien-Dindo grade 1 Nominal	3	2
Clavien-Dindo grade 2	1	0

Outcome	Cryoablation, , N = 56	Partial nephrectomy, , N = 47
Nominal		
Clavien-Dindo grade 3b Nominal	1	2

Duration of hospital stay

Outcome	Cryoablation, , N = 56	Partial nephrectomy, , N = 47
Duration of hospital stay Mean (SD)	1.68 (0.18)	1.38 (0.12)

Duration of hospital stay - Polarity - Lower values are better

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All complication and duration of stay outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders or matching undertaken. Limited information about missing data or inclusion criteria. No protocol identified so unable to fully assess bias in selection of reported result.)*
Overall bias	Directness	Directly applicable

Fraisse, 2019

Bibliographic Reference	Fraisse, Guillaume; Colleter, Loic; Peyronnet, Benoit; Khene, Zine-Eddine; Mandoorah, Qusay; Soorojebally, Yanish; Bourgi, Ali; De La Taille, Alexandre; Roupret, Morgan; De Kerviler, Eric; Desgrandchamps, Francois; Bensalah, Karim; Masson-Lecomte, Alexandra; Peri-operative and local control outcomes of robot-assisted partial nephrectomy versus percutaneous cryoablation for renal masses: comparison after matching on radiological stage and renal score.; BJU international; 2019; vol. 123 (no. 4); 632-638

Study details

Study type	Retrospective cohort study

Study location	France
Study setting	Hospital setting
Study dates	Between 2009 and 2016
Sources of funding	Not reported
Inclusion criteria	Patients with T1 renal tumour
Exclusion criteria	Patients lacking radiological follow-up Patients with missing information regarding RENAL nephrometry score or histological data Patients with a history of contralateral kidney tumour Patients with other metastatic cancers
Intervention(s)	Robot-assisted partial nephrectomy (RAPN)
Comparator	Percutaneous cryoablation (PCA)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: 354 RAPN: 177 PCA: 177
Duration of follow-up	After matching, the median follow-up was 39.03 months for the RAPN group and 62.59 months for the PCA group.
Loss to follow-up	After recurrence in the PCA group, four were lost to follow-up.
Methods of analysis	To reduce differences between the two groups attributable to selection bias and confounding was performed a 1:1 matched analysis on radiological tumour stage and RENAL nephrometry score. Survival curves were modelled using Kaplan–Meier analysis and compared using a log-rank test. Cox regression analysis, adjusted for standard clinicopathological variables, was performed to identify factors associated with oncological outcomes.

Study arms

Robot-assisted partial nephrectomy (N = 177)

Percutaneous cryoablation (N = 177)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 177)	Percutaneous cryoablation (N = 177)
% Female No of events	n = 49 ; % = 27.7	n = 57 ; % = 32.2
Age Mean (SD)	59.89 (10.75)	69.94 (9.38)
T1a No of events	n = 170 ; % = 96	n = 170 ; % = 96
T1b No of events	n = 7 ; % = 4	n = 7 ; % = 4
Tumour size, mm Mean (SD)	27.65 (9.19)	25.94 (8.55)

Outcomes

Survival

Outcome	Robot-assisted partial nephrectomy, , N = 177	Percutaneous cryoablation, , N = 177
Cancer-specific mortality No of events	n = 1 ; % = 0.6	n = 0 ; % = 0

Cancer-specific mortality - Polarity - Lower values are better

Survival

Outcome	Percutaneous cryoablation versus Robot-assisted partial nephrectomy, , N2 = 177, N1 = 177
local recurrence	2.99 (1.02 to 8.74)

Outcome	Percutaneous cryoablation versus Robot-assisted partial nephrectomy, , N2 = 177, N1 = 177
Hazard ratio/95% CI	

local recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Grant, 2020

Bibliographic Reference	Grant, S.R.; Lei, X.; Hess, K.R.; Smith, G.L.; Matin, S.F.; Wood, C.G.; Nguyen, Q.; Frank, S.J.; Anscher, M.S.; Smith, B.D.; Karam, J.A.; Tang, C.; Stereotactic Body Radiation Therapy for the Definitive Treatment of Early Stage Kidney Cancer: A Survival Comparison With Surgery, Tumor Ablation, and Observation; Advances in Radiation Oncology; 2020; vol. 5 (no. 3); 495-502

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	From 2004 to 2014
Sources of funding	Sources of support: none
Inclusion criteria	Patients with T1N0M0 kidney cancer (7 cm or less with no nodal or distant metastases)

Exclusion criteria	Metastatic disease at diagnosis Patients with nodal disease Patient with stage T2-T4 Patients with benign or rare histology, bilateral disease, or involving renal pelvis Patients with missing or inadequate survival follow-up data Patients who received systemic therapy Patients who receive conventionally fractionated radiation or non-standard procedures
Intervention(s)	Surgery (including partial and total nephrectomy)
Comparator	Tumour ablation (including cryoablation and thermal ablation), stereotactic body radiation therapy (SBRT), or observation
Outcome measures	Survival
Number of participants	Total number of participants: 200,839 Surgery: 165,298 Tumour ablation: 17,196 SBRT (BED <100): 42 SBRT (BED ≥100): 62 Observation: 18,241
Duration of follow-up	Surgery (median: 57 months), tumour ablation (median: 50 months), SBRT (median: 37 months), and observed (median: 19 months)
Loss to follow-up	Not reported
Methods of analysis	A propensity score was generated by multinomial logistic regression, and a Cox proportional hazard model was fit to determine association between treatment group and overall survival (OS) with propensity score adjustments for patient, demographic, and treatment characteristics, including age at diagnosis, race, sex, year of diagnosis, Charlson-Deyo comorbidity score, tumour size, laterality, histology, grade, insurance plan, rurality, median income, education, academic hospital, and distance travelled for treatment.

Study arms

Surgery (N = 165298)

Tumour ablation (N = 17196)

SBRT, BED <100 (N = 42)

SBRT, BED > 100 (N = 62)

Observation (N = 18241)

SBRT (N = 104)

Characteristics

Arm-level characteristics

Characteristic	Surgery (N = 165298)	Tumour ablation (N = 17196)	SBRT, BED <100 (N = 42)	Observation (N = 18241)
% Female No of events	n = 65644 ; % = 39.7	n = 6411 ; % = 37.3	n = 37 ; % = 35.6	n = 7655 ; % = 42
Age Median (IQR)	61 (*empty data* to *empty data*)	69 (*empty data* to *empty data*)	75 (*empty data* to *empty data*)	74 (*empty data* to *empty data*)
T1a No of events	n = 110014 ; % = 66.6	n = 15188 ; % = 88.3	n = 63 ; % = 60.6	n = 11837 ; % = 64.9
T1b No of events	n = 55284 ; % = 33.4	n = 2008 ; % = 11.7	n = 41 ; % = 39.4	n = 6404 ; % = 35.1
Clear cell carcinoma No of events	n = 92157 ; % = 55.8	n = 6779 ; % = 39.4	n = 37 ; % = 35.6	n = 2693 ; % = 14.8
Papillary carcinoma No of events	n = 26457 ; % = 16	n = 2465 ; % = 14.3	n = 13 ; % = 12.5	n = 1088 ; % = 6
Renal cell carcinoma NOS No of events	n = 46382 ; % = 28.1	n = 7545 ; % = 43.9	n = 47 ; % = 45.2	n = 12792 ; % = 70.1
Carcinoma NOS No of events	n = 302 ; % = 0.2	n = 407 ; % = 2.4	n = 7 ; % = 6.7	n = 1668 ; % = 9.1

Outcomes

Survival

Outcome	SBRT, BED <100 versus Observation, , N2 = 42, N1 = 18241	Surgery versus Observation, , N2 = 165298, N1 = 18241	Tumour ablation versus Observation, , N2 = 17196, N1 = 18241	SBRT, BED > 100 versus Observation, , N2 = 62, N1 = 18241	SBRT versus Observation, , N2 = 104, N1 = 18241
Overall survival Hazard ratio/95% CI	0.9 (0.58 to 1.4)	0.25 (0.24 to 0.26)	0.36 (0.35 to 0.38)	0.34 (0.19 to 0.6)	0.56 (0.39 to 0.79)

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Overall survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Appropriate adjustments made, sensitivity analysis carried out)*
Overall bias	Directness	Indirectly Applicable *(Observation considered in place of active surveillance. Will need to consider downgrading at GRADE depending on other evidence identified)*

Haber, 2012

Bibliographic Reference	Haber, Georges-Pascal; Lee, Michael C; Crouzet, Sebastien; Kamoi, Kazumi; Gill, Inderbir S; Tumour in solitary kidney: laparoscopic partial nephrectomy versus laparoscopic cryoablation.; BJU international; 2012; vol. 109 (no. 1); 118-24

Study details

Study type	Retrospective cohort study
Study location	US

Study setting	Hospital. Single institution.
Study dates	February 1998 to September 2008
Sources of funding	No financial support reported. Conflict of interest: none declared
Inclusion criteria	Radiologically-suspicious enhancing mass Mass 7cm or less (clinical stage 1)
Exclusion criteria	Not reported
Intervention(s)	Partial nephrectomy (PN) Laparoscopic. Surgical treatment at the discretion of the surgeon.
Comparator	Cryoablation. Laparoscopic. Performed under real-time laparoscopic ultrasound guidance. Intra-operative core needle biopsies of the tumour were obtained immediately before cryoablation.
Outcome measures	Recurrence Survival Duration of hospital stay
Number of participants	N=78 PN: 48 Cryoablation: 30
Duration of follow-up	Mean follow-up PN: 42.7 months Cryoablation: 60.2 months
Loss to follow-up	Not reported
Methods of analysis	No adjustments for confounders or matching. Mean ± SD is used to summarize continuous variables. Frequencies and proportions are used to summarize categorical variables. Statistical comparisons of continuous variables were made using the student t-test.
Additional comments	Limitations: retrospective design, lack of adjustments for confounders (difference between frequency of ipsilateral renal surgery - cryoablation had significantly more than PN arm). Percentages presented in the paper converted into events by NICE staff.

Study arms

Partial nephrectomy (N = 48)

Laparoscopic

Cryoablation (N = 30)

Laparoscopic

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 48)	Cryoablation (N = 30)
% Female No of events	n = 23 ; % = 47.9	n = 8 ; % = 26.7
Age Mean (SD)	60.6 (13.7)	60.9 (11.4)
Tumour size cm Mean (SD)	3.2 (1.33)	2.6 (1.08)
Pathological tumour stage - pT1a No of events	n = 38 ; % = 79	n = 24 ; % = 80
Pathological tumour stage - pT1b No of events	n = 9 ; % = 19	n = 6 ; % = 20
Pathological tumour stage - pT2 No of events	n = 1 ; % = 2	n = 0 ; % = 0

Outcomes

Duration of hospital stay

Outcome	Partial nephrectomy, , N = 48	Cryoablation, , N = 30
Duration of hospital stay Mean (SD)	4.6 (2.9)	2.4 (2.2)

Duration of hospital stay - Polarity - Lower values are better

Recurrence and survival

Outcome	Partial nephrectomy, , N = 48	Cryoablation, , N = 30
Overall survival - 5 years No of events	n = 45 ; % = 93.75	n = 26 ; % = 86.66
Overall survival - 7 years No of events	n = 41 ; % = 85.42	n = 25 ; % = 83.33
Cancer-specific survival - 5 years No of events	n = 48 ; % = 100	n = 26 ; % = 86.66
Cancer-specific survival - 7 years No of events	n = 48 ; % = 100	n = 25 ; % = 83.33
local recurrence No of events	n = 0 ; % = 0	n = 4 ; % = 13.3
Metastases No of events	n = 1 ; % = 2.1	n = 4 ; % = 3.3

Metastases - Polarity - Lower values are better

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Overall survival and cancer-specific survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, and protocol not identified)*
Overall bias	Directness	Directly applicable

Recurrence (local and metastatic)

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, and protocol not identified)*
Overall bias	Directness	Directly applicable

Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, potential for lack of blinding to affect discharge decisions, and protocol not identified)*
Overall bias	Directness	Directly applicable

Jasinski, 2024

Bibliographic Reference	Jasinski, Milosz; Wisniewski, Przemyslaw; Bielinska, Marta; Siekiera, Jerzy; Kamecki, Krzysztof; Salagierski, Maciej; Perioperative and Oncological Outcomes of Percutaneous Radiofrequency Ablation versus Partial Nephrectomy for cT1a Renal Cancers: A Retrospective Study on Groups with Similar Clinical Characteristics.; Cancers; 2024; vol. 16 (no. 8)

Study details

Study type	Retrospective cohort study
Study location	Poland
Study setting	Hospital
Study dates	Between August 2016 and February 2022
Sources of funding	This study received no external funding
Inclusion criteria	Patients age under 67 Patients with functional contralateral kidney, no significant comorbidities that would be a contraindication to partial nephrectomy Patients with exophytic lesions and one of the following: not larger than 30 mm and located in the central part of the kidney; not larger than 30 mm and located in the lower pole of the kidney; not larger than 25 mm
Exclusion criteria	Patients without histopathology confirmed renal cell carcinoma Patients with missing biopsy data, with inconclusive biopsy, lost from follow-up (no follow-up contrast-enhanced imaging available), or with lacking diagnostic imaging data
Intervention(s)	Partial nephrectomy (laparoscopic or open)
Comparator	Percutaneous radiofrequency ablation

Outcome measures	Duration of hospital stay
Number of participants	N = 85 Partial nephrectomy (laparoscopic or open) = 44 Percutaneous radiofrequency ablation = 41
Duration of follow-up	The mean follow-up time was 29 months, and the median was 28 months (range 3–71 months)
Loss to follow-up	Not reported
Methods of analysis	Differences between variables were assessed using Mann–Whitney U-test. The χ-square test was employed to evaluate differences in qualitative variables
Additional comments	

Study arms

Partial nephrectomy (laparoscopic or open) (N = 44)

Percutaneous radiofrequency ablation (N = 41)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (laparoscopic or open) (N = 44)	Percutaneous radiofrequency ablation (N = 41)
Age Mean (SD)	55.2 (9)	56.3 (9.8)

Outcomes

Hospital stay (days)

Outcome	Partial nephrectomy (laparoscopic or open), , N = 44	Percutaneous radiofrequency ablation, , N = 41
Hospital stay (days) Mean (SD)	5.04 (0.67)	2.12 (0.94)

Hospital stay (days) - Polarity - Lower values are better

Critical appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Hospital stay (days)

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The outcomes were not adjusted for all important confounder factors)*
Overall bias	Directness	Directly applicable

Junker, 2022

Bibliographic Reference	Junker, Theresa; Duus, Louise; Rasmussen, Benjamin S B; Azawi, Nessn; Lund, Lars; Norgaard, Birgitte; Gerke, Oke; Graumann, Ole; Partial Nephrectomy versus Percutaneous Cryoablation of Small Renal Cell Carcinomas: A Comparison of Adverse Events in a Prospective Multicenter Cohort Study.; Journal of vascular and interventional radiology : JVIR; 2022; vol. 33 (no. 11); 1375-1383e7

Study details

Trial registration number and/or trial name	NCT04040530
Study type	Prospective cohort study

Study location	Denmark
Study setting	Hospital setting, two university hospitals: Odense University Hospital and Zealand University Hospital. Data collection was prospective and protocol-driven.
Study dates	June 2019 to February 2021
Sources of funding	Not provided
Inclusion criteria	Patients aged ≥18 years Histologically verified primary renal cell carcinoma stage cT1N0M0 Treated with partial nephrectomy or cryoablation
Exclusion criteria	Metastatic disease at the time of diagnosis Conversion from partial to radical nephrectomy Salvage procedures
Intervention(s)	Percutaneous cryoablation performed by two radiologists under computed tomography guidance. Double 10-minute freeze with an 8-minute thaw period in between was used. Expanding ice ball covered the entire tumour with a minimum 5-mm margin.
Comparator	Partial nephrectomy performed by six experienced urologists. Both robot-assisted partial nephrectomy and open partial nephrectomy were included. Arterial clamping or off-clamp techniques were used, and endoscopic ultrasound was used to identify tumour margins.
Outcome measures	Intraoperative severe adverse events Postoperative severe adverse events Duration of hospital stay
Number of participants	Total number of participants: N = 190 Cryoablation: 104 (54.7%) Partial nephrectomy: 86 (45.3%)
Duration of follow-up	All patients had a follow-up period of 90 days.
Loss to follow-up	Not reported
Methods of analysis	Univariate and multivariable logistic regression analyses were performed, adjusted for age and sex. No propensity score matching was described.
Additional comments	The authors acknowledged several limitations of this study. The nonrandomised design contributed to the risk of selection bias, considering the heterogeneity of comorbidity, age, and performance status across treatment groups. The sample size was relatively small, reducing the number of events in some outcome variables and resulting in wide confidence intervals that affected precision and generalisability. Furthermore, cryoablation was performed at a single site, which may limit external validity. However, the study has several strengths. The data were prospectively collected and driven by a predefined protocol. The cohort represents

	consecutively treated patients from two highly specialised institutions, covering one-third of the population in Denmark treated with nephron-sparing procedures for renal cell carcinoma. All patients were discussed at a multidisciplinary team conference, and treatment decisions were reached based on shared decision-making, ensuring a solid foundation for the decision-making process. The study did not report on several important outcomes, such as recurrence, survival, renal functional impairment, cardiovascular events, and quality of life. These outcomes are crucial for assessing the long-term effectiveness and safety of the interventions. The absence of these data may warrant downgrading the certainty of evidence for this study. Another aspect to consider is the short follow-up period of 90 days. While this may be sufficient for capturing short-term complications, it does not allow for the assessment of long-term outcomes. Future studies with longer follow-up periods are needed to better understand the comparative effectiveness and safety of cryoablation and partial nephrectomy.

Study arms

Cryoablation (N = 104)

Partial nephrectomy (N = 86)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 104)	Partial nephrectomy (N = 86)
% Female No of events	n = 39 ; % = 37	n = 32 ; % = 37
Age Median (IQR)	72 (66 to 78)	64 (54 to 71)
TNM staging: cT1a No of events	n = 91 ; % = 88	n = 54 ; % = 63
TNM staging: cT1b No of events	n = 13 ; % = 12	n = 32 ; % = 37
Clear cell adenocarcinoma No of events	n = 74 ; % = 82	n = 62 ; % = 85
Papillary adenocarcinoma No of events	n = 9 ; % = 10	n = 10 ; % = 14
Chromophobe adenocarcinoma No of events	n = 5 ; % = 6	n = 1 ; % = 1

Characteristic	Cryoablation (N = 104)	Partial nephrectomy (N = 86)
Oncocytoma No of events	n = 2 ; % = 2	n = 0 ; % = 0
Charlson comorbidity index Median (IQR)	5 (4 to 6)	4 (2 to 5)
ASA score: 1 No of events	n = 3 ; % = 3	n = 14 ; % = 16
ASA score: 2 No of events	n = 39 ; % = 38	n = 55 ; % = 64
ASA score 3 (three) No of events	n = 59 ; % = 57	n = 17 ; % = 20
ASA score: 4 No of events	n = 2 ; % = 2	n = 0 ; % = 0
Performance status: 0 No of events	n = 49 ; % = 48	n = 71 ; % = 85
Performance status: 1 No of events	n = 31 ; % = 30	n = 11 ; % = 13
Performance status: 2 No of events	n = 16 ; % = 16	n = 2 ; % = 2
Performance status: 3 No of events	n = 6 ; % = 6	n = 0 ; % = 0

Outcomes

Study timepoints

- 90 days

Adverse events

Outcome	Cryoablation, 90 days, N = 104	Partial nephrectomy, 90 days, N = 86
Postoperative severe adverse events: Clavien-Dindo grades 1-5, within 90 days No of events	n = 24 ; % = 23	n = 20 ; % = 23
Postoperative severe adverse events: Clavien-Dindo grades 1-2, within 90 days No of events	n = 14 ; % = 13	n = 17 ; % = 20

Outcome	Cryoablation, 90 days, N = 104	Partial nephrectomy, 90 days, N = 86
Postoperative severe adverse events: Clavien-Dindo grades 3-5, within 90 days No of events	n = 10 ; % = 10	n = 3 ; % = 3

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Complications at 90 days

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as it used a nonrandomised design and did not use propensity score matching for all important baseline characteristics. The risk of bias due to selection of participants, classification of interventions, deviations from intended interventions, measurement of outcomes, and selection of the reported result was low to moderate. However, there was insufficient information to judge the risk of bias due to missing data. Considering all domains, the overall risk of bias for this study is serious, mainly driven by the potential for confounding.)*
Overall bias	Directness	Directly applicable *(The study appears to provide direct evidence relevant to the UK NHS setting. The study was conducted in Denmark, and the population, interventions (cryoablation and partial nephrectomy), and outcomes (complications, hospital stay, and readmission rates) are likely to be similar to those encountered in the UK NHS. However, some minor differences in healthcare systems and practices between Denmark and the UK may exist. The study did not report on quality of life or cost-effectiveness outcomes, but this alone does not affect the directness of the evidence. Overall, the study provides direct evidence with minimal sources of indirectness.)*

Junker, 2022

Bibliographic Reference	Junker, Theresa; Duus, Louise; Rasmussen, Benjamin S B; Azawi, Nessn; Lund, Lars; Norgaard, Birgitte; Graumann, Ole; Impact of Partial Nephrectomy and Percutaneous Cryoablation on Short-term Health-related Quality of Life-A Prospective Comparative Cohort Study.; European urology open science; 2022; vol. 45; 99-107

Study details

Trial registration number and/or trial name	NCT04040530
Study type	Prospective cohort study
Study location	Denmark
Study setting	Hospital setting. Data obtained from two university hospitals, Odense University Hospital (OUH) and Zeeland University Hospital (ZUH), covering one-third of the Danish population of 5.8 million people.
Study dates	June 2019 to February 2021
Sources of funding	This work was supported by the Region of Southern Denmark, The University of Southern Denmark.
Inclusion criteria	Patients older than 18 years Partial nephrectomy or percutaneous ablation of histologically verified primary renal cell carcinoma clinical stage cT1
Exclusion criteria	Patients with diagnosed dementia or under evaluation for dementia Patients with multiple tumours treated with nephron-sparing surgery more than once within 3 months
Intervention(s)	Partial nephrectomy (PN), including both robot-assisted PN (RAPN) and open PN (OPN), with RAPN as the preferred choice if surgically possible.
Comparator	Percutaneous cryoablation (PCA) performed by specialised interventional radiologists under computed tomography guidance, with the patient under sedation, if possible.
Outcome measures	Postoperative severe adverse events Quality of life -The European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire
Number of participants	Total number of participants: N = 165 Partial nephrectomy: 79 (47.9%) Percutaneous cryoablation: 86 (52.1%)
Duration of follow-up	90 days
Loss to follow-up	The completion rates of the questionnaire were 98% at 14-d and 96% at 90-d follow-up. Patients lost to follow-up were considered random for both PN and PCA.
Methods of analysis	A linear mixed-effect model (restricted maximum likelihood estimation [REML]) with patients as random effects, and treatment (PN versus PCA) and visits (baseline, 14 d, and 90 d) as fixed effects was used to analyse

	the changes from baseline to follow-up between PN and PCA treatment. Standard model selection was performed using the likelihood ratio test. Standard model assumptions were not violated. Adjusted models included age and sex as covariates as these were considered potential confounding factors. Statistical significance was set at 0.05.
Additional comments	The authors acknowledged several limitations of the study. Firstly, patients were not randomised, which poses a risk of confounding by indication, potentially compromising internal validity. However, the design followed the clinical practice of providing information about HRQoL outcomes from a broader patient perspective. The authors argue that this feature, combined with a high response rate throughout the study, contributes to the external and internal validity, thus limiting the magnitude of the indication bias. Secondly, the inclusion of open procedures is another limitation since postoperative outcomes after minimally invasive procedures such as RAPN, compared with open PN, may differ, especially in the short-term outcome. However, this study reflects the standard clinical practice and real-life data. The study would have been strengthened if more patients had been included, generating a larger sample size. However, patients treated with NSS were consecutively recruited for almost 2 years, from an uptake area covering 2 million people. One weakness of the study is the lack of randomisation, which could lead to selection bias and confounding. Additionally, the follow-up period of 90 days is relatively short, and longer-term outcomes were not assessed. The study does not report on important outcomes such as recurrence, survival, and adverse events, which could have provided a more comprehensive understanding of the comparative effectiveness of PN and PCA. A strength of the study is the prospective design and the high response rate, which enhances the validity of the findings. The study also provides valuable information on patient-reported HRQoL outcomes, which are often overlooked in clinical decision-making.

Study arms

Partial nephrectomy (N = 79)

Percutaneous cryoablation (N = 86)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 79)	Percutaneous cryoablation (N = 86)
% Female No of events	n = 21 ; % = 27	n = 24 ; % = 28
Age Median (IQR)	62.1 (52.7 to 71)	69.1 (62.2 to 76.1)
TNM staging: cT1a No of events	n = 53 ; % = 66	n = 79 ; % = 88
TNM staging: cT1b No of events	n = 27 ; % = 34	n = 11 ; % = 12
Histological subtype: Unclassified RCC No of events	n = 1 ; % = 1	n = 2 ; % = 2
Histological subtype: Clear cell No of events	n = 59 ; % = 74	n = 57 ; % = 63
Histological subtype: Papillary No of events	n = 11 ; % = 14	n = 25 ; % = 28
Histological subtype: Chromophobe No of events	n = 5 ; % = 6	n = 5 ; % = 6
Histological subtype: Epithelioid angiomyolipoma No of events	n = 3 ; % = 4	n = 1 ; % = 1
Performance status: ECOG 0 No of events	n = 67 ; % = 85	n = 51 ; % = 59
Performance status: ECOG 1 No of events	n = 10 ; % = 13	n = 23 ; % = 27
Performance status: ECOG 2 No of events	n = 2 ; % = 3	n = 11 ; % = 13
Performance status: ECOG 3 No of events	n = 0 ; % = 0	n = 1 ; % = 1

Outcomes

Study timepoints

- See below (The study assessed health-related quality of life (HRQoL) using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire, which was distributed before treatment (baseline), and 14 and 90 days postoperatively. The follow-up cutoffs of 14 and 90 days were chosen to reflect the standard follow-ups and convalescence after treatment at the participating institutions. The study did not report any data extraction timepoints beyond 90 days post-treatment, which falls within the 0 to 5 years range of interest. There were no data extraction timepoints reported for the 5 to 10 years range or beyond 10 years.)

Quality of life: Mean difference

Outcome	Percutaneous cryoablation versus Partial nephrectomy, See below, N2 = 86, N1 = 76
Quality of life: Global health status, 14 days post-treatment Mean (95% CI)	9.6 (3.2 to 16)
Quality of life: Global health status, 90 days post-treatment Mean (95% CI)	-0.26 (-6.7 to 6.2)

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Quality of life

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(The study has a moderate risk of bias due to potential confounding from unmeasured factors (as the study was not randomised) and the possibility of outcome assessors being influenced by their knowledge of the intervention received by participants. However, the risk of bias is low for the other domains assessed, including selection of participants, classification of interventions, deviations from intended interventions, missing data, and selection of the reported result.)*

Section	Question	Answer
Overall bias	Directness	Directly applicable *(For the purpose of this systematic review, we are assuming that all studies meeting the predefined inclusion criteria for the PICO will be graded as 'direct' in terms of their evidence. This assumption is based on the notion that studies satisfying the PICO criteria will directly address the research question at hand, without significant indirectness in terms of population, interventions, comparisons, or outcomes measured. Upon assessing the directness of this particular study, no significant sources of indirectness have been identified that would impact its applicability to the UK NHS. The study population, interventions, and outcomes appear to be relevant and comparable to what would be expected in the UK healthcare setting. Therefore, the evidence provided by this study can be considered direct for the purposes of this systematic review.)*

Kawaguchi, 2022

Bibliographic Reference	Kawaguchi, Shohei; Izumi, Kouji; Naito, Renato; Kadomoto, Suguru; Iwamoto, Hiroaki; Yaegashi, Hiroshi; Nohara, Takahiro; Shigehara, Kazuyoshi; Yoshida, Kotaro; Kadono, Yoshifumi; Mizokami, Atsushi; Comparison of Clinical Outcomes between Robot-Assisted Partial Nephrectomy and Cryoablation in Elderly Patients with Renal Cancer.; Cancers; 2022; vol. 14 (no. 23)

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital setting. Data obtained from a single institute, Kanazawa University Hospital.
Study dates	October 2016 to December 2021
Sources of funding	This research received no external funding.
Inclusion criteria	Patients aged ≥70 years Diagnosed with renal cell carcinoma Underwent robotic-assisted partial nephrectomy or partial cystectomy at Kanazawa University Hospital between October 2016 and December 2021.
Exclusion criteria	Not provided
Intervention(s)	Robot-assisted partial nephrectomy (RAPN) using the transperitoneal or retroperitoneal approach based on tumour location and size and renal

	vessel anatomy. Tumour resection was performed with warm ischemia using a renal artery clamp.
Comparator	Percutaneous cryoablation (PCA) performed under CT guidance using the CryoHit cryoablation system and 17-guage cryoneedles with local anaesthesia. In patients at high risk of bleeding, arterial embolisation was performed a day before PCA.
Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment
Number of participants	Total number of participants: N = 99 Robot-assisted partial nephrectomy (RAPN): 50 (50.5%) Percutaneous cryoablation (PCA): 49 (49.5%)
Duration of follow-up	The mean follow-up period was 24.3 (2–60) months for the RAPN group and 20.1 (2–60) months for the PCA group.
Loss to follow-up	Not provided
Methods of analysis	Chi-square, Wilcoxon's signed-rank, and Mann–Whitney U tests were used to compare features between RAPN and PCA groups. Univariable and multivariable logistic regression were used to determine risk factors for eGFR decline. Survival curves were measured using the Kaplan–Meier method, and log-rank tests evaluated differences in overall and recurrence-free survival. No propensity score matching was described.
Additional comments	Mean change in eGFR calculated by NICE team. The main limitations of this study, as acknowledged by the authors, were its retrospective design and small sample size. The study used real-world data, with significantly more T1b tumours in the RAPN group and more solitary kidney patients in the PCA group, which may have impacted oncological outcomes and post-treatment renal function. The follow-up period was relatively short, and only a few patients in the PCA group could be evaluated for renal function at 2 years. Patients with stage 3b or higher chronic kidney disease were also included, and follow-up imaging might not have accurately assessed recurrence due to the need to reduce or omit contrast media. The lack of clear criteria for treatment selection and significant differences in baseline age between the groups limit the ability to accurately compare oncological outcomes and changes in renal function. The study did not investigate patients on a no-treatment follow-up, which is a potential option for older patients with more comorbidities and slower-growing tumours. Strengths of the study include its comparison of real-world outcomes for two treatment approaches in an elderly population, providing valuable information for clinical decision-making in this age group. The study also assessed a range of relevant outcomes, including recurrence, survival, postoperative complications, and renal function.

	Some additional information that would have been useful includes the exclusion criteria, loss to follow-up data, and more detailed descriptions of the interventions and comparators, particularly regarding "usual care" components. The lack of randomisation and potential for selection bias may warrant downgrading of certain outcomes, particularly those related to oncological outcomes and renal function, which could be influenced by baseline differences between the groups.

Study arms

Robot-assisted partial nephrectomy (N = 50)

Percutaneous cryoablation (N = 49)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 50)	Percutaneous cryoablation (N = 49)
% Female No of events	n = 16 ; % = 32	n = 14 ; % = 28.6
Age (years) median Nominal	75	78
TNM staging: Clinical T1a No of events	n = 42 ; % = 84	n = 46 ; % = 93.9
TNM staging: Clinical T1b No of events	n = 8 ; % = 16	n = 1 ; % = 4
TNM staging: Clinical T3a No of events	n = 0 ; % = 0	n = 2 ; % = 4.1
R.E.N.A.L. score: Low (4-6) No of events	n = 29 ; % = 59.2	n = 32 ; % = 65.3
R.E.N.A.L. score: Moderate (7-9) No of events	n = 20 ; % = 40	n = 17 ; % = 34.7
R.E.N.A.L. score: Highest (10-12) No of events	n = 1 ; % = 2	n = 0 ; % = 0
Histologic subtype: Clear cell No of events	n = 35 ; % = 50	n = 38 ; % = 77.6
Histologic subtype: Papillary No of events	n = 6 ; % = 12	n = 1 ; % = 2

Characteristic	Robot-assisted partial nephrectomy (N = 50)	Percutaneous cryoablation (N = 49)
Histologic subtype: Chromophobe No of events	n = 3 ; % = 6	n = 1 ; % = 2
Histologic subtype: Benign No of events	n = 2 ; % = 4	n = 2 ; % = 4.1
Histologic subtype: Others No of events	n = 4 ; % = 8	n = 0 ; % = 0
Histologic subtype: Nondiagnostic No of events	n = 0 ; % = 0	n = 7 ; % = 14.3
Preoperative eGFR (mL/min/1.73 m2) Mean (SD)	65 (17.6)	65.7 (39.1)
Preoperative CKD stage: 1 No of events	n = 3 ; % = 6	n = 9 ; % = 18.4
Preoperative CKD stage: 2 No of events	n = 26 ; % = 52	n = 12 ; % = 24.5
Preoperative CKD stage: 3a No of events	n = 15 ; % = 30	n = 15 ; % = 30.6
Preoperative CKD stage: 3b No of events	n = 6 ; % = 12	n = 11 ; % = 22.4
Preoperative CKD stage: 4 No of events	n = 0 ; % = 0	n = 1 ; % = 2
Preoperative CKD stage: 5 No of events	n = 0 ; % = 0	n = 1 ; % = 2
Preoperative CKD stage: Greater than or equal to stage 3b No of events	n = 6 ; % = 12	n = 13 ; % = 26.5

Outcomes

Study timepoints

- See below (The mean follow-up period was 24.3 (2-60) months for the RAPN group and 20.1 (2-60) months for the PCA group. Renal function was assessed by determining estimated glomerular filtration rates (eGFR) at 1, 3, 6, 12, and 24 months after RAPN and PCA. Postoperative local recurrence and distant metastasis were evaluated using thoracoabdominal contrast CT, or plain CT or MRI in patients not suitable for contrast media due to severe renal dysfunction.)

Survival

Outcome	Robot-assisted partial nephrectomy, See below, N = 50	Percutaneous cryoablation, See below, N = 49
Overall survival: All-cause mortality, follow-up timepoint is not specified Nominal	1	4

Severe adverse events

Outcome	Robot-assisted partial nephrectomy, See below, N = 50	Percutaneous cryoablation, See below, N = 49
Severe adverse events: Postoperative, Clavien-Dindo grade greater than or equal to 3, follow-up timepoint is not specified Custom value	1/50 (grade 3a pneumothorax)	0/49

Renal function impairment

Outcome	Robot-assisted partial nephrectomy, See below, N = 50	Percutaneous cryoablation, See below, N = 49
Change in eGFR at 24 months postoperative (ml/min/1.73 m2) Mean (SD)	-0.9 (18.97)	-19.3 (33.92)

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Renal functional impairment

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(This retrospective cohort study has a serious risk of bias due to potential confounding factors that were not adequately controlled for, such as significant differences in baseline age between the intervention groups. The lack of propensity score matching or other*

Section	Question	Answer
		appropriate statistical adjustments to account for these differences raises concerns about the validity of the reported effect estimates. While other domains, such as classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results, had a low to moderate risk of bias, the critical issue of confounding remains inadequately addressed. Therefore, the overall risk of bias for this study is considered serious, and the findings should be interpreted with caution.)
Overall bias	Directness	Directly applicable *(For the purpose of this systematic review, we assume that this study is directly applicable because it meets the PICO inclusion criteria. However, there are some potential differences between the study and the UK NHS setting that should be considered. The study was conducted in a Japanese hospital setting, which may have some differences compared to the typical UK NHS setting in terms of healthcare system organisation, patient characteristics, and clinical practices. For example, there may be variations in the availability and accessibility of robot-assisted partial nephrectomy and percutaneous cryoablation between Japan and the UK. The study population included patients aged 70 years or older with renal cell carcinoma, which is likely to be similar to the target population encountered in the UK NHS. However, there may be some differences in the distribution of comorbidities, performance status, or other patient characteristics between the Japanese and UK populations. These differences could potentially impact the generalisability of the study findings to the UK NHS setting. The interventions, robot-assisted partial nephrectomy and percutaneous cryoablation, are both used in the UK NHS for the treatment of renal cell carcinoma in elderly patients. The techniques and protocols described in the study appear to be broadly comparable to those employed in UK clinical practice. However, there may be some variations in the specific equipment, expertise, or treatment guidelines between the two settings. In summary, while there are some potential sources of indirectness related to the healthcare system, patient population, and reported outcomes, the overall directness of the study remains high, given its adherence to the PICO inclusion criteria. The differences identified are not likely to substantially impact the applicability of the study findings to the UK NHS setting. However, it is important to consider these potential sources of indirectness when interpreting the results and making decisions based on the evidence provided by this study.)*

Severe complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(This retrospective cohort study has a serious risk of bias due to potential confounding factors that were not adequately controlled for, such as significant differences in baseline age between the intervention groups. The lack of propensity score matching or other appropriate statistical adjustments to account for these differences raises concerns about the validity of the reported effect estimates. While other domains, such as classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results, had a low to moderate risk of bias, the critical issue of confounding remains inadequately addressed. Therefore, the overall risk of bias for this study is considered serious, and the findings should be interpreted with caution.)*
Overall bias	Directness	Directly applicable *(For the purpose of this systematic review, we assume that this study is directly applicable because it meets the PICO inclusion criteria. However, there are some potential differences between the study and the UK NHS setting that should be considered. The study was conducted in a Japanese hospital setting, which may have some differences compared to the typical UK NHS setting in terms of healthcare system organisation, patient characteristics, and clinical practices. For example, there may be variations in the availability and accessibility of robot-assisted partial nephrectomy and percutaneous cryoablation between Japan and the UK. The study population included patients aged 70 years or older with renal cell carcinoma, which is likely to be similar to the target population encountered in the UK NHS. However, there may be some differences in the distribution of comorbidities, performance status, or other patient characteristics between the Japanese and UK populations. These differences could potentially impact the generalisability of the study findings to the UK NHS setting. The interventions, robot-assisted partial nephrectomy and percutaneous cryoablation, are both used in the UK NHS for the treatment of renal cell carcinoma in elderly patients. The techniques and protocols described in the study appear to be broadly comparable to those employed in UK clinical practice. However, there may be some variations in the specific equipment, expertise, or treatment guidelines between the two settings. In summary, while there are some potential sources of indirectness related to the healthcare system, patient population, and reported outcomes, the overall directness of the study remains high, given its adherence to the PICO inclusion criteria. The differences identified are not likely to substantially impact the applicability of the study findings to the UK*

Section	Question	Answer
		NHS setting. However, it is important to consider these potential sources of indirectness when interpreting the results and making decisions based on the evidence provided by this study.)

Mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(This retrospective cohort study has a serious risk of bias due to potential confounding factors that were not adequately controlled for, such as significant differences in baseline age between the intervention groups. The lack of propensity score matching or other appropriate statistical adjustments to account for these differences raises concerns about the validity of the reported effect estimates. While other domains, such as classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results, had a low to moderate risk of bias, the critical issue of confounding remains inadequately addressed. Therefore, the overall risk of bias for this study is considered serious, and the findings should be interpreted with caution.)*
Overall bias	Directness	Directly applicable *(For the purpose of this systematic review, we assume that this study is directly applicable because it meets the PICO inclusion criteria. However, there are some potential differences between the study and the UK NHS setting that should be considered. The study was conducted in a Japanese hospital setting, which may have some differences compared to the typical UK NHS setting in terms of healthcare system organisation, patient characteristics, and clinical practices. For example, there may be variations in the availability and accessibility of robot-assisted partial nephrectomy and percutaneous cryoablation between Japan and the UK. The study population included patients aged 70 years or older with renal cell carcinoma, which is likely to be similar to the target population encountered in the UK NHS. However, there may be some differences in the distribution of comorbidities, performance status, or other patient characteristics between the Japanese and UK populations. These differences could potentially impact the generalisability of the study findings to the UK NHS setting. The interventions, robot-assisted partial nephrectomy and percutaneous cryoablation, are both used in the UK NHS for the treatment of renal cell carcinoma in elderly patients. The techniques and protocols described in the study appear to be broadly comparable to those employed in UK clinical practice. However, there may be some*

Section	Question	Answer
		variations in the specific equipment, expertise, or treatment guidelines between the two settings. In summary, while there are some potential sources of indirectness related to the healthcare system, patient population, and reported outcomes, the overall directness of the study remains high, given its adherence to the PICO inclusion criteria. The differences identified are not likely to substantially impact the applicability of the study findings to the UK NHS setting. However, it is important to consider these potential sources of indirectness when interpreting the results and making decisions based on the evidence provided by this study.)

Kiriluk, 2011

Bibliographic Reference	Kiriluk, Kyle J; Shikanov, Sergey A; Steinberg, Gary D; Shalhav, Arieh L; Lifshitz, David A; Laparoscopic partial nephrectomy versus laparoscopic ablative therapy: a comparison of surgical and functional outcomes in a matched control study.; Journal of endourology; 2011; vol. 25 (no. 12); 1867-72

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Surgeries performed by three surgeons from a single institution.
Study dates	November 2002 to December 2008
Sources of funding	Reported that no competing financial interests exist. No further detail reported.
Inclusion criteria	Patients who underwent nephron sparing surgery
Exclusion criteria	Not reported
Intervention(s)	Partial nephrectomy (laparoscopic) (PN)
Comparator	Thermal ablation (TA), 21 laparoscopic RFA and 30 laparoscopic cryoablation
Outcome measures	Postoperative severe adverse events
Number of participants	N=102 PN: 51 TA: 51

Duration of follow-up	PN: mean 18 months (range 13.0-26.8) TA: mean 27 months (range 0.4-40.0)
Loss to follow-up	Not reported
Methods of analysis	Authors state that ablation patients were matched by preoperative estimated glomerular filtration rate (eGFR), comorbidities, age, comorbidities, BMI and tumour size to 51 patients who underwent LPN. Pairwise matching was performed individually between the groups. The bigger LPN group was used as controls. This is not named as propensity score matching. Analysis of categorical variables was performed using chi-square or Fisher exact tests where appropriate. Analysis of continuous variables was performed using a paired t test.
Additional comments	Mean hospital stay and renal function not extracted as within search period of included systematic reviews (Yanagisawa 2022 and Patel 2017). Limitations: small sample size so reduced power, retrospective study design, treatment decision dependent on surgeon and patient preference,

Study arms

Partial nephrectomy (N = 51)

Laparoscopic

Thermal ablation (N = 51)

Radiofrequency and cryoablation, laparoscopic

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 51)	Thermal ablation (N = 51)
% Female No of events	n = 25 ; % = 49	n = 25 ; % = 49
Age Custom value	mean 66, range 23-83	mean 65.7, range 27-75
Tumour size cm Custom value	mean 2.27, range 0.80-5.10	mean 2.35, range 0.99-4.90

Characteristic	Partial nephrectomy (N = 51)	Thermal ablation (N = 51)
Preoperative eGFR ml/min/1.73 m2 Mean (SD)	87 (NR)	88 (NR)
Single kidney No of events	n = 3 ; % = 5.9	n = 5 ; % = 9.8

Outcomes

Complications

Outcome	Partial nephrectomy, , N = 51	Thermal ablation, , N = 51
Complications (Clavien-Dindo 1-5) all complications were grade 1 or 2 only No of events	n = 6 ; % = 11.7	n = 12 ; % = 23.5

Complications (Clavien-Dindo 1-5) - Polarity - Lower values are better

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Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Most important confounders used in matching, but protocol not identified and some limited reporting on missing data)*
Overall bias	Directness	Directly applicable

Kitley, 2019

Bibliographic Reference	Kitley, Weston; Sulek, Jay; Sundaram, Chandru; Bahler, Clint D; Treatment Trends and Long-Term Survival Associated with Cryotherapy and Partial Nephrectomy for Small Renal Masses in the National Cancer Database Using Propensity Score Matching.; Journal of endourology; 2019; vol. 33 (no. 5); 408-414

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	Between 1998 and 2012
Sources of funding	No competing financial interests exist
Inclusion criteria	Patients with T1a
Exclusion criteria	cN(+) and cM(+)
Intervention(s)	Cryoablation (CA)
Comparator	Partial nephrectomy (PN)
Outcome measures	Survival
Number of participants	Total number of participants: 12458 CA: 6229 PN: 6229
Duration of follow-up	96 months
Loss to follow-up	Not reported
Methods of analysis	Propensity score matching was performed in a 1:1 nearest neighbour fashion using tumour diameter, Charlson score, race, age, geographic region, facility type, insurance type, and income to generate the conditional treatment probability. A Kaplan–Meier survival analysis was used to compare OS between CA and PN as well as other significant predictors on multivariable analysis. A Cox proportional hazards model was used on the matched data to adjust for potential confounders. Variables adjusted for were year of surgery, tumour diameter, Charlson score, race, age, geographic region, facility type, insurance type, and income.

Study arms

Cryoablation (N = 6229)

Partial nephrectomy (N = 6229)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 6229)	Partial nephrectomy (N = 6229)
% Female No of events	n = 2495 ; % = 40	n = 2518 ; % = 40.4
Age Mean (SD)	66.5 (11.7)	63.4 (11.4)
T1 (not otherwise specified) No of events	n = 870 ; % = 14	n = 754 ; % = 12.1
T1a No of events	n = 4607 ; % = 74	n = 3637 ; % = 58.4
Unknown No of events	n = 752 ; % = 12.1	n = 1838 ; % = 38.5
Tumor diameter (cm) Mean (SD)	2.5 (7.6)	2.5 (8.2)

Outcomes

Survival

Outcome	Cryoablation versus Partial nephrectomy, , N2 = 6229, N1 = 6229
Overall survival Hazard ratio/95% CI	1.46 (1.32 to 1.63)

Overall survival - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Lane, 2010

Bibliographic Reference	Lane BR, Abouassaly R, Gao T, Weight CJ, Hernandez AV, Larson BT, Kaouk JH, Gill IS CS; Active Treatment of Localized Renal Tumors May Not Impact Overall Survival in Patients Aged 75 Years or Older; Cancer; 2010; (no. 116); 3119-3126

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Kidney cancer registry for single institution.
Study dates	January 2000 to December 2006
Sources of funding	No sources of funding reported.
Inclusion criteria	Patients older than 75 years Suspected clinical stage T1 renal cancer
Exclusion criteria	Patients who underwent nephrectomy for reasons other than renal cancer
Intervention(s)	Active surveillance Management selected by patient and treating physician. Patients who elected active surveillance were followed clinically every 6 months with renal imaging.
Comparator	Radical nephrectomy. Follow-up in surgical patients was tailored according to pathologic cancer stage.
Outcome measures	Recurrence Survival

	Renal functional impairment
Number of participants	N=251 Active surveillance (AS): 105 Radical nephrectomy (RN): 146
Duration of follow-up	Median years [IQR] AS: 3.7 [2.4-5.1] RN: 4.4 [2.8-5.50]
Loss to follow-up	148 patients died during follow-up period. Not further reported.
Methods of analysis	The Kaplan-Meier method was used to evaluate survival, and differences among management types were tested with the log-rank test. Multivariate analyses evaluating the association between management type and all-cause mortality while adjusting for prespecified clinical characteristics (age, sex, race, Charlson-Romano index, presence of solitary kidney, preoperative glomerular filtration rate [GFR]) were performed using Cox proportional hazard models.
Additional comments	Study included in an included systematic review (Patel 2017), but not reported fully in that SR. It is therefore extracted in full here. Study also reports a nephron sparing intervention arm. This is not included as it does not separate out ablation and partial nephrectomy. Limitations: retrospective nature, selection biases, reliance on date and cause of death information from publicly accessible databases (SSDI and NDI), and lack of pathologic confirmation of malignancy in most patients who underwent surveillance.

Study arms

Active surveillance (N = 105)

Radical nephrectomy (N = 146)

Characteristics

Arm-level characteristics

Characteristic	Active surveillance (N = 105)	Radical nephrectomy (N = 146)
% Female No of events	n = 47 ; % = 45	n = 64 ; % = 44
Age Median (IQR)	81 (78 to 86)	79 (77 to 83)

Characteristic	Active surveillance (N = 105)	Radical nephrectomy (N = 146)
TNM classification - T1b (remainder are T1a) No of events	n = 15 ; % = 14	n = 86 ; % = 59
Primary RCC type - conventional RCC No of events	n = 2 ; % = 1.9	n = 88 ; % = 60
Primary RCC type - Benign No of events	n = 4 ; % = 3.8	n = 27 ; % = 18
Primary RCC type - unknown No of events	n = 99 ; % = 94	n = 0 ; % = 0
Baseline renal function - eGFR ml/min/1.73m2 Median (IQR)	54 (41 to 67)	64 (55 to 76)

Outcomes

Survival

Outcome	Radical nephrectomy versus Active surveillance , , N2 = 146, N1 = 105
Overall survival Multivariate analysis Hazard ratio/95% CI	0.75 (0.45 to 1.26)

Overall survival - Polarity - Lower values are better

Survival

Outcome	Active surveillance , , N = 105	Radical nephrectomy, , N = 146
Kidney cancer-specific mortality No of events	n = 6 ; % = 5.7	n = 7 ; % = 4.8
Metastasis No of events	n = 0 ; % = 0	n = 1 ; % = 0.7

Kidney cancer-specific mortality - Polarity - Lower values are better
Metastasis - Polarity - Lower values are better

Renal functional impairment

Outcome	Active surveillance , , N = 105	Radical nephrectomy, , N = 146
Newly diagnosed CKD No of events	n = 5 ; % = 5	n = 32 ; % = 47

Newly diagnosed CKD - Polarity - Lower values are better

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Overall survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Insufficient adjustment for confounders, limited reporting on missing data and protocol not identififed)*
Overall bias	Directness	Directly applicable

Kidney cancer-specific mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identififed)*
Overall bias	Directness	Directly applicable

Metastasis

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identififed)*
Overall bias	Directness	Directly applicable

Newly diagnosed CKD

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identififed)*
Overall bias	Directness	Directly applicable

Lehrer, 2023

Bibliographic Reference	Lehrer, Raphael; Cornelis, Francois; Bernhard, Jean-Christophe; Bigot, Pierre; Champy, Cecile; Bruyere, Franck; Roupret, Morgan; Doumerc, Nicolas; Bensalah, Charles-Karim; Olivier, Jonathan; Audenet, Francois; Tricard, Thibault; Parier, Bastien; Durand, Xavier; Durand, Matthieu; Charles, Thomas; Branger, Nicolas; Surlemont, Louis; Xylinas, Evanguelos; Beauval, Jean-Baptiste; Barral, Matthias; Minimally invasive nephron-sparing treatments for T1 renal cell cancer in patients over 75 years: a comparison of outcomes after robot-assisted partial nephrectomy and percutaneous ablation.; European radiology; 2023; vol. 33 (no. 12); 8426-8435

Study details

Trial registration number and/or trial name	NCT03293563
Study type	Retrospective cohort study
Study location	France
Study setting	Data obtained from the French national multicentre prospective database URO-CCR, involving multiple hospitals/institutions.
Study dates	January 2010 to January 2021
Sources of funding	The authors state that this work has not received any funding.
Inclusion criteria	Patients older than 75 years Treated for a T1 renal cell cancer by robot-assisted partial nephrectomy or percutaneous thermal ablation between January 2010 and January 2021
Exclusion criteria	Presence of metastases Suspected of having lymph node metastasis on CT/MRI Less than 75 years of age

	Insufficient tumour data (histological type or tumour size) Multiple tumours on the same kidney Underwent concomitant treatment of multiple tumours in the same procedure
Intervention(s)	Percutaneous thermal ablation, including radiofrequency ablation, cryoablation, and microwave ablation, performed under CT, ultrasound, or MRI guidance.
Comparator	Robot-assisted partial nephrectomy performed laparoscopically using Da Vinci generation robots.
Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants: N = 205 patients for 209 procedures Percutaneous thermal ablation: 66 (31.6%) Robot-assisted partial nephrectomy: 143 (68.4%)
Duration of follow-up	The mean follow-up was 22 ± 16.1 months [1–68 months] for the robot-assisted partial nephrectomy group and 22 ± 15.5 months [1–64 months] for the percutaneous thermal ablation group.
Loss to follow-up	A total of 4 patients (6%) in the percutaneous thermal ablation group and 18 patients (12.7%) in the robot-assisted partial nephrectomy group had less than 3 months follow-up and were therefore excluded from the oncological results analysis.
Methods of analysis	Quantitative variables were compared with Student's t-test and qualitative variables using chi-square or Fisher's test. Disease-free survival and overall survival were analyzed by patient and time to progression was analyzed by lesion, estimated using the Kaplan-Meier method and group comparison using log-rank or Wilcoxon tests. A Cox proportional hazards regression model was used to measure the association between treatment and oncological outcomes, adjusting for relevant prognostic factors. No propensity score matching was performed.
Additional comments	This study has several limitations, as acknowledged by the authors. Firstly, it is a retrospective analysis of a prospective cohort with a limited number of patients, especially for percutaneous thermal ablation. The diagnosis of oncocytoma treated with percutaneous thermal ablation relying on a core biopsy is limited. However, only one patient had oncocytoma in the percutaneous thermal ablation group, and no recurrence was observed. Cancer-specific survival was not studied in this cohort due to the lack of events and data on the causes of death. Although the populations were significantly different, with notably younger and healthier patients in the robot-assisted partial nephrectomy group, population matching could not be performed due to the relatively small number of patients. The authors also did not perform a subgroup analysis, particularly of the different ablation techniques, given the small sample and the low number of events.

	Finally, the number of patients lost to follow-up was relatively high, particularly in the robot-assisted partial nephrectomy group. A strength of this study is that it specifically compares robot-assisted partial nephrectomy and percutaneous thermal ablation approaches in an elderly population over 75 years, which is an under-represented group in clinical trials. The study also provides data on several important outcomes, including oncological outcomes, renal function preservation, and perioperative outcomes. However, some important outcomes are missing, such as intraoperative severe adverse events, cardiovascular events, and quality of life measures. The lack of these outcomes may limit the comprehensive assessment of the safety and patient-reported outcomes of the two treatment approaches. Additionally, the relatively short mean follow-up duration of 22 months in both groups may not be sufficient to capture long-term oncological outcomes and late complications. Given the retrospective nature of the study, the potential for selection bias, and the imbalance in baseline characteristics between the two treatment groups, the oncological outcomes may need to be interpreted with caution and potentially downgraded. The lack of propensity score matching or other advanced statistical methods to account for potential confounders may also limit the robustness of the findings.

Study arms

Percutaneous thermal ablation (N = 66)

Robot-assisted partial nephrectomy (N = 143)

Characteristics

Arm-level characteristics

Characteristic	Percutaneous thermal ablation (N = 66)	Robot-assisted partial nephrectomy (N = 143)
% Female No of events	n = 20 ; % = 30.4	n = 46 ; % = 32.9
Age Mean (SD)	80.4 (3.7)	79 (3.7)
ASA score: 1 No of events	n = 1 ; % = 1.5	n = 16 ; % = 11.3
ASA score: 2 No of events	n = 36 ; % = 54.5	n = 86 ; % = 60.6
ASA score 3 (three)	n = 28 ; % = 42.4	n = 40 ; % = 28.2

Characteristic	Percutaneous thermal ablation (N = 66)	Robot-assisted partial nephrectomy (N = 143)
No of events		
ASA score: 4 No of events	n = 1 ; % = 1.5	n = 0 ; % = 0
Tumour size (cm) Mean (SD)	2.7 (0.7)	3.2 (0.9)
Primary RCC type: Clear cell renal cell carcinoma No of events	n = 52 ; % = 78.8	n = 99 ; % = 69.2
Primary RCC type: Papillary carcinoma No of events	n = 5 ; % = 7.6	n = 22 ; % = 15.4
Primary RCC type: Chromophobe renal carcinoma No of events	n = 8 ; % = 1.12	n = 18 ; % = 12.6
Primary RCC type: Oncocytoma No of events	n = 1 ; % = 1.5	n = 4 ; % = 2.8
Preoperative creatinine serum level (µmol/L) Mean (SD)	94.2 (35.5)	88.9 (25)
History of kidney surgery No of events	n = 11 ; % = 16.7	n = 8 ; % = 5.6

Outcomes

Study timepoints

- See below (The study did not explicitly mention the timepoints for data extraction. The authors reported that the mean follow-up was 22 ± 16.1 months [1–68 months] for the robot-assisted partial nephrectomy group and 22 ± 15.5 months [1–64 months] for the percutaneous thermal ablation group. The study included patients treated between January 2010 and January 2021. The oncological outcomes, including disease-free survival, time to progression, and overall survival, were analysed based on the available follow-up data. The study did not report outcomes at specific follow-up timepoints, such as 0-5 years or 5-10 years. Perioperative outcomes, such as operation time, length of hospital stay, and postoperative increase in serum creatinine level, were likely measured during the immediate postoperative period and hospital stay. Postoperative complications were divided into three groups according to the time of onset: Perioperative complications were complications that occurred during hospitalisation. Early postoperative complications were complications that occurred during the first 3 months of follow-up. Late postoperative complications were complications that occurred after 3 months. The study did not provide further details on the specific timepoints for data extraction for each outcome measure.)

Survival

Outcome	Percutaneous thermal ablation versus Robot-assisted partial nephrectomy, See below, N2 = 66, N1 = 143
Overall mortality, follow-up timepoint is not specified Hazard ratio/95% CI	3.3 (0.87 to 12.72)

Duration of hospital stay

Outcome	Percutaneous thermal ablation, See below, N = 66	Robot-assisted partial nephrectomy, See below, N = 143
Duration of hospital stay, follow-up timepoint is not specified Mean (SD)	1.7 (1.4)	4.2 (3.4)

Recurrence

Outcome	Percutaneous thermal ablation versus Robot-assisted partial nephrectomy, See below, N2 = 66, N1 = 143
Disease free survival Hazard ratio/95% CI	2.2 (0.88 to 5.5)

Disease free survival - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there*

Section	Question	Answer
		was an imbalance in baseline characteristics between the two treatment groups, and the authors did not use advanced statistical methods to adequately control for potential confounders. There is also a serious risk of bias due to missing data, as a relatively high number of patients were lost to follow-up, particularly in the robot-assisted partial nephrectomy group. The risk of bias in other domains, such as selection of participants, classification of interventions, deviations from intended interventions, measurement of outcomes, and selection of the reported result, is considered moderate or low. Overall, the study's findings should be interpreted with caution due to the serious risk of bias in key domains.)
Overall bias	Directness	Directly applicable

Overall mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was an imbalance in baseline characteristics between the two treatment groups, and the authors did not use advanced statistical methods to adequately control for potential confounders. There is also a serious risk of bias due to missing data, as a relatively high number of patients were lost to follow-up, particularly in the robot-assisted partial nephrectomy group. The risk of bias in other domains, such as selection of participants, classification of interventions, deviations from intended interventions, measurement of outcomes, and selection of the reported result, is considered moderate or low. Overall, the study's findings should be interpreted with caution due to the serious risk of bias in key domains.)*
Overall bias	Directness	Directly applicable

Disease-free survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was an imbalance in baseline characteristics between the two treatment groups, and the authors did not use advanced statistical methods to adequately control for potential confounders. There is also a serious risk of bias due to missing data, as a relatively high*

Section	Question	Answer
		number of patients were lost to follow-up, particularly in the robot-assisted partial nephrectomy group. The risk of bias in other domains, such as selection of participants, classification of interventions, deviations from intended interventions, measurement of outcomes, and selection of the reported result, is considered moderate or low. Overall, the study's findings should be interpreted with caution due to the serious risk of bias in key domains.)
Overall bias	Directness	Directly applicable

Long, 2017

Bibliographic Reference	Long, Jean-Alexandre; Bernhard, Jean-Christophe; Bigot, Pierre; Lanchon, Cecilia; Paparel, Philippe; Rioux-Leclercq, Nathalie; Albiges, Laurence; Bodin, Thomas; Nouhaud, Francois-Xavier; Boissier, Romain; Gimel, Pierre; Mejean, Arnaud; Masson-Lecomte, Alexandra; Grenier, Nicolas; Cornelis, Francois; Grassano, Yohann; Comat, Vincent; Le Clerc, Quentin Come; Rigaud, Jerome; Salomon, Laurent; Descotes, Jean-Luc; Sengel, Christian; Roupret, Morgan; Verhoest, Gregory; Ouzaid, Idir; Arnoux, Valentin; Bensalah, Karim; Partial nephrectomy versus ablative therapy for the treatment of renal tumors in an imperative setting.; World journal of urology; 2017; vol. 35 (no. 4); 649-656

Study details

Study type	Retrospective cohort study
Study location	France
Study setting	Hospital. National database (URO CCR) in France.
Study dates	2000 to 2015
Sources of funding	Authors declare that they have no conflict of interest. No funding information reported.
Inclusion criteria	Patients undergoing thermal ablation or partial nephrectomy for a renal tumour in an imperative indication
Exclusion criteria	Not reported
Intervention(s)	Partial nephrectomy (PN) Performed in an open (n = 146), laparoscopic (n = 9), or robotic (n = 17) approach.
Comparator	Thermal ablation Radiofrequency ablation (n = 104) or cryoablation (n = 8)

Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	N= 284 PN: 172 Thermal ablation: 112
Duration of follow-up	Mean follow-up (months) PN: 43 (SD 53.70) Thermal ablation: 38 (SD (24.17)
Loss to follow-up	Not reported.
Methods of analysis	Data are presented as means and standard deviation (SD) or frequency (%) for continuous and categorical variables, respectively. Bivariable comparisons were made using independent t test or Mann–Whitney U test for continuous data, and Chi-square or Fisher's exact test for categorical data as appropriate. Statistical analysis was performed on the entire cohort and in three subgroups according to the type of imperative indication.
Additional comments	PN (n = 172) and thermal ablation (n = 112) were performed in patients with either a solitary kidney (n = 146), a bilateral tumour (n = 78), or CKD (n = 60). Limitations: The group of imperative indications includes different kind of patients (solitary kidney, chronic kidney disease (CKD), and bilateral renal masses) that might not behave similarly in terms of renal function outcome. eGFR change from baseline and SD calculated from baseline and follow-up figures by NICE team. T stage not reported as an inclusion criteria, but 92.5% of participants are T1 (7.5% T2).

Study arms

Partial nephrectomy (N = 172)

Open, laparoscopic or robotic

Thermal ablation (N = 112)

Radiofrequency and cryoablation

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 172)	Thermal ablation (N = 112)
Age Mean (SD)	62.7 (12.4)	64.6 (14.8)
Tumour size mm Mean (SD)	36.4 (21.2)	24.6 (9)
Primary RCC type - Clear cell No of events	n = 129 ; % = 75	n = 80 ; % = 72
Primary RCC type - Papillary No of events	n = 34	n = 24 ; % = 22
Primary RCC type - Chromophobe No of events	n = 9 ; % = 5	n = 8 ; % = 7
Preoperative eGFR Mean (SD)	65.9 (28.8)	65.9 (30.1)
Imperative indication - solitary kidney No of events	n = 79 ; % = 46	n = 67 ; % = 60
Imperative indication - bilateral tumour No of events	n = 51 ; % = 30	n = 27 ; % = 24
Imperative indication - eGFR < 60 ml/min No of events	n = 42 ; % = 24	n = 18 ; % = 16

Outcomes

Survival and recurrence

Outcome	Partial nephrectomy, , N = 172	Thermal ablation, , N = 112
Recurrence (local or metastatic) No of events	n = 34 ; % = 19	n = 29 ; % = 25
Death (overall) No of events	n = 14 ; % = 11	n = 10 ; % = 11
Death of kidney cancer No of events	n = 5 ; % = 5	n = 1 ; % = 1

Recurrence (local or metastatic) - Polarity - Lower values are better
Death (overall) - Polarity - Lower values are better
Death of kidney cancer - Polarity - Lower values are better

Renal functional impairment

Outcome	Partial nephrectomy, , N = 172	Thermal ablation, , N = 112
Change in eGFR (ml/min/1.73 m2) at latest follow up Mean (SD)	-10.32 (30.47)	-7.39 (29.28)

Complications

Outcome	Partial nephrectomy, , N = 172	Thermal ablation, , N = 112
Postoperative complications (any Clavien-Dindo grade) No of events	n = 36 ; % = 20	n = 11 ; % = 10
Major complications (Clavien-Dindo III and IV) No of events	n = 15 ; % = 8	n = 2 ; % = 2

Postoperative complications (any Clavien-Dindo grade) - Polarity - Lower values are better
Major complications (Clavien-Dindo III and IV) - Polarity - Lower values are better

Length of stay

Outcome	Partial nephrectomy, , N = 172	Thermal ablation, , N = 112
Hospital stay (days)	10.69 (5.52)	2.44 (2.55)

Outcome	Partial nephrectomy, , N = 172	Thermal ablation, , N = 112
Mean (SD)		

Hospital stay - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Lucignani, 2023

Bibliographic Reference	Lucignani, G.; De Lorenzis, E.; Ierardi, A.M.; Silvani, C.; Marmiroli, A.; Nizzardo, M.; Albo, G.; Carrafiello, G.; Montanari, E.; Boeri, L.; Perioperative and Survival Outcomes of Patients Treated With Robot-Assisted Partial Nephrectomy and Percutaneous Microwave Ablation for Small Renal Masses: A Single Center Experience; Clinical Genitourinary Cancer; 2023

Study details

Study type	Retrospective cohort study
Study location	Italy
Study setting	Hospital setting. Data obtained from a single academic centre (IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy).
Study dates	January 2016 to October 2022
Sources of funding	This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Inclusion criteria	Patients older than 18 years Small renal mass (< 4 cm)
Exclusion criteria	Masses showing extrarenal and vascular invasion

Intervention(s)	Robot-assisted partial nephrectomy was performed with the Da Vinci Si and Xi surgical system through a laparoscopic transperitoneal approach and under general anaesthesia.
Comparator	Microwave ablation was performed percutaneously through the Emprint Ablation System under local anaesthesia and mild sedation with the support of an anaesthesiologist.
Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants: N = 171 Robot-assisted partial nephrectomy (RAPN): 109 (63.7%) Microwave ablation (MWA): 62 (36.3%)
Duration of follow-up	The follow up period was 24 (7-24) and 24 (12-36) months for MWA and RAPN, respectively.
Loss to follow-up	Not reported
Methods of analysis	The Mann-Whitney and Fisher exact tests were used to compare clinical and perioperative variables between RAPN and MWA groups. Log-rank analyses were used to detect any possible difference in recurrence between the 2 groups. Kaplan Meier analyses were used to create recurrence plots. Factors associated with recurrence were investigated by means of univariate Cox proportional hazard models. The limited number of events did not allow for multivariate regression analysis. Propensity score matching was not performed.
Additional comments	The authors acknowledged several limitations of their study. Firstly, the retrospective nature did not allow for exact control of patients' perioperative management. For example, patients treated by MWA systematically underwent a CT scan on postoperative day 1 to check for complications, which may have increased the incidental detection of otherwise asymptomatic haematomas. Secondly, selection bias related to allocation to either RAPN or MWA may have influenced the results, though this is a recurrent issue in series regarding thermal ablation. The authors suggest that future studies should focus on overcoming these limitations by using a randomised design. Thirdly, the study reports a relatively high rate of tumour persistence after MWA, which might be related to the presence of enhancement at the early evaluation of 1 month, not necessarily indicating persistent disease. In fact, most of the persistent lesions did not display any signs of local progression at subsequent follow-up. Due to this uncertainty, the authors are now planning the first follow-up at 3 months post-MWA. Lastly, the high rate of non-diagnostic biopsies did not allow a histology-based evaluation of treatment efficacy. A strength of this study is the direct comparison between RAPN and MWA, two advanced techniques for managing small renal masses, in terms of

	perioperative, functional, and oncological outcomes. The study provides valuable insights into the potential benefits and drawbacks of each approach. However, some information is missing from the report. The authors did not provide details on the loss to follow-up, which could potentially impact the validity of the results. Additionally, the study did not assess quality of life outcomes, which are important when comparing different treatment modalities. Given the retrospective nature of the study and the potential for selection bias, the outcomes may need more downgrading. The lack of randomisation and the differences in baseline characteristics between the two groups could have influenced the observed results. Furthermore, the relatively short follow-up period may not be sufficient to capture long-term oncological outcomes and complications. In conclusion, while this study provides valuable insights into the comparison between RAPN and MWA for small renal masses, the limitations, particularly the retrospective design and potential for selection bias, should be considered when interpreting the results. Future randomised controlled trials with longer follow-up periods and more comprehensive outcome measures would help to further clarify the relative benefits and drawbacks of these two treatment approaches.

Study arms

Robot-assisted partial nephrectomy (N = 109)

Microwave ablation (N = 62)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 109)	Microwave ablation (N = 62)
% Female No of events	n = 35 ; % = 32.1	n = 19 ; % = 30.6
Age Median (IQR)	65 (53 to 73)	73 (61 to 79)
Tumour size: Diameter (cm) Median (IQR)	3 (2.1 to 3.7)	2.5 (1.8 to 3.1)
Primary RCC type: Clear cell carcinoma No of events	n = 62 ; % = 56.9	n = 13 ; % = 31.7

Characteristic	Robot-assisted partial nephrectomy (N = 109)	Microwave ablation (N = 62)
Primary RCC type: Papillary carcinoma No of events	n = 17 ; % = 15.6	n = 2 ; % = 4.9
Primary RCC type: Chromophobe carcinoma No of events	n = 8 ; % = 7.3	n = 0 ; % = 0
Primary RCC type: Oncocytoma No of events	n = 12 ; % = 11	n = 7 ; % = 17.1
Primary RCC type: Angiomyolipoma No of events	n = 4 ; % = 3.7	n = 4 ; % = 9.8
Primary RCC type: Cystic renal neoplasm of low malignant potential No of events	n = 2 ; % = 1.8	n = 0 ; % = 0
Baseline renal function: Chronic kidney disease No of events	n = 21 ; % = 19.3	n = 24 ; % = 38.7
Preoperative eGFR, mL/min Median (IQR)	79.1 (64.3 to 92.7)	67 (51.7 to 87.6)

Outcomes

Study timepoints

- See below (The study did not clearly specify the timepoints for data extraction. The authors reported that the follow-up period was 24 (7-24) and 24 (12-36) months for MWA and RAPN, respectively. No other timepoints were mentioned for the outcomes of interest.)

Survival

Outcome	Robot-assisted partial nephrectomy , See below, N = 109	Microwave ablation, See below, N = 62
Disease free survival No of events	n = 99 ; % = 96.5	n = 45 ; % = 83.2
Disease free survival Sample size	n = 103	n = 54
Overall survival No of events	n = 103 ; % = 94.5	n = 54 ; % = 86.4

Adverse events

Outcome	Robot-assisted partial nephrectomy , See below, N = 109	Microwave ablation, See below, N = 62
Overall complications, follow-up timepoint is not specified No of events	n = 38 ; % = 34.9	n = 12 ; % = 19.7
Major complications (Clavien-Dindo > 2), follow-up timepoint is not specified No of events	n = 6 ; % = 5.5	n = 3 ; % = 4.8

Duration of hospital stay

Outcome	Robot-assisted partial nephrectomy , See below, N = 109	Microwave ablation, See below, N = 62
Duration of hospital stay, follow-up timepoint is not specified Median (IQR)	4 (3 to 5)	2 (1 to 3)

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Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was insufficient information on how important confounding factors were controlled for in the analysis. The risk of bias in selection of participants into the study and due to deviations from intended interventions was moderate, while the risk of bias in classification of interventions and measurement of outcomes was low. However, there was no information to assess the risk of bias due to missing data and selection of the reported result. Overall, the study has a serious risk of bias.)*
Overall bias	Directness	Directly applicable

Major complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was insufficient information on how important confounding factors were controlled for in the analysis. The risk of bias in selection of participants into the study and due to deviations from intended interventions was moderate, while the risk of bias in classification of interventions and measurement of outcomes was low. However, there was no information to assess the risk of bias due to missing data and selection of the reported result. Overall, the study has a serious risk of bias.)*
Overall bias	Directness	Directly applicable

Overall complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was insufficient information on how important confounding factors were controlled for in the analysis. The risk of bias in selection of participants into the study and due to deviations from intended interventions was moderate, while the risk of bias in classification of interventions and measurement of outcomes was low. However, there was no information to assess the risk of bias due to missing data and selection of the reported result. Overall, the study has a serious risk of bias.)*
Overall bias	Directness	Directly applicable

Disease-free survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was insufficient information on how important confounding factors were controlled for in the analysis. The risk of bias in selection of participants into the study and due to deviations from intended interventions was moderate, while the risk of bias in classification of interventions and measurement of outcomes was low. However, there was no information to assess the risk of bias due to missing*

Section	Question	Answer
		data and selection of the reported result. Overall, the study has a serious risk of bias.)
Overall bias	Directness	Directly applicable

Overall survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as there was insufficient information on how important confounding factors were controlled for in the analysis. The risk of bias in selection of participants into the study and due to deviations from intended interventions was moderate, while the risk of bias in classification of interventions and measurement of outcomes was low. However, there was no information to assess the risk of bias due to missing data and selection of the reported result. Overall, the study has a serious risk of bias.)*
Overall bias	Directness	Directly applicable

Mason, 2018

Bibliographic Reference	Mason, Ross J; Atwell, Thomas; Lohse, Christine; Bhindi, Bimal; Schmit, Grant; Schmitz, John; Leibovich, Bradley C; Boorjian, Stephen A; Thompson, R Houston; Synchronous nephron-sparing approaches for bilateral renal masses: peri-operative and renal functional outcomes.; BJU international; 2018; vol. 122 (no. 2); 243-248

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Review of data from a single institution
Study dates	Partial nephrectomy: 1974 to 2013 Cryoablation: 2003 to 2013
Sources of funding	No funding received, authors report that there are no conflicts of interest

Inclusion criteria	People with synchronous bilateral tumours undergoing bilateral partial nephrectomy or bilateral cryoablation
Exclusion criteria	Presence of metastases
Intervention(s)	Partial nephrectomy (PN) Bilateral, synchronous. All but one procedure was open.
Comparator	Cryoablation Bilateral, synchronous. Performed under either CT or ultrasonography guidance at the discretion of the radiologist.
Outcome measures	Recurrence
Number of participants	N= 88 PN: 76 Cryoablation: 12
Duration of follow-up	Years, median (IQR) PN: 3.2 (1.5-7.5) Cryoablation: 1.2 (0.3, 3.6)
Loss to follow-up	Not reported. 37/88 patients provided eGFR measurements at 3 months but numbers contributing to recurrence outcome unclear.
Methods of analysis	Data collected by a trained nurse abstractor with data checks and periodic auditing. Clinical and pathological features are summarized with medians and interquartile ranges (IQRs) or frequency counts and percentages. Because of the limited number of patients undergoing PCA, statistical comparisons between the PN and PCA groups were not performed. No adjustments for confounding or matching carried out.
Additional comments	Clavien-Dindo outcomes not extracted as the maximum Clavien-Dindo complication grade per patient is reported. This will under-report the number of low grade complications, potentially in a biased way if the number of high-grade complications is unevenly distributed between arms. Limitations: no adjustments for confounders or matching undertaken. Small number of patients in the cryoablation arm. Shorter follow up in the cryoablation arm may have detected fewer metastasis events than longer follow up in the PN arm.

Study arms

Partial nephrectomy (N = 76)

Synchronous bilateral

Cryoablation (N = 12)

Synchronous bilateral, percutaneous

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 76)	Cryoablation (N = 12)
% Female No of events	n = 22 ; % = 28.9	n = 1 ; % = 8
Age Median (IQR)	62 (50 to 71)	67 (56 to 72)
Surgery technique used - open No of events	n = 75 ; % = 98.7	*empty data*
Surgery technique used - Laparoscopic No of events	n = 1 ; % = 1.3	*empty data*
Maximum tumour size Median (IQR)	4.6 (3.4 to 6.5)	2.6 (2.4 to 3.2)
Total number of renal masses Nominal	249	30
Benign masses Nominal	48	6
RCC tumours Nominal	151	15

Outcomes

Recurrence

Outcome	Partial nephrectomy, , N = 61	Cryoablation, , N = 12
Metastases At longest follow up No of events	n = 9 ; % = 11.8	n = 0 ; % = 0

Metastases - Polarity - Lower values are better

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Metastasis

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, unclear extent of missing data, no protocol identified.)*
Overall bias	Directness	Directly applicable

Millan, 2022

Bibliographic Reference	Millan, Braden; Breau, Rodney H; Bhindi, Bimal; Mallick, Ranjeeta; Tanguay, Simon; Finelli, Antonio; Lavallee, Luke T; Pouliot, Frederic; Rendon, Ricardo; So, Alan I; Dean, Lucas; Lattouf, Jean-Baptiste; Basappa, Naveen S; Kapoor, Anil; A Comparison of Percutaneous Ablation Therapy to Partial Nephrectomy for cT1a Renal Cancers: Results from the Canadian Kidney Cancer Information System.; The Journal of urology; 2022; vol. 208 (no. 4); 804-812

Study details

Study type	Retrospective cohort study
Study location	Canada
Study setting	Hospital setting. Data obtained from the Canadian Kidney Cancer information system (CKCis) database, a prospective national cohort collecting data on patients with any renal malignancy from 14 Canadian academic institutions.
Study dates	2011 to 2021
Sources of funding	The Kidney Cancer Research Network of Canada (KCRNC) and The Canadian Kidney Cancer information system (CKCis) have received unrestricted grants from BMS, Eisai, EMD Serono, GSK, Ipsen, Pfizer, Merck, Novartis and Roche. There is no direct role or influence from this funding on this work.
Inclusion criteria	Underwent a partial nephrectomy or ablation therapy (radiofrequency ablation or cryoablation) as the primary treatment method for clinical T1a N0 M0 renal cancers from 2011 to 2021
Exclusion criteria	Multiple tumours

	Age less than 18 years No post-procedure/-surgery follow-up Benign or missing tumour pathology Non-RCC histology cT1b disease and above Any radiographic adenopathy or metastases
Intervention(s)	Percutaneous ablation therapy (AT), including radiofrequency ablation (RFA) or cryoablation
Comparator	Partial nephrectomy (PN)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: N = 2,276 Percutaneous ablation therapy (AT): 275 (12.1%) Partial nephrectomy (PN): 2,001 (87.9%)
Duration of follow-up	The median followup for patients who were treated with PN was 2.0 years (IQR 0.6-4.2) in comparison to 2.6 years for AT (IQR 1.1-4.2, p=0.001).
Loss to follow-up	480/2,001 of the patients who underwent PN were lost to follow-up, in comparison to 47/228 of the patients who underwent AT.
Methods of analysis	Inverse probability of treatment weighting (IPTW) using propensity score (PS) was used. The primary outcomes, RFS and OS, were compared using Kaplan-Meier log-rank test analyses and Cox proportional hazard regression models. Sensitivity analyses were performed using other PS techniques, including adjusting for PS using a multivariable model, PS quintile stratification, PS matching and overlap weight, and 1:4 PS matching.
Additional comments	The authors acknowledged several limitations in this observational study. The allocation of patients to treatment groups was based on referral patterns and physician decision making, leading to confounding by indication. Patients with cT1aN0M0 renal masses who underwent AT had higher median age, baseline serum creatinine, and Charlson Comorbidity Index score compared to those who underwent PN, suggesting that choice of intervention was related to patient comorbidities and demographics. As with all observational studies, unmeasured differences between groups cannot be accounted for. The study follow-up was relatively short, limiting the impact of the results, especially considering the high cancer-specific survival of pT1a renal cell carcinoma. The loss to follow-up was significant

	and differed between the two treatment cohorts, which could have an unpredictable effect on the data. Additionally, data on nephrometry score were not available, which could have influenced local recurrence and complications. Strengths of the study include the use of a large, multi-institutional national cohort, improving the generalisability of the findings. All patients who underwent AT had pathologically confirmed renal cell carcinoma, addressing a limitation of previous studies. The authors employed several propensity score techniques to adjust for baseline differences between groups. The AT cohort included a large proportion of younger patients compared to previous studies, making the findings more applicable to a broader population of patients with small renal masses. The study did not report on several important outcomes, such as intraoperative and postoperative severe adverse events, renal functional impairment, cardiovascular events, duration of hospital stay, and quality of life. These outcomes could provide a more comprehensive understanding of the risks and benefits associated with each treatment modality.

Study arms

Percutaneous ablation therapy (N = 275

Partial nephrectomy (N = 2001)

Characteristics

Arm-level characteristics

Characteristic	Percutaneous ablation therapy (N = 275)	Partial nephrectomy (N = 2001)
% Female No of events	n = 88 ; % = 32	n = 751 ; % = 38
Age Median (IQR)	67 (59 to 74)	60 (52 to 67)
TNM classification: T1a No of events	n = 275 ; % = 100	n = 2001 ; % = 100

Characteristic	Percutaneous ablation therapy (N = 275)	Partial nephrectomy (N = 2001)
Primary RCC type: clear cell No of events	n = 187 ; % = 68	n = 1334 ; % = 67
Primary RCC type: Papillary (I, II and unclassified) No of events	n = 51 ; % = 19	n = 364 ; % = 18
Primary RCC type: chromophobe No of events	n = 9 ; % = 3	n = 161 ; % = 8
Primary RCC type: Clear cell papillary No of events	n = 11 ; % = 4	n = 77 ; % = 4
Primary RCC type: Other No of events	n = 17 ; % = 6	n = 65 ; % = 3
Charlson comorbidity index Median (IQR)	5 (4 to 6)	4 (3 to 5)

Outcomes

Study timepoints

- See below (The study reported recurrence-free survival (RFS) and overall survival (OS) at 2-year and 5-year time points. The median follow-up for patients who were treated with partial nephrectomy was 2.0 years (IQR 0.6-4.2) in comparison to 2.6 years for ablation therapy (IQR 1.1-4.2, p=0.001). The study did not report any data extraction time points beyond 5 years.)

Survival and recurrence

Outcome	Partial nephrectomy versus Percutaneous ablation therapy , See below, N2 = 164, N1 = 164
Overall survival: All-cause mortality, 5-year follow-up Hazard ratio/95% CI	0.96 (0.38 to 2.44)

Outcome	Partial nephrectomy versus Percutaneous ablation therapy , See below, N2 = 164, N1 = 164
Recurrence-free survival: 5-year follow-up Hazard ratio/95% CI	0.36 (0.18 to 0.71)
Local recurrence-free survival: 5-year follow-up Hazard ratio/95% CI	0.31 (0.13 to 0.73)

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Recurrence and survival outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(While the study has a low risk of bias in several domains, including the classification of interventions, deviations from intended interventions, measurement of outcomes, and selection of the reported result, there is a serious risk of bias due to confounding and missing data. The authors did not include all the important confounding domains considered essential by the NICE committee for proper propensity score matching, and there was a significant amount of missing data that differed between the intervention groups. These issues could potentially influence the study results and lead to biased effect estimates.)*
Overall bias	Directness	Directly applicable *(The study is directly applicable to the systematic review, as it meets the PICO inclusion criteria. However, there may be some differences between the study population and the UK NHS setting. The study was conducted in Canada, and the patient population may have different demographic and clinical characteristics compared to those typically encountered in the UK NHS. Additionally, the healthcare system and standard practices in Canada may differ from those in the UK, which could influence the implementation and outcomes of the interventions. Despite these potential differences, the study provides valuable information on the comparative effectiveness of percutaneous ablation therapy and partial nephrectomy for the management of cT1a renal cancers, which is relevant to the UK NHS setting.)*

Mues, 2012

Bibliographic Reference	Mues, Adam C; Korets, Ruslan; Graversen, Joseph A; Badani, Ketan K; Bird, Vincent G; Best, Sara L; Cadeddu, Jeffrey A; Clayman, Ralph V; McDougall, Elspeth; Barwari, Kurdo; Laguna, Pilar; de la Rosette, Jean; Kavoussi, Louis; Okhunov, Zhamshid; Munver, Ravi; Patel, Sutchin R; Nakada, Stephen; Tsivian, Matvey; Polascik, Thomas J; Shalhav, Arieh; Shingleton, W Bruce; Johnson, Emilie K; Wolf, J Stuart Jr; Landman, Jaime; Clinical, pathologic, and functional outcomes after nephron-sparing surgery in patients with a solitary kidney: a multicenter experience.; Journal of endourology; 2012; vol. 26 (no. 10); 1361-6

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. 12 institutions across the US and possibly the Netherlands. Unclear reporting.
Study dates	1990 to 2010
Sources of funding	Authors report that no competing financial interests exist.
Inclusion criteria	Solitary kidney (functional or anatomic) Patients who underwent nephron-sparing surgery for one or more renal masses
Exclusion criteria	Presence of metastases
Intervention(s)	Thermal ablation (TA) Laparoscopic and percutaneous cryoablation or radiofrequency ablation. No further detail reported.
Comparator	Robot-assisted partial nephrectomy (PN)
Outcome measures	Recurrence Postoperative severe adverse events
Number of participants	N=198 TA: 98 PN: 100

Duration of follow-up	TA: mean 31 months PN: mean 24 months
Loss to follow-up	Not reported
Methods of analysis	Univariate analyses were performed with chi-square andt test for categorical and continuous variables, respectively. For variables where the distribution did not conform to the normality assumption, the Mann-Whitney and Kruskal-Wallis tests were used. No adjustments for confounders or matching was undertaken.
Additional comments	Renal functional outcomes not extracted as within the search period of an included systematic review (Patel 2017). There was no standardised definition (estimated glomerular filtration rate [eGFR]) of a non-functioning kidney. Complications outcomes covers Clavien-Dindo grades 1-5: there were no complications of grade 4 or 5 to report.

Study arms

Thermal ablation (N = 98)

Cryoablation or radiofrequency ablation (laparoscopic or percutaneous)

Partial nephrectomy (N = 100)

Open or laparoscopic

Characteristics

Arm-level characteristics

Characteristic	Thermal ablation (N = 98)	Partial nephrectomy (N = 100)
% Female Custom value	NR	NR
Age Custom value	mean 64, range 38 to 86	mean 64, range 35 to 92

Characteristic	Thermal ablation (N = 98)	Partial nephrectomy (N = 100)
Tumour size cm Custom value	mean 2.5, range 1-4.4)	mean 3.9, range 1-10
Primary RCC type - Clear cell No of events	n = 51 ; % = 49	n = 70 ; % = 70
Primary RCC type - Papillary No of events	n = 5 ; % = 4.7	n = 18 ; % = 18
Primary RCC type - Chromophobe No of events	n = 0 ; % = 0	n = 6 ; % = 6
Primary RCC type - oncocytoma No of events	n = 13 ; % = 12	n = 3 ; % = 3
Primary RCC type - acute myeloid leukemia No of events	n = 6 ; % = 5.7	n = 3 ; % = 3
Primary RCC type - nondiagnostic No of events	n = 8 ; % = 7.6	n = 0 ; % = 0
Primary RCC type - no biopsy No of events	n = 22 ; % = 21	n = 0 ; % = 0

Outcomes

Recurrence and survival

Outcome	Thermal ablation, , N = 98	Partial nephrectomy , , N = 100
local recurrence No of events	n = 7 ; % = 6.7	n = 3 ; % = 3
Metastasis No of events	n = 2 ; % = 1.9	n = 1 ; % = 1

Outcome	Thermal ablation, , N = 98	Partial nephrectomy , , N = 100
Mortality No of events	n = 0 ; % = 0	n = 1 ; % = 1

local recurrence - Polarity - Lower values are better
Metastasis - Polarity - Lower values are better
Mortality - Polarity - Lower values are better

Complications

Outcome	Thermal ablation, , N = 98	Partial nephrectomy , , N = 100
Clavien-Dindo grade 1 No of events	n = 5 ; % = 5.1	n = 10 ; % = 10
Clavien-Dindo grade 2 No of events	n = 1 ; % = 1	n = 2 ; % = 2
Clavien-Dindo grade 3 No of events	n = 3 ; % = 3.1	n = 6 ; % = 6

Clavien-Dindo grade 1 - Polarity - Lower values are better
Clavien-Dindo grade 2 - Polarity - Lower values are better
Clavien-Dindo grade 3 - Polarity - Lower values are better

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All recurrence and survival outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders or matching undertaken. No protocol identified so unable to fully assess bias in selection of reported result.)*
Overall bias	Directness	Directly applicable

Palumbo, 2020

Bibliographic Reference	Palumbo, Carlotta; Mistretta, Francesco A; Knipper, Sophie; Mazzone, Elio; Pecoraro, Angela; Tian, Zhe; Perrotte, Paul; Antonelli, Alessandro; Montorsi, Francesco; Shariat, Shahrokh F; Saad, Fred; Simeone, Claudio; Briganti, Alberto; Lavallee, Luke T; Karakiewicz, Pierre I; Assessment of local tumor ablation and non-interventional management versus partial nephrectomy in T1a renal cell carcinoma.; Minerva urologica e nefrologica = The Italian journal of urology and nephrology; 2020; vol. 72 (no. 3); 350-359

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	From 2004 to 2015
Sources of funding	Not reported
Inclusion criteria	Patients with T1a
Exclusion criteria	All autopsy or death certificate cases and those with missing follow-up data
Intervention(s)	Local tumour ablation (LTA) and non-interventional management (NIM)
Comparator	Partial nephrectomy (PN)
Outcome measures	Survival
Number of participants	Total number of participants: 31613 LTA: 4524 NIM: 1654 PN: 25435
Duration of follow-up	Not reported
Loss to follow-up	Not reported
Methods of analysis	Propensity score matching (PSM) (1:1) was performed according to the nearest neighbour to minimise differences that may distinguish LTA or NIM patients from their PN counterparts. The PSM cohorts (LTA versus. PN and

	NIM versus. PN) were balanced according to age at diagnosis, gender, race, year of diagnosis, population density, marital status, socioeconomic status, tumour grade, histology and tumour size. The analysis relied on PSM data for purpose of multivariable comparisons between LTA versus. PN and NIM versus. PN. Specifically, multivariable competing risks regression models (CRR) predicted cancer-specific mortality and other cause mortality according to treatment type. Adjustment variables consisted of age at diagnosis, gender, race, year of diagnosis, population density, marital status, socioeconomic status, tumour grade, histology and tumour size.

Study arms

Local tumour ablation (N = 4524)

Non-interventional management (N = 1654)

Partial nephrectomy (N = 25435)

Characteristics

Arm-level characteristics

Characteristic	Local tumor ablation (N = 4524)	Non-interventional management (N = 1654)	Partial nephrectomy (N = 25435)
% Female No of events	n = 1642 ; % = 36.3	n = 607 ; % = 36.7	n = 9748 ; % = 38.3
Age Median (IQR)	68 (60 to 76)	70 (61 to 78)	59 (50 to 67)
Clear-cell renal cell carcinoma No of events	n = 2457 ; % = 54.3	n = 794 ; % = 48	n = 15899 ; % = 62.5
Papillary renal cell carcinoma No of events	n = 812 ; % = 17.9	n = 261 ; % = 15.8	n = 4401 ; % = 17.3

Characteristic	Local tumor ablation (N = 4524)	Non-interventional management (N = 1654)	Partial nephrectomy (N = 25435)
Chromophobe renal cell carcinoma No of events	n = 194 ; % = 4.3	n = 62 ; % = 3.7	n = 1583 ; % = 6.2
Renal cell carcinoma not otherwise specified No of events	n = 1061 ; % = 23.5	n = 537 ; % = 32.5	n = 3435 ; % = 14

Outcomes

Survival

Outcome	Local tumor ablation versus Partial nephrectomy, , N2 = 4524, N1 = 25435	Non-interventional management versus Partial nephrectomy, , N2 = 1654, N1 = 25435
Cancer specific mortality - Overall Hazard ratio/95% CI	1.6 (1.2 to 2.2)	3.3 (1.9 to 5.6)
Cancer specific mortality - Younger than 65 years Hazard ratio/95% CI	1.3 (0.6 to 2.6)	5.1 (1.9 to 13.6)
Cancer specific mortality - 65 years and older Hazard ratio/95% CI	1.8 (1.2 to 2.7)	2.9 (1.6 to 5.1)

Cancer specific mortality - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Pandolfo, 2023

Bibliographic Reference	Pandolfo, Savio Domenico; Beksac, Alp T; Derweesh, Ithaar; Celia, Antonio; Schiavina, Riccardo; Bianchi, Lorenzo; Costa, Giovanni; Carbonara, Umberto; Loizzo, Davide; Lucarelli, Giuseppe; Cerrato, Clara; Imbimbo, Ciro; Mirone, Vicenzo; Elbich, Jeffrey; Basile, Giuseppe; Hampton, Lance J; Kim, Fernando J; Capitanio, Umberto; Kaouk, Jihad; Autorino, Riccardo; Percutaneous Ablation versus Robot-Assisted Partial Nephrectomy for Completely Endophytic Renal Masses: A Multicenter Trifecta Analysis with a Minimum 3-Year Follow-Up.; Journal of endourology; 2023; vol. 37 (no. 3); 279-285

Study details

Study type	Retrospective cohort study
Study location	USA and Europe
Study setting	Hospital setting. Data obtained from seven high-volume US and European centers.
Study dates	2010 to 2020
Sources of funding	The sources of funding are not stated.
Inclusion criteria	Patients who underwent robot-assisted partial nephrectomy (RAPN) or percutaneous tumour ablation (PTA) for the treatment of a renal mass between 2010 and 2020
Exclusion criteria	Patients with previous kidney cancer surgery or multiple renal tumours
Intervention(s)	Robot-assisted partial nephrectomy (RAPN)

Comparator	Percutaneous tumour ablation (PTA), including cryoablation, radiofrequency, or microwave ablation
Outcome measures	Recurrence Survival Intraoperative severe adverse events Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants: N = 152 Robot-assisted partial nephrectomy: 60 (39.5%) Percutaneous tumour ablation: 92 (60.5%)
Duration of follow-up	Mean follow-up was 44.4 (32) months for RAPN and 35.6 (35.1) months for PTA.
Loss to follow-up	Not reported
Methods of analysis	Baseline characteristics, clinical, surgical, and postoperative outcomes were compared between the two groups (RAPN versus PTA). Kolmogorov–Smirnov (test K–S) was assessed to evaluate the data distribution. Mean ± standard deviation was adopted for normal distribution data. When no-normal distribution data, median and interquartile range was employed. Frequency (%) was reported for categorical data. To compare continuous variables t-test and Kruskal–Wallis H test were used according to the distribution. For categorical ones, Fisher's exact or Pearson chi-squared test were adopted to assess differences. Recurrence-free survival (RFS) was calculated with Kaplan–Meier analysis and long-rank test was used to assess differences among treatments. Multivariable logistic regression model assessed predictors of trifecta failure.
Additional comments	The authors acknowledged several limitations in this study, mostly related to its retrospective design, which may introduce patient-selection bias. The absence of standardised pre- and postoperative management among the different centres could have also influenced the outcomes. Merging different ablation modalities in the specific setting of endophytic masses might be regarded as another bias to be accounted for. A strength of this study is that it provides a direct comparison between RAPN and PTA for the specific subset of patients with completely endophytic renal masses, which has been scarcely reported in the

	literature. The multicentric nature of the study, involving seven high-volume centres, enhances the generalisability of the findings. However, some important information is missing, such as the sources of funding, loss to follow-up, and whether any propensity score matching was performed. The lack of randomisation and the potential for selection bias may warrant downgrading the level of evidence for certain outcomes. Additionally, the study did not report on cardiovascular events or quality of life outcomes, which are important considerations when comparing treatment modalities. The follow-up duration, although not statistically different between groups, may not be sufficient to capture long-term oncologic outcomes, particularly in the context of slow-growing renal masses.

Study arms

Robot-assisted partial nephrectomy (N = 60

Percutaneous tumour ablation (N = 92)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 60)	Percutaneous tumour ablation (N = 92)
% Female No of events	n = 18 ; % = 30	n = 26 ; % = 28.3
Age Median (IQR)	56.4 (19 to 79)	63.4 (20 to 88)
TNM classification: cT stage 1a No of events	n = 46 ; % = 76.7	n = 85 ; % = 92.4
TNM classification: cT stage 1b No of events	n = 10 ; % = 16.6	n = 5 ; % = 5.4
TNM classification: cT stage 2a No of events	n = 4 ; % = 6.7	n = 2 ; % = 2.2

Characteristic	Robot-assisted partial nephrectomy (N = 60)	Percutaneous tumour ablation (N = 92)
Tumour size (cm) Mean (SD)	2.8 (0.99)	2.6 (1.57)
Baseline renal function: Preoperative eGFR, mL/min Mean (SD)	89.1 (20.8)	69.7 (26.8)
Preoperative CKD stage: CKD greater than stage III No of events	n = 3 ; % = 5	n = 29 ; % = 31.5
Preoperative CKD stage: Solitary kidney No of events	n = 3 ; % = 5	n = 19 ; % = 20.6
Performance status at baseline: ASA score 1 No of events	n = 2 ; % = 3.3	n = 1 ; % = 1.1
Performance status at baseline: ASA score 2 No of events	n = 35 ; % = 58.3	n = 35 ; % = 38
Performance status at baseline: ASA score 3 No of events	n = 23 ; % = 38.3	n = 50 ; % = 54.3

Outcomes

Survival

Outcome	Robot-assisted partial nephrectomy , , N = 60	Percutaneous tumour ablation, , N = 92
Overall mortality: All-cause death, follow-up timepoint not specified No of events	n = 9 ; % = 15	n = 15 ; % = 15.1

Recurrence

Outcome	Robot-assisted partial nephrectomy , , N = 60	Percutaneous tumour ablation, , N = 92
Recurrence: Local recurrence, follow-up timepoint not specified No of events	n = 2 ; % = 3.3	n = 6 ; % = 6.5
Recurrence: Metastasis, follow-up timepoint not specified No of events	n = 0 ; % = 0	n = 3 ; % = 3.3

Adverse events

Outcome	Robot-assisted partial nephrectomy , , N = 60	Percutaneous tumour ablation, , N = 92
Overall complications: Postprocedural complications, Clavien-Dindo Classification, follow-up timepoint not specified No of events	n = 10 ; % = 16.7	n = 2 ; % = 2.2
Major complications: Postprocedural complications, Clavien-Dindo Classification grade 3 or higher, follow-up timepoint not specified No of events	n = 1 ; % = 3.3	n = 1 ; % = 1.1
Minor complications: Postprocedural complications, Clavien-Dindo Classification grade 1-2, follow-up timepoint not specified No of events	n = 9 ; % = 15	n = 1 ; % = 1.1

Minor complications: Postprocedural complications, Clavien-Dindo Classification grade 1-2, follow-up timepoint not specified - Polarity - Lower values are better

Kidney function

Outcome	Robot-assisted partial nephrectomy , , N = 60	Percutaneous tumour ablation, , N = 92
Renal functional impairment: New onset CKD III, follow-up timepoint not specified No of events	n = 7 ; % = 11.7	n = 23 ; % = 25
Renal functional impairment: DeGFR at latest follow-up, mL/min Mean (SD)	-13.5 (19.2)	-19.3 (28.7)

Duration of hospital stay

Outcome	Robot-assisted partial nephrectomy , , N = 60	Percutaneous tumour ablation, , N = 92
Duration of hospital stay, days Standardised Mean (SD)	4.03 (3.3)	3.1 (4.5)

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Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)*
Overall bias	Directness	Directly applicable

Renal functional impairment

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)*
Overall bias	Directness	Directly applicable

Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)*
Overall bias	Directness	Directly applicable

Metastasis

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)*
Overall bias	Directness	Directly applicable

Local recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding,*

Section	Question	Answer
		as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)
Overall bias	Directness	Directly applicable

Overall mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to potential confounding, as the authors did not use an appropriate analysis method to control for important confounding domains. There is insufficient information to assess the risk of bias in several other domains, including deviations from intended interventions and missing data.)*
Overall bias	Directness	Directly applicable

Pantelidou, 2016

Bibliographic Reference	Pantelidou, Maria; Challacombe, Ben; McGrath, Andrew; Brown, Matthew; Ilyas, Shahzad; Katsanos, Konstantinos; Adam, Andreas; Percutaneous Radiofrequency Ablation Versus Robotic-Assisted Partial Nephrectomy for the Treatment of Small Renal Cell Carcinoma.; Cardiovascular and interventional radiology; 2016; vol. 39 (no. 11); 1595-1603

Study details

Study type	Retrospective cohort study
Study location	UK
Study setting	Hospital setting. Institutional database from Guy's and St Thomas' Hospitals.
Study dates	2005 to 2013
Sources of funding	No conflicts of interest. No funding reported.
Inclusion criteria	Histologically confirmed RCC

	T1 stage RCC <7cm Data for follow-up and baseline pre-procedure CT imaging available.
Exclusion criteria	Benign renal tumour on histology >7cm renal tumours Lost to follow-up or no post-procedure follow-up imaging Nephrectomy or ablation techniques other than those listed under 'arms'
Intervention(s)	Radiofrequency ablation (RFA) Percutaneously under CT guidance. At least one cycle of up to 12 minutes in duration. Contrast-enhanced CT performed the next day to assess technical result. Follow-up included contrast-enhanced computed tomography every 4–6 months during the 2 years and annually thereafter. In cases of local recurrence, the radiological diagnosis was based on recurrent contrast enhancement, and repeat ablation or open/laparoscopic nephrectomy was performed without repeat biopsy
Comparator	Partial nephrectomy (PN). Robot-assisted, performed laparoscopically. Follow-up included transabdominal ultrasound in those treated with RPN every 4–6 months during the 2 years and annually thereafter. In cases of local recurrence, the radiological diagnosis was based on recurrent contrast enhancement, and repeat ablation or open/laparoscopic nephrectomy was performed without repeat biopsy
Outcome measures	Recurrence Postoperative severe adverse events
Number of participants	N=126 RFA: 63 PN: 63
Duration of follow-up	Months: median (range) RFA: 47.5 (11.8–80.2) PN: 18.5 (6.2–29.5)

Loss to follow-up	Follow-up CT scan is an inclusion criteria. No further information.
Methods of analysis	Disease-free survival (DFS) was defined as the percentage of patients free from any recurrence and metastasis on follow-up. Disease-free Survival was analysed with the Kaplan–Meier method. Survival curves for the two groups were compared using the log-rank test and corresponding hazard ratios were calculated. Cox regression model used to report DFS. Adjustments for baseline tumour size, PADUA score, age and type of treatment offered. Unclear how type of treatment offered was adjusted for. Did not adjust for baseline eGFR or RCC type.
Additional comments	Limitations: retrospective design. The duration of follow-up for the partial nephrectomy group was significantly shorter (median 18 months) than the RFA group (median 47.5 months) due to later introduction of robotic PN to the institution. This may bias towards the partial nephrectomy group for disease-free survival. Older and frailer patients are usually sent for FRA rather than PN, resulting in baseline differences. Authors state that loss to follow-up was significant, especially in the RFA arm (no further detail).

Study arms

Radiofrequency ablation (N = 63)

Percutaneous

Partial nephrectomy (N = 63)

Robotic-assisted

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 63)	Partial nephrectomy (N = 63)
Age Mean (SD)	61 (21)	54 (7)
Tumour size cm	2.11 (0.19)	2.88 (0.13)

Characteristic	Radiofrequency ablation (N = 63)	Partial nephrectomy (N = 63)
Mean (SD)		
Primary RCC type - Clear cell No of events	n = 48 ; % = 76.2	n = 54 ; % = 85.7
Primary RCC type - Papillary No of events	n = 9 ; % = 14.3	n = 7 ; % = 11.1
Primary RCC type - Chromophobe No of events	n = 2 ; % = 3.2	n = 2 ; % = 3.2
Primary RCC type - unspecified No of events	n = 4 ; % = 6.3	n = 0 ; % = 0
Baseline eGFR mls/min/1.73 m2 Mean (SD)	51.5 (20)	87.8 (15.1)
Single kidney No of events	n = 16 ; % = 25.4	n = 1 ; % = 1.6

Outcomes

Survival

Outcome	Partial nephrectomy versus Radiofrequency ablation, , N2 = 63, N1 = 63
Disease-free survival Hazard ratio/95% CI	0.6 (0.1 to 3.7)

Disease-free survival - Polarity - Lower values are better

Complications

Outcome	Radiofrequency ablation, , N = 63	Partial nephrectomy, , N = 63
All complications (Clavien-Dindo I-V) No of events	n = 5 ; % = 7.9	n = 11 ; % = 17.5
Minor complications (Clavien I and II) No of events	n = 4 ; % = 6.3	n = 10 ; % = 15.9
Major complications (Clavien III and IV) No of events	n = 1 ; % = 1.6	n = 1 ; % = 1.6

All complications (Clavien-Dindo I-V) - Polarity - Lower values are better
Minor complications (Clavien I and II) - Polarity - Lower values are better
Major complications (Clavien III and IV) - Polarity - Lower values are better

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Disease free survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Insufficient adjustment (no eGFR at baseline or primary RCC type); imbalance in follow-up duration; loss to follow up greater in RFA arm; no protocol identified.)*
Overall bias	Directness	Directly applicable

All complication outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders; loss to follow up greater in RFA arm; no protocol identified.)*
Overall bias	Directness	Directly applicable

Panumatrassamee, 2013

Bibliographic Reference	Panumatrassamee, Kamol; Kaouk, Jihad H; Autorino, Riccardo; Lenis, Andrew T; Laydner, Humberto; Isac, Wahib; Long, Jean-Alexandre; Eyraud, Remi; Kassab, Ahmad; Khalifeh, Ali; Hillyer, Shahab; Rizkala, Emad; Haber, Georges-Pascal; Stein, Robert J; Cryoablation versus minimally invasive partial nephrectomy for small renal masses in the solitary kidney: impact of approach on functional outcomes.; The Journal of urology; 2013; vol. 189 (no. 3); 818-22

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Single institution retrospective review.
Study dates	2000 to 2012
Sources of funding	Authors report financial interest and/or other relationship with Ethicon, Covidien, Intuitive and Endocare (producers of medical technologies with involvement in both ablation and nephrectomy).
Inclusion criteria	Solitary kidney Patients who underwent RCA with a percutaneous or laparoscopic approach or minimally invasive PN with a laparoscopic or robotic approach
Intervention(s)	Cryoablation. Performed with double freeze-thaw cycles to extend the iceball 5 to 10 mm beyond the tumour edge. Intraoperative pre-cryoablation needle biopsies were performed in all patients. The choice of laparoscopic or percutaneous approach was based on tumour location and technical capability depending on the year of treatment.
Comparator	Partial nephrectomy (PN) Performed with a laparoscopic or robotic approach. After PN with pathology confirmed malignant tumour, renal function and imaging studies were performed at 6 months postoperatively and then yearly.
Outcome measures	Postoperative severe adverse events
Number of participants	N=62

	Cryoablation: 29 PN: 33
Duration of follow-up	Cryoablation: median IQR: 41 (26-59) PN: median IQR: 17 (5-62)
Loss to follow-up	Not reported
Methods of analysis	All patients were included in the analysis in an intent to treat fashion including those who underwent radical nephrectomy after RCA and PN. Postoperative complications were graded using the Clavien classification system.
Additional comments	Baseline characteristics reported for tumours, not people. The cryoablation arm has 29 people with 43 tumours. Information for people not available. The most common solitary kidney etiology was contralateral RCC in both groups. Two-thirds of patients (63%) in the RCA group had previous RCC surgery in a treated kidney while none had prior surgery in the PN group. Limitations: retrospective design, longer follow up in cryoablation arm (not a concern for postoperative complications).

Study arms

Cryoablation (N = 43)

29 patients with 43 tumours - characteristics reported for tumours not people

Partial nephrectomy (N = 33)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 43)	Partial nephrectomy (N = 33)
% Female No of events	n = 8 ; % = 19	n = 11 ; % = 33
Age	64 (57 to 72)	60 (51 to 69)

Characteristic	Cryoablation (N = 43)	Partial nephrectomy (N = 33)
Median (IQR)		
Tumour size on CT Median (IQR)	2.2 (1.6 to 3.2)	2.9 (1.8 to 4.2)
Preoperative eGFR ml/min/1.73m2 Median (IQR)	57 (51 to 63)	62 (51 to 73)
RENAL score 4-6 tumour complexity No of events	n = 18 ; % = 42	n = 13 ; % = 40
RENAL score 7-9 No of events	n = 18 ; % = 42	n = 14 ; % = 42
RENAL score 10-12 No of events	n = 7 ; % = 16	n = 6 ; % = 18

Outcomes

Complications

Outcome	Cryoablation, , N = 29	Partial nephrectomy, , N = 33
Major postoperative complications (Clavien-Dindo grade 3-5) No of events	n = 1 ; % = 5.6	n = 6 ; % = 18
Minor postoperative complications (Clavien-Dindo grade 1-2) No of events	n = 2 ; % = 4	n = 7 ; % = 21
Overall postoperative complications (Clavien-Dindo grade 1-5) No of events	n = 3 ; % = 7	n = 13 ; % = 39

Major postoperative complications (Clavien-Dindo grade 3-5) - Polarity - Lower values are better
Minor postoperative complications (Clavien-Dindo grade 1-2) - Polarity - Lower values are better

Overall postoperative complications (Clavien-Dindo grade 1-5) - Polarity - Lower values are better

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All complication outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustments for confounders, no protocol identified and limited information on missing data)*
Overall bias	Directness	Directly applicable

Park, 2018

Bibliographic Reference	Park, B.K.; Gong, I.H.; Kang, M.Y.; Sung, H.H.; Jeon, H.G.; Jeong, B.C.; Jeon, S.S.; Lee, H.M.; Seo, S.I.; RFA versus robotic partial nephrectomy for T1a renal cell carcinoma: a propensity score-matched comparison of mid-term outcome; European Radiology; 2018; vol. 28 (no. 7); 2979-2985

Study details

Study type	Retrospective cohort study
Study location	South Korea
Study setting	Hospital. Review of data from a single institution
Study dates	2008 to 2016
Sources of funding	No funding. Study reports that there are no conflicts of interest
Inclusion criteria	Solitary renal mass and histologically-confirmed RCC
Exclusion criteria	Small (<4 cm) pathological T3a RCC, multiple RCC, bilateral RCC, metastatic RCC and hereditary RCC
Intervention(s)	Partial nephrectomy (PN) Robot-assisted. Performed by an experienced urologist. Histological diagnosis made using surgical specimens.

Comparator	Radiofrequency ablation (RFA) Performed by an experienced radiologist. Histological diagnosis made using biopsy cores.
Outcome measures	Renal functional impairment
Number of participants	N=126 PN: 63 RFA: 63
Duration of follow-up	Months, median PN: 24.6 RFA: 21
Loss to follow-up	Not reported
Methods of analysis	Propensity score matching was undertaking with the following variables: age, sex, American Society of Anaesthesiologists (ASA) score, tumour size, tumour laterality, tumour histology, R.E.N.A.L. nephrometry score and preoperative estimated glomerular filtration rate (eGFR). Matching was performed without replacement, and non-matched results were discarded. Pre-treatment and post-treatment eGFR was calculated using the modification of diet in renal disease equation to compare the two group. The number of patients upgraded to chronic kidney disease (CKD) stage III-IV in each group was also evaluated and compared.
Additional comments	Duration of hospital stay outcomes not extracted as reported in an included systematic review (Yanagisawa 2018)

Study arms

Radiofrequency ablation (N = 63)

Partial nephrectomy (N = 63)

Robot-assisted

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 63)	Partial nephrectomy (N = 63)
% Female No of events	n = 22 ; % = 35	n = 16 ; % = 25
Age Mean (SD)	57.7 (10.8)	57.1 (13.1)
Tumour size Assumed cm Mean (SD)	2 (0.6)	2.1 (0.5)
Primary RCC type - Clear cell No of events	n = 54 ; % = 85.7	n = 48 ; % = 76.2
Primary RCC type - non clear cell No of events	n = 9 ; % = 14.3	n = 15 ; % = 23.8
Pre-treatment eGFR Mean (SD)	85.1 (18.4)	92.1 (25.6)

Outcomes

Renal functional impairment

Outcome	Radiofrequency ablation, , N = 63	Partial nephrectomy, , N = 63
Upgrade to CKD 3-5 No of events	n = 6 ; % = 9.5	n = 8 ; % = 12.7

Upgrade to CKD 3-5 - Polarity - Lower values are better

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Renal functional impairment

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Propensity score matching includes important confounders, possible residual confounding remains. No protocol identified.)*
Overall bias	Directness	Directly applicable

Park, 2019

Bibliographic Reference	Park, Jong Mok; Yang, Seung Woo; Shin, Ju Hyun; Na, Yong Gil; Song, Ki Hak; Lim, Jae Sung; Oncological and Functional Outcomes of Laparoscopic Radiofrequency Ablation and Partial Nephrectomy for T1a Renal Masses: A Retrospective Single-center 60 Month Follow-up Cohort Study.; Urology journal; 2019; vol. 16 (no. 1); 44-49

Study details

Study type	Retrospective cohort study
Study location	Korea
Study setting	Hospital setting
Study dates	Between January 2005 and October 2014
Sources of funding	
Inclusion criteria	Histologically confirmed RCC Patients with T1a Patients with a small (< 4 cm) solitary tumour Patients followed up for at least 2 years after surgery by contrast imaging studies
Exclusion criteria	Metastatic disease at evaluation

	Patients with, bilateral renal masses Patients with hereditary renal tumour
Intervention(s)	Radiofrequency ablation (RFA)
Comparator	Partial nephrectomy (PN)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: 115 RFA: 62 PN: 53
Duration of follow-up	Average follow-ups were 60 and 68 months for RFA and PN, respectively
Loss to follow-up	There was no patient lost to follow-up.
Methods of analysis	The RFA and PN groups were compared in terms of survival using the Kaplan-Meier method and the log-rank test.

Study arms

Radiofrequency ablation (N = 62

Partial nephrectomy (N = 53)

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 62)	Partial nephrectomy (N = 53)
% Female No of events	n = 17 ; % = 26.5	n = 13 ; % = 24.5
Age Mean (95% CI)	58 (32 to 84)	53 (17 to 77)

Characteristic	Radiofrequency ablation (N = 62)	Partial nephrectomy (N = 53)
Baseline renal function (ml/min) Mean (95% CI)	94.2 (35.82 to 193)	97.5 (30.2 to 155)
Tumour size (cm) Mean (95% CI)	2.14 (0.8 to 3.6)	2.75 (1.3 to 4)

Outcomes

Survival

Outcome	Radiofrequency ablation, , N = 62	Partial nephrectomy, , N = 53
local recurrence No of events	n = 0 ; % = 0	n = 0 ; % = 0
Disease-specific mortality No of events	n = 0 ; % = 0	n = 0 ; % = 0
Overall mortality No of events	n = 2 ; % = 3.2	n = 0 ; % = 0

local recurrence - Polarity - Lower values are better
Disease-specific mortality - Polarity - Lower values are better
Overall mortality - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not adjust the results presented to control possible confounding factors)*

Section	Question	Answer
Overall bias	Directness	Directly applicable

Patel, 2012

Bibliographic Reference	Patel, Nilay; Cranston, David; Akhtar, M Zeeshan; George, Caroline; Jones, Andrew; Leiblich, Aaron; Protheroe, Andrew; Sullivan, Mark; Active surveillance of small renal masses offers short-term oncological efficacy equivalent to radical and partial nephrectomy.; BJU international; 2012; vol. 110 (no. 9); 1270-5

Study details

Study type	Retrospective cohort study
Study location	UK
Study setting	Hospital. Cancer Research Uro-Oncology Database used to identify patients retrospectively.
Study dates	2005 to 2010
Sources of funding	None declared, no conflicts of interest declared
Inclusion criteria	Suspected clinical stage T1 renal cancer Solid enhancing or cystic enhancing T1a small renal mass managed by radical nephrectomy, partial nephrectomy or active surveillance.
Exclusion criteria	Not reported
Intervention(s)	Active surveillance (AS) A follow-up surveillance protocol for patients managed with AS had not been prospectively established before this study. Patient assessment and follow-up were dependent upon individual physician preferences. Patients were followed up with CT, MRI or ultrasound scans of the abdomen and chest every 3 – 6 months. Routine percutaneous renal biopsy of T1 lesions was not undertaken. Patients on AS were advised to have definitive treatment if their tumours grew to > 4 cm in maximal diameter or had rapid tumour growth rates.
Comparator	Radical nephrectomy (RN). Open or laparoscopic. Patients were followed up postoperatively every 6 – 12 months with a CT scan of the chest and abdomen.

Outcome measures	Survival
Number of participants	N=112 AS: 71 RN: 41
Duration of follow-up	AS: mean 34 months RN: mean 37 months
Loss to follow-up	Not reported.
Methods of analysis	Limited reporting: "Statistical analysis was performed using Microsoft EXCEL and GRAPHPAD PRISM 4; using the following tests; chi squared, Student' s t test and Kaplan–Meier curves". No adjustments or matching conducted.
Additional comments	Study also contains a partial nephrectomy (PN) arm. AS versus PN comparisons are not extracted here as they are reported on in an included systematic review (Guo 2019). Baseline characteristics for radical nephrectomy arm not reported - only reported for both surgery arms combined, and split by tumours 0-4cm and 4+cm. Overall 14/71 (19.7%) patients managed with AS subsequently went on to receive definitive therapy; RN (2/14), PN (7/14), radiofrequency ablation (3/14) and high-intensity focused ultrasound (2/14). The trigger for intervention in these patients was an increase in size (9/14), patient choice (4/14) and a change in radiological diagnosis (1/14).

Study arms

Active surveillance (N = 71)

<4cm tumours

Radical nephrectomy (N = 41)

<4cm tumours

Characteristics

Arm-level characteristics

Characteristic	Active surveillance (N = 71)	Radical nephrectomy (N = 41)
% Female Nominal	19	NR
Age Custom value	mean 71.9, range 24-93	NR
Tumour size cm Mean (SD)	2.2 (NR)	NR (NR)
Biopsy undertaken Nominal	7	NR
Of biopsied, RCC Nominal	2	NR
Of biopsied, oncocytoma Nominal	2	NR
Of biopsied, non-diagnostic Nominal	3	NR

Outcomes

Survival

Outcome	Active surveillance, , N = 71	Radical nephrectomy, , N = 41
Mortality No of events	n = 12 ; % = 17	n = 8 ; % = 19.6
Cancer-specific mortality No of events	n = 1 ; % = 1.4	n = 3 ; % = 7.4

Mortality - Polarity - Lower values are better

Cancer-specific mortality - Polarity - Lower values are better

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Mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, different follow up schedules between arms, some unclear reporting about AS and missing data)*
Overall bias	Directness	Directly applicable

Cancer-specific mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, different follow up schedules between arms, some unclear reporting about AS and missing data)*
Overall bias	Directness	Directly applicable

Pecoraro, 2019

Bibliographic Reference	Pecoraro, A.; Palumbo, C.; Knipper, S.; Mistretta, F.A.; Tian, Z.; Shariat, S.F.; Saad, F.; Briganti, A.; Fiori, C.; Porpiglia, F.; Karakiewicz, P.I.; Cryoablation predisposes to higher cancer specific mortality relative to partial nephrectomy in patients with nonmetastatic pT1b kidney cancer; Journal of Urology; 2019; vol. 202 (no. 6); 1120-1125

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	From 2004 to 2015

Sources of funding	Not reported
Inclusion criteria	Patients aged ≥18 years Patients with T1b histologically confirmed nmRCC
Exclusion criteria	Patients with missing or inadequate survival follow-up data
Intervention(s)	Cryoablation (CA)
Comparator	Partial nephrectomy (PN)
Outcome measures	Survival
Number of participants	Total number of participants: 662 CA: 228 PN: 434
Duration of follow-up	Median followup was 38 months
Loss to follow-up	Not reported
Methods of analysis	The 1:2 PS matched cohort was balanced by age, gender, ethnicity, educational status, socioeconomic status, marital status, population density by patient residence type, tumour size, tumour grade, histological type and diagnosis year. Additional multivariable adjustment was made for age, tumour size, tumour grade and histological type

Study arms

Cryoablation (N = 228)

Partial nephrectomy (N = 434)

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 228)	Partial nephrectomy (N = 434)
% Female No of events	n = 71 ; % = 31.1	n = 140 ; % = 32.3

Characteristic	Cryoablation (N = 228)	Partial nephrectomy (N = 434)
Age Mean (SD)	69.3 (0.7)	68 (0.5)
Clear cell No of events	n = 139 ; % = 60.4	n = 268 ; % = 61.8
Papillary No of events	n = 31 ; % = 13.5	n = 54 ; % = 12.4
Chromophobe No of events	n = 8 ; % = 3.5	n = 16 ; % = 3.7
Others No of events	n = 52 ; % = 22.6	n = 96 ; % = 22.1
Tumour size Mean (SD)	47.1 (0.3)	47 (0.2)

Outcomes

Survival

Outcome	Cryoablation versus Partial nephrectomy, , N2 = 228, N1 = 434
Cancer-specific mortality Hazard ratio/95% CI	2.5 (1.08 to 5.63)

Cancer-specific mortality - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the*

Section	Question	Answer
		study did not control the analysis for all the important confounding domains.)
Overall bias	Directness	Directly applicable

Pedraza-Sanchez, 2023

Bibliographic Reference	Pedraza-Sanchez, Jose Pablo; Chaves-Marcos, Reyes; Mazuecos-Quiros, Javier; Bisono-Castillo, Alvaro Luis; Osman-Garcia, Ignacio; Gutierrez-Marin, Carlos Miguel; Medina Lopez, Rafael Antonio; Juarez Soto, Alvaro; Percutaneous radiofrequency ablation is an effective treatment option for small renal masses, comparable to partial nephrectomy.; European radiology; 2023; vol. 33 (no. 11); 7371-7379

Study details

Study type	Retrospective cohort study Retrospective analysis of a prospectively maintained registry
Study location	Spain
Study setting	Hospital setting. Data obtained from two hospitals belonging to the Andalusian Public Health System (SSPA) in Spain.
Study dates	June 2014 to June 2021
Sources of funding	Not reported
Inclusion criteria	Patients older than 18 years Radiologic imaging diagnoses of small renal mass (SRMs) including benign lesions Extension study (chest-abdomen CT) without evidence of distant metastatic disease Suitable to undergo radiofrequency or partial nephrectomy Patients who underwent radiofrequency had to be elderly (> 60 years) and have comorbidities, thus, with high surgical risk
Exclusion criteria	Radiological evidence of tumour extension beyond the kidney or vascular involvement

	Metastatic disease at diagnosis Inability to undergo any of these two surgical procedures
Intervention(s)	Percutaneous radiofrequency ablation (PRFA) under contrast-enhanced power ultrasound (CEPUS) guidance. All tumours were ablated for at least one cycle of up to 7-12 min.
Comparator	Partial nephrectomy (PN) performed through three approaches: robotic-assisted, laparoscopic, and open.
Outcome measures	Recurrence Survival Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants: N = 291 Percutaneous radiofrequency ablation: 111 (38.1%) Partial nephrectomy: 180 (61.9%)
Duration of follow-up	Median follow-up time was 38 months (range, 12-109) for PRFA and 48 months (range, 12-78) for PN.
Loss to follow-up	Not reported
Methods of analysis	Comparisons of treatment features were evaluated using the t test, Wilcoxon-Mann-Whitney U test, chi-square test, Fisher test, and Cochran-Armitage trend test. Kaplan-Meier curves depicted overall survival, local recurrence-free survival, and metastasis-free survival rates. A multivariate analysis was carried out to eliminate the effect of confounding variables that could modify the result such as malignant histology and tumour size - p value<0.05 was considered significant. No propensity score matching was reported.
Additional comments	The authors identified several limitations of this study. Firstly, due to the retrospective design, selection bias in performing the procedures (PRFA or PN) could not be avoided. Confounding variables such as malignant histology and tumour size may have favoured the PN group. A randomised controlled trial would be needed to address this limitation. Secondly, the sample size and statistical power of 70% may not be sufficient to determine non-inferiority or superiority conclusively. Increasing the sample size could resolve this issue.

	A strength of this study is that it is the first to compare patients undergoing CEPUS-guided PRFA and PN at two centres with experience in each procedure. The study also has a reasonable number of patients. Some information is missing from the report, such as the trial registration number, sources of funding, and loss to follow-up data. The study did not assess intraoperative severe adverse events, cardiovascular events, or quality of life as outcomes. The difference in follow-up protocols between the PRFA and PN groups (mainly CEPUS for RFA and CT for PN) may make the comparison of local recurrence-free survival and metastasis-free survival less reliable, potentially necessitating the downgrading of these outcomes. Overall, while this study provides valuable insights into the comparison of PRFA and PN for small renal masses, its limitations should be considered when interpreting the results. The retrospective design and potential for selection bias are notable weaknesses. However, the study's strengths, such as the comparison of CEPUS-guided PRFA and PN at experienced centres, contribute to the growing body of evidence in this field.

Study arms

Percutaneous radiofrequency ablation (N = 111)

Partial nephrectomy (N = 180)

Characteristics

Arm-level characteristics

Characteristic	Percutaneous radiofrequency ablation (N = 111)	Partial nephrectomy (N = 180)
% Female No of events	n = 31 ; % = 27.9	n = 71 ; % = 39.4
Age Mean (SD)	64.56 (11)	57.47 (11.9)
TNM staging: T1a No of events	n = 109 ; % = 98.2	n = 140 ; % = 81.2

Characteristic	Percutaneous radiofrequency ablation (N = 111)	Partial nephrectomy (N = 180)
TNM staging: T1b No of events	n = 2 ; % = 1.8	n = 29 ; % = 17
TNM staging: T2 No of events	n = 0 ; % = 0	n = 2 ; % = 1.2
Tumour size, mm Mean (SD)	21.47 (8.48)	32.3 (14.39)
Primary RCC type: Clear cells No of events	n = 32 ; % = 29.1	n = 105 ; % = 58.3
Primary RCC type: papillary No of events	n = 20 ; % = 18.2	n = 37 ; % = 20.6
Primary RCC type: chromophobe No of events	n = 9 ; % = 8.2	n = 5 ; % = 2.8
Primary RCC type: Oncocytoma No of events	n = 9 ; % = 8.2	n = 5 ; % = 2.8
Primary RCC type: Angiomyolipoma No of events	n = 2 ; % = 1.8	n = 7 ; % = 3.9
Primary RCC type: Eosinophilic cells No of events	n = 1 ; % = 0.9	n = 2 ; % = 1.1
Primary RCC type: Absence of neoplasia No of events	n = 17 ; % = 15.5	n = 11 ; % = 6.1
Primary RCC type: Inconclusive No of events	n = 15 ; % = 13.6	n = 0 ; % = 0
Baseline renal function: Preoperative creatinine, mg/dL Mean (SD)	1.07 (0.61)	0.92 (0.37)

Characteristic	Percutaneous radiofrequency ablation (N = 111)	Partial nephrectomy (N = 180)
Baseline renal function: Preoperative estimated glomerular filtration rate, mL/min/1.73 m2 Mean (SD)	77.42 (22.99)	86.72 (19.42)
Performance status at baseline: ASA score 1 No of events	n = 4 ; % = 3.6	n = 12 ; % = 6.7
Performance status at baseline: ASA score 2 No of events	n = 67 ; % = 60.4	n = 142 ; % = 78.9
Performance status at baseline: ASA score 3 No of events	n = 40 ; % = 36	n = 25 ; % = 13.9
Performance status at baseline: ASA score 4 No of events	n = 0 ; % = 0	n = 1 ; % = 0.6

Outcomes

Survival

Outcome	Percutaneous radiofrequency ablation, , N = 111	Partial nephrectomy, , N = 180
Metastasis: follow-up timepoint is not specified Nominal	0	6
Cancer-specific mortality: follow-up timepoint is not specified Nominal	0	1

Survival

Outcome	Percutaneous radiofrequency ablation versus Partial nephrectomy, , N2 = 111, N1 = 180
Local recurrence-free survival: follow-up timepoint is not specified Hazard ratio/95% CI	0.9 (0.28 to 2.9)
Overall survival: follow-up timepoint is not specified Hazard ratio/95% CI	1.2 (0.42 to 3.1)

Overall survival: follow-up timepoint is not specified - Polarity - Lower values are better

Adverse events

Outcome	Percutaneous radiofrequency ablation, , N = 111	Partial nephrectomy, , N = 180
Postoperative severe adverse events: Clavien-Dindo complications grade 3 or higher, follow-up timepoint is not specified No of events	n = 1 ; % = 0.9	n = 12 ; % = 6.7
Postoperative severe adverse events: Clavien-Dindo complications grade 1-2, follow-up timepoint is not specified No of events	n = 110 ; % = 99	n = 168 ; % = 85.5

Postoperative severe adverse events: Clavien-Dindo complications grade 1-2, follow-up timepoint is not specified - Polarity - Lower values are better

Kidney function

Outcome	Percutaneous radiofrequency ablation, , N = 111	Partial nephrectomy, , N = 180
Renal functional impairment: Change in estimated glomerular filtration rate pre- and postoperatively in mL/min/1.73 m2, follow-up timepoint is not specified	-2.42 (13.14)	-3.79 (16)

Outcome	Percutaneous radiofrequency ablation, , N = 111	Partial nephrectomy, , N = 180
Mean (SD)		

Duration of hospital stay

Outcome	Percutaneous radiofrequency ablation, , N = 111	Partial nephrectomy, , N = 180
Duration of hospital stay, follow-up timepoint is not specified Mean (SD)	1.04 (0.2)	3.57 (3.06)

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Renal functional impairment

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the authors identified several potential confounders that may have favoured the partial nephrectomy group, and the study did not use an appropriate analysis method to control for all the important confounding domains. Additionally, there is a serious risk of bias in the measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study participants, and the methods of outcome assessment were probably not comparable across intervention groups due to differences in follow-up protocols. The study has a moderate risk of bias in the selection of participants and deviations from intended interventions. There was insufficient information to assess the risk of bias due to missing data.)*
Overall bias	Directness	Directly applicable

Complications

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the*

Section	Question	Answer
		authors identified several potential confounders that may have favoured the partial nephrectomy group, and the study did not use an appropriate analysis method to control for all the important confounding domains. Additionally, there is a serious risk of bias in the measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study participants, and the methods of outcome assessment were probably not comparable across intervention groups due to differences in follow-up protocols. The study has a moderate risk of bias in the selection of participants and deviations from intended interventions. There was insufficient information to assess the risk of bias due to missing data.)
Overall bias	Directness	Directly applicable

Survival event data

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the authors identified several potential confounders that may have favoured the partial nephrectomy group, and the study did not use an appropriate analysis method to control for all the important confounding domains. Additionally, there is a serious risk of bias in the measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study participants, and the methods of outcome assessment were probably not comparable across intervention groups due to differences in follow-up protocols. The study has a moderate risk of bias in the selection of participants and deviations from intended interventions. There was insufficient information to assess the risk of bias due to missing data.)*
Overall bias	Directness	Directly applicable

Survival hazard ratios

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the authors identified several potential confounders that may have favoured the partial nephrectomy group, and the study did not use an appropriate analysis method to control for all the important confounding domains. Additionally, there is a serious risk of bias in*

Section	Question	Answer
		the measurement of outcomes, as the outcome assessors were likely aware of the intervention received by study participants, and the methods of outcome assessment were probably not comparable across intervention groups due to differences in follow-up protocols. The study has a moderate risk of bias in the selection of participants and deviations from intended interventions. There was insufficient information to assess the risk of bias due to missing data.)
Overall bias	Directness	Directly applicable

Qiu, 2023

Bibliographic Reference	Qiu, Jessica; Ballantyne, Christopher; Lange, Moritz; Kennady, Emmett; Yeaman, Clinton; Culp, Stephen; Schenkman, Noah; Lobo, Jennifer M; Comparison of microwave ablation and partial nephrectomy for T1a small renal masses.; Urologic oncology; 2023; vol. 41 (no. 10); 434e9-434e16

Study details

Study type	Prospective cohort study Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	Data were collected retrospectively from 2009 to 2015 and prospectively since 2015
Sources of funding	Not reported
Inclusion criteria	Patients with T1a Malignant tumors ≤4 cm Biopsy proven RCC
Exclusion criteria	Metastatic disease at diagnosis Genetic predispositions to multiple renal masses such as VHL or Lynch syndrome Lack of follow-up

Intervention(s)	Partial nephrectomy (PN) (robotic-assisted laparoscopic partial nephrectomy and open partial nephrectomy)
Comparator	Microwave ablation (MWA)
Outcome measures	Recurrence Survival Intraoperative severe adverse events Postoperative severe adverse events
Number of participants	Total number of participants = 206 MWA <3cm = 62 MWA 3-4cm = 64 PN <3cm = 36 PN 3-4cm = 44
Duration of follow-up	Median follow-up for PN <3 cm was 35.9 months (IQR 18.7−46.4) and 25.6 months (IQR 18.5−49.9) for MWA. Median follow-up for SRMs 3-4 cm was 36.1 months (IQR 18.8−50.7) for PN and 27.3 months (IQR 12.3−48.6) for MWA.
Loss to follow-up	Not reported
Methods of analysis	Kaplan-Meier survival analysis, log-rank test, and Cox proportional-hazard analysis were performed to compare LRFS of MWA and PN for the <3 cm and 3−4 cm cohorts.

Study arms

Microwave ablation (overall) (N = 126)

Partial nephrectomy (overall) (N = 80)

Characteristics

Arm-level characteristics

Characteristic	Microwave ablation (overall) (N = 126)	Partial nephrectomy (overall) (N = 80)
% Female, <3cm No of events	n = 25 ; % = 40.3	n = 8 ; % = 22.2
% Female, 3-4cm No of events	n = 23 ; % = 34.9	n = 14 ; % = 31.8
Age, <3cm Median (IQR)	65 (59 to 72)	53 (42 to 59)
Age, 3-4cm Median (IQR)	68 (59 to 73)	56 (49 to 62)
RCC type clear cell <3cm No of events	n = 39 ; % = 65	n = 28 ; % = 82.4
RCC type clear cell 3-4cm No of events	n = 45 ; % = 75	n = 32 ; % = 78.1
RCC type papillary, <3cm No of events	n = 19 ; % = 31.7	n = 5 ; % = 14.7
RCC type papillary, 3-4cm No of events	n = 5 ; % = 8.3	n = 8 ; % = 19.5
RCC type chromophobe, <3cm No of events	n = 1 ; % = 1.7	n = 3 ; % = 5

Characteristic	Microwave ablation (overall) (N = 126)	Partial nephrectomy (overall) (N = 80)
RCC type chromophobe, 3-4cm No of events	n = 0 ; % = 0	n = 0 ; % = 0

Outcomes

Survival

Outcome	Microwave ablation (overall), , N = 126	Partial nephrectomy (overall), , N = 80
Overall recurrences No of events	n = 8 ; % = 13	n = 5 ; % = 13
local recurrence No of events	n = 6 ; % = 10	n = 3 ; % = 8
Mortality No of events	n = 5	n = 3

Overall recurrences - Polarity - Lower values are better
local recurrence - Polarity - Lower values are better
Mortality - Polarity - Lower values are better

Complications

Outcome	Microwave ablation (overall), , N = 106	Partial nephrectomy (overall), , N = 80
Total complications No of events	n = 15	n = 20
CD 1-3A No of events	n = 10	n = 16
CD-3B+ No of events	n = 5	n = 4

Total complications - Polarity - Lower values are better

CD 1-3A - Polarity - Lower values are better
CD-3B+ - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Rembeyo, 2020

Bibliographic Reference	Rembeyo, Gregory; Correas, Jean-Michel; Jantzen, Rodolphe; Audenet, Francois; Dariane, Charles; Delavaud, Christophe; Mejean, Arnaud; Timsit, Marc-Olivier; Percutaneous Ablation Versus Robotic Partial Nephrectomy in the Treatment of cT1b Renal Tumors: Oncologic and Functional Outcomes of a Propensity Score-weighted Analysis.; Clinical genitourinary cancer; 2020; vol. 18 (no. 2); 138-147

Study details

Study type	Retrospective cohort study
Study location	France
Study setting	Hospital setting
Study dates	Between February 2010 and May 2016
Sources of funding	Not reported
Inclusion criteria	Patients with solitary renal mass > 4 cm Patients with cT1b Patients with absence of nodal or distant metastasis (N0 and M0).

Exclusion criteria	Metastatic disease at evaluation Patients with multiple RCC Patients with an American Society of Anesthesiologists score > 4
Intervention(s)	Robot-assisted partial nephrectomy (RAPN)
Comparator	Cryoablation (CA) and radiofrequency ablation (RFA)
Outcome measures	Recurrence Survival Renal functional impairment
Number of participants	Total number of participants: 102 RARP: 36 CA: 55 RFA: 11
Duration of follow-up	Median (range): 23.7 months (15.5-32.2), 19.9 months (15.5-27.2), and 51.3 (31.1-56.5) in the groups RARP, CA, and RFA, respectively
Loss to follow-up	No patients have been lost to follow-up. All patients included in the study were analysed.
Methods of analysis	Multivariate models were used to compare RAPN (reference) to PTA treatments for logistic regression (CKD upstaging and onset of CKD) and lineal regression (median eGFR change, percentage change in eGFR, and eGFR preservation). Adjustment variables were the age, the pretreatment eGFR, the RENAL score, and the presence of hypertension. CSS and recurrence-free survival (RFS) were estimated at 2 years using the Kaplan-Meier method and compared with Cox proportional hazards regression model to calculate hazard ratios (HRs). To control for selection bias between the different treatments, we adjusted our models with an Inverse Probability of Treatment Weighting propensity score. The propensity score of each patient was calculated using preoperative variables, which included age, pretreatment eGFR, American Society of Anesthesiologists score, RENAL score, Charlson comorbidity index, diabetes, and hypertension. Adjusted ORs and corresponding 95% CIs and P values were obtained according to the treatment reference (RAPN)

Study arms

Robot-assisted partial nephrectomy (N = 36)

Cryoablation (N = 55)

Radiofrequency ablation (N = 11)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 36)	Cryoablation (N = 55)	Radiofrequency ablation (N = 11)
% Female No of events	n = 8 ; % = 22.2	n = 18 ; % = 32.7	n = 4 ; % = 36.4
Age Median (IQR)	60 (54.8 to 66)	72 (60 to 80)	84 (76 to 86)
Angiomyolipoma No of events	n = 1 ; % = 2.8	n = 10 ; % = 18.2	n = 0 ; % = 0
Oncocytoma No of events	n = 3 ; % = 8.3	n = 1 ; % = 1.8	n = 0 ; % = 0
Clear-cell RCC No of events	n = 20 ; % = 55.5	n = 39 ; % = 70.1	n = 10 ; % = 90.9
Papillary RCC No of events	n = 9 ; % = 25	n = 2 ; % = 3.6	n = 1 ; % = 9.1
Chromophobe RCC No of events	n = 3 ; % = 8.3	n = 3 ; % = 5.5	n = 0 ; % = 0
Tumour size, mm Median (IQR)	45 (40 to 54.5)	46 (41 to 54)	42 (40 to 45)

Outcomes

Renal function impairment

Outcome	Robot-assisted partial nephrectomy, , N = 36	Cryoablation, , N = 55	Radiofrequency ablation, , N = 11
Onset of CKD e eGFR < 60 mL/min/1.73m2 No of events	n = 2 ; % = 6.5	n = 6 ; % = 15.4	n = 4 ; % = 66.7

Onset of CKD e eGFR < 60 mL/min/1.73m2 - Polarity - Higher values are better

Survival

Outcome	Robot-assisted partial nephrectomy, , N = 32	Cryoablation, , N = 44	Radiofrequency ablation, , N = 11
local recurrence No of events	n = 3 ; % = 9	n = 12 ; % = 27	n = 2 ; % = 18
Overall mortality No of events	n = 1 ; % = 3.1	n = 3 ; % = 6.8	n = 1 ; % = 9
Cancer specific mortality No of events	n = 0 ; % = 0	n = 2 ; % = 4.5	n = 0 ; % = 0

local recurrence - Polarity - Lower values are better
Overall mortality - Polarity - Lower values are better
Cancer specific mortality - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study presents a serious risk of bias due to confounding, as the study did not control the analysis for all important confounding domains. Furthermore, there is a moderate risk of bias due to deviations from intended interventions. Patients in the percutaneous thermal ablation group (cryoablation or radiofrequency ablation)*

Section	Question	Answer
		were assessed through early imaging evaluation on day 1, which allowed detect incomplete treatment and performing a salvage PTA intervention)
Overall bias	Directness	Directly applicable

Rusinek, 2022

Bibliographic Reference	Rusinek, M.; Salagierski, M.; Rozanski, W.; Jakobczyk, B.; Markowski, M.; Lipinski, M.; Wilkosz, J.; Comparison of the Results of Therapy for cT1 Renal Carcinoma with Nephron-Sparing Surgery (NSS) versus. Percutaneous Thermal Ablation (TA); Journal of Personalized Medicine; 2022; vol. 12 (no. 3); 495

Study details

Study type	Retrospective cohort study
Study location	Poland
Study setting	Hospital
Study dates	2014 to 2017
Sources of funding	This research received no external funding
Inclusion criteria	Patients with T1a Renal tumours were diagnosed with the use of ultrasonography, computed tomography and magnetic resonance imaging. Histopathology examination of removed tumour was performed afterwards. In patients treated with TA, ultrasonography-guided biopsy was performed.
Exclusion criteria	Not reported
Intervention(s)	Percutaneous thermal ablation • Patients with small T1 renal tumours with peripheral or intermediate location per R.E.N.A.L. score but who had objections related to age or general conditions, had renal contraindications (single kidney,

	• tumours in both kidneys) or who had not consented to surgery were qualified to thermal ablation. • Thermal ablation was performed with monopolar Cool-tip RF ablation system
Comparator	Nephron sparing surgery • Patients with small T1 renal tumours with peripheral or intermediate location per R.E.N.A.L. score were qualified to NSS • NSS was open laparotomy (ONSS) without clamping renal vessels.
Outcome measures	Survival Intraoperative severe adverse events
Number of participants	140
Duration of follow-up	3 years Imaging examinations such as ultrasound, CT, MRI, PET/CT were performed 3, 6 and 12 months after ablation followed by CT and MRI 6-monthly for 2 years. Patient follow-up was completed in 2020. Unclear if this was the same for NSS arm
Loss to follow-up	None
Methods of analysis	Nominal variables were displayed as a count of observations and percentage values calculated for investigated and control groups. Chi-squared test was used for comparison. For low count of observations to increase conservatism of the test, the Fisher's exact test was used. For survival analysis Kaplan-Meier's curve and single regression Cox proportional hazards model were applied. To eliminate the bias caused by clinical variables which substantially varied between investigated and control groups, multiple regression Cox proportional hazards model was used considering only those variables which were significant or almost significant ($p < 0.1$) in single regression model.
Additional comments	The observed overall survival of patients in both groups did not depend on the cancer but on the age of the patients. Patients treated with renal-saving surgery were at an average 10 years younger than patients treated with thermoablation.

	Patients treated with thermoablation had statistically significantly more co-morbidities than those treated with renal sparing surgery.

Study arms

Percutaneous thermal ablation (N = 84)

Nephron sparing surgery (N = 56)

Characteristics

Study-level characteristics

Characteristic	Study (N = 140)
Age Median (IQR)	67.5 (59 to 74.5)

Arm-level characteristics

Characteristic	Percutaneous thermal ablation (N = 84)	Nephron sparing surgery (N = 56)
% Female No of events	n = 35 ; % = 42.86	n = 28 ; % = 50
TNM classification: cT1a No of events	n = 75 ; % = 89.29	n = 51 ; % = 91.07
TNM classification: cT1b No of events	n = 9 ; % = 10.71	n = 14 ; % = 10
RCC type: Clear-cell No of events	n = 74 ; % = 94.05	n = 44 ; % = 78.57
RCC type: Papillary type 1 No of events	n = 2 ; % = 2.38	n = 4 ; % = 7.14

Characteristic	Percutaneous thermal ablation (N = 84)	Nephron sparing surgery (N = 56)
RCC type: Papillary type 2 No of events	n = 2 ; % = 2.38	n = 6 ; % = 91.07
RCC type: Chromophobe No of events	n = 1 ; % = 1.19	n = 2 ; % = 3.58
CHARLSON score Median (IQR)	5 (2.28 to 3)	3 (1.86 to 1)

Outcomes

Mortality

Outcome	Percutaneous thermal ablation, , N = 84	Nephron sparing surgery, , N = 56
Deaths in follow-up period No of events	n = 23 ; % = 27.3	n = 2 ; % = 3.5

Complications

Outcome	Percutaneous thermal ablation, , N = 84	Nephron sparing surgery, , N = 56
Clavien-Dindo grade 1 No of events	n = 82 ; % = 97.62	n = 51 ; % = 91.07
Clavien-Dindo grade 2 No of events	n = 0 ; % = 0	n = 3 ; % = 5.36
Clavien-Dindo grade 3 No of events	n = 1 ; % = 1.19	n = 1 ; % = 1.79

Outcome	Percutaneous thermal ablation, , N = 84	Nephron sparing surgery, , N = 56
Clavien-Dindo grade 5 No of events	n = 1 ; % = 1.19	n = 1 ; % = 1.79

Clavien-Dindo grade 1 - Polarity - Lower values are better
Clavien-Dindo grade 2 - Polarity - Lower values are better
Clavien-Dindo grade 3 - Polarity - Lower values are better
Clavien-Dindo grade 5 - Polarity - Lower values are better

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All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders. Event data only. Those with TA tended to be older.)*
Overall bias	Directness	Directly applicable

Ryoo, 2022

Bibliographic Reference	Ryoo, H.; Kang, M.; Sung, H.H.; Jeon, H.G.; Jeong, B.C.; Jeon, S.S.; Lee, H.M.; Park, B.K.; Seo, S.I.; A Comparison of Functional and Oncologic Outcomes between Partial Nephrectomy and Radiofrequency Ablation in Patients with Chronic Kidney Disease after Propensity Score Matching; Diagnostics; 2022; vol. 12 (no. 10); 2292

Study details

Study type	Retrospective cohort study
Study location	Korea
Study setting	Hospital setting.
Study dates	From 2005 to 2019
Sources of funding	This research received no external funding.

Inclusion criteria	Patients with cT1aN0M0 renal masses
Exclusion criteria	Patients with multiple renal masses Patients with, bilateral renal masses Patients with a history of hereditary renal cell carcinoma
Intervention(s)	Partial nephrectomy (PN)
Comparator	Radiofrequency ablation (RFA)
Outcome measures	Renal functional impairment
Number of participants	Total number of participants = 511 PN CKD Stage 2 (60 ≤ eGFR < 90) = 270 RFA CKD Stage 2 (60 ≤ eGFR < 90) = 135 PN CKD stage 3 or Higher (eGFR < 60) = 53 RFA CKD stage 3 or Higher (eGFR < 60) = 53
Duration of follow-up	PN CKD Stage 2 (60 ≤ eGFR < 90) (mean - SD) = 51.4 - 34.2 RFA CKD Stage 2 (60 ≤ eGFR < 90) (mean - SD) = 51.0 - 36.0 PN CKD stage 3 or Higher (eGFR < 60) (mean - SD) = 54.3 - 40.3 RFA CKD stage 3 or Higher (eGFR < 60) (mean - SD) = 43.3 - 39.0
Loss to follow-up	Not reported
Methods of analysis	Propensity scores were estimated using a logistic regression model. Demographic and clinical characteristics were analysed using Student's t-tests for continuous variables and the chi-squared test for categorical variables.

Study arms

Partial nephrectomy (CKD Stage 2) (N = 270)

Radiofrequency ablation (CKD Stage 2) (N = 135)

Partial nephrectomy (CKD stage 3 or Higher) (N = 53)

Radiofrequency ablation (CKD stage 3 or Higher) (N = 53)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (CKD Stage 2) (N = 270)	Radiofrequency ablation (CKD Stage 2) (N = 135)	Partial nephrectomy (CKD stage 3 or Higher) (N = 53)	Radiofrequency ablation (CKD stage 3 or Higher) (N = 53)
% Female No of events	n = 75 ; % = 27.8	n = 35 ; % = 25.9	n = 15 ; % = 28.3	n = 12 ; % = 22.6
Age Mean (SD)	62.8 (10.9)	63 (12.4)	66.6 (8.8)	66.5 (11.7)
Unknown (not biopsied) No of events	n = 0 ; % = 0	n = 47 ; % = 34.8	n = 0 ; % = 0	n = 19 ; % = 35.8
Benign No of events	n = 8 ; % = 3	n = 12 ; % = 8.9	n = 2 ; % = 3.8	n = 9 ; % = 17
Clear cell RCC No of events	n = 213 ; % = 78.9	n = 62 ; % = 45.9	n = 46 ; % = 86.8	n = 22 ; % = 41.5
Non-clear cell RCC No of events	n = 49 ; % = 18.1	n = 14 ; % = 10.4	n = 5 ; % = 9.4	n = 3 ; % = 5.7
Baseline renal function	76.3 (8.2)	75.9 (7.9)	48.6 (10.6)	33.2 (18.8)

Characteristic	Partial nephrectomy (CKD Stage 2) (N = 270)	Radiofrequency ablation (CKD Stage 2) (N = 135)	Partial nephrectomy (CKD stage 3 or Higher) (N = 53)	Radiofrequency ablation (CKD stage 3 or Higher) (N = 53)
Mean (SD)				
Tumour size (cm) Mean (SD)	2.19 (0.74)	2.13 (0.83)	2.27 (0.7)	2.2 (0.85)

Outcomes

Renal functional impairment

Outcome	Partial nephrectomy (CKD Stage 2), , N = 270	Radiofrequency ablation (CKD Stage 2), , N = 135	Partial nephrectomy (CKD stage 3 or Higher), , N = 53	Radiofrequency ablation (CKD stage 3 or Higher), , N = 53
Upstaging to CKD stage 3 at 1 year post-treatment No of events	n = 35 ; % = 13	n = 19 ; % = 14.1	*empty data*	*empty data*
CKD upstaging at 3 years post-treatment No of events	*empty data*	*empty data*	n = 6 ; % = 7.1	n = 9 ; % = 17
Upstaging to stage 4 No of events	*empty data*	*empty data*	n = 2 ; % = 2.4	n = 3 ; % = 5.7
Upstaging to stage 5 No of events	*empty data*	*empty data*	n = 4 ; % = 4.7	n = 6 ; % = 11.3

CKD upstaging - CKD stage 2 (60 ≤ eGFR < 90) - Polarity - Lower values are better
CKD upstaging - CKD Stage 3 or Higher (eGFR < 60) - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not adjust the results presented to control possible confounding factors. There is no information on how propensity score matching was performed)*
Overall bias	Directness	Directly applicable

Shapiro, 2020

Bibliographic Reference	Shapiro, Daniel D; Wells, Shane A; Best, Sara L; Hedican, Sean P; Ziemlewicz, Timothy J; Lubner, Meghan G; Hinshaw, James Louis; Lee, Fred T Jr; Jarrard, David F; Richards, Kyle A; Downs, Tracy M; Allen, Glenn O; Nakada, Stephen Y; Abel, Edwin Jason; Comparing Outcomes for Patients with Clinical T1b Renal Cell Carcinoma Treated With Either Percutaneous Microwave Ablation or Surgery.; Urology; 2020; vol. 135; 88-94

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	Between January 2000 and June 2018
Sources of funding	None
Inclusion criteria	cT1b renal mass (between 4 and 7cm)
Exclusion criteria	Advanced RCC (presence of tumor thrombus or metastatic disease) Patients with hereditary RCC syndromes
Intervention(s)	Microwave Ablation (MW)

Comparator	Partial nephrectomy (PN) Radical nephrectomy (RN)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: 325 MW: 40 PN: 74 RN: 211
Duration of follow-up	Median follow-up was 34, 35, and 49 months following MW, PN, and RN, respectively.
Loss to follow-up	Not reported
Methods of analysis	Survival analysis was performed between the MW, PN, and RN cohorts. Local recurrence-free survival (LRFS), metastasis-free survival (MFS), and cancer-specific survival (CSS) were determined using the Kaplan-Meier method. Univariable and multivariable Cox proportional hazard regression was performed to assess the relationships between variables and survival outcomes.

Study arms

Microwave Ablation (N = 40)

Partial Nephrectomy (N = 74)

Radical Nephrectomy (N = 211)

Characteristics

Arm-level characteristics

Characteristic	Microwave Ablation (N = 40)	Partial Nephrectomy (N = 74)	Radical Nephrectomy (N = 211)
% Female	n = 10 ; % = 25	n = 25 ; % = 34	n = 75 ; % = 35

Characteristic	Microwave Ablation (N = 40)	Partial Nephrectomy (N = 74)	Radical Nephrectomy (N = 211)
No of events			
Age Median (IQR)	69 (65 to 77)	58 (51 to 65)	59 (51 to 71)
Open No of events	*empty data*	n = 60 ; % = 81	n = 44 ; % = 21
Laparoscopic/robotic No of events	*empty data*	n = 14 ; % = 19	n = 167 ; % = 79
Clear cell No of events	n = 35 ; % = 87.5	n = 54 ; % = 73	n = 173 ; % = 82
Papillary No of events	n = 3 ; % = 7.5	n = 13 ; % = 18	n = 19 ; % = 9
Chromophobe No of events	n = 1 ; % = 2.5	n = 5 ; % = 7	n = 8 ; % = 4
Unclassified No of events	n = 1 ; % = 2.5	n = 2 ; % = 3	n = 11 ; % = 5
Radiographic tumor diameter, cm Median (IQR)	4.4 (4.1 to 5)	4.7 (4.1 to 5.3)	5 (4.5 to 6)

Outcomes

Survival

Outcome	Microwave Ablation, , N = 40	Partial Nephrectomy, , N = 74	Radical Nephrectomy, , N = 211
local recurrence No of events	n = 2 ; % = 5	n = 1 ; % = 1.4	n = 1 ; % = 0.5

Outcome	Microwave Ablation, , N = 40	Partial Nephrectomy, , N = 74	Radical Nephrectomy, , N = 211
metastatic recurrence No of events	n = 0 ; % = 0	n = 4 ; % = 5.4	n = 19 ; % = 9
Cancer specific mortality No of events	n = 0 ; % = 0	n = 3 ; % = 4.1	n = 12 ; % = 5.7

local recurrence - Polarity - Lower values are better
metastatic recurrence - Polarity - Lower values are better
Cancer specific mortality - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study presents a serious risk of bias due to confounding, as the study did not adjust the results presented to control possible confounding factors. Furthermore, there is a statistical difference in some baseline characteristics e.g. patients in the microwave ablation arm were older and had higher Charlson comorbidity index, which may have affected the outcomes.)*
Overall bias	Directness	Partially Applicable *(The study was conducted in the US, which has a different healthcare system than the UK NHS. However, the interventions (microwave ablation, partial and radical nephrectomy) and the patient population (T1b) are relevant to the UK NHS setting. The outcomes assessed in the study, such as mortality and recurrence are important for decision-making in the UK NHS context.)*

Staehler, 2022

Bibliographic Reference	Staehler, Michael; Schuler, Tina; Spek, Annabel; Rodler, Severin; Tamalunas, Alexander; Furweger, Christoph; Muacevic, Alexander; Propensity Score-Matched Analysis of Single Fraction Robotic Radiosurgery Versus Open Partial Nephrectomy in Renal Cell Carcinoma: Oncological Outcomes.; Cureus; 2022; vol. 14 (no. 1); e21623

Study details

Study type	Retrospective cohort study
Study location	Germany
Study setting	Hospital
Study dates	January 2009 and December 2017
Sources of funding	All authors have declared that no financial support was received from any organization for the submitted work
Inclusion criteria	Patients with histologically proven clear cell RCC
Exclusion criteria	Not reported
Intervention(s)	High-dose local stereotactic robotic radiosurgery (RRS) RRS was performed using a radiosurgical device (Cyberknife® G6, Accuray Incorporated, Sunnyvale, California, United States) with real-time tumour tracking
Comparator	Open partial nephrectomy OPN was performed according to the surgeon's discretion following standard surgical principles
Outcome measures	Recurrence Survival
Number of participants	70
Duration of follow-up	Median follow-up was 28.1 months in both groups (range 6.0-78.3 months).
Loss to follow-up	None
Methods of analysis	• The PSM method was applied to eliminate any significant difference in oncological and clinical characteristics. Nonparsimonious and multivariate logistic regression was utilized to calculate the propensity scores on the basis of ECOG performance status, age, and tumour size. • 35 patients in the RRS group were perfectly matched to 35 patients in the OPN group in a 1:1 ratio according to the nearest neighbour matching method

	• Kaplan-Meier analysis, Cox regression, and log-rank calculations were used to estimate overall survival (OS) with a one-sided p value. • Differences in matching categories were calculated with the Mann-Whitney U test and statistical significance was set at a two-sided p<.05.
Additional comments	• Limitations in the literature so far are the lack of prospective data and the selection bias of patients especially as ablative techniques are used in patients unfit for surgery. • The authors noted that that there is a size limitation to single fraction RRS of below 5cm and that larger tumours are not suitable for this kind of therapy. • Median OS not yet reached

Study arms

High-dose local stereotactic robotic radiosurgery (N = 35)

Partial nephrectomy (N = 35)

Characteristics

Arm-level characteristics

Characteristic	High-dose local stereotactic robotic radiosurgery (N = 35)	Partial nephrectomy (N = 35)
Age Median (IQR)	65 (58 to 75)	71 (56 to 76)

Outcomes

Survival

Outcome	Partial nephrectomy versus High-dose local stereotactic robotic radiosurgery, , N2 = 35, N1 = 35
Overall survival	1.48 (0.5 to 4.16)

Outcome	Partial nephrectomy versus High-dose local stereotactic robotic radiosurgery, , N2 = 35, N1 = 35
Hazard ratio/95% CI	

Recurrence

Outcome	High-dose local stereotactic robotic radiosurgery, , N = 35	Partial nephrectomy, , N = 35
local recurrence No of events	n = 1 ; % = 2.86	n = 0 ; % = 0

local recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Adjusted for confounders but might not have been all the important ones)*
Overall bias	Directness	Directly applicable

Takaki, 2014

Bibliographic Reference	Takaki, Haruyuki; Soga, Norihito; Kanda, Hideki; Nakatsuka, Atsuhiro; Uraki, Junji; Fujimori, Masashi; Yamanaka, Takashi; Hasegawa, Takaaki; Arima, Kiminobu; Sugimura, Yoshiki; Sakuma, Hajime; Yamakado, Koichiro; Radiofrequency ablation versus radical nephrectomy: clinical outcomes for stage T1b renal cell carcinoma.; Radiology; 2014; vol. 270 (no. 1); 292-9

Study details

Study type	Retrospective cohort study
Study location	Japan

Study setting	Hospital. Single institutional review
Study dates	2002 to 2012
Sources of funding	None reported.
Inclusion criteria	Patients with a single renal cell carcinoma measuring 4.1-7.0cm in maximum diameter (stage T1b) Tumours without extrarenal spread or vascular invasion With at least 6 months follow up
Exclusion criteria	Not reported
Intervention(s)	Radiofrequency ablation (RFA) The RF electrodes were inserted into the tumour through the normal renal parenchyma to minimize the risk of haemorrhage and tumour seeding. The diagnosis of RCC was established with needle biopsy in 10 of the 21 patients (48%). RCC was diagnosed on the basis of imaging findings in the other patients.
Comparator	Radical nephrectomy (RN) Approaches of radical nephrectomy (open or laparoscopic) were determined by the surgeons on the basis of tumour location, patient wishes, and history of previous abdominal surgery. Of the 39 patients who underwent radical nephrectomy, 28 (72%) received open radical nephrectomy and 11 (28%) received laparoscopic radical nephrectomy.
Number of participants	N=60 RFA: 21 RN: 39
Duration of follow-up	Months, mean (SD) RFA: 41.3 (31.1) RN: 48.6 (33.2)
Loss to follow-up	Not reported.
Methods of analysis	The two patient groups were compared by using the Mann-Whitney U test for continuous variables and the Fisher exact test for categoric variables. The survival intervals were defined from each treatment to death from any cause (overall survival), death related to RCC (RCC-related survival), and RCC recurrence or death related to RCC (disease-free survival). These

	survival curves were generated by using the Kaplan-Meier method and compared with the log-rank test. No confounders adjusted for in the analysis.
Additional comments	Renal functional outcomes are not extracted here as they are reported in an included systematic review (Patel 2017).

Study arms

Radiofrequency ablation (N = 21)

Radical nephrectomy (N = 39)

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 21)	Radical nephrectomy (N = 39)
% Female No of events	n = 2 ; % = 9.5	n = 11.28
Age Mean (SD)	71.6 (12.3)	61.8 (12.9)
Tumour size cm Mean (SD)	4.6 (0.5)	5.2 (0.9)
Single kidney No of events	n = 3 ; % = 14	n = 0 ; % = 0

Outcomes

Survival

Outcome	Radiofrequency ablation, , N = 21	Radical nephrectomy, , N = 39
Mortality At 46 months No of events	n = 5 ; % = 24	n = 1 ; % = 2.6
Kidney cancer-specific mortality No of events	n = 1 ; % = 4.8	n = 0 ; % = 0
Recurrence Local and metastatic No of events	n = 2 ; % = 9.5	n = 4 ; % = 10.25
local recurrence No of events	n = 0 ; % = 0	n = 1 ; % = 2.6
Metastasis No of events	n = 2 ; % = 9.5	n = 3 ; % = 7.7

Mortality - Polarity - Lower values are better
Kidney cancer-specific mortality - Polarity - Lower values are better
Recurrence - Polarity - Lower values are better
local recurrence - Polarity - Lower values are better
Metastasis - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All survival and recurrence outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounding or matching, and arms are not similar at baseline. Limited information available on missing data, and no protocol identified to verify bias in selection of reported result.)*

Section	Question	Answer
Overall bias	Directness	Directly applicable

Takaki, 2010

Bibliographic Reference	Takaki, Haruyuki; Yamakado, Koichiro; Soga, Norihito; Arima, Kiminobu; Nakatsuka, Atsuhiro; Kashima, Masataka; Uraki, Junji; Yamada, Tomomi; Takeda, Kan; Sugimura, Yoshiki; Midterm results of radiofrequency ablation versus nephrectomy for T1a renal cell carcinoma.; Japanese journal of radiology; 2010; vol. 28 (no. 6); 460-8

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital. Review of a single institution.
Study dates	2002 to 2008
Sources of funding	Information on funding not reported
Inclusion criteria	With at least 6 months follow up Patients with a single RCC of 4cm or less in maximum diameter (T1a)
Exclusion criteria	Patients with RCCs with vascular invasion or extrarenal spread
Intervention(s)	Radiofrequency ablation (RFA) Single session with additional session if residual tumour remained. RCC was diagnosed based on imaging findings in 39 patients (76.5%, 39/51). Needle biopsy was performed in the other 12 patients (23.5%, 12/51) to determine the presence of a primary or metastatic renal cancer (n = 8) or whose imaging findings were not typical for RCC (n = 4).
Comparator	Radical nephrectomy (RN) open or laparoscopic. The diagnosis of RCC was confirmed by pathological findings in all patients from the radical nephrectomy group. Of 54 patients, 33 (61.1%, 33/54) underwent open radical nephrectomy and 21 patients (38.9%, 21/54) laparoscopic radical nephrectomy.
Number of participants	Months, mean, SD

	RFA: 51 RN: 54
Duration of follow-up	RFA: 34.0 ± 23.2 RN: 40.9 ± 23.2
Loss to follow-up	Not reported
Methods of analysis	The cumulative overall survival, RCC-related survival, and DFS curves were generated using the Kaplan-Meier method and were compared using the log-rank test.
Additional comments	Study contains three arms (thermal ablation, radical nephrectomy and partial nephrectomy). Only TA versus RN comparison is extracted here. TA versus PN comparison is reported in an included systematic review (Xu 2019) and RN versus PN is not within the scope of this review question. All but five patients (90.2%, 46/51) in the RF ablation group were judged not to be surgical candidates due to high surgical and general anaesthesia risk because of medical comorbidities (n = 22), association of other cancers (n = 15), risk for newly requiring dialysis (n = 11), and advanced age (>80 years) (n = 5). The other five patients refused surgical intervention. The survival intervals were defined from each treatment to death from any cause (overall survival), death related to RCC (RCC-related survival), and death related to RCC or RCC recurrence (disease-free survival; DFS).

Study arms

Radiofrequency ablation (N = 51)

Radical nephrectomy (N = 54)

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 51)	Radical nephrectomy (N = 54)
% Female No of events	n = 15 ; % = 29.4	n = 15 ; % = 27.8

Characteristic	Radiofrequency ablation (N = 51)	Radical nephrectomy (N = 54)
Age Mean (SD)	69.4 (9.6)	57.6 (11.7)
Tumour size cm Mean (SD)	2.4 (0.7)	2.8 (0.7)
Presence of comorbid disease (other cancer, cerebrovascular, cardiopulmonary, liver cirrhosis, renal disease/dysfunction, diabetes, other) No of events	n = 46 ; % = 90.2	n = 31 ; % = 57.4
Haemodialysis No of events	n = 5 ; % = 9.8	n = 7 ; % = 13

Outcomes

Recurrence and survival

Outcome	Radiofrequency ablation, , N = 51	Radical nephrectomy, , N = 54
Mortality No of events	n = 8 ; % = 15.7	n = 0 ; % = 0
Cancer-specific mortality No of events	n = 0 ; % = 0	n = 0 ; % = 0
local recurrence No of events	n = 0 ; % = 0	n = 0 ; % = 0
Distant recurrence No of events	n = 1 ; % = 2	n = 2 ; % = 3.7

Mortality - Polarity - Lower values are better
Cancer-specific mortality - Polarity - Lower values are better
local recurrence - Polarity - Lower values are better

Distant recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All recurrence and survival outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders or matching undertaken. No protocol identified so unable to fully assess bias in selection of reported result.)*
Overall bias	Directness	Directly applicable

Tanagho, 2013

Bibliographic Reference	Tanagho, Youssef S; Bhayani, Sam B; Kim, Eric H; Figenshau, R Sherburne; Renal cryoablation versus robot-assisted partial nephrectomy: Washington University long-term experience.; Journal of endourology; 2013; vol. 27 (no. 12); 1477-86

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Single institution (Washington University)
Study dates	2000 to 2012 (Cryoablation: 2000 to 2011; partial nephrectomy: 2007 to 2012)
Sources of funding	Midwest Stone Institute. One author is a consultant for Surgiquest (manufactures technologies for minimally invasive surgery)
Inclusion criteria	Patients with contrast enhancing renal masses concerning for RCC on preoperative imaging
Exclusion criteria	Not reported
Intervention(s)	Cryoablation (laparoscopic and percutaneous)

	Patient comorbidity and surgical risk, tumour location and size, and the preference of the patient and treating surgeon all contributed to the choice of treatment.
Comparator	Robot-assisted partial nephrectomy (PN)
Outcome measures	Recurrence Postoperative severe adverse events
Number of participants	N=500 Cryoablation: 267 PN: 233
Duration of follow-up	Mean radiographic follow up (SD), months Cryoablation: 39.8 (34.3) PN: 21.9 (18.8)
Loss to follow-up	Not reported
Methods of analysis	For the subset of patients with pathologically confirmed, localised RCC, Kaplan-Meier analysis of disease-free survival (DFS), cancer-specific survival (CSS), and overall survival (OS) was performed in each treatment group. The log-rank test was used to compare DFS, CSS, and OS between the two groups. A multivariate Cox proportional hazards model identified variables that predicted cancer recurrence in the same patient subset. Authors report that model adjusted for baseline patient and tumour characteristics, but does not specify which.
Additional comments	Loss to follow up not reported, but study authors report that unavailable data and patient loss to follow-up may impact overall outcomes. Mortality and cancer specific mortality calculated by NICE team from percentages reported from a Kaplan-Meier analysis. This analysis was conducted in a subset of confirmed localised RCC.

Study arms

Cryoablation (N = 267)

Partial nephrectomy (N = 233)

Robot-assisted

Characteristics

Arm-level characteristics

Characteristic	Cryoablation (N = 267)	Partial nephrectomy (N = 233)
% Female No of events	n = 104 ; % = 39	n = 106 ; % = 45.5
Age Mean (SD)	69.3 (11)	57.4 (11.9)
Tumour size cm Mean (SD)	2.5 (1)	2.9 (1.5)
Nephrometry score Mean (SD)	6.4 (1.7)	7.3 (1.9)
Tumour pathology - RCC No of events	n = 80 ; % = 52.3	n = 185 ; % = 79.4
Tumour pathology - RCC Sample size	n = 153	n = 233
Tumour pathology - other No of events	n = 73 ; % = 47.7	n = 48 ; % = 20.6
Tumour pathology - other Sample size	n = 153	n = 233
Solitary kidney No of events	n = 26 ; % = 10.1	n = 3 ; % = 1.3

Outcomes

Complications

Outcome	Cryoablation, , N = 267	Partial nephrectomy, , N = 233
Clavien-Dindo grade 1 No of events	n = 1 ; % = 0.4	n = 5 ; % = 2.1
Clavien-Dindo grade 2 No of events	n = 2 ; % = 0.8	n = 10 ; % = 4.3
Clavien-Dindo grade 3 No of events	n = 2 ; % = 0.8	n = 3 ; % = 1.3
Clavien-Dindo grade 4 No of events	n = 2 ; % = 0.8	n = 3 ; % = 1.3

Clavien-Dindo grade 1 - Polarity - Lower values are better
Clavien-Dindo grade 2 - Polarity - Lower values are better
Clavien-Dindo grade 3 - Polarity - Lower values are better
Clavien-Dindo grade 4 - Polarity - Lower values are better

Survival and recurrence

Outcome	Cryoablation versus Partial nephrectomy, , N2 = 80, N1 = 185
Disease free survival Odds ratio/95% CI	11.41 (1.9 to 68.67)

Disease free survival - Polarity - Lower values are better

Survival and recurrence

Outcome	Cryoablation, , N = 80	Partial nephrectomy, , N = 185
Mortality At 5 years, from K-M analysis No of events	n = 19 ; % = 22.9	n = 15 ; % = 8.3
Cancer specific mortality At 5 years, from K-M analysis No of events	n = 4 ; % = 5.6	n = 0 ; % = 0

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All complication and mortality outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, likely to be at risk of high levels of missing data, longer follow-up time for cryoablation arm affecting recurrence results, no protocol identified.)*
Overall bias	Directness	Directly applicable

Disease-free survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Result from a multivariate model, but confounders adjusted for not reported. Likely to be at risk of high levels of missing data, longer follow-up time for cryoablation arm affecting recurrence results, no protocol identified.)*
Overall bias	Directness	Directly applicable

Tang, 2017

Bibliographic Reference	Tang, Dominic H; Nawlo, Jude; Chipollini, Juan; Gilbert, Scott M; Poch, Michael; Pow-Sang, Julio M; Sexton, Wade J; Spiess, Philippe E; Management of Renal Masses in an Octogenarian Cohort: Is There a Right Approach?.; Clinical genitourinary cancer; 2017; vol. 15 (no. 6); 696-703

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Retrospective review from a single institution.
Study dates	2000 to 2013
Sources of funding	No conflicts of interest. No funding information reported.

Inclusion criteria	Patients with incidentally found enhancing solid renal mass. Patients aged 80 to 89
Exclusion criteria	Metastatic disease at evaluation
Intervention(s)	Active surveillance (AS): Active surveillance was performed with repeat cross-sectional imaging studies of the abdomen and pelvis within a minimum of 6 months after diagnosis. The decision to proceed with delayed intervention for active surveillance was influenced by the tumour growth rate, disease progression, and patient and surgeon discretion. Partial nephrectomy (PN): laparoscopic, robotic-assisted or open approach. Radical nephrectomy (RN): laparoscopic, robotic-assisted or open approach. Treatment decisions in all cases were determined by the patient and treating physician after consideration of the tumour characteristics, radiologic appearance, patient life expectancy, treatment options, and patient and surgeon preference. Surgical follow-up protocol determined by pathologic stage.
Comparator	Interventions compared with each other
Outcome measures	Survival
Number of participants	N=115 AS: 31 PN: 31 RN: 53
Duration of follow-up	Median follow-up period: 51 months (IQR, 23-81 months). Not reported at arm level.
Loss to follow-up	Not reported.
Methods of analysis	The Kaplan-Meier method and log-rank test were used to evaluate differences in unadjusted survival curves. The Cox proportional hazards model was used to perform multivariable analysis for survival. The variables included in the multivariable analysis were age, Charlson comorbidity index, clinical stage, and management type.

Additional comments	AS versus PN results not extracted as included in an included systematic review (Guo 2019). Only AS versus RN results extracted here. The follow-up duration for survival was defined as the interval from date of surgery to the date of the last follow-up examination or death. The follow-up duration for survival for active surveillance patients was defined the interval from the start of active surveillance to the date of the last follow-up visit or death. All follow-up data were obtained through the institutional tumour registry. Five patients (16%) receiving active surveillance eventually underwent surgical intervention owing to a concerning increase in size or disease progression. Two patients with cT1a disease underwent cryoablation and partial nephrectomy. Two patients with cT1b disease also underwent partial nephrectomy. 1 patient receiving active surveillance initially with cT2 disease developed renal vein involvement 6 months after diagnosis and underwent radical nephrectomy. Limitations: AS arm did not undergo biopsy of the renal mass. Small study underpowered to detect an effect. All patients undergoing intervention were acceptable surgical candidates. Follow-up data not reported at arm level.

Study arms

Active surveillance (N = 31)

Partial nephrectomy (N = 31)

Radical nephrectomy (N = 53)

Characteristics

Arm-level characteristics

Characteristic	Active surveillance (N = 31)	Partial nephrectomy (N = 31)	Radical nephrectomy (N = 53)
% Female No of events	n = 13	n = 7	n = 23
Age Median (IQR)	83 (82 to 86)	81 (80 to 84)	82 (81 to 85)

Characteristic	Active surveillance (N = 31)	Partial nephrectomy (N = 31)	Radical nephrectomy (N = 53)
Tumour size cm Median (IQR)	2.7 (2.3 to 3.7)	3.2 (2.5 to 4.3)	5.5 (4 to 8)
TNM classification - cT1a No of events	n = 28 ; % = 81	n = 23 ; % = 74	n = 11 ; % = 21
TNM classification - cT1b No of events	n = 5 ; % = 16	n = 6 ; % = 19	n = 20 ; % = 38
TNM classification - cT2 No of events	n = 1 ; % = 3	n = 2 ; % = 7	n = 14 ; % = 26
TNM classification - cT3 No of events	n = 0 ; % = 0	n = 0 ; % = 0	n = 8 ; % = 15
Primary RCC type - Clear cell No of events	n = 3 ; % = 60	n = 14 ; % = 45	n = 40 ; % = 76
Primary RCC type - Papillary No of events	n = 2 ; % = 40	n = 6 ; % = 19	n = 5 ; % = 9
Primary RCC type - Chromophobe No of events	n = 0 ; % = 0	n = 3 ; % = 10	n = 1 ; % = 2
Primary RCC type - mixed No of events	n = 0 ; % = 0	n = 3 ; % = 10	n = 1 ; % = 2
Primary RCC type - other No of events	n = 0 ; % = 0	n = 2 ; % = 7	n = 2 ; % = 4

Characteristic	Active surveillance (N = 31)	Partial nephrectomy (N = 31)	Radical nephrectomy (N = 53)
Primary RCC type - Benign No of events	n = 0 ; % = 0	n = 5 ; % = 16	n = 2 ; % = 6
Nephrometry score Median (IQR)	6 (6 to 8)	6 (4 to 8)	8 (6 to 10)

Outcomes

Survival

Outcome	Radical nephrectomy versus Active surveillance, , N2 = 53, N1 = 31
Overall survival - whole cohort Hazard ratio/95% CI	0.9 (0.5 to 1.9)
Overall survival - T1a only Hazard ratio/95% CI	1 (0.3 to 2.8)

Overall survival - whole cohort - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Overall survival outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Insufficient adjustment for confounders (renal function at baseline not adjusted for); insufficient reporting on missing data; unclear follow-up duration at arm level; no protocol identified.)*
Overall bias	Directness	Directly applicable

Turna, 2009

Bibliographic Reference	Turna, Burak; Kaouk, Jihad H; Frota, Rodrigo; Stein, Robert J; Kamoi, Kazumi; Gill, Inderbir S; Novick, Andrew C; Minimally invasive nephron sparing management for renal tumors in solitary kidneys.; The Journal of urology; 2009; vol. 182 (no. 5); 2150-7

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Data registry from single institution.
Study dates	September 1997 to October 2006
Sources of funding	No funding reported. One author listed as having a financial interested and / or other relationship with Intuitive Surgical (maker of robotic surgical products).
Inclusion criteria	Patients who underwent minimally invasive nephron sparing management for renal tumours Solitary kidney
Exclusion criteria	Not reported
Intervention(s)	Partial nephrectomy (PN) Laparoscopic. Initially reserved for small peripheral exophytic tumours but more complex tumours were treated with increasing experience. The ideal surgical treatment in an individual was chosen at surgeon discretion.
Comparator	2 separate arms. Ablative procedures were done for localised, less than 4 cm, enhancing solid renal masses in select patients with significant comorbidities, particularly percutaneous RFA in patients at greater risk for surgery under general anaesthesia. Followup protocol for ablative procedures includes MRI on postoperative day 1, and at 3, 6, 12, 24, 36, 48 and 60 months. Kidney biopsy at the treatment site is often done 6 months after treatment and tissue is analysed. 1) Cryoablation: A 3-port retroperitoneal laparoscopic approach was used to create renal cryolesions. Puncture cryoablation was performed with a 4.8-mm cryoprobe. 2) Radiofrequency ablation (RFA): Fine needle biopsy and RFA probe introduction are performed under CT guidance. Ablation is done at a 200 W power setting, generating a core temperature of 105C, which is maintained

	for 10 minutes per treatment cycle. The number of cycles is determined by tumour size.
Outcome measures	Recurrence Survival
Number of participants	N=101 PN: 36 Cryoablation: 36 RFA: 29
Duration of follow-up	PN: median 42.5 months Cryoablation: median 24 months RFA: Not reported
Loss to follow-up	Not reported
Methods of analysis	Nominal data were analyzed using the chi-square test. Continuous data were analyzed using ANOVA and means were compared using Student's t test. Univariate analysis was done using contingency table analysis and logistic fit model for nominal and continuous data, respectively. Multivariate regression analysis using the ordinal logistic fit model included variables with p <0.20 on univariate analysis.
Additional comments	Study had 3 arms. Renal functional outcomes not extracted as reported in an included systematic review (Patel 2017). Limitations: retrospective study, different follow up regimes across arms, limited reporting. Complete pathological analysis is not available for ablation arms since probe ablative procedures rely on radiographic imaging and postoperative needle biopsy instead of on whole specimen histopathological analysis.

Study arms

Partial nephrectomy (N = 36)

Laparoscopic

Cryoablation (N = 36)

Radiofrequency ablation (N = 29)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 36)	Cryoablation (N = 36)	Radiofrequency ablation (N = 29)
% Female No of events	n = 15 ; % = 42	n = 13 ; % = 36	n = 11 ; % = 38
Age Mean (SD)	60.3 (15.5)	64.1 (11.1)	60.7 (14.3)
Tumour size Mean (SD)	3.7 (1.9)	2.5 (1.1)	2.6 (1)
Benign tumours (at biopsy - not fully conducted for ablation arms) No of events	n = 13 ; % = 36.2	n = 8 ; % = 26.7	n = 5 ; % = 17.2

Outcomes

Duration of hospital stay

Outcome	Partial nephrectomy, , N = 36	Cryoablation, , N = 36	Radiofrequency ablation, , N = 29
Duration of hospital stay Mean (SD)	3.3 (2.6)	1.8 (1.3)	1 (0)

Duration of hospital stay - Polarity - Lower values are better

Survival

Outcome	Partial nephrectomy, , N = 36	Cryoablation, , N = 36	Radiofrequency ablation, , N = 29
Overall mortality 2 years No of events	n = 3 ; % = 8.3	n = 4 ; % = 11	n = 4 ; % = 13.8
Cancer specific mortality 2 years No of events	n = 0 ; % = 0	n = 3 ; % = 8.3	n = 3 ; % = 10.3
local recurrence 2 years No of events	n = 0 ; % = 0	n = 6 ; % = 16.67	n = 13 ; % = 44.8
Distant recurrence No of events	n = 0 ; % = 0	n = 3 ; % = 8.33	n = 4 ; % = 13.79

Overall mortality - Polarity - Lower values are better
Cancer specific mortality - Polarity - Lower values are better
local recurrence - Polarity - Lower values are better
Distant recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Overall mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Cancer-specific mortality

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Local recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Distant recurrence

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders, limited reporting on missing data and protocol not identified)*
Overall bias	Directness	Directly applicable

Uemura, 2021

Bibliographic Reference	Uemura, Toshihiro; Kato, Taigo; Nagahara, Akira; Kawashima, Atsunari; Hatano, Koji; Ujike, Takeshi; Ono, Yusuke; Higashihara, Hiroki; Fujita, Kazutoshi; Fukuhara, Shinichiro; Kiuchi, Hiroshi; Imamura, Ryoichi; Tomiyama, Noriyuki; Nonomura, Norio; Uemura, Motohide; Therapeutic and Clinical Outcomes of Robot-assisted Partial Nephrectomy Versus Cryoablation for T1 Renal Cell Carcinoma.; In vivo (Athens, Greece); 2021; vol. 35 (no. 3); 1573-1579

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital setting
Study dates	Between March 2016 and November 2019
Sources of funding	Not reported
Inclusion criteria	Patients with cT1 renal tumour
Exclusion criteria	Not reported
Intervention(s)	Robot-assisted partial nephrectomy (RAPN)
Comparator	Percutaneous cryoablation (PCA)
Outcome measures	Recurrence Survival
Number of participants	Total number of participants: 126 RAPN: 78 PCA: 48
Duration of follow-up	Median (IQR) RAPN: 18.5 months (12-30) PCA: 12 months (6-32)
Loss to follow-up	Not reported
Methods of analysis	Multiple logistic regression analysis was used to evaluate factors associated with trifecta achievement in the RAPN group and decline in

	renal function at 6 months postoperatively in all patients. The Kaplan-Meier method was used to calculate survival rates and log-rank tests were used to compare the two groups.
Additional comments	Postoperative complication outcomes not extracted as within the search period of an included systematic review (Yanagisawa 2022)

Study arms

Robot-assisted partial nephrectomy (N = 78)

Percutaneous cryoablation (N = 48)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 78)	Percutaneous cryoablation (N = 48)
% Female No of events	n = 15 ; % = 19	n = 7 ; % = 14.6
Age Median (IQR)	61 (52 to 69)	78 (70 to 82)
T1a No of events	n = 73 ; % = 93.6	n = 46 ; % = 95.8
T1b No of events	n = 5 ; % = 6.4	n = 2 ; % = 4.2
Clear cell No of events	n = 58 ; % = 74.3	n = 41 ; % = 85.4
Papillary No of events	n = 11 ; % = 14.1	n = 4 ; % = 8.3
Chromophobe No of events	n = 6 ; % = 7.7	n = 2 ; % = 4.2

Characteristic	Robot-assisted partial nephrectomy (N = 78)	Percutaneous cryoablation (N = 48)
Oncocytoma No of events	n = 2 ; % = 2.6	n = 0 ; % = 0
AML No of events	n = 1 ; % = 1.3	n = 0 ; % = 0
Unknown No of events	n = 0 ; % = 0	n = 1 ; % = 2.1
Maximum tumour diameter, mm Median (IQR)	73.2 (64 to 84.4)	53.6 (36.4 to 61.3)

Outcomes

Survival

Outcome	Robot-assisted partial nephrectomy, , N = 78	Percutaneous cryoablation, , N = 48
Recurrence No of events	n = 2 ; % = 2.6	n = 3 ; % = 6.2
Mortality cancer specific No of events	n = 0 ; % = 0	n = 0 ; % = 0
Mortality other causes No of events	n = 0 ; % = 0	n = 1 ; % = 2.1

Recurrence - Polarity - Lower values are better
Mortality cancer specific - Polarity - Lower values are better
Mortality other causes - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study presents a serious risk of bias due to confounding, as the study did not control the analysis for all important confounding domains. Furthermore, there is a statistical difference in some baseline characteristics (favour RAPN arm) (e.g., age, tumour size, and ASA score), which may have affected the outcomes.)*
Overall bias	Directness	Directly applicable

Uhlig, 2020

Bibliographic Reference	Uhlig, A.; Uhlig, J.; Trojan, L.; Kim, H.S.; Stereotactic Body Radiotherapy for Stage I Renal Cell Carcinoma: National Treatment Trends and Outcomes Compared to Partial Nephrectomy and Thermal Ablation; Journal of Vascular and Interventional Radiology; 2020; vol. 31 (no. 4); 564-571

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital setting
Study dates	Between 2004 and 2015
Sources of funding	A.U. was supported by a Ferdinand Eisenberger Grant of the Deutsche Gesellschaft für Urologie (German Society of Urology) (Grant UhA1/FE-17). H.S.K. is supported by the United States Department of Defense (Grant CA160741). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript
Inclusion criteria	Patients with stage I renal cell carcinoma (RCC)
Exclusion criteria	Under 18 years old at the time of treatment RCC stage II and above Radiation to metastatic RCC sites

	Unknown primary cancer side Unknown cancer histology Unknown survival status or follow-up time
Intervention(s)	Partial nephrectomy (PN)
Comparator	Cryoablation (CRYO), radiofrequency (RF) or microwave (MW) ablation, or stereotactic body radiotherapy (SBRT)
Outcome measures	Survival
Number of participants	Total number of participants in the matched cohort: 636 PN: 159 CRYO: 159 RF/MW ablation: 159 SBRT: 159
Duration of follow-up	Median follow-up time in the matched cohort was 58.1 months (IQR: 34.7–86.6 months)
Loss to follow-up	Not reported
Methods of analysis	Kaplan-Meier plots with log-rank tests and Cox proportional hazard regression models with robust variance (sandwich) estimators were used to evaluate OS. People were propensity score–matched to account for potential confounders, including patient age, sex, race, comorbidities, tumour size, histology, grade, tumour sequence, administration of systemic therapy, treatment in academic versus non-academic centres, treatment location, and year of diagnosis.

Study arms

Partial nephrectomy (N = 82913)

Cryoablation (N = 5446)

Radiofrequency ablation (N = 3432)

SBRT (N = 174)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 82913)	Cryoablation (N = 5446)	Radiofrequency ablation (N = 3432)	SBRT (N = 174)
% Female No of events	n = 68 ; % = 42.8	n = 58 ; % = 37.1	n = 53 ; % = 33.3	n = 59 ; % = 37.1
Age Median (IQR)	70 (63 to 77)	70 (65 to 78)	72 (63 to 78.5)	73 (64 to 82)
Clear cell RCC No of events	n = 134 ; % = 84.3	n = 133 ; % = 83.6	n = 130 ; % = 81.8	n = 131 ; % = 82.4
Chromophobe RCC No of events	n = 1 ; % = 0.6	n = 2 ; % = 1.3	n = 3 ; % = 1.9	n = 2 ; % = 1.3
Other histology No of events	n = 2 ; % = 1.3	n = 1 ; % = 0.6	n = 1 ; % = 0.6	n = 2 ; % = 1.3
Papillary RCC No of events	n = 22 ; % = 13.8	n = 23 ; % = 14.5	n = 25 ; % = 15.7	n = 24 ; % = 15.1
Tumor size, mm Median (IQR)	24 (18.5 to 32)	26 (21 to 31.5)	25 (20 to 33)	35 (25.5 to 45)

Outcomes

Survival

Outcome	Partial nephrectomy versus SBRT, , N2 = 159, N1 = 159	Cryoablation versus SBRT, , N2 = 159, N1 = 159	Radiofrequency ablation versus SBRT, , N2 = 159, N1 = 159	Cryoablation versus Partial nephrectomy, , N2 = 159, N1 = 159
Overall survival Hazard ratio/95% CI	0.29 (0.19 to 0.46)	0.4 (0.26 to 0.6)	0.46 (0.31 to 0.67)	1.35 (0.8 to 2.28)

Overall survival - Polarity - Higher values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Umari, 2022

Bibliographic Reference	Umari, Paolo; Rizzo, Michele; Billia, Michele; Stacul, Fulvio; Bertolotto, Michele; Cova, Maria A; Bondonno, Gianmarco; Perri, Davide; Liguori, Giovanni; Volpe, Alessandro; Trombetta, Carlo; Oncological outcomes of active surveillance and percutaneous cryoablation of small renal masses are similar at intermediate term follow-up.; Minerva urology and nephrology; 2022; vol. 74 (no. 3); 321-328

Study details

Study type	Retrospective cohort study
Study location	Italy
Study setting	Hospital setting
Study dates	Percutaneous cryoablation data were collected and analysed since 2011 and active surveillance since 2010
Sources of funding	Not reported
Inclusion criteria	Patients with a single cT1a renal tumour
Exclusion criteria	Not reported
Intervention(s)	Active surveillance (AS)
Comparator	Percutaneous cryoablation (PCA)
Outcome measures	Recurrence
Number of participants	Total number of participants = 134 AS = 75 PCA = 59
Duration of follow-up	Mean 35.31 (SD = 21.19)
Loss to follow-up	Not reported
Methods of analysis	The Chi-square test and t-test were used to compare categorical and continuous variables respectively. Survival analysis was performed using the Kaplan-Meier method
Additional comments	

Study arms

Active surveillance (N = 75)

Cryoablation (N = 59)

Characteristics

Arm-level characteristics

Characteristic	Active surveillance (N = 75)	Cryoablation (N = 59)
% Female No of events	n = 28 ; % = 37.3	n = 13 ; % = 22
Age Mean (SD)	69.47 (13.16)	70.27 (9.12)
RCC No of events	n = 10 ; % = 76.9	n = 31 ; % = 81.6
Oncocytoma No of events	n = 3 ; % = 23.1	n = 6 ; % = 15.8
Angiomyolipoma No of events	n = 0 ; % = 0	n = 1 ; % = 2.6
Tumour size, mm Mean (SD)	19.52 (8.85)	22.2 (8.18)

Outcomes

Survival

Outcome	Active surveillance, , N = 75	Cryoablation, , N = 59
Distant metastasis No of events	n = 1 ; % = 1.3	n = 1 ; % = 1.7

Distant metastasis - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Weinberg, 2015

Bibliographic Reference	Weinberg, Aaron C; Woldu, Solomon L; Wen, Timothy; Deibert, Christopher M; Korets, Ruslan; Badani, Ketan K; Utilization and perioperative complications of laparoscopic cryoablation versus. robotic partial nephrectomy for localized renal tumors.; International braz j urol : official journal of the Brazilian Society of Urology; 2015; vol. 41 (no. 3); 473-85

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospital. Data from a national database (Nationwide Inpatient Sample, NIS) which includes all inpatient hospital discharge data collected via federal-state partnerships.
Study dates	2008 to 2010
Sources of funding	No funding reported. Paper states that no conflicts of interests were declared.
Inclusion criteria	Patients with contrast enhancing renal masses concerning for RCC on preoperative imaging Patients with a primary diagnosis code of cancer of the kidney
Exclusion criteria	Admission types other than elective With diagnoses of transplant, renal pelvis tumour or pyelonephritis

	Patients undergoing the following concomitant procedures: splenectomy, liver resection, pancreas resection, bowel or colon resection, or thrombectomy with vascular reconstruction.
Intervention(s)	Laparoscopic cryoablation (LCA)
Comparator	Robotic partial nephrectomy (PN)
Outcome measures	Duration of hospital stay
Number of participants	N=14,455 LCA: 4,421 PN: 10,034
Duration of follow-up	Not reported. Length of hospital stay is the only outcome of relevance from this study, so duration of follow up is less important.
Loss to follow-up	Not reported
Methods of analysis	Fisher’s exact test, Chi-square test, and Mantel-Haenszel test were used to assess differences in distribution among the categorical variables. The median test and t-test were used to assess the difference in distributions among continuous variables. Means, medians and ranges were reported for any continuously coded variable. Multivariable models were presented, but no outcomes were relevant.
Additional comments	For the outcomes presented here, no adjustment for confounders or matching was undertaken. Study aim is to explore the utilisation and perioperative complications of LCA and PN.

Study arms

Partial nephrectomy (N = 10034)

Robot-assisted

Cryoablation (N = 4421)

Laparoscopic

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 10034)	Cryoablation (N = 4421)
% Female No of events	n = 58089 ; % = 57.9	n = 2506 ; % = 59.1
Age category: 50 years or less No of events	n = 2750 ; % = 27.4	n = 448 ; % = 10.6
Age category: 51-60 No of events	n = 2784 ; % = 27.7	n = 688 ; % = 16.2
Age category: 61-70 No of events	n = 2878 ; % = 28.7	n = 1306 ; % = 30.8
Age category: 71-80 No of events	n = 1440 ; % = 14.4	n = 1306 ; % = 30.8
Age category: over 80 No of events	n = 181 ; % = 1.8	n = 493 ; % = 11.6

Outcomes

Duration of hospital stay

Outcome	Partial nephrectomy, , N = 10034	Cryoablation, , N = 4421
Duration of hospital stay (days) Mean (SD)	3.04 (0.13)	2.89 (0.18)

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Duration of hospital stay

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(No adjustment for confounders or matching was conducted. Potential for lack of blinding to affect discharge decisions. No protocol identified.)*
Overall bias	Directness	Directly applicable

Xing, 2018

Bibliographic Reference	Xing, Minzhi; Kokabi, Nima; Zhang, Di; Ludwig, Johannes M; Kim, Hyun S; Comparative Effectiveness of Thermal Ablation, Surgical Resection, and Active Surveillance for T1a Renal Cell Carcinoma: A Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked Population Study.; Radiology; 2018; vol. 288 (no. 1); 81-90

Study details

Study type	Retrospective cohort study
Study location	US
Study setting	Hospitals. SEER-Medicare-linked database was used (Surveillance, Epidemiology and End Results database)
Study dates	2002 to 2011 (with at least one year of follow-up to 2012)
Sources of funding	No funding, no conflicts of interest
Inclusion criteria	Node-negative, nonmetastatic T1a RCC (≤4cm) With a recognisable RCC histological subtype recorded in the database Patients at least 66 years old At least 1 year of follow-up
Exclusion criteria	Autopsy or death certificate diagnoses, absence of continuous Medicare Part A or B enrolment, and pre-existing end-stage renal disease before diagnosis

Intervention(s)	1. Active surveillance (AS): those with absence of active procedural codes who had biopsy-proven RCC with at least one relevant follow-up diagnostic imaging examination within 6 months after initial diagnosis. 2. Thermal ablation (TA): Further detail not reported, likely to be all techniques. 3. Radical nephrectomy (RN): Further detail not reported, likely to be all techniques.
Comparator	Interventions compared to each other.
Outcome measures	Survival Cardiovascular events
Number of participants	N= 7398 AS: 1978 TA: 898 RN: 4522 These numbers are total numbers from the unmatched cohort. For each comparison, matching affects the total number of participants analysed.
Duration of follow-up	Median months AS versus TA: 42.2 versus 42.3 AS versus RN: 60.1 versus 63.0 RN versus TA: 46.9 versus 46.8
Loss to follow-up	Not reported
Methods of analysis	Propensity score matching: For each pair of treatment groups, propensity scores were calculated on the basis of 17 predefined covariates: age, sex, race, Charlson comorbidity index, cardiovascular disease, hypertension, diabetes, moderate or severe renal disease, socioeconomic status, marital status, region, urban or rural location, tumour size, histologic characteristics, Fuhrman grade, year of diagnosis, and length of follow-up. For each pair, a greedy 1:1 algorithm was used to match randomly treated patients to one of the two treatment groups by using the closest propensity score.

	Differences in survival were calculated via Kaplan-Meier estimation, and stratified log-rank tests were used to compare the equality be - tween survival curves in matched comparison groups. Cox regression analysis was used to evaluate influence of individual therapies on cause-specific mortality Cardiovascular outcomes: A cardiovascular event was defined as hospitalization for coronary disease, heart failure, stroke, or peripheral arterial disease. Multivariable logistic regression was used to evaluate risk for complications based on therapeutic modality, and unadjusted differences were assessed by using the McNemar test for matched pairs.
Additional comments	This study also reports PN versus TA and AS versus PN. These comparisons are not extracted as they are also reported in Palumbo 2020 from the SEER database. Palumbo includes a wider data range with more recent data and so was selected over Xing 2018 for these comparisons. Characteristics not reported at arm level, but at comparison level (as matching was conducted for each comparison, total number and characteristics were different per comparison). All reported characteristics were well matched according to tests for significance in all three comparisons. Limitations: SEER database only includes patients aged at least 65 years. Confounding may not be entirely removed. The Active surveillance arm may be more similar to watchful waiting than a prospectively planned surveillance program. Thermal ablation type or technique and surgery technique is not reported.

Study arms

Active surveillance (N = 1978)

Thermal ablation (N = 898)

Radical nephrectomy (N = 4522)

Outcomes

Survival

Outcome	Radical nephrectomy versus Thermal ablation, , N2 = 733, N1 = 733	Active surveillance versus Thermal ablation, , N2 = 647, N1 = 647	Active surveillance versus Radical nephrectomy, , N2 = 1674, N1 = 1674
Cancer-specific mortality Hazard ratio/95% CI	1.12 (0.59 to 1.7)	1.45 (1.13 to 2.59)	1.08 (0.82 to 1.42)
Cancer-specific mortality ≥75 Sample size	n1 = 386, n2 = 386	n1 = 319, n2 = 319	n1 = 661, n2 = 661
Cancer-specific mortality ≥75 Hazard ratio/95% CI	1.05 (0.57 to 1.95)	1.62 (1.16 to 2.86)	0.96 (0.67 to 1.39)

Cancer-specific mortality - Polarity - Lower values are better

Cardiovascular

Outcome	Thermal ablation, , N = 733	Radical nephrectomy, , N = 733
Cardiovascular events hospitalization for coronary disease, heart failure, stroke, or peripheral arterial disease No of events	n = 270 ; % = 36.9	n = 331 ; % = 45.2

Cardiovascular events - Polarity - Lower values are better

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Cancer specific survival and cardiovascular events

Section	Question	Answer
Overall bias	Risk of bias judgement	Moderate *(Comparisons including AS: Serious. Comparisons not including AS: moderate. Propensity score matching adjusts for important confounders, but residual confounding may remain. Deviations from interventions not reported clearly. No protocol identified. AS arm not well described and may not match protocol.)*
Overall bias	Directness	Directly applicable

Cancer specific survival - over 75

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(Propensity score matching adjusts for important confounders, but subgrouping might break matching and possible residual confounding remains. Deviations from interventions not reported clearly. No protocol identified.)*
Overall bias	Directness	Directly applicable

Yamanoi, 2024

Bibliographic Reference	Yamanoi, Tomoaki; Bekku, Kensuke; Yoshinaga, Kasumi; Maruyama, Yuki; Nagao, Kentaro; Kawada, Tatsushi; Tominaga, Yusuke; Umakoshi,

Noriyuki; Sadahira, Takuya; Katayama, Satoshi; Iwata, Takehiro; Uka, Mayu; Nishimura, Shingo; Edamura, Kohei; Kobayashi, Tomoko; Kobayashi, Yasuyuki; Hiraki, Takao; Araki, Motoo; Propensity score-matched analysis comparing robot-assisted partial nephrectomy and image-guided percutaneous cryoablation for cT1 renal cell carcinoma.; Urologic oncology; 2024; vol. 42 (no. 12); 453e15-453e22

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital
Study dates	Between June 2012 and May 2021
Sources of funding	The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
Inclusion criteria	Patients with cT1 renal cell carcinoma
Exclusion criteria	non-renal cell carcinoma histology Prior history of renal cell carcinoma Intrarenal metastasis of other cancers No control imaging History of renal replacement therapy, such as dialysis and transplantation
Intervention(s)	Robot-assisted partial nephrectomy
Comparator	Percutaneous cryoablation
Outcome measures	Survival Renal functional impairment Distant metastasis Complications
Number of participants	N = 216 Robot-assisted partial nephrectomy = 108 Percutaneous cryoablation = 108

Duration of follow-up	The median follow-up period was 53 months (interquartile range [IQR]: 26−70 months) for the robot-assisted partial nephrectomy group and 61 months (IQR: 44−77 months) for the image-guided percutaneous cryoablation group
Loss to follow-up	Not reported
Methods of analysis	All patients were matched 1:1 with the nearest neighbour propensity score, using the nearest neighbour matching algorithm without replacement. To minimise treatment bias, we used a calliper size 0.2 times the standard deviation of the logistic regression model of the propensity scores. After matching, the Kaplan−Meier method was applied to estimate overall survival, cancer-specific survival, metastasis-free survival, and local recurrence-free survival, and log-rank tests were employed for intertreatment comparison. A conditional logistic regression was performed to analyse the odds ratios (ORs) and 95% confidence intervals (CIs) regarding the incidence of perioperative complications and >90% eGFR preservation at each time in the matched groups.

Study arms

Robot-assisted partial nephrectomy (N = 108)

Percutaneous cryoablation (N = 108)

Characteristics

Arm-level characteristics

Characteristic	Robot-assisted partial nephrectomy (N = 108)	Percutaneous cryoablation (N = 108)
% Female No of events	n = 39 ; % = 36.1	n = 34 ; % = 31.5
Age Median (IQR)	66 (58 to 71)	65 (57 to 74)
TNM classification - cT1a No of events	n = 101 ; % = 93.5	n = 100 ; % = 92.6

Characteristic	Robot-assisted partial nephrectomy (N = 108)	Percutaneous cryoablation (N = 108)
TNM classification - cT1b No of events	n = 7 ; % = 6.5	n = 8 ; % = 7.4
Primary RCC type - Clear-cell renal cell carcinoma No of events	n = 90 ; % = 83.3	n = 90 ; % = 83.3
Primary RCC type - Non clear cell renall cell carcinoma No of events	n = 18 ; % = 16.7	n = 18 ; % = 16.7
Baseline renal function - Baseline eGFR, mL/min/1.73m2 Mean (SD)	68.5 (16)	66.7 (20.7)
Tumor size, mm Mean (SD)	25.7 (8.6)	26.8 (9.5)

Outcomes

Distant metastasis

Outcome	Robot-assisted partial nephrectomy, , N = 108	Percutaneous cryoablation, , N = 108
Distant metastasis No of events	n = 1 ; % = 0.93	n = 2 ; % = 1.85

Distant metastasis - Polarity - Lower values are better

Renal functional impairment

Outcome	Robot-assisted partial nephrectomy versus Percutaneous cryoablation, , N2 = 108, N1 = 108
>90% eGFR preservation at 60 months Odds ratio/95% CI	1.42 (0.62 to 3.24)

>90% eGFR preservation at 60 months - Polarity - Higher values are better

Survival

Outcome	Robot-assisted partial nephrectomy, , N = 108	Percutaneous cryoablation, , N = 108
Mortality of any cause No of events	n = 3 ; % = 2.78	n = 9 ; % = 8.33
Mortality due to renal cell carcinoma No of events	n = 0 ; % = 0	n = 0 ; % = 0
Complications All complications (Clavien-Dindo) - All complications (Clavien-Dindo) No of events	n = 9 ; % = 8.3	n = 11 ; % = 10.2
Complications - All complications (Clavien-Dindo) - Complications (Clavien-Dindo ≥ Ⅲ) No of events	n = 4 ; % = 3.7	n = 6 ; % = 5.6

Mortality of any cause - Polarity - Lower values are better
Mortality due to renal cell carcinoma - Polarity - Lower values are better

Critical appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Distant metastasis

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The outcomes were not adjusted for all important confounder factors)*
Overall bias	Directness	Directly applicable

Yanagisawa, 2020

Bibliographic Reference	Yanagisawa, Takafumi; Miki, Jun; Shimizu, Kanichiro; Fukuokaya, Wataru; Urabe, Fumihiko; Mori, Keiichiro; Sasaki, Hiroshi; Kimura, Takahiro; Miki, Kenta; Egawa, Shin; Functional and oncological outcome of percutaneous

cryoablation versus laparoscopic partial nephrectomy for clinical T1 renal tumors: A propensity score-matched analysis.; Urologic oncology; 2020; vol. 38 (no. 12); 938e1-938e7

Study details

Study type	Retrospective cohort study
Study location	Japan
Study setting	Hospital setting. Data obtained from two hospitals in Japan
Study dates	September 2011 to December 2019.
Sources of funding	Not reported
Inclusion criteria	Patients with cT1 renal tumour
Exclusion criteria	Patients with benign tumours, diagnosed by biopsy or resection
Intervention(s)	Laparoscopic partial nephrectomy was performed using either a transperitoneal or retroperitoneal approach
Comparator	Percutaneous cryoablation was performed under CT or MRI guidance.
Outcome measures	Intraoperative severe adverse events Postoperative severe adverse events Renal functional impairment Duration of hospital stay
Number of participants	Total number of participants = 180 Percutaneous cryoablation (PCA) = 90 Laparoscopic partial nephrectomy (LPN) = 90
Duration of follow-up	Median follow-up was 26.5 months for PCA and 18 months for LPN
Loss to follow-up	Not reported
Methods of analysis	The chi-square test, Fisher's exact test, Student's t-test, and the Mann-Whitney U test were used to compare the features of each treatment. Propensity scores were calculated through logistic regression modelling based on the following covariates: Age, gender, Charlson's comorbidity index (CCI), the R.E.N.A.L nephrometry score, clinical T-stage, tumour diameter, and pre-operative eGFR. Each patient underwent either PCA or

	LPN and was matched 1:1 with the nearest neighbour's propensity score, using the nearest neighbour matching algorithm without replacement. Kaplan-Meier method was used to estimate OS, CSS, LRFS, MFS, and LCS. Log-rank tests were used for intertreatment comparisons.
Additional comments	

Study arms

Percutaneous cryoablation (N = 90)

Laparoscopic partial nephrectomy (N = 90)

Characteristics

Arm-level characteristics

Characteristic	Percutaneous cryoablation (N = 90)	Laparoscopic partial nephrectomy (N = 90)
% Female No of events	n = 22 ; % = 24	n = 17 ; % = 19
Age Median (IQR)	68.5 (61 to 76)	69.5 (63 to 75)
cT1a No of events	n = 78 ; % = 86.7	n = 77 ; % = 85.6
cT1b No of events	n = 12 ; % = 13.3	n = 13 ; % = 14.4
Clear cell No of events	n = 60 ; % = 92	n = 76 ; % = 84
Papillary No of events	n = 3 ; % = 3.3	n = 6 ; % = 6.7
Chromophobe No of events	n = 2 ; % = 2.2	n = 6 ; % = 6.7

Characteristic	Percutaneous cryoablation (N = 90)	Laparoscopic partial nephrectomy (N = 90)
Unclassified No of events	n = 0 ; % = 0	n = 2 ; % = 2.2
Baseline renal function Mean (SD)	62.5 (18.6)	63.2 (18.8)
Tumour size, mm Mean (SD)	27.6 (9.7)	28.8 (9.5)

Outcomes

Hospital stay

Outcome	Percutaneous cryoablation, , N = 90	Laparoscopic partial nephrectomy, , N = 90
Hospital stay (days) Mean (SD)	5.3 (5.3)	8.8 (3.4)

Hospital stay - Polarity - Lower values are better

Complications

Outcome	Percutaneous cryoablation, , N = 90	Laparoscopic partial nephrectomy, , N = 90
All No of events	n = 5 ; % = 5.5	n = 10 ; % = 11.1
Severe (Clavien grade ≥ Ⅲ) No of events	n = 1 ; % = 1.1	n = 3 ; % = 3.3

All - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not control the analysis for all the important confounding domains.)*
Overall bias	Directness	Directly applicable

Yang, 2024

Bibliographic Reference	Yang, Bo; Zheng, Yang; Zheng, Mengqin; Wang, Dong; Ren, Shangqing; Tian, Jingzhi; Partial nephrectomy versus radiofrequency ablation in patients with cT1a renal cell carcinoma: A surveillance, epidemiology, end results (SEER) analysis.; Medicine; 2024; vol. 103 (no. 48); e40721

Study details

Study type	Retrospective cohort study
Study location	United States of America
Study setting	Data was collected via the National Cancer Institute's Surveillance, Epidemiology, End Results (SEER) database
Study dates	Between January 1, 2004 and December 31, 2015.
Sources of funding	Not reported
Inclusion criteria	Patients diagnosed with renal cell carcinoma by positive histology and underwent partial nephrectomy or radiofrequency ablation The size of the tumour is no more than 4 cm, consistent with TNM stage T1a
Exclusion criteria	Patients with metastatic diseases Patients with the unknown tumour grade, which affect the clinical outcomes
Intervention(s)	Radiofrequency ablation
Comparator	Partial nephrectomy

Outcome measures	Survival
Number of participants	N = 15692 Radiofrequency ablation = 300 Partial nephrectomy = 15392
Duration of follow-up	The median duration of follow-up for radiofrequency ablation and partial nephrectomy was 45.5 and 55 months in the entire cohort, respectively
Loss to follow-up	Not reported
Methods of analysis	Kaplan–Meier method and log-rank test were performed to explore the difference in overall survival and cancer-specific survival between 2 groups. Cox proportional hazards regression model adjusting for baseline characteristics was also conducted to calculate the hazard ratio (HR) and 95% confidence interval (CI)
Additional comments	The log-rank test and Cox proportional hazards regression model were adjusted for race, gender, year of diagnosis, age

Study arms

Radiofrequency ablation (N = 300)

Partial nephrectomy (N = 15392)

Characteristics

Arm-level characteristics

Characteristic	Radiofrequency ablation (N = 300)	Partial nephrectomy (N = 15392)
% Female No of events	n = 125 ; % = 41.67	n = 6217 ; % = 40.39
Age Mean (SD)	66.34 (12.91)	56.51 (12.32)

Characteristic	Radiofrequency ablation (N = 300)	Partial nephrectomy (N = 15392)
Primary RCC type - Clear cell No of events	n = 199 ; % = 66.33	n = 10221 ; % = 66.4
Primary RCC type - Non–clear cell No of events	n = 101 ; % = 33.67	n = 5171 ; % = 33.6
Tumor size, mm No of events	n = 25.2 ; % = 6.89	n = 24.72 ; % = 8.26

Outcomes

Survival

Outcome	Partial nephrectomy versus Radiofrequency ablation, , N2 = 300, N1 = 15392
Overall survival - All cohort T1a Hazard ratio/95% CI	0.46 (0.32 to 0.67)
Overall survival - ≦2 cm Hazard ratio/95% CI	0.93 (0.49 to 1.75)
Overall survival - 2–3 cm Hazard ratio/95% CI	0.52 (0.32 to 0.84)
Overall survival - >3 cm Hazard ratio/95% CI	0.27 (0.15 to 0.5)
Cancer-specific survival - All cohort T1a Hazard ratio/95% CI	0.59 (0.34 to 1.04)
Cancer-specific survival - ≦2 cm Hazard ratio/95% CI	0.61 (0.17 to 2.19)

Outcome	Partial nephrectomy versus Radiofrequency ablation, , N2 = 300, N1 = 15392
Cancer-specific survival - 2–3 cm Hazard ratio/95% CI	0.8 (0.24 to 2.68)
Cancer-specific survival - >3 cm Hazard ratio/95% CI	0.38 (0.18 to 0.81)

Overall survival - Polarity - Higher values are better
Cancer-specific survival - Polarity - Higher values are better

Critical appraisal - ROBINS-I: a tool for non-randomised studies of interventions

Survival

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The outcomes were not adjusted for all important confounder factors)*
Overall bias	Directness	Directly applicable

Yasuda, 2023

Bibliographic Reference	Yasuda, Yosuke; Zhang, Jj H; Attawettayanon, Worapat; Rathi, Nityam; Wilkins, Lamont; Roversi, Gustavo; Zhang, Ao; Accioly, Joao Pedro Emrich; Shah, Snehi; Munoz-Lopez, Carlos; Palacios, Diego Aguilar; Hofmann, Martin; Campbell, Rebecca A; Kaouk, Jihad; Haber, Georges-Pascal; Eltemamy, Mohamad; Krishnamurthi, Venkatesh; Abouassaly, Robert; Martin, Charles 3rd; Li, Jianbo; Weight, Christopher; Campbell, Steven C; Comprehensive Management of Renal Masses in Solitary Kidneys.; European urology oncology; 2023; vol. 6 (no. 1); 84-94

Study details

Study type	Retrospective cohort study
Study location	US

Study setting	Hospital setting
Study dates	Patients were identified from the Cleveland Clinic kidney cancer database (IRM 20-836) between 1975 and 2022
Sources of funding	Funding/Support and role of the sponsor: None
Inclusion criteria	Solitary kidney Total contralateral absence or severe contralateral atrophy (<15% global renal function)
Exclusion criteria	Patients with horseshoe kidneys
Intervention(s)	Partial nephrectomy (PN)
Comparator	Cryoablation (CA) and active surveillance (AS)
Outcome measures	Recurrence Survival Postoperative severe adverse events
Number of participants	Total number of participants = 970 Partial nephrectomy (PN) = 842 Cryoablation (CA) = 102 Active surveillance (AS) = 26
Duration of follow-up	Follow-up (months), median I (IQR) PN: 57.4 (47.2–71.1) CA: 31.2 (6.8–114.9) AS: 39.4 (11.8–74.2)
Loss to follow-up	Not reported
Methods of analysis	Continuous variables were expressed as median and interquartile range, or means and standard deviations, and were compared using Kruskal-Wallis and Wilcoxon tests depending on the number of groups in comparison and data distribution. Categorical variables were compared using chi-square test or Fisher's exact test. A Kaplan-Meier analysis was used to assess overall survival (OS), recurrence-free survival (RFS), and dialysis-free survival with comparisons made by the log-rank test. A Cox proportional hazard model was used to assess the effect of patient demographics and

	clinical/pathologic variables on survival and to calculate hazard ratios and 95% confidence intervals for influential variables.

Study arms

Partial nephrectomy (N = 842)

Cryoablation (N = 102)

Active surveillance (N = 26)

Characteristics

Arm-level characteristics

Characteristic	Partial nephrectomy (N = 842)	Cryoablation (N = 102)	Active surveillance (N = 26)
% Female No of events	n = 307 ; % = 36.5	n = 33 ; % = 32.4	n = 4 ; % = 15.4
Age Median (IQR)	64 (55 to 70)	67 (58 to 73)	70 (65 to 79)
Open No of events	n = 756 ; % = 89.8	n = 0 ; % = 0	n = NA ; % = NA
Minimally invasive surgery No of events	n = 86 ; % = 10.2	n = 102 ; % = 100	n = NA ; % = NA
T1a No of events	n = 410 ; % = 51	n = 77 ; % = 92	n = 19 ; % = 79
T1b No of events	n = 280 ; % = 35	n = 7 ; % = 8	n = 4 ; % = 17
T2 No of events	n = 78 ; % = 10	n = 0 ; % = 0	n = 1 ; % = 4

Characteristic	Partial nephrectomy (N = 842)	Cryoablation (N = 102)	Active surveillance (N = 26)
T3a No of events	n = 26 ; % = 3.6	n = 0 ; % = 0	n = 0 ; % = 0
T3b-c, T4 No of events	n = 3 ; % = 0.4	n = 0 ; % = 0	n = 0 ; % = 0
Baseline renal function Median (IQR)	57 (44 to 71)	53 (40 to 65)	45 (31 to 59)
Tumor size (cm) Median (IQR)	3.9 (2.8 to 5.3)	2.3 (1.6 to 3.1)	2.2 (1.3 to 3.2)

Outcomes

Complications

Outcome	Partial nephrectomy, , N = 842	Cryoablation, , N = 102	Active surveillance, , N = 26
CD 3–5 (90-days) No of events	n = 69 ; % = 8	n = 6 ; % = 6	n = NA ; % = NA

CD 3–5 (90-days) - Polarity - Lower values are better

Survival

Outcome	Partial nephrectomy, , N = 842	Cryoablation, , N = 102	Active surveillance, , N = 26
Overall mortality No of events	n = 381 ; % = 45.2	n = 28 ; % = 27.5	n = 10 ; % = 62.5
Recurrence No of events	n = 128 ; % = 15.2	n = 10 ; % = 9.8	n = NA ; % = NA
Local No of events	n = 99 ; % = 11.8	n = 5 ; % = 4.9	n = NA ; % = NA

Outcome	Partial nephrectomy, , N = 842	Cryoablation, , N = 102	Active surveillance, , N = 26
metastatic No of events	n = 50 ; % = 5.9	n = 8 ; % = 7.8	n = 2 ; % = 7.7

Overall mortality - Polarity - Lower values are better
Recurrence - Polarity - Lower values are better

Critical appraisal - Critical Appraisal - ROBINS-I: a tool for non-randomised studies of interventions

All outcomes

Section	Question	Answer
Overall bias	Risk of bias judgement	Serious *(The study has a serious risk of bias due to confounding, as the study did not adjust the results presented to control possible confounding factors. Furthermore, there are some missing data, indicating a study limitation. However, the authors did not describe the proportion of participants and reasons for missing data across intervention arms.)*
Overall bias	Directness	Directly applicable

Appendix E – Forest plots

Thermal ablation versus partial nephrectomy RCT

Figure 2 Postoperative severe adverse events - Clavien-Dindo I

Figure 3 Postoperative severe adverse events - Clavien-Dindo 2

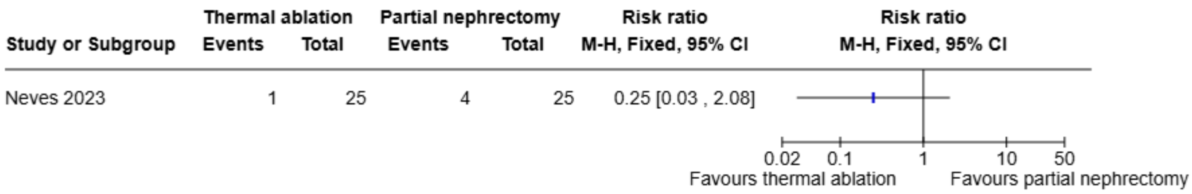
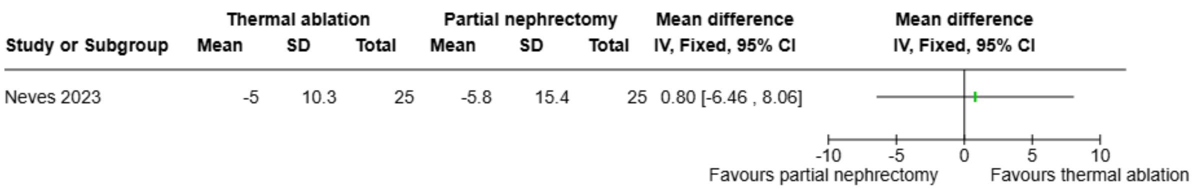


Figure 4 Postoperative severe adverse events - Clavien-Dindo 3-5

No events for this outcome so no forest plot presented.

Figure 5 Renal functional impairment: Change in eGFR at 6 months (mL/min/1.73 m2)



Thermal ablation versus partial nephrectomy non-randomised evidence

Figure 6 Disease-free survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Fossati 2015	0.058268908123975824	0.4394893506502429	27.1%	1.06 [0.45 , 2.51]
Pantelidou 2016	0.5108256237659907	0.9211694554330034	6.2%	1.67 [0.27 , 10.14]
Millan 2022	1.0216512475319814	0.35008503471449026	42.7%	2.78 [1.40 , 5.52]
Lehrer 2023	0.7884573603642703	0.4675038618536366	24.0%	2.20 [0.88 , 5.50]
Total (95% CI)			**100.0%**	**1.96 [1.25 , 3.07]**

Heterogeneity: Chi² = 3.04, df = 3 (P = 0.39); I² = 1%
Test for overall effect: Z = 2.94 (P = 0.003)
Test for subgroup differences: Not applicable

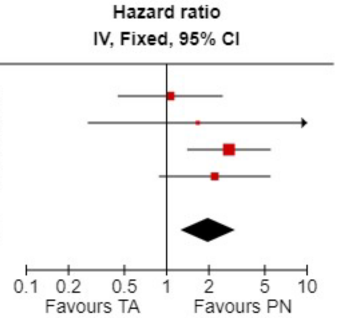


Figure 7 Disease-free survival >5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Olweny 2012	-0.16251892949777494	0.6676343145889025	0.85 [0.23 , 3.15]

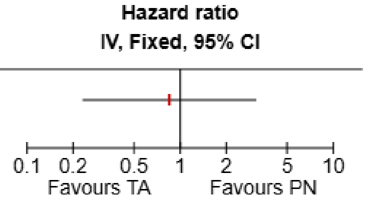
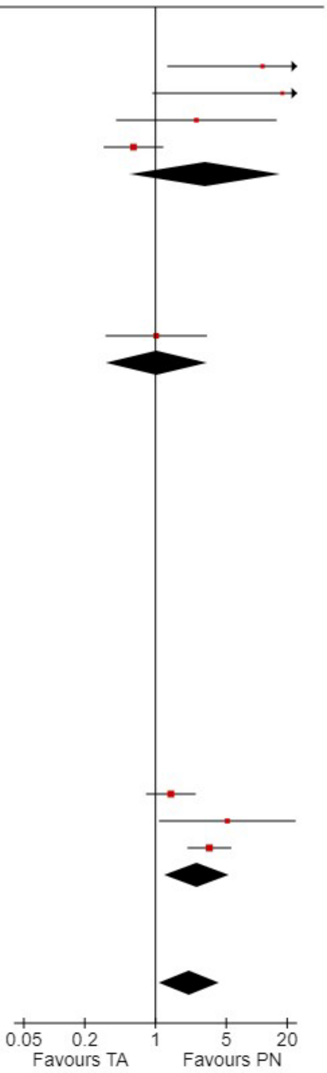


Figure 8 Recurrence ≤5 years - subgroup by ablation type



Study or Subgroup	log[OR]	SE	Weight	Odds ratio IV, Random, 95% CI
2.3.1 Cryotherapy				
Tanagho 2013	2.4344901638739844	1.1058042322322306	6.8%	11.41 [1.31 , 99.67]
Caputo 2017	2.885598	1.507995	4.3%	17.91 [0.93 , 344.20]
Uemura 2021	0.929536	0.932048	8.5%	2.53 [0.41 , 15.74]
Yasuda 2022	-0.500351	0.346529	18.0%	0.61 [0.31 , 1.20]
Subtotal (95% CI)			**37.7%**	**3.08 [0.56 , 17.03]**
Heterogeneity: Tau² = 2.11; Chi² = 11.59, df = 3 (P = 0.009); I² = 74%				
Test for overall effect: Z = 1.29 (P = 0.20)				
2.3.2 Microwave ablation				
Anglickis 2019	Not estimable	Not estimable		Not estimable
Qiu 2023	0.016807	0.588904	13.5%	1.02 [0.32 , 3.23]
Subtotal (95% CI)			**13.5%**	**1.02 [0.32 , 3.23]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.03 (P = 0.98)				
2.3.3 Radiofrequency ablation				
Bird 2009	Not estimable	Not estimable		Not estimable
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
2.3.4 Thermal ablation NS				
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
2.3.5 Thermal ablation combined				
Long 2017	0.349348	0.288425	19.0%	1.42 [0.81 , 2.50]
Rembeyo 2019	1.633535	0.793191	10.3%	5.12 [1.08 , 24.24]
Almadalal 2022	1.225006	0.254354	19.6%	3.40 [2.07 , 5.60]
Subtotal (95% CI)			**48.9%**	**2.54 [1.22 , 5.30]**
Heterogeneity: Tau² = 0.26; Chi² = 6.13, df = 2 (P = 0.05); I² = 67%				
Test for overall effect: Z = 2.48 (P = 0.01)				
Total (95% CI)			**100.0%**	**2.13 [1.07 , 4.22]**
Heterogeneity: Tau² = 0.56; Chi² = 24.73, df = 7 (P = 0.0008); I² = 72%				
Test for overall effect: Z = 2.17 (P = 0.03)				
Test for subgroup differences: Chi² = 1.96, df = 2 (P = 0.38), I² = 0%				

Figure 9 Funnel plot for recurrence ≤5 years - subgroup by ablation type

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

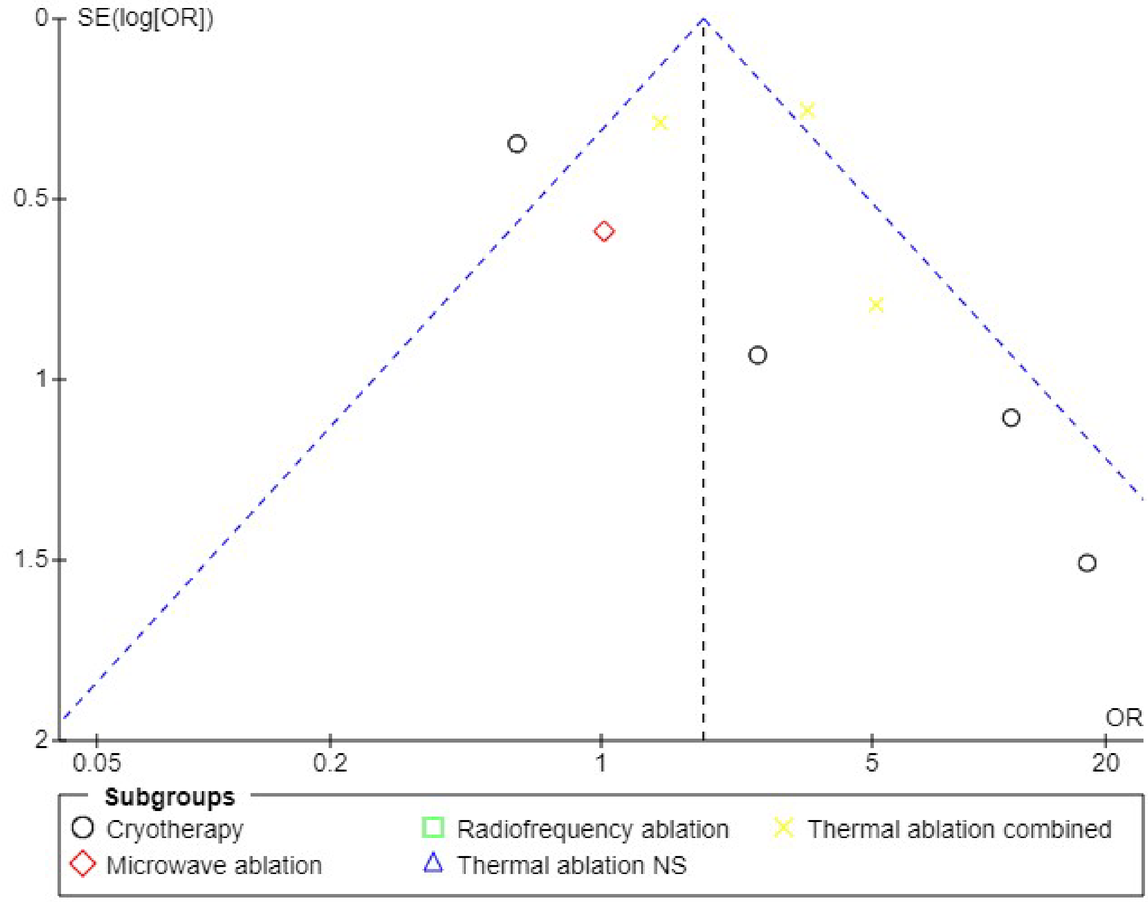


Figure 10 Recurrence ≤5 years - subgroup by TNM stage

Study or Subgroup	log[OR]	SE	Weight	Odds ratio IV, Random, 95% CI
2.4.1 T1b-T2				
Bird 2009	Not estimable	Not estimable		Not estimable
Tanagho 2013	2.4344901638739844	1.1058042322322306	6.8%	11.41 [1.31 , 99.67]
Long 2017	0.349348	0.288425	19.0%	1.42 [0.81 , 2.50]
Caputo 2017	2.885598	1.507995	4.3%	17.91 [0.93 , 344.20]
Rembeyo 2019	1.633535	0.793191	10.3%	5.12 [1.08 , 24.24]
Anglickis 2019	Not estimable	Not estimable		Not estimable
Uemura 2021	0.929536	0.932048	8.5%	2.53 [0.41 , 15.74]
Yasuda 2022	-0.500351	0.346529	18.0%	0.61 [0.31 , 1.20]
Subtotal (95% CI)			**67.0%**	**2.25 [0.93 , 5.47]**
Heterogeneity: Tau² = 0.67; Chi² = 15.31, df = 5 (P = 0.009); I² = 67%				
Test for overall effect: Z = 1.79 (P = 0.07)				
2.4.2 T1a				
Almadalal 2022	1.225006	0.254354	19.6%	3.40 [2.07 , 5.60]
Qiu 2023	0.016807	0.588904	13.5%	1.02 [0.32 , 3.23]
Subtotal (95% CI)			**33.0%**	**2.09 [0.65 , 6.68]**
Heterogeneity: Tau² = 0.52; Chi² = 3.55, df = 1 (P = 0.06); I² = 72%				
Test for overall effect: Z = 1.24 (P = 0.21)				
2.4.3 Not reported				
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
Total (95% CI)			**100.0%**	**2.13 [1.07 , 4.22]**
Heterogeneity: Tau² = 0.56; Chi² = 24.73, df = 7 (P = 0.0008); I² = 72%				
Test for overall effect: Z = 2.17 (P = 0.03)				
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%				

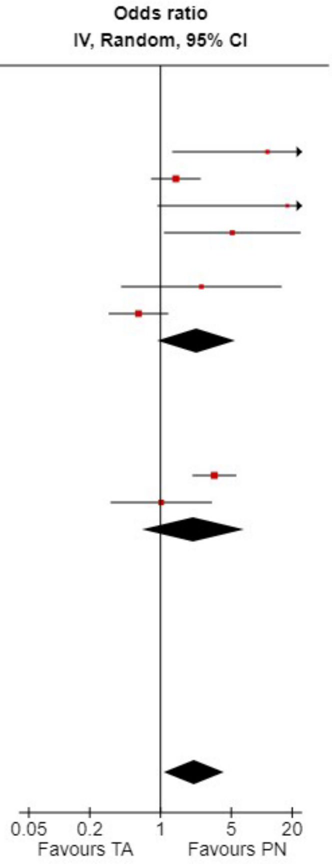


Figure 11 Local recurrence-free survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Fraisse 2019	1.095273387402595	0.5479966926171489	25.3%	2.99 [1.02 , 8.75]
Millan 2022	1.171182981502945	0.4401892323744399	39.1%	3.23 [1.36 , 7.64]
Aikawa 2023	1.6094379124341003	0.7287047692529413	14.3%	5.00 [1.20 , 20.86]
Pedraza-Sanchez 2023	-0.10536051565782628	0.5963569818693407	21.3%	0.90 [0.28 , 2.90]
Total (95% CI)			**100.0%**	**2.57 [1.50 , 4.40]**
Heterogeneity: Chi² = 4.27, df = 3 (P = 0.23); I² = 30%				
Test for overall effect: Z = 3.42 (P = 0.0006)				
Test for subgroup differences: Not applicable				

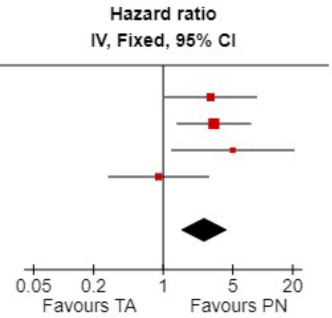


Figure 12 Local recurrence-free survival >5 years

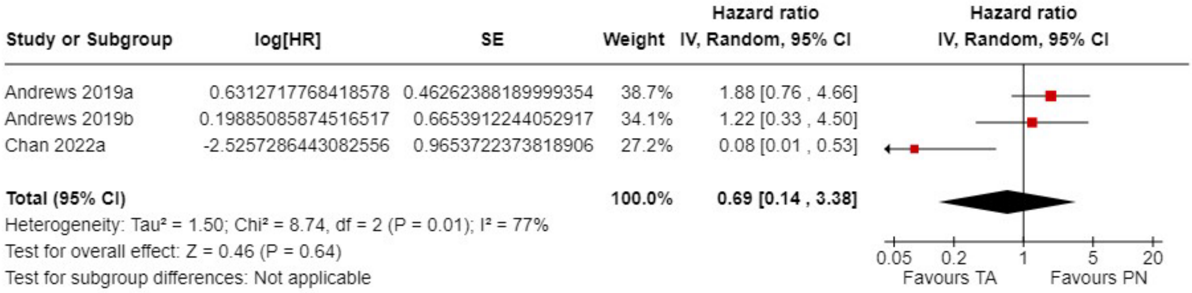
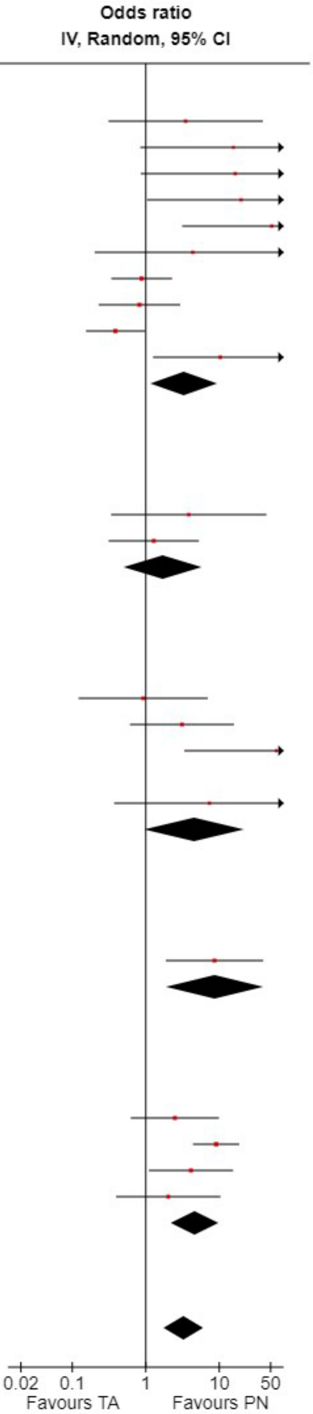


Figure 13 Local recurrence ≤5 years - subgroup by ablation type

Study or Subgroup	log[OR]	SE	Weight	Odds ratio IV, Random, 95% CI
2.7.1 Cryotherapy				
Desai 2005	1.2499017362143359	1.233963914495755	3.8%	3.49 [0.31 , 39.19]
Turna 2009 (1)	2.744535	1.487962	1.6%	15.56 [0.84 , 287.40]
Haber 2011	2.801644	1.510158	3.0%	16.47 [0.85 , 317.82]
Klatte 2011	2.9856819377004897	1.5034922567016462	3.0%	19.80 [1.04 , 377.09]
Guillotreau 2012	3.9460378840154235	1.431240794094354	3.2%	51.73 [3.13 , 855.10]
Emara 2014	1.472472057360943	1.567012185918466	2.8%	4.36 [0.20 , 94.04]
Thompson 2015	-0.127833	0.485464	7.4%	0.88 [0.34 , 2.28]
Fossati 2015	-0.19845093872383832	0.6526237071270896	6.5%	0.82 [0.23 , 2.95]
Yasuda 2022	-0.949697	0.47091	7.5%	0.39 [0.15 , 0.97]
Beksac 2022	2.333357	1.074938	4.4%	10.31 [1.25 , 84.79]
Subtotal (95% CI)			**43.3%**	**3.28 [1.15 , 9.33]**
Heterogeneity: Tau² = 1.64; Chi² = 28.23, df = 9 (P = 0.0009); I² = 68%				
Test for overall effect: Z = 2.23 (P = 0.03)				
2.7.2 Microwave ablation				
Shapiro 2020	1.34602	1.240973	3.8%	3.84 [0.34 , 43.74]
Qiu 2023	0.249461	0.722025	6.1%	1.28 [0.31 , 5.28]
Subtotal (95% CI)			**9.9%**	**1.69 [0.50 , 5.75]**
Heterogeneity: Tau² = 0.00; Chi² = 0.58, df = 1 (P = 0.45); I² = 0%				
Test for overall effect: Z = 0.84 (P = 0.40)				
2.7.3 Radiofrequency ablation				
Stern 2007	-0.08338160893905101	1.0332676143899622	4.6%	0.92 [0.12 , 6.97]
Lucas 2008	1.1346227261911428	0.8314838444267316	5.6%	3.11 [0.61 , 15.87]
Turna 2009 (1)	4.089789	1.4704	1.6%	59.73 [3.35 , 1066.05]
Takaki 2010	Not estimable	Not estimable		Not estimable
Park 2018	1.9947003132247452	1.5236430396233471	3.0%	7.35 [0.37 , 145.62]
Subtotal (95% CI)			**14.8%**	**4.53 [0.95 , 21.65]**
Heterogeneity: Tau² = 1.17; Chi² = 5.64, df = 3 (P = 0.13); I² = 47%				
Test for overall effect: Z = 1.89 (P = 0.06)				
2.7.4 Thermal ablation NS				
Attawettayanon 2023	2.15355	0.778643	5.8%	8.62 [1.87 , 39.63]
Subtotal (95% CI)			**5.8%**	**8.62 [1.87 , 39.63]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 2.77 (P = 0.006)				
2.7.5 Thermal ablation combined				
Mues 2012	0.911149	0.705329	6.2%	2.49 [0.62 , 9.91]
Almadalal 2022	2.203253	0.370092	8.0%	9.05 [4.38 , 18.70]
Cazalas 2023	1.417066	0.673614	6.4%	4.12 [1.10 , 15.45]
Pandolfo 2023	0.704708	0.833988	5.6%	2.02 [0.39 , 10.37]
Subtotal (95% CI)			**26.1%**	**4.60 [2.18 , 9.72]**
Heterogeneity: Tau² = 0.21; Chi² = 4.70, df = 3 (P = 0.20); I² = 36%				
Test for overall effect: Z = 4.00 (P < 0.0001)				
Total (95% CI)			**100.0%**	**3.24 [1.74 , 6.03]**
Heterogeneity: Tau² = 1.15; Chi² = 53.74, df = 19 (P < 0.0001); I² = 65%				
Test for overall effect: Z = 3.72 (P = 0.0002)				
Test for subgroup differences: Chi² = 3.15, df = 4 (P = 0.53), I² = 0%				



Footnotes

(1) Results combined for overall total.

Figure 14 Funnel plot for local recurrence ≤5 years - subgroup by ablation type

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

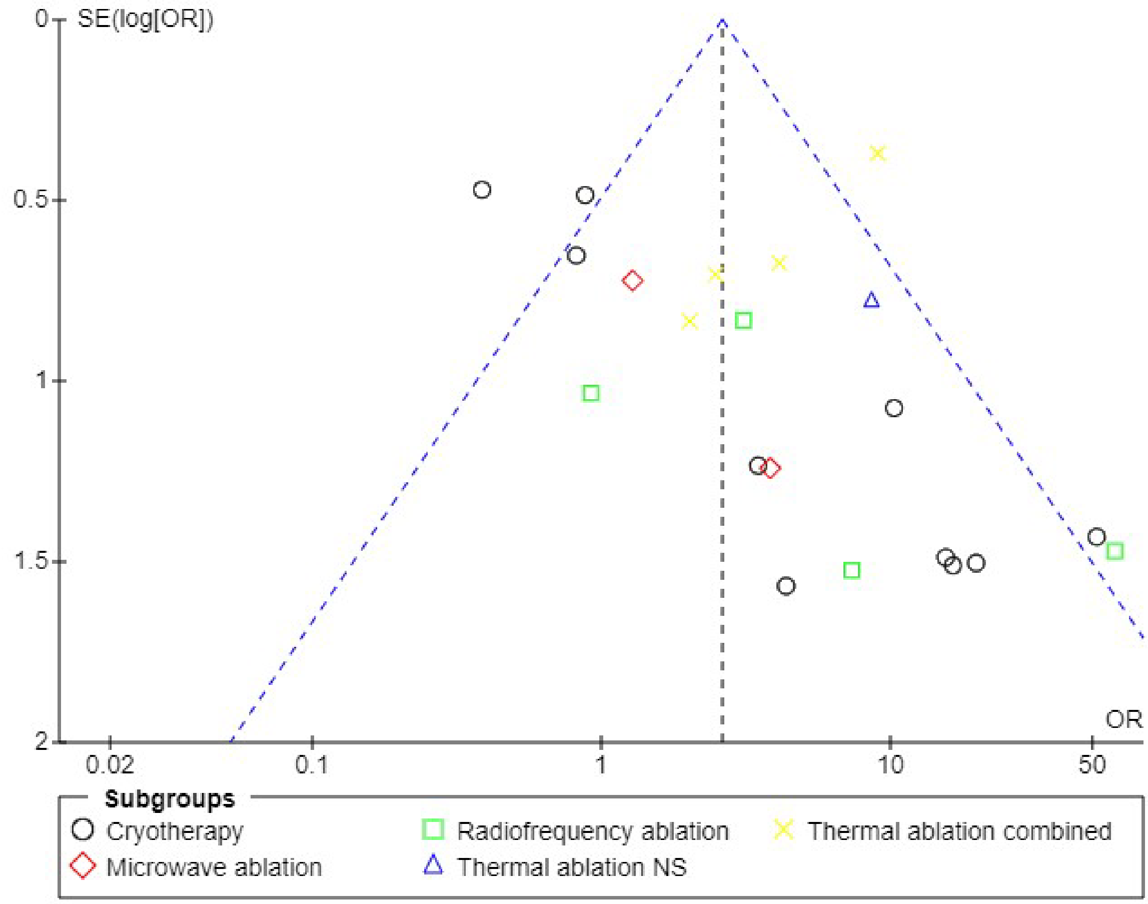


Figure 15 Local recurrence >5 years

Study or Subgroup	log[OR]	SE	Weight	Odds ratio IV, Random, 95% CI
Bianchi 2021a	1.924141	0.334152	58.2%	6.85 [3.56 , 13.18]
Olweny 2012	0	0.8495878159795025	41.8%	1.00 [0.19 , 5.29]
Park 2019	Not estimable	Not estimable		Not estimable
Total (95% CI)			**100.0%**	**3.07 [0.48 , 19.70]**

Heterogeneity: Tau² = 1.43; Chi² = 4.44, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 1.18 (P = 0.24)
Test for subgroup differences: Not applicable

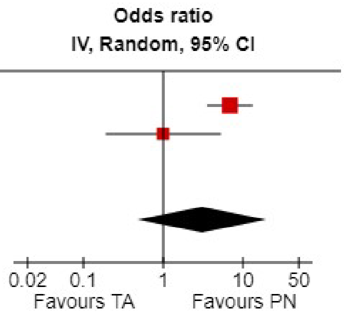


Figure 16 Metastasis-free survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Bhindi 2018	-0.5108256237659907	0.35365301914811886	78.3%	0.60 [0.30 , 1.20]
Aikawa 2023	0.994252273343867	0.6714125516781708	21.7%	2.70 [0.72 , 10.08]
Total (95% CI)			**100.0%**	**0.83 [0.45 , 1.54]**

Heterogeneity: Chi² = 3.93, df = 1 (P = 0.05); I² = 75%
Test for overall effect: Z = 0.59 (P = 0.56)
Test for subgroup differences: Not applicable

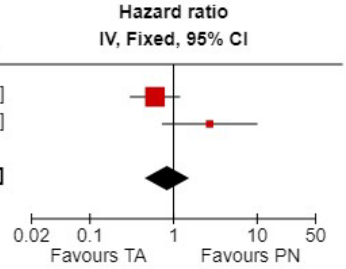


Figure 17 Metastasis-free survival >5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Andrews 2019a	-1.4696759700589417	1.0328970889385358	30.0%	0.23 [0.03 , 1.74]
Andrews 2019b	-0.05129329438755058	0.7749368091936031	53.2%	0.95 [0.21 , 4.34]
Chan 2022a	-2.0402208285265546	1.3782593518153576	16.8%	0.13 [0.01 , 1.94]
Total (95% CI)			**100.0%**	**0.44 [0.15 , 1.35]**

Heterogeneity: Chi² = 2.16, df = 2 (P = 0.34); I² = 8%
Test for overall effect: Z = 1.43 (P = 0.15)
Test for subgroup differences: Not applicable

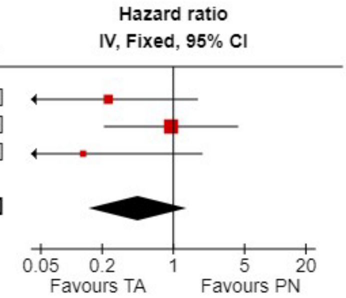
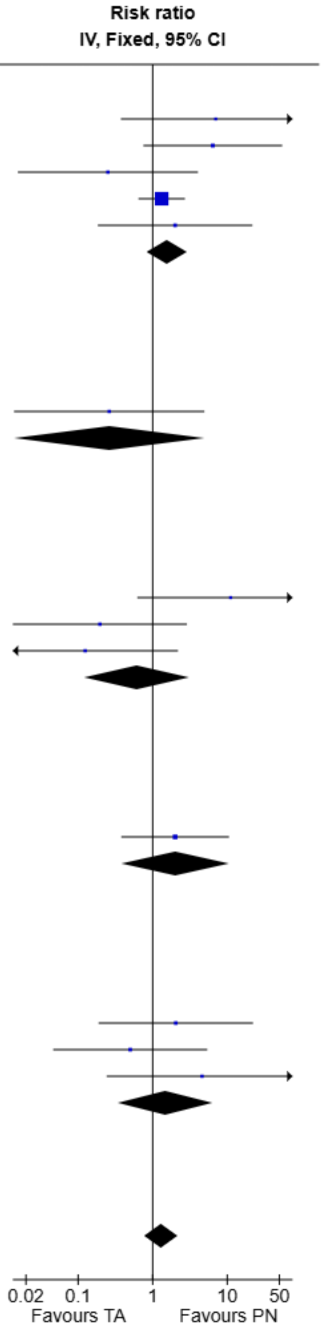


Figure 18 Metastasis ≤5 years - subgroup by ablation type

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Partial nephrectomy Events	Partial nephrectomy Total	Weight	Risk ratio IV, Fixed, 95% CI
2.11.1 Cryotherapy						
Turna 2009[a]	3	36	0	36	1.6%	7.00 [0.37 , 130.82]
Haber 2011	4	30	1	48	5.7%	6.40 [0.75 , 54.58]
Mason 2018	0	12	9	61	3.4%	0.25 [0.02 , 4.05]
Yasuda 2022	8	102	50	842	51.2%	1.32 [0.64 , 2.71]
Yamanoi 2024	2	108	1	108	4.6%	2.00 [0.18 , 21.73]
Subtotal		**288**		**1095**	**66.6%**	**1.54 [0.83 , 2.87]**
Total events:	17		61			
Test for overall effect: Z = 1.36 (P = 0.17)						
Heterogeneity: Chi² = 4.58, df = 4 (P = 0.33); I² = 13%						
2.11.2 Microwave ablation						
Shapiro 2020	0	40	3	74	3.1%	0.26 [0.01 , 4.94]
Subtotal		**40**		**74**	**3.1%**	**0.26 [0.01 , 4.94]**
Total events:	0		3			
Test for overall effect: Z = 0.90 (P = 0.37)						
Heterogeneity: Not applicable						
2.11.3 Radiofrequency ablation						
Turna 2009[a]	4	29	0	36	1.7%	11.10 [0.62 , 198.09]
Takaki 2010	1	51	1	10	3.6%	0.20 [0.01 , 2.88]
Pedraza-Sanchez 2023	0	111	6	180	3.2%	0.12 [0.01 , 2.19]
Subtotal		**191**		**226**	**8.5%**	**0.61 [0.12 , 3.08]**
Total events:	5		7			
Test for overall effect: Z = 0.60 (P = 0.55)						
Heterogeneity: Chi² = 5.76, df = 2 (P = 0.06); I² = 65%						
2.11.4 Thermal ablation NS						
Attawettayanon 2023	4	66	2	66	9.5%	2.00 [0.38 , 10.55]
Subtotal		**66**		**66**	**9.5%**	**2.00 [0.38 , 10.55]**
Total events:	4		2			
Test for overall effect: Z = 0.82 (P = 0.41)						
Heterogeneity: Not applicable						
2.11.5 Thermal ablation combined						
Mues 2012	2	98	1	100	4.6%	2.04 [0.19 , 22.14]
Cazalas 2023	1	75	2	75	4.7%	0.50 [0.05 , 5.40]
Pandolfo 2023	3	92	0	60	3.0%	4.59 [0.24 , 87.33]
Subtotal		**265**		**235**	**12.3%**	**1.47 [0.34 , 6.32]**
Total events:	6		3			
Test for overall effect: Z = 0.51 (P = 0.61)						
Heterogeneity: Chi² = 1.44, df = 2 (P = 0.49); I² = 0%						
Total		**850**		**1660**	**100.0%**	**1.28 [0.77 , 2.14]**
Total events:	32		76			
Test for overall effect: Z = 0.95 (P = 0.34)						
Test for subgroup differences: Chi² = 2.53, df = 4 (P = 0.64), I² = 0%						
Heterogeneity: Chi² = 12.60, df = 11 (P = 0.28); I² = 13%						



Footnotes
[a]Results combined for overall total.

Figure 19 Funnel plot for metastasis ≤5 years - subgroup by ablation type

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

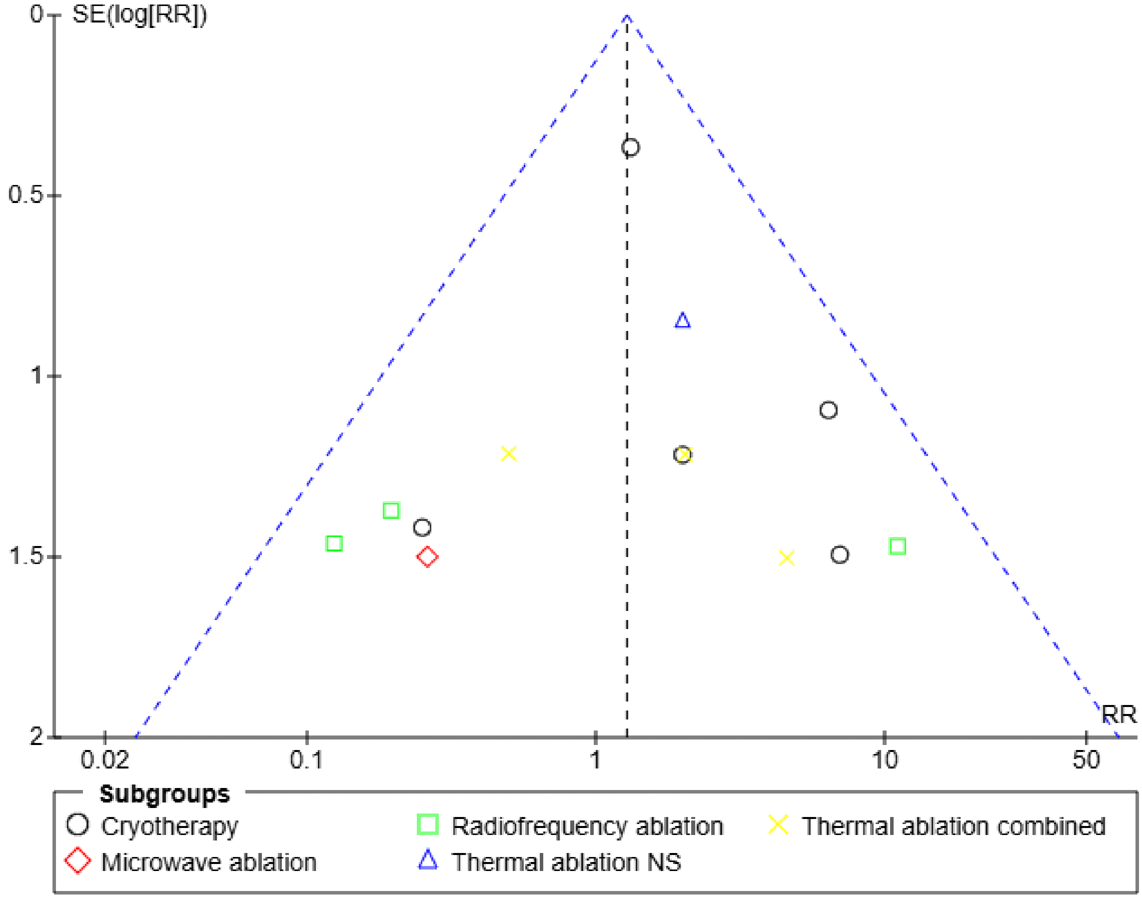


Figure 20 Metastasis >5 years

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Bianchi 2021a	4	151	15	665	1.17 [0.40 , 3.49]

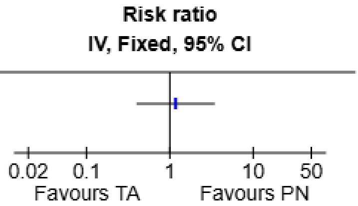


Figure 21 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Takaki 2012	1.247032293786383	1.048201062662636	1.0%	3.48 [0.45 , 27.15]
Thompson 2015	0.542324	0.232344	21.4%	1.72 [1.09 , 2.71]
Bhindi 2018	0.9555114450274365	0.30370512148392564	12.5%	2.60 [1.43 , 4.72]
Alam 2019	0.8064758658669486	0.6103513504607835	3.1%	2.24 [0.68 , 7.41]
Uhlig 2020	0.30010459245033816	0.267178122285140 65	16.1%	1.35 [0.80 , 2.28]
Millan 2022	0.040821994520255166	0.47439189705001217	5.1%	1.04 [0.41 , 2.64]
Aikawa 2023	1.7719568419318752	0.9094113038640351	1.4%	5.88 [0.99 , 34.97]
Lehrer 2023	1.1939224684724346	0.6843078868749242	2.5%	3.30 [0.86 , 12.62]
Pedraza-Sanchez 2023	0.1823215567939546	0.509933522999976	4.4%	1.20 [0.44 , 3.26]
Yang 2024	0.776529	0.188513	32.4%	2.17 [1.50 , 3.15]
Total			**100.0%**	**1.89 [1.53 , 2.34]**

Test for overall effect: Z = 5.94 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Chi² = 8.41, df = 9 (P = 0.49); I² = 0%

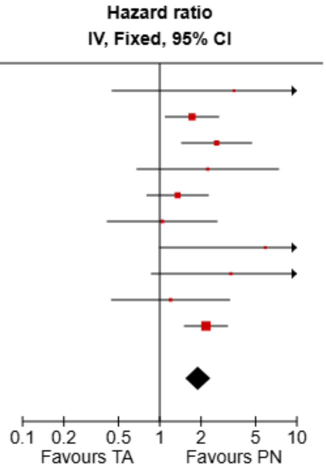


Figure 22 Funnel plot for overall survival ≤5 years

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate

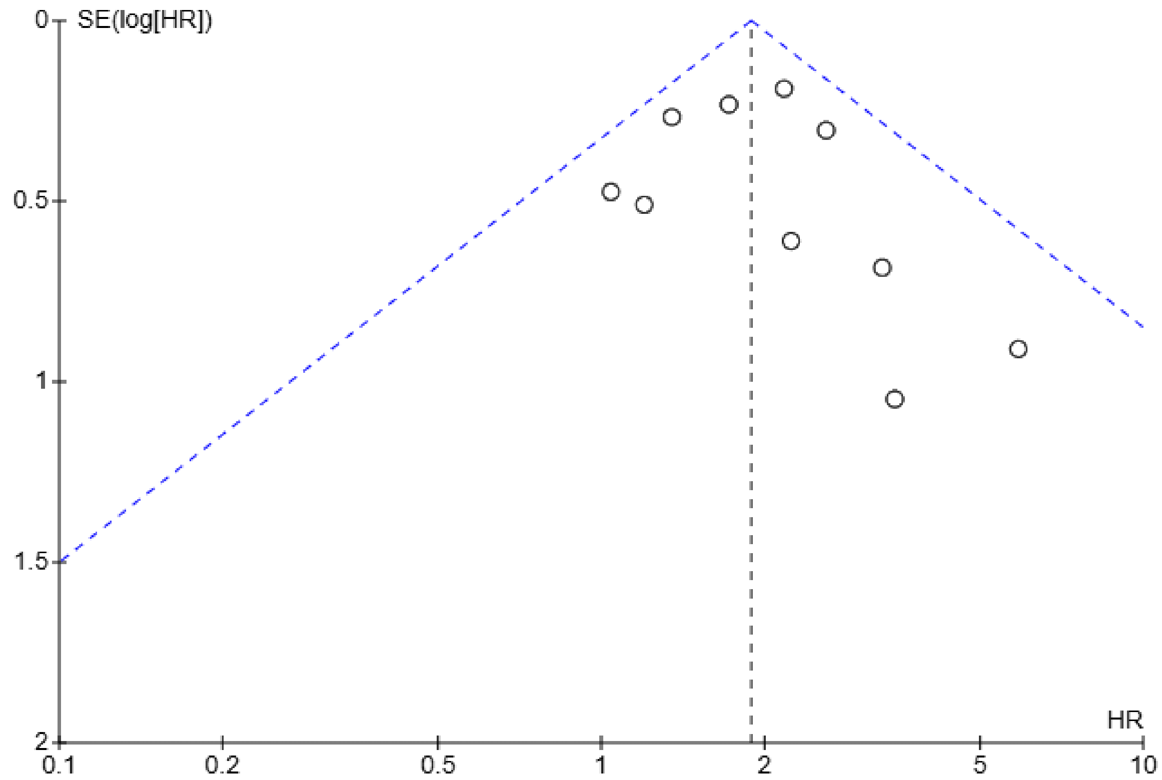


Figure 23 Overall survival >5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
Olweny 2012	0.02955880224154443	1.3688965861881273	1.4%	1.03 [0.07 , 15.07]
Andrews 2019a	0.7080357930536959	0.15200490270947678	30.2%	2.03 [1.51 , 2.73]
Kitley 2019	0.37843643572024505	0.05381432513111617	38.7%	1.46 [1.31 , 1.62]
Andrews 2019b	1.007957920399979	0.27112265263938684	19.5%	2.74 [1.61 , 4.66]
Chan 2022a	-0.31471074483970024	0.45280228741381856	10.2%	0.73 [0.30 , 1.77]
Total (95% CI)			**100.0%**	**1.69 [1.22 , 2.35]**

Heterogeneity: Tau² = 0.07; Chi² = 11.59, df = 4 (P = 0.02); I² = 65%
Test for overall effect: Z = 3.15 (P = 0.002)
Test for subgroup differences: Not applicable

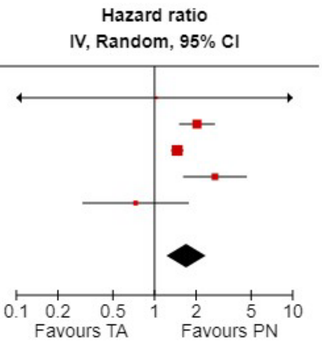
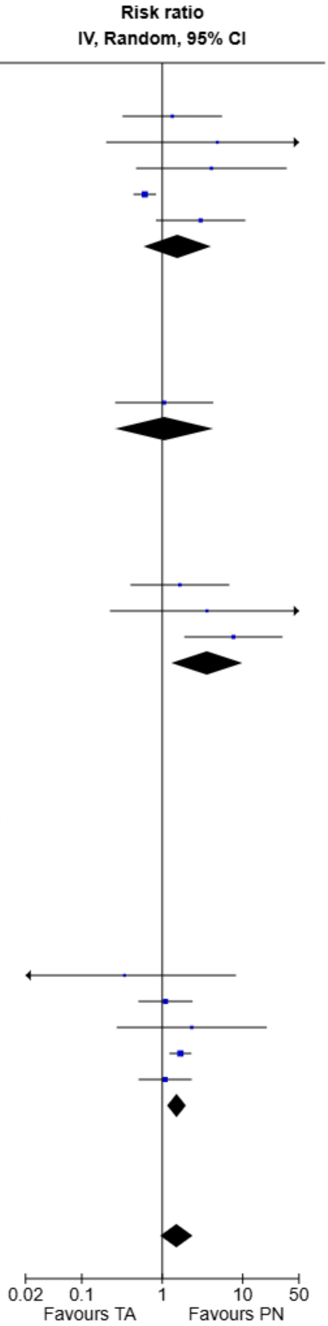


Figure 24 Mortality ≤5 years - subgroup by ablation type

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Partial nephrectomy Events	Partial nephrectomy Total	Weight	Risk ratio IV, Random, 95% CI
2.15.1 Cryotherapy						
Turna 2009[a]	4	36	3	36	3.7%	1.33 [0.32 , 5.54]
Uemura 2021	1	48	0	78	1.8%	4.84 [0.20 , 116.39]
Kawaguchi 2022	4	49	1	50	3.6%	4.08 [0.47 , 35.24]
Yasuda 2022	28	102	381	842	17.0%	0.61 [0.44 , 0.84]
Yamanoi 2024	9	108	3	108	7.5%	3.00 [0.83 , 10.78]
Subtotal (Wald[b])		**343**		**1114**	**33.7%**	**1.54 [0.58 , 4.04]**
Total events:	46		388			
Test for overall effect: Z = 0.87 (P = 0.38)						
Heterogeneity: Tau² (DL[c]) = 0.65; Chi² = 10.44, df = 4 (P = 0.03); I² = 62%						
2.15.2 Microwave ablation						
Qiu 2023	5	126	3	80	6.7%	1.06 [0.26 , 4.31]
Subtotal		**126**		**80**	**6.7%**	**1.06 [0.26 , 4.31]**
Total events:	5		3			
Test for overall effect: Z = 0.08 (P = 0.94)						
Heterogeneity: Not applicable						
2.15.3 Radiofrequency ablation						
Turna 2009[a]	4	29	3	36	3.7%	1.66 [0.40 , 6.81]
Takaki 2010	8	51	0	10	2.3%	3.60 [0.22 , 57.79]
Rusinek 2022	23	84	2	56	6.7%	7.67 [1.88 , 31.24]
Subtotal (Wald[b])		**164**		**102**	**12.8%**	**3.58 [1.29 , 9.93]**
Total events:	35		5			
Test for overall effect: Z = 2.45 (P = 0.01)						
Heterogeneity: Tau² (DL[c]) = 0.10; Chi² = 2.27, df = 2 (P = 0.32); I² = 12%						
2.15.4 Thermal ablation NS						
Subtotal		**0**		**0**		**Not estimable**
Total events:	0		0			
Test for overall effect: Not applicable						
Heterogeneity: Not applicable						
2.15.5 Thermal ablation combined						
Mues 2012	0	98	1	100	1.8%	0.34 [0.01 , 8.25]
Long 2017	10	112	14	172	12.1%	1.10 [0.50 , 2.38]
Rembeyo 2019	4	55	1	32	3.6%	2.33 [0.27 , 19.93]
Almadalal 2022	42	169	109	738	17.1%	1.68 [1.23 , 2.30]
Pandolfo 2023	15	92	9	60	12.2%	1.09 [0.51 , 2.32]
Subtotal (Wald[b])		**526**		**1102**	**46.9%**	**1.50 [1.15 , 1.97]**
Total events:	71		134			
Test for overall effect: Z = 2.97 (P = 0.003)						
Heterogeneity: Tau² (DL[c]) = 0.00; Chi² = 2.82, df = 4 (P = 0.59); I² = 0%						
Total (Wald[b])		**1159**		**2362**	**100.0%**	**1.50 [0.94 , 2.38]**
Total events:	157		527			
Test for overall effect: Z = 1.71 (P = 0.09)						
Test for subgroup differences: Chi² = 2.91, df = 3 (P = 0.41), I² = 0%						
Heterogeneity: Tau² (DL[c]) = 0.31; Chi² = 33.68, df = 12 (P = 0.001); I² = 64%						



Footnotes
[a]Results combined for overall total.
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.

Figure 25 Funnel plot for mortality ≤5 years - subgroup by ablation type

Vertical dotted line shows effect estimate.

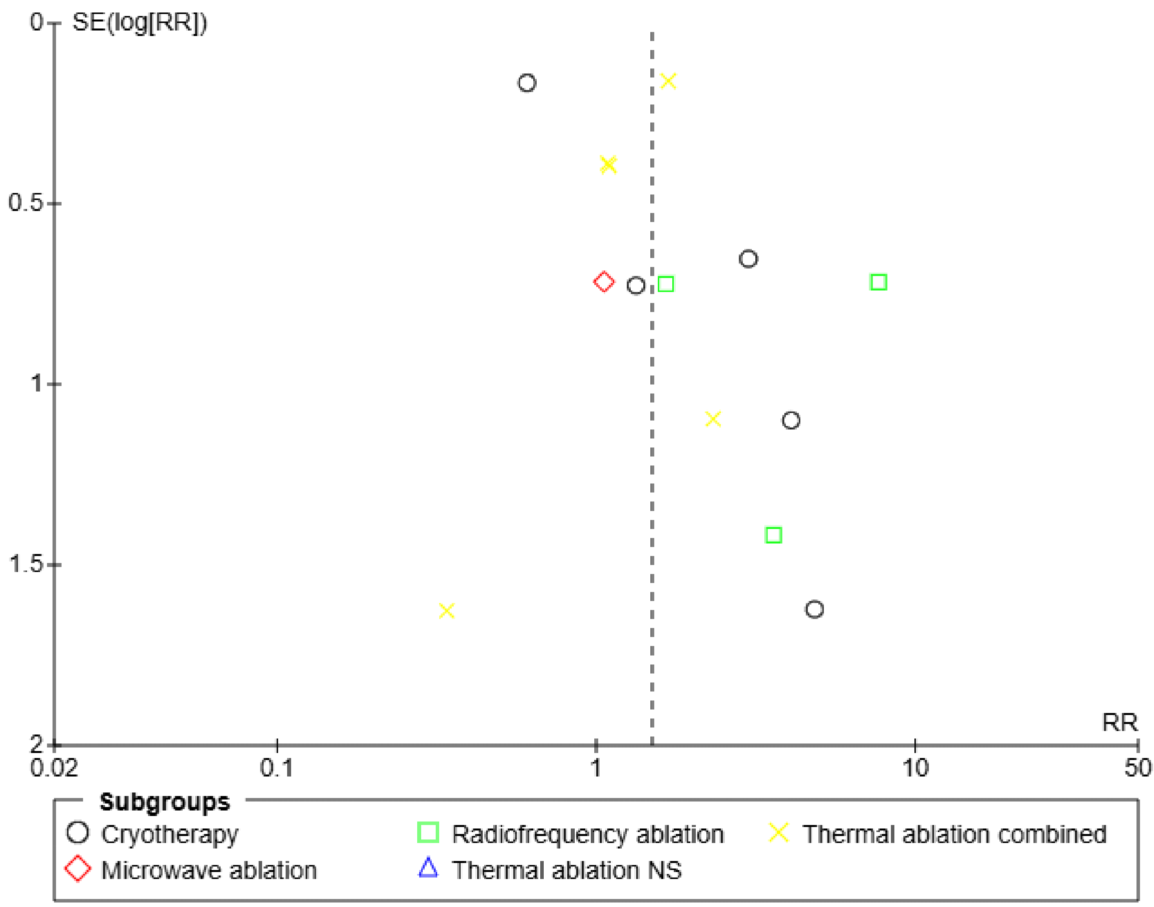
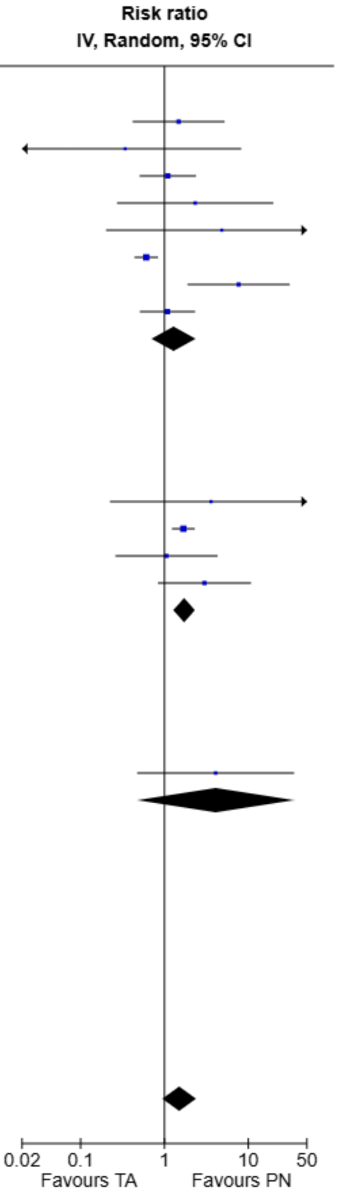


Figure 26 Mortality ≤5 years - subgroup by TNM stage

	Thermal ablation		Partial nephrectomy			Risk ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**IV, Random, 95% CI**
2.16.1 T1b-T2						
Turna 2009	8	65	3	36	7.7%	1.48 [0.42 , 5.22]
Mues 2012	0	98	1	100	1.9%	0.34 [0.01 , 8.25]
Long 2017	10	112	14	172	12.0%	1.10 [0.50 , 2.38]
Rembeyo 2019	4	55	1	32	3.7%	2.33 [0.27 , 19.93]
Uemura 2021	1	48	0	78	1.9%	4.84 [0.20 , 116.39]
Yasuda 2022	28	102	381	842	16.6%	0.61 [0.44 , 0.84]
Rusinek 2022	23	84	2	56	6.8%	7.67 [1.88 , 31.24]
Pandolfo 2023	15	92	9	60	12.2%	1.09 [0.51 , 2.32]
Subtotal (Wald[a])		**656**		**1376**	**62.8%**	**1.28 [0.70 , 2.35]**
Total events:	89		411			
Test for overall effect: Z = 0.81 (P = 0.42)						
Heterogeneity: Tau² (DL[b]) = 0.35; Chi² = 17.34, df = 7 (P = 0.02); I² = 60%						
2.16.2 T1a						
Takaki 2010	8	51	0	10	2.4%	3.60 [0.22 , 57.79]
Almadalal 2022	42	169	109	738	16.7%	1.68 [1.23 , 2.30]
Qiu 2023	5	126	3	80	6.8%	1.06 [0.26 , 4.31]
Yamanoi 2024	9	108	3	108	7.6%	3.00 [0.83 , 10.78]
Subtotal (Wald[a])		**454**		**936**	**33.5%**	**1.71 [1.27 , 2.31]**
Total events:	64		115			
Test for overall effect: Z = 3.57 (P = 0.0004)						
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 1.48, df = 3 (P = 0.69); I² = 0%						
2.16.3 Not reported						
Kawaguchi 2022	4	49	1	50	3.7%	4.08 [0.47 , 35.24]
Subtotal		**49**		**50**	**3.7%**	**4.08 [0.47 , 35.24]**
Total events:	4		1			
Test for overall effect: Z = 1.28 (P = 0.20)						
Heterogeneity: Not applicable						
2.16.4 T1a-T2						
Subtotal		**0**		**0**		**Not estimable**
Total events:	0		0			
Test for overall effect: Not applicable						
Heterogeneity: Not applicable						
Total (Wald[a])		**1159**		**2362**	**100.0%**	**1.50 [0.94 , 2.38]**
Total events:	157		527			
Test for overall effect: Z = 1.71 (P = 0.09)						
Test for subgroup differences: Chi² = 1.40, df = 2 (P = 0.50), I² = 0%						
Heterogeneity: Tau² (DL[b]) = 0.31; Chi² = 33.68, df = 12 (P = 0.0008); I² = 64%						



Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Figure 27 Mortality >5 years

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Park 2019	2	62	0	53	4.29 [0.21 , 87.34]

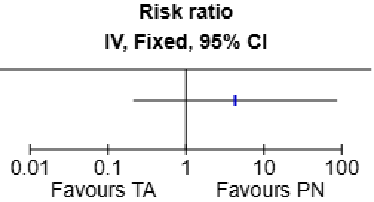


Figure 28 Cancer-specific survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Bhindi 2018	0.12221763272424911	0.6430516382818217	3.8%	1.13 [0.32 , 3.99]
Alam 2019	-1.171182981502945	1.3201100493558056	0.9%	0.31 [0.02 , 4.12]
Pecoraro 2019	0.9162907318741551	0.42121906678534765	8.9%	2.50 [1.09 , 5.71]
Palumbo 2020	0.4700036292457356	0.15462932185141784	66.0%	1.60 [1.18 , 2.17]
Aikawa 2023	0.7765287894989963	1.2417407893230425	1.0%	2.17 [0.19 , 24.79]
Yang 2024	0.527633	0.285217	19.4%	1.69 [0.97 , 2.96]
Total			**100.0%**	**1.64 [1.28 , 2.10]**

Test for overall effect: Z = 3.95 (P < 0.0001)
Test for subgroup differences: Not applicable
Heterogeneity: Chi² = 3.02, df = 5 (P = 0.70); I² = 0%

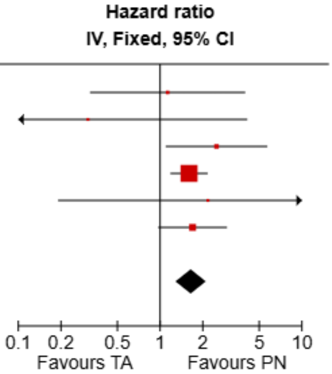


Figure 29 Cancer-specific survival >5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Olweny 2012	0.029558802241544 43	1.3688965861881273	20.9%	1.03 [0.07 , 15.07]
Andrews 2019a	-1.2378743560016174	1.6365343980092448	14.7%	0.29 [0.01 , 7.17]
Andrews 2019b	0.6626879730752367	0.7806956706360618	64.4%	1.94 [0.42 , 8.96]
Total (95% CI)			**100.0%**	**1.29 [0.38 , 4.39]**

Heterogeneity: Chi² = 1.13, df = 2 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.40 (P = 0.69)
Test for subgroup differences: Not applicable

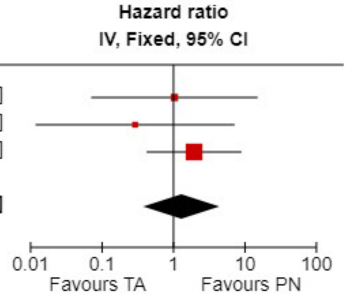
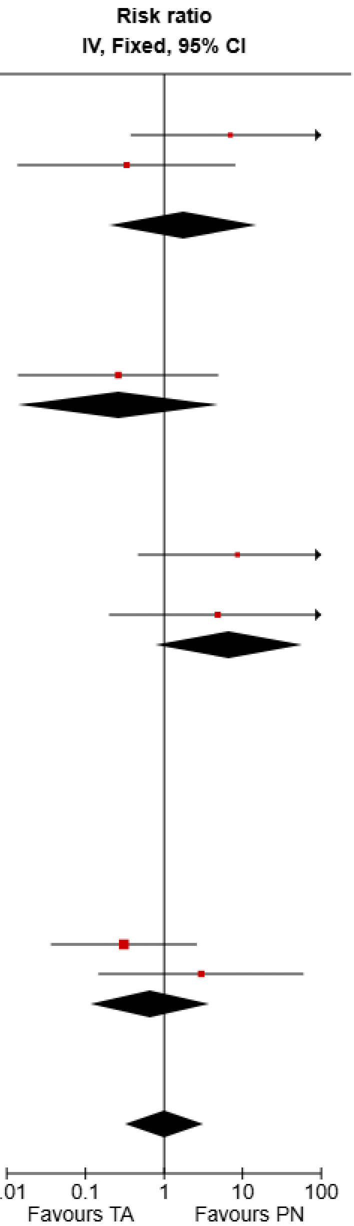


Figure 30 Cancer-specific mortality ≤5 years - subgroup by ablation type

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
2.20.1 Cryotherapy				
Turna 2009[a]	1.94591	1.493874	8.0%	7.00 [0.37 , 130.82]
Fraisse 2019	-1.098612	1.629549	12.8%	0.33 [0.01 , 8.13]
Yamanoi 2024	Not estimable	Not estimable		Not estimable
Subtotal			**20.8%**	**1.74 [0.20 , 15.09]**
Test for overall effect: Z = 0.50 (P = 0.61)				
Heterogeneity: Chi² = 1.90, df = 1 (P = 0.17); I² = 47%				
2.20.2 Microwave ablation				
Shapiro 2020	-1.341994	1.49933	15.1%	0.26 [0.01 , 4.94]
Subtotal			**15.1%**	**0.26 [0.01 , 4.94]**
Test for overall effect: Z = 0.90 (P = 0.37)				
Heterogeneity: Not applicable				
2.20.3 Radiofrequency ablation				
Turna 2009[a]	2.155631	1.491762	8.1%	8.63 [0.46 , 160.68]
Takaki 2010	Not estimable	Not estimable		Not estimable
Pedraza-Sanchez 2023	1.57861	1.628562	12.8%	4.85 [0.20 , 117.98]
Subtotal			**20.9%**	**6.64 [0.77 , 57.30]**
Test for overall effect: Z = 1.72 (P = 0.09)				
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%				
2.20.4 Thermal ablation NS				
Subtotal				**Not estimable**
Test for overall effect: Not applicable				
Heterogeneity: Not applicable				
2.20.5 Thermal ablation combined				
Long 2017	-1.180442	1.088695	28.7%	0.31 [0.04 , 2.59]
Rembeyo 2019	1.080594	1.533571	14.5%	2.95 [0.15 , 59.52]
Subtotal			**43.1%**	**0.66 [0.12 , 3.73]**
Test for overall effect: Z = 0.48 (P = 0.63)				
Heterogeneity: Chi² = 1.45, df = 1 (P = 0.23); I² = 31%				
Total			**100.0%**	**1.00 [0.32 , 3.12]**



Test for overall effect: Z = 0.01 (P = 0.99)
Test for subgroup differences: Chi² = 4.01, df = 3 (P = 0.26), I² = 25.1%
Heterogeneity: Chi² = 5.74, df = 5 (P = 0.28); I² = 13%

Footnotes
[a]Results combined for overall total.

Figure 31 Cancer-specific mortality >5 years

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Bianchi 2021a	4	151	4	665	4.40 [1.11 , 17.41]
Park 2019	0	62	0	53	Not estimable

Risk ratio
IV, Fixed, 95% CI

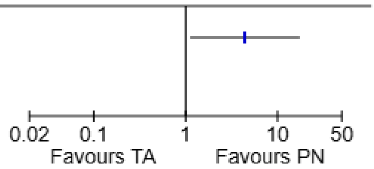
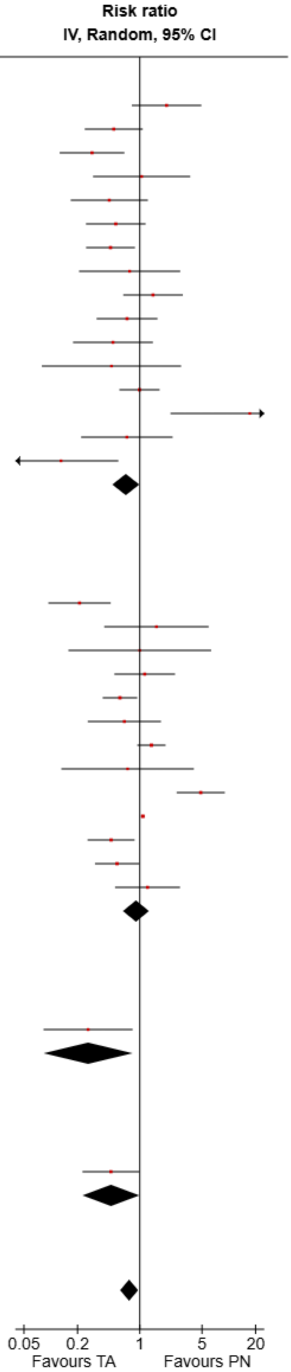


Figure 32 Postoperative severe adverse events - Clavien-Dindo I-V - subgroup by TNM stage

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Random, 95% CI
2.22.1 T1b-T2				
Kiriluk 2011	0.693147	0.459113	3.2%	2.00 [0.81 , 4.92]
Mues 2012	-0.672944	0.382704	3.7%	0.51 [0.24 , 1.08]
Tanagho 2013	-1.234822	0.427129	3.4%	0.29 [0.13 , 0.67]
Emara 2014	0.047939	0.640989	2.2%	1.05 [0.30 , 3.68]
Pantelidou 2016	-0.788457	0.509081	2.9%	0.45 [0.17 , 1.23]
Caputo 2017	-0.6205764877251099	0.3934013085231626	3.6%	0.54 [0.25 , 1.16]
Long 2017	-0.756628	0.322404	4.2%	0.47 [0.25 , 0.88]
Yanagisawa 2018	-0.26236426446749106	0.6674491359374831	2.1%	0.77 [0.21 , 2.85]
Rembeyo 2019	0.342490308946776	0.3929778947687665	3.6%	1.41 [0.65 , 3.04]
Shapiro 2020	-0.3293037471426003	0.40151068780248905	3.6%	0.72 [0.33 , 1.58]
Yanagisawa 2020	-0.693147	0.527046	2.8%	0.50 [0.18 , 1.40]
Acosta Ruiz 2021	-0.7323678937132266	0.9189971657476939	1.3%	0.48 [0.08 , 2.91]
Junker 2022	-0.007722	0.265374	4.6%	0.99 [0.59 , 1.67]
Chan 2022c	2.844414	1.04586	1.1%	17.19 [2.21 , 133.52]
Aikawa 2023	-0.333823	0.603873	2.4%	0.72 [0.22 , 2.34]
Pandolfo 2023	-2.036882	0.756613	1.8%	0.13 [0.03 , 0.57]
Subtotal (Wald[a])			**46.4%**	**0.70 [0.49 , 0.99]**
Test for overall effect: Z = 2.03 (P = 0.04)				
Heterogeneity: Tau² (DL[b]) = 0.25; Chi² = 33.04, df = 15 (P = 0.005); I² = 55%				
2.22.2 T1a				
Desai 2005	-1.55814461804655	0.4115392956046335	3.5%	0.21 [0.09 , 0.47]
Stern 2007	0.4307829160924542	0.6888331025333729	2.0%	1.54 [0.40 , 5.94]
Ko 2008	0	0.9418539347001843	1.3%	1.00 [0.16 , 6.33]
Klatte 2011	0.12783337150988489	0.4001644750295952	3.6%	1.14 [0.52 , 2.49]
Guillotreau 2012	-0.5128236264286636	0.22747651994804577	5.0%	0.60 [0.38 , 0.94]
Haramis 2012	-0.3987761199573678	0.48286609821806764	3.0%	0.67 [0.26 , 1.73]
Fossati 2015	0.3011050927839216	0.1866395166320698	5.3%	1.35 [0.94 , 1.95]
Garcia 2021	-0.3148107398400336	0.8743130275875858	1.4%	0.73 [0.13 , 4.05]
Chan 2022b	1.57649	0.317856	4.2%	4.84 [2.59 , 9.02]
Pedraza-Sanchez 2023	0.079027	0.022829	6.0%	1.08 [1.03 , 1.13]
Qiu 2023	-0.741937	0.31021	4.3%	0.48 [0.26 , 0.87]
Lucignani 2023	-0.588466	0.290423	4.4%	0.56 [0.31 , 0.98]
Yamanoi 2024	0.200671	0.428371	3.4%	1.22 [0.53 , 2.83]
Subtotal (Wald[a])			**47.4%**	**0.91 [0.65 , 1.27]**
Test for overall effect: Z = 0.58 (P = 0.56)				
Heterogeneity: Tau² (DL[b]) = 0.23; Chi² = 59.89, df = 12 (P < 0.00001); I² = 80%				
2.22.3 Not reported				
Panumatrassamee 2013	-1.337125	0.587767	2.4%	0.26 [0.08 , 0.83]
Subtotal			**2.4%**	**0.26 [0.08 , 0.83]**
Test for overall effect: Z = 2.27 (P = 0.02)				
Heterogeneity: Not applicable				
2.22.4 T1a-T2				
Bhindi 2018	-0.746392	0.375309	3.8%	0.47 [0.23 , 0.99]
Subtotal			**3.8%**	**0.47 [0.23 , 0.99]**
Test for overall effect: Z = 1.99 (P = 0.05)				
Heterogeneity: Not applicable				
Total (Wald[a])			**100.0%**	**0.76 [0.60 , 0.96]**



Test for overall effect: Z = 2.32 (P = 0.02)
Test for subgroup differences: Chi² = 5.98, df = 3 (P = 0.11), I² = 49.8%
Heterogeneity: Tau² (DL[b]) = 0.23; Chi² = 116.85, df = 30 (P < 0.00001); I² = 74%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Figure 33 Funnel plot for postoperative severe adverse events - Clavien-Dindo I-V - subgroup by TNM stage

Vertical dotted line shows effect estimate.

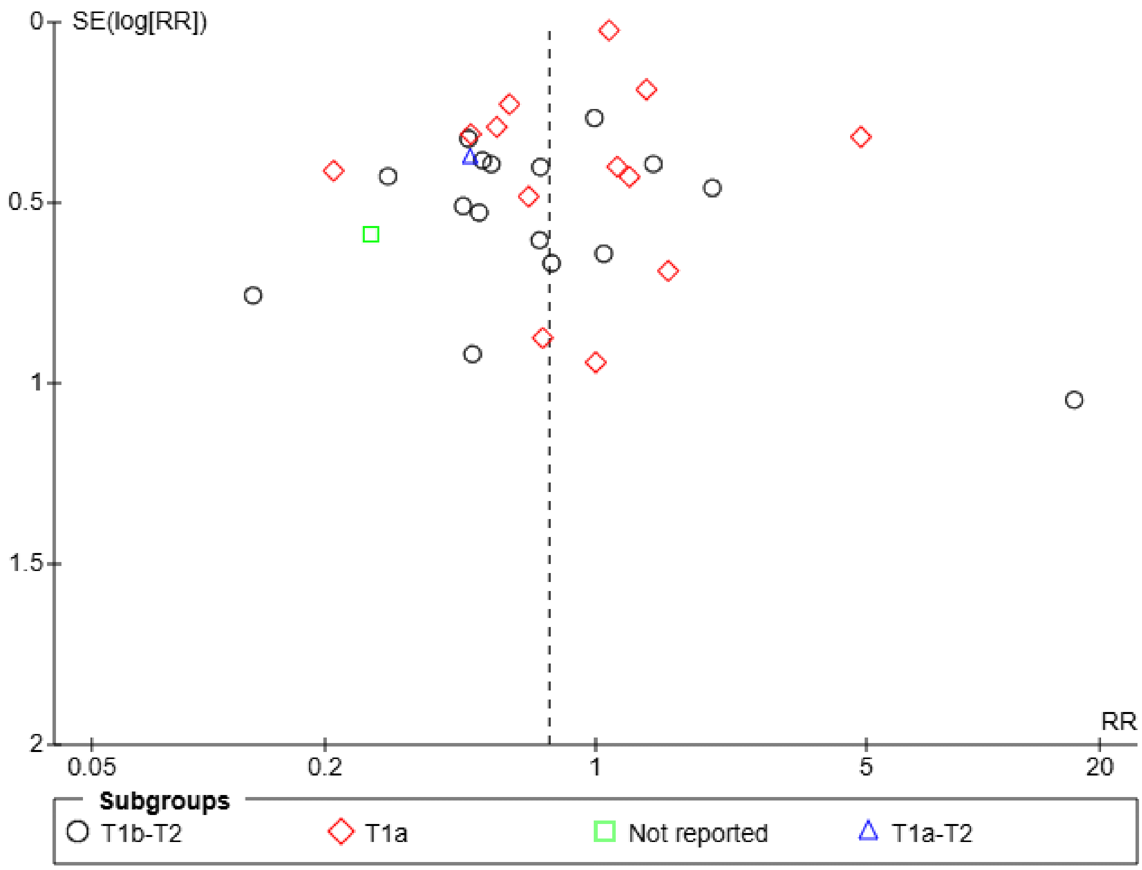


Figure 34 Postoperative severe adverse events - Clavien-Dindo I-II - subgroup by TNM stage

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Random, 95% CI
2.23.1 T1b-T2				
Kiriluk 2011	0.693147	0.459113	4.0%	2.00 [0.81 , 4.92]
Mues 2012	-0.672944	0.47937	3.7%	0.51 [0.20 , 1.31]
Tanagho 2013	-1.745648	0.626069	2.3%	0.17 [0.05 , 0.60]
Emara 2014	0.517943	0.843129	1.3%	1.68 [0.32 , 8.76]
Pantelidou 2016	-0.916291	0.56414	2.8%	0.40 [0.13 , 1.21]
Chan 2022a	0.3576744442718159	0.6727613064054431	2.0%	1.43 [0.38 , 5.35]
Junker 2022	-0.3842	0.330165	7.0%	0.68 [0.36 , 1.30]
Rusinek 2022	0.069429	0.045178	33.4%	1.07 [0.98 , 1.17]
Pandolfo 2023	-2.624669	1.040949	0.9%	0.07 [0.01 , 0.56]
Subtotal (95% CI)			**57.4%**	**0.70 [0.43 , 1.15]**
Heterogeneity: Tau² = 0.30; Chi² = 24.41, df = 8 (P = 0.002); I² = 67%				
Test for overall effect: Z = 1.40 (P = 0.16)				
2.23.2 T1a				
Pedraza-Sanchez 2023	0.059943	0.02188	35.4%	1.06 [1.02 , 1.11]
Qiu 2023	-0.924259	0.376913	5.7%	0.40 [0.19 , 0.83]
Subtotal (95% CI)			**41.0%**	**0.70 [0.27 , 1.81]**
Heterogeneity: Tau² = 0.41; Chi² = 6.80, df = 1 (P = 0.009); I² = 85%				
Test for overall effect: Z = 0.74 (P = 0.46)				
2.23.3 Not reported				
Panumatrassamee 2013	-1.123551	0.76031	1.6%	0.33 [0.07 , 1.44]
Subtotal (95% CI)			**1.6%**	**0.33 [0.07 , 1.44]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.48 (P = 0.14)				
Total (95% CI)			**100.0%**	**0.88 [0.73 , 1.07]**
Heterogeneity: Tau² = 0.03; Chi² = 33.67, df = 11 (P = 0.0004); I² = 67%				
Test for overall effect: Z = 1.27 (P = 0.21)				
Test for subgroup differences: Chi² = 0.94, df = 2 (P = 0.62), I² = 0%				

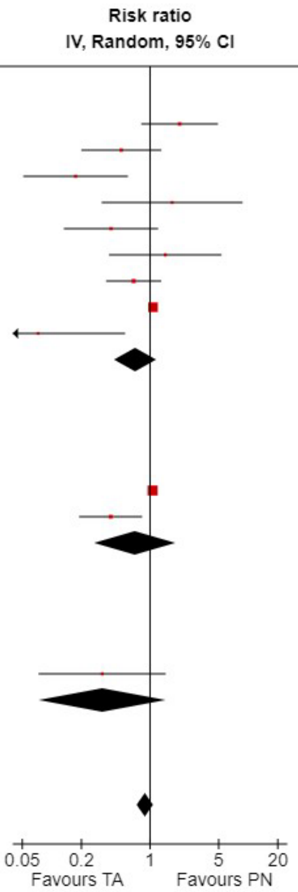


Figure 35 Funnel plot for postoperative severe adverse events - Clavien-Dindo I-II - subgroup by TNM stage

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

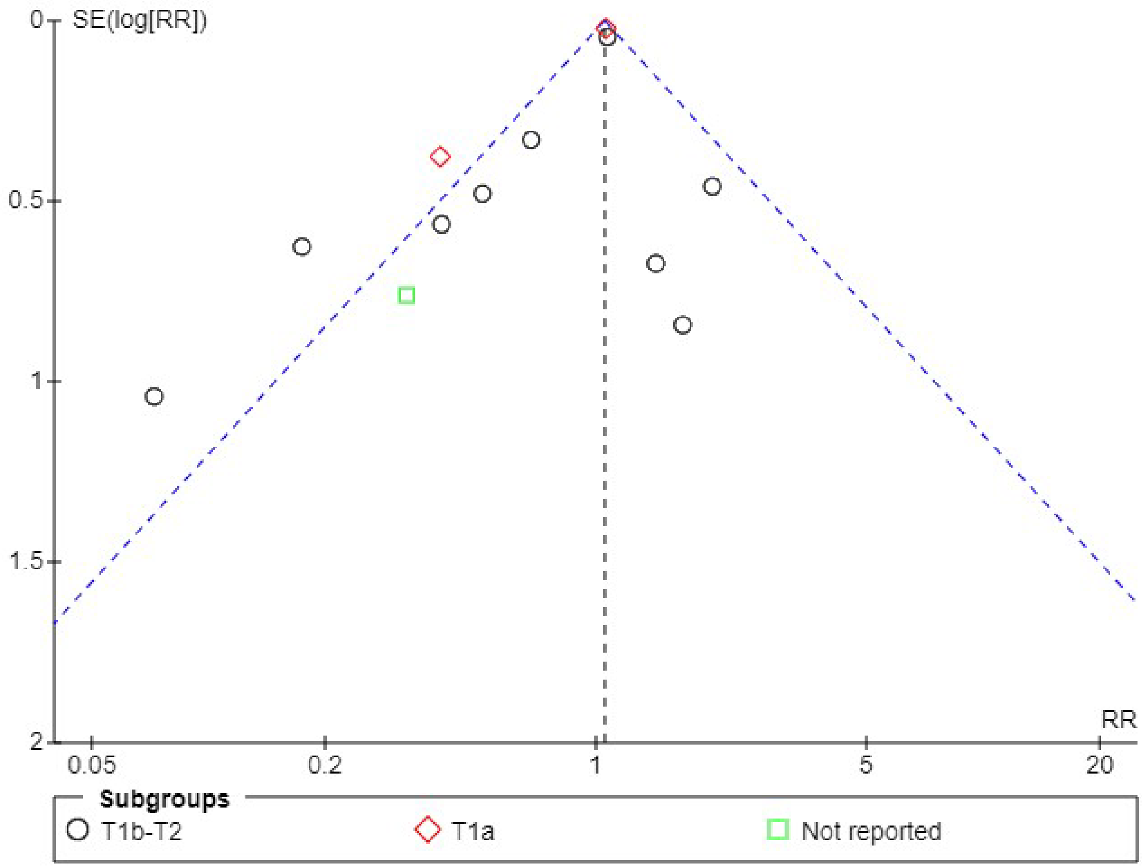
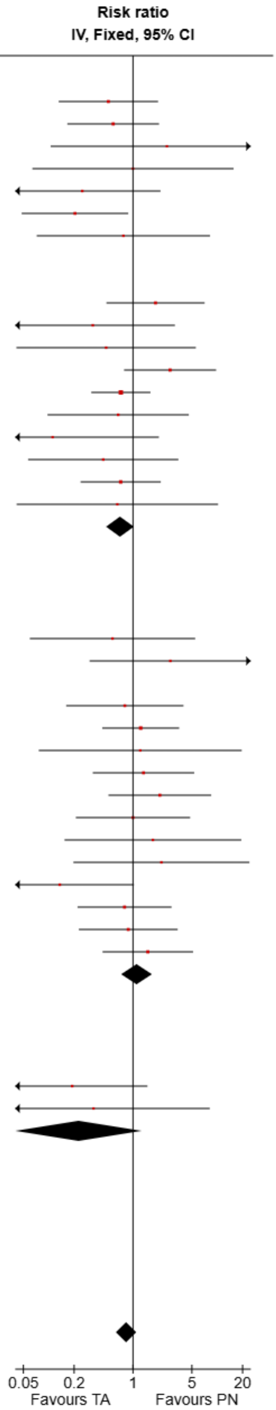


Figure 36 Postoperative severe adverse events - Clavien-Dindo III-V - subgroup by TNM stage

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
2.24.1 T1b-T2				
Mues 2012	-0.672944	0.692673	4.2%	0.51 [0.13 , 1.98]
Tanagho 2013	-0.541675	0.639241	4.9%	0.58 [0.17 , 2.04]
Emara 2014	0.926762	1.6212	0.8%	2.53 [0.11 , 60.60]
Pantelidou 2016	0	1.402945	1.0%	1.00 [0.06 , 15.64]
Caputo 2017	-1.3862943611198906	1.0906290928534212	1.7%	0.25 [0.03 , 2.12]
Long 2017	-1.585907	0.742916	3.6%	0.20 [0.05 , 0.88]
Yanagisawa 2018	-0.26236426446749106	1.2084225049095934	1.4%	0.77 [0.07 , 8.22]
Rembeyo 2019	Not estimable	Not estimable		Not estimable
Anglickis 2019	Not estimable	Not estimable		Not estimable
Shapiro 2020	0.616186139423817	0.6846943797619374	4.3%	1.85 [0.48 , 7.09]
Yanagisawa 2020	-1.098612	1.145038	1.5%	0.33 [0.04 , 3.14]
Chan 2022a	-0.733969	1.250896	1.3%	0.48 [0.04 , 5.57]
Junker 2022	1.013929	0.641942	4.9%	2.76 [0.78 , 9.70]
Yasuda 2022	-0.33154	0.412514	11.8%	0.72 [0.32 , 1.61]
Rusinek 2022	-0.405465	0.985007	2.1%	0.67 [0.10 , 4.60]
Cazalas 2023	-2.197225	1.481859	0.9%	0.11 [0.01 , 2.03]
Aikawa 2023	-0.813396	1.047503	1.8%	0.44 [0.06 , 3.45]
Attawettayanon 2023	-0.336472	0.559065	6.4%	0.71 [0.24 , 2.14]
Pandolfo 2023	-0.427444	1.404444	1.0%	0.65 [0.04 , 10.23]
Subtotal			**53.7%**	**0.70 [0.48 , 1.02]**
Test for overall effect: Z = 1.84 (P = 0.07)				
Heterogeneity: Chi² = 13.45, df = 16 (P = 0.64); I² = 0%				
2.24.2 T1a				
Desai 2005	-0.5596157879354227	1.1529217454492278	1.5%	0.57 [0.06 , 5.47]
Stern 2007	1.0216512475319814	1.126506417733136	1.6%	2.78 [0.31 , 25.27]
Ko 2008	Not estimable	Not estimable		Not estimable
Klatte 2011	-0.22314355131420976	0.8178704364720286	3.0%	0.80 [0.16 , 3.97]
Guillotreau 2012	0.21072103131565253	0.5361112525378064	7.0%	1.23 [0.43 , 3.53]
Haramis 2012	0.19845093872383832	1.415010369770119	1.0%	1.22 [0.08 , 19.53]
Kim 2015	0.2876820724517809	0.7073060382962376	4.0%	1.33 [0.33 , 5.33]
Fossati 2015	0.7339691750802004	0.7164412706216458	3.9%	2.08 [0.51 , 8.48]
Park 2018	0	0.796697	3.2%	1.00 [0.21 , 4.77]
Park 2019	0.544727175441672	1.2325503596670315	1.3%	1.72 [0.15 , 19.31]
Garcia 2021	0.7765287894989963	1.2271015703799606	1.3%	2.17 [0.20 , 24.09]
Pedraza-Sanchez 2023	-2.00148	1.033813	1.9%	0.14 [0.02 , 1.03]
Qiu 2023	-0.231112	0.655411	4.7%	0.79 [0.22 , 2.87]
Lucignani 2023	-0.128934	0.688982	4.2%	0.88 [0.23 , 3.39]
Yamanoi 2024	0.405465	0.63099	5.1%	1.50 [0.44 , 5.17]
Subtotal			**43.7%**	**1.10 [0.72 , 1.68]**
Test for overall effect: Z = 0.45 (P = 0.65)				
Heterogeneity: Chi² = 7.24, df = 13 (P = 0.89); I² = 0%				
2.24.3 Not reported				
Panumatrassamee 2013	-1.662548	1.049705	1.8%	0.19 [0.02 , 1.48]
Kawaguchi 2022	-1.07881	1.62082	0.8%	0.34 [0.01 , 8.15]
Subtotal			**2.6%**	**0.23 [0.04 , 1.27]**
Test for overall effect: Z = 1.69 (P = 0.09)				
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%				
2.24.4 T1a-T2				
Subtotal				**Not estimable**
Test for overall effect: Not applicable				
Heterogeneity: Not applicable				
Total			**100.0%**	**0.83 [0.63 , 1.09]**



Test for overall effect: Z = 1.33 (P = 0.18)
Test for subgroup differences: Chi² = 4.70, df = 2 (P = 0.10), I² = 57.5%
Heterogeneity: Chi² = 25.48, df = 32 (P = 0.79); I² = 0%

Figure 37 Funnel plot for postoperative severe adverse events - Clavien-Dindo III-V - subgroup by TNM stage

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

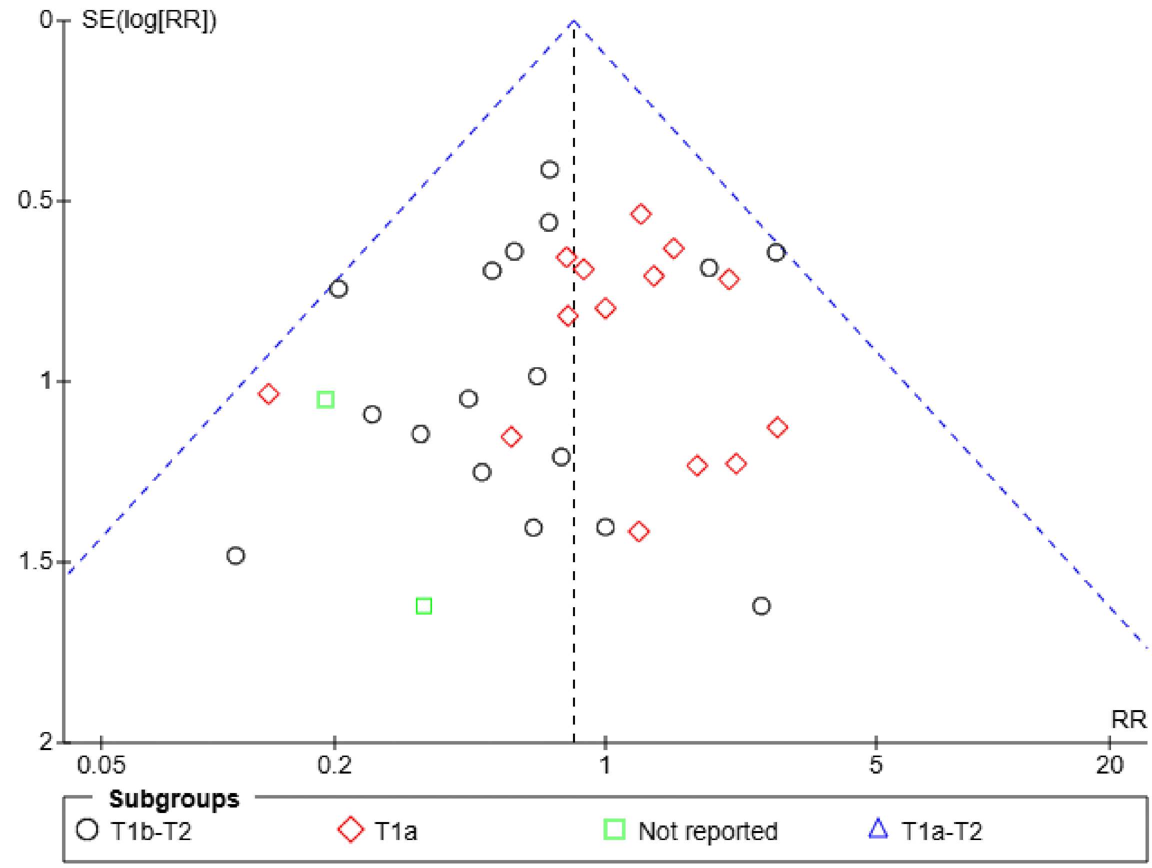
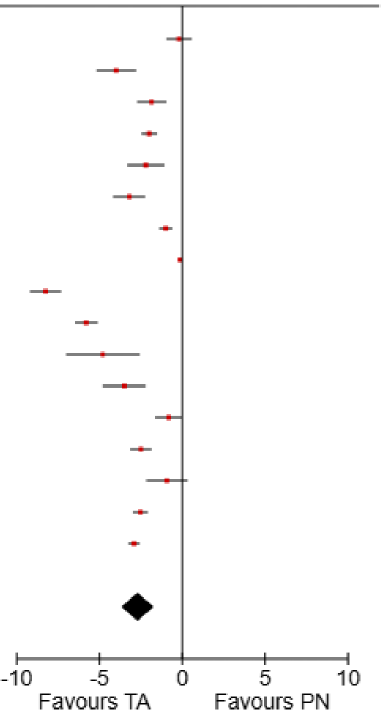


Figure 38 Duration of hospital stay (days) (lower is better)

Study or Subgroup	MD	SE	Weight	Mean difference IV, Random, 95% CI
Desai 2005	-0.2	0.395943	6.0%	-0.20 [-0.98 , 0.58]
Ko 2008	-3.99	0.612529	5.7%	-3.99 [-5.19 , -2.79]
Turna 2009	-1.856923	0.452181	5.9%	-1.86 [-2.74 , -0.97]
Bird 2009	-2	0.2394	6.1%	-2.00 [-2.47 , -1.53]
Haber 2011	-2.2	0.580122	5.7%	-2.20 [-3.34 , -1.06]
Kim 2015	-3.2	0.498344	5.9%	-3.20 [-4.18 , -2.22]
Fossati 2015	-1	0.20825	6.2%	-1.00 [-1.41 , -0.59]
Weinberg 2015	-0.15	0.003002	6.2%	-0.15 [-0.16 , -0.14]
Long 2017	-8.25	0.484986	5.9%	-8.25 [-9.20 , -7.30]
Park 2018	-5.8	0.353664	6.0%	-5.80 [-6.49 , -5.11]
Yanagisawa 2018	-4.8	1.137876	4.7%	-4.80 [-7.03 , -2.57]
Yanagisawa 2020	-3.5	0.663744	5.6%	-3.50 [-4.80 , -2.20]
Garcia 2021	-0.83	0.409426	6.0%	-0.83 [-1.63 , -0.03]
Lehrer 2023	-2.5	0.33247	6.1%	-2.50 [-3.15 , -1.85]
Pandolfo 2023	-0.93	0.633726	5.7%	-0.93 [-2.17 , 0.31]
Pedraza-Sanchez 2023	-2.53	0.228868	6.1%	-2.53 [-2.98 , -2.08]
Jasinski 2024	-2.92	0.178195	6.2%	-2.92 [-3.27 , -2.57]
Total (Wald[a])			**100.0%**	**-2.70 [-3.68 , -1.73]**

Mean difference IV, Random, 95% CI



Test for overall effect: Z = 5.45 (P < 0.00001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 3.95; Chi² = 1159.20, df = 16 (P < 0.00001); I² = 99%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Figure 39 Funnel plot for duration of hospital stay

Vertical dotted line shows effect estimate.

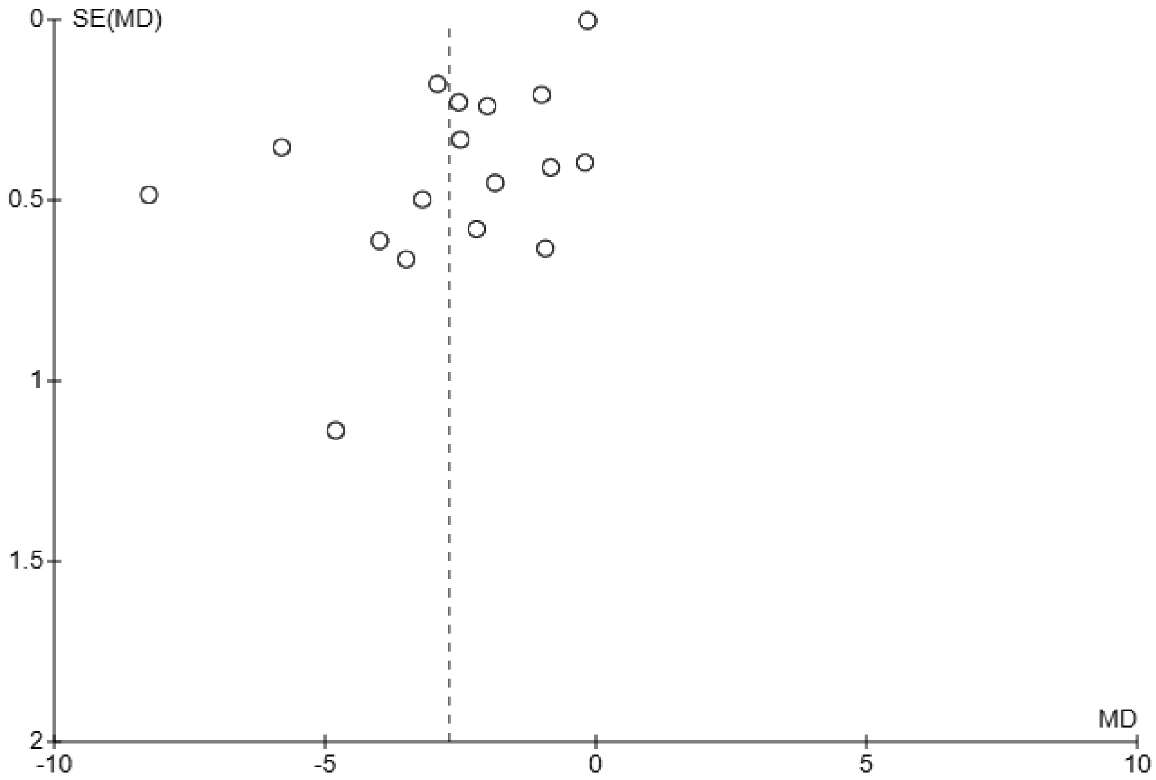
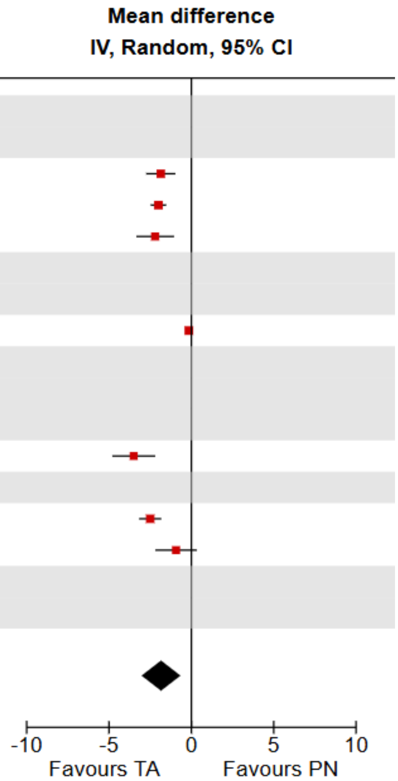


Figure 40 Duration of hospital stay (days): sensitivity analysis (lower is better)

Sensitivity analysis removed all studies that included open surgery or did not specify surgery type. Remaining studies used minimally invasive surgical techniques for partial nephrectomy.

Study or Subgroup	MD	SE	Weight	Mean difference IV, Random, 95% CI
✗ Desai 2005	-0.2	0.395943	0.0%	-0.20 [-0.98 , 0.58]
✗ Ko 2008	-3.99	0.612529	0.0%	-3.99 [-5.19 , -2.79]
✓ Turna 2009	-1.856923	0.452181	14.3%	-1.86 [-2.74 , -0.97]
✓ Bird 2009	-2	0.2394	15.3%	-2.00 [-2.47 , -1.53]
✓ Haber 2011	-2.2	0.580122	13.5%	-2.20 [-3.34 , -1.06]
✗ Kim 2015	-3.2	0.498344	0.0%	-3.20 [-4.18 , -2.22]
✗ Fossati 2015	-1	0.20825	0.0%	-1.00 [-1.41 , -0.59]
✓ Weinberg 2015	-0.15	0.003002	15.8%	-0.15 [-0.16 , -0.14]
✗ Long 2017	-8.25	0.484986	0.0%	-8.25 [-9.20 , -7.30]
✗ Park 2018	-5.8	0.353664	0.0%	-5.80 [-6.49 , -5.11]
✗ Yanagisawa 2018	-4.8	1.137876	0.0%	-4.80 [-7.03 , -2.57]
✓ Yanagisawa 2020	-3.5	0.663744	12.9%	-3.50 [-4.80 , -2.20]
✗ Garcia 2021	-0.83	0.409426	0.0%	-0.83 [-1.63 , -0.03]
✓ Lehrer 2023	-2.5	0.33247	15.0%	-2.50 [-3.15 , -1.85]
✓ Pandolfo 2023	-0.93	0.633726	13.2%	-0.93 [-2.17 , 0.31]
✗ Pedraza-Sanchez 2023	-2.53	0.228868	0.0%	-2.53 [-2.98 , -2.08]
✗ Jasinski 2024	-2.92	0.178195	0.0%	-2.92 [-3.27 , -2.57]
Total (Wald[a])			**100.0%**	**-1.84 [-2.95 , -0.74]**



Test for overall effect: Z = 3.27 (P = 0.001)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (DL[b]) = 2.01; Chi² = 163.35, df = 6 (P < 0.00001); I² = 96%

Footnotes
[a]CI calculated by Wald-type method.
[b]Tau² calculated by DerSimonian and Laird method.

Figure 41 Renal function impairment: Change in eGFR ≤5 years (mL/min/1.73 m2, higher is better)

Study or Subgroup	MD	SE	Weight	Mean difference IV, Random, 95% CI
Lucas 2008	3.5	3.743643	3.4%	3.50 [-3.84 , 10.84]
Foyil 2008	-6.1	2.175607	5.8%	-6.10 [-10.36 , -1.84]
Turna 2009	13.2	3.501748	3.7%	13.20 [6.34 , 20.06]
Takaki 2010	3.8	4.588805	2.6%	3.80 [-5.19 , 12.79]
Deklaj 2010	-0.1	9.897037	0.7%	-0.10 [-19.50 , 19.30]
Kiriluk 2011	-2.8	9.123115	0.8%	-2.80 [-20.68 , 15.08]
Pascal 2011	7.2	3.21338	4.0%	7.20 [0.90 , 13.50]
Mitchell 2011	1.8	2.371623	5.4%	1.80 [-2.85 , 6.45]
Mues 2012	-1	9.025723	0.8%	-1.00 [-18.69 , 16.69]
Klatte 2011	1.1	2.778109	4.7%	1.10 [-4.34 , 6.54]
Guillotreau 2012	2.3	2.94726	4.4%	2.30 [-3.48 , 8.08]
Tanagho 2013	6.1	2.998034	4.4%	6.10 [0.22 , 11.98]
Youn 2013	0.8	1.022064	8.2%	0.80 [-1.20 , 2.80]
Faddegon 2013	0	1.647576	6.9%	0.00 [-3.23 , 3.23]
Takaki 2014	22.4	10.037626	0.7%	22.40 [2.73 , 42.07]
Cooper 2015	-0.3	2.476526	5.2%	-0.30 [-5.15 , 4.55]
Danzig 2015	-1	1.633725	7.0%	-1.00 [-4.20 , 2.20]
Long 2017	2.93	3.612814	3.5%	2.93 [-4.15 , 10.01]
Bertolo 2019	1.2	3.891501	3.2%	1.20 [-6.43 , 8.83]
Acosta Ruiz 2021	-0.01	1.660813	6.9%	-0.01 [-3.27 , 3.25]
Kawaguchi 2022	-18.4	5.538787	1.9%	-18.40 [-29.26 , -7.54]
Cazalas 2023	-2.5	12.280852	0.5%	-2.50 [-26.57 , 21.57]
Duus 2023	1	2.48578	5.2%	1.00 [-3.87 , 5.87]
Pandolfo 2023	-5.8	3.885505	3.2%	-5.80 [-13.42 , 1.82]
Pedraza-Sanchez 2023	1.37	1.725605	6.8%	1.37 [-2.01 , 4.75]
Total (95% CI)			**100.0%**	**0.99 [-0.70 , 2.68]**

Heterogeneity: Tau² = 7.99; Chi² = 53.19, df = 24 (P = 0.0005); I² = 55%
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Not applicable

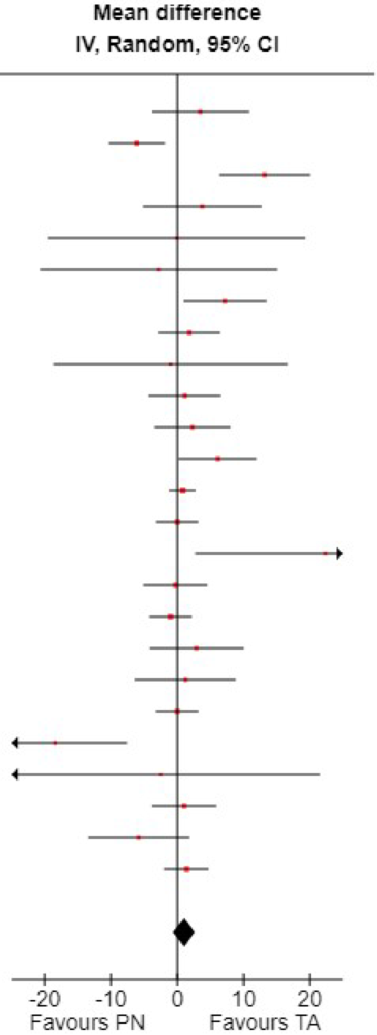


Figure 42 Funnel plot for renal function impairment: Change in eGFR ≤5 years

Blue dotted line shows confidence interval, vertical dotted line shows effect estimate.

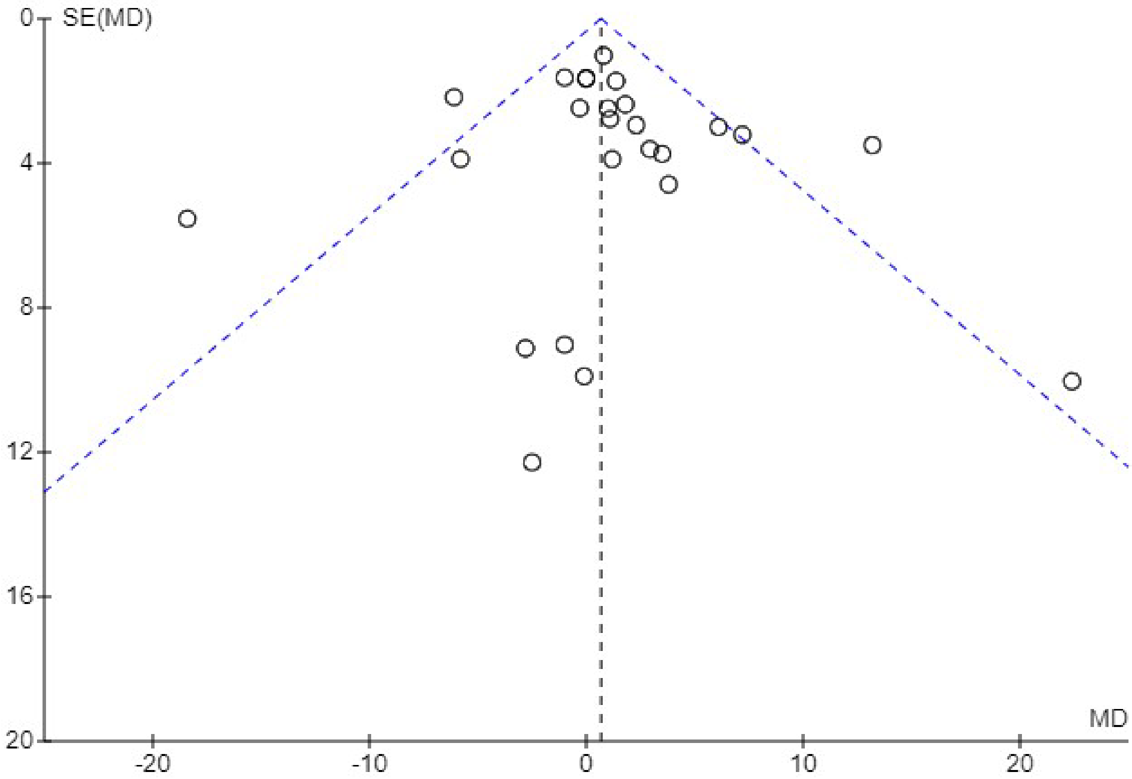


Figure 43 Renal function impairment: New onset eGFR <60 mL/min/1.73 m2

	Thermal ablation		Partial nephrectomy			Risk ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Fixed, 95% CI
Park 2018	6	63	8	63	13.3%	0.75 [0.28 , 2.04]
Rembeyo 2019	10	66	2	36	6.2%	2.73 [0.63 , 11.78]
Ryoo 2022	19	135	35	270	49.2%	1.09 [0.65 , 1.82]
Beksac 2022	4	43	6	31	9.6%	0.48 [0.15 , 1.56]
Pandolfo 2023	23	92	7	60	21.7%	2.14 [0.98 , 4.68]
Total (95% CI)		**399**		**460**	**100.0%**	**1.17 [0.82 , 1.69]**
Total events:	62		58			

Heterogeneity: Chi² = 6.62, df = 4 (P = 0.16); I² = 40%
Test for overall effect: Z = 0.86 (P = 0.39)
Test for subgroup differences: Not applicable

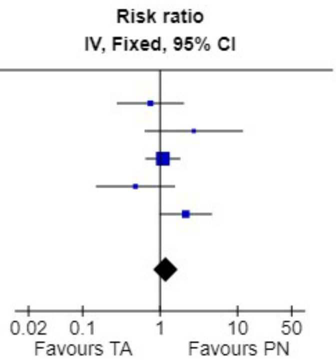


Figure 44 Renal function impairment: New onset eGFR <45 mL/min/1.73 m2

Study or Subgroup	log[OR]	SE	Odds ratio IV, Fixed, 95% CI
Alam 2019	0.5423242908253616	0.7552443833146022	1.72 [0.39 , 7.56]

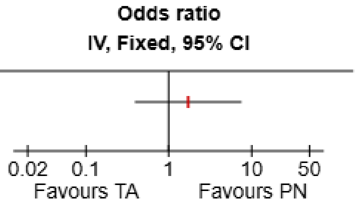


Figure 45 Renal function impairment: New onset eGFR <30 mL/min/1.73 m2

	Thermal ablation		Partial nephrectomy		Risk ratio
Study or Subgroup	Events	Total	Events	Total	IV, Fixed, 95% CI
Ryoo 2022	3	53	2	53	1.50 [0.26 , 8.62]

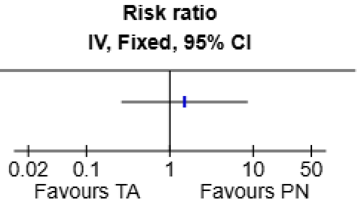


Figure 46 Renal function impairment: New onset eGFR <15 mL/min/1.73 m2

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
2.30.1 Cryotherapy				
Guillotreau 2012	2.6736487743848776	1.4522945519272574	6.9%	14.49 [0.84 , 249.66]
Beksac 2022	0.183613	0.691245	30.5%	1.20 [0.31 , 4.66]
Subtotal (95% CI)			**37.4%**	**1.90 [0.56 , 6.47]**
Heterogeneity: Chi² = 2.40, df = 1 (P = 0.12); I² = 58%				
Test for overall effect: Z = 1.03 (P = 0.30)				
2.30.2 Microwave ablation				
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
2.30.3 Radiofrequency ablation				
Lucas 2008	-0.011928570865273812	1.4072189927091063	7.4%	0.99 [0.06 , 15.58]
Ryoo 2022	0.405465	0.615574	38.5%	1.50 [0.45 , 5.01]
Subtotal (95% CI)			**45.8%**	**1.40 [0.46 , 4.24]**
Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%				
Test for overall effect: Z = 0.60 (P = 0.55)				
2.30.4 Thermal ablation NS				
Pascal 2011	-0.8919980393051105	1.5637130382601647	6.0%	0.41 [0.02 , 8.78]
Subtotal (95% CI)			**6.0%**	**0.41 [0.02 , 8.78]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				
2.30.5 Thermal ablation combined				
Turna 2009	-1.9307965112452652	1.5679922096598782	5.9%	0.15 [0.01 , 3.13]
Mues 2012	-0.688134638736401	1.72442287810397	4.9%	0.50 [0.02 , 14.76]
Subtotal (95% CI)			**10.8%**	**0.25 [0.03 , 2.47]**
Heterogeneity: Chi² = 0.28, df = 1 (P = 0.59); I² = 0%				
Test for overall effect: Z = 1.18 (P = 0.24)				
Total (95% CI)			**100.0%**	**1.21 [0.57 , 2.57]**
Heterogeneity: Chi² = 5.64, df = 6 (P = 0.47); I² = 0%				
Test for overall effect: Z = 0.51 (P = 0.61)				
Test for subgroup differences: Chi² = 2.88, df = 3 (P = 0.41), I² = 0%				

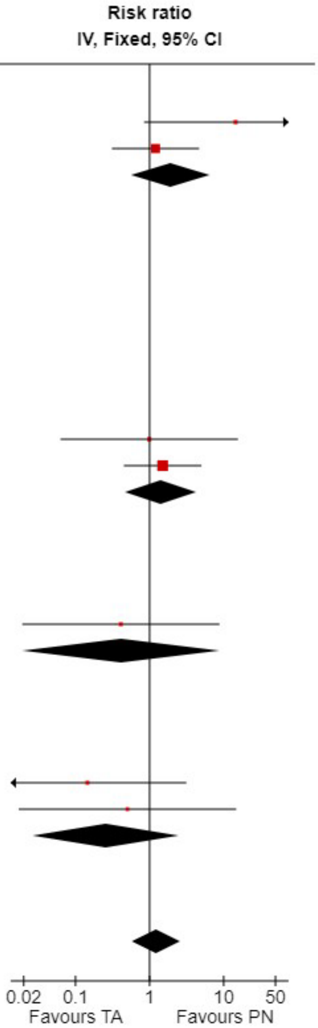


Figure 47 Quality of life at 14 days (EORTC questionnaire, higher is better)

Study or Subgroup	MD	SE	Mean difference IV, Fixed, 95% CI
Junker 2022	-9.6	3.240668	-9.60 [-15.95 , -3.25]

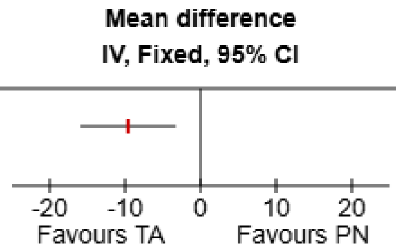
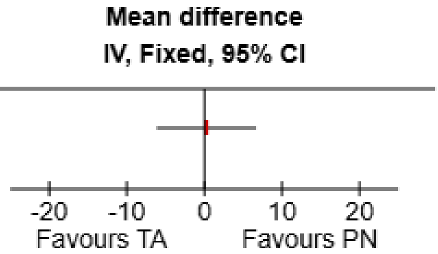


Figure 48 Quality of life at 90 days (EORTC questionnaire, higher is better)

Study or Subgroup	MD	SE	Mean difference IV, Fixed, 95% CI
Junker 2022	0.26	3.265986	0.26 [-6.14 , 6.66]



Thermal ablation versus radical nephrectomy non-randomised evidence

Figure 49 Disease-free survival ≤5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Almadalal 2022	1.7351891177396608	0.2870181347211293	5.67 [3.23 , 9.95]

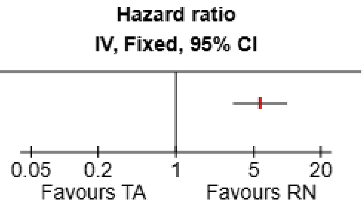


Figure 50 Recurrence ≤5 years

Study or Subgroup	log[RR]	SE	Risk ratio IV, Fixed, 95% CI
Takaki 2014	-0.074108	0.822642	0.93 [0.19 , 4.66]

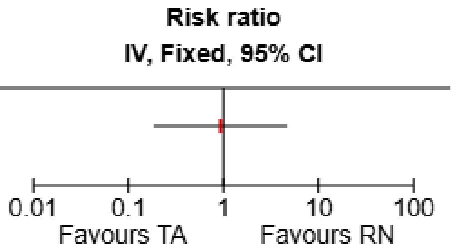


Figure 51 Local recurrence ≤5 years

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
Takaki 2010	Not estimable	Not estimable		Not estimable
Takaki 2014	1.696449	1.611277	36.2%	5.45 [0.23 , 128.32]
Shapiro 2020	2.356126	1.212543	63.8%	10.55 [0.98 , 113.60]
Total (95% CI)			**100.0%**	**8.31 [1.24 , 55.51]**

Heterogeneity: Chi² = 0.11, df = 1 (P = 0.74); I² = 0%
Test for overall effect: Z = 2.19 (P = 0.03)
Test for subgroup differences: Not applicable

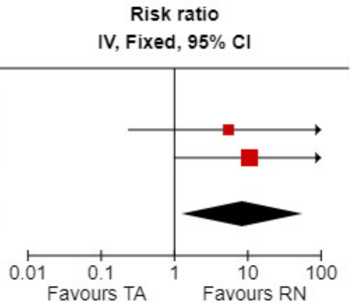


Figure 52 Metastasis ≤5 years

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
Takaki 2010	-0.635989	1.20908	27.4%	0.53 [0.05 , 5.66]
Takaki 2014	0.213574	0.871822	52.7%	1.24 [0.22 , 6.84]
Shapiro 2020	-2.020547	1.422032	19.8%	0.13 [0.01 , 2.15]
Total (95% CI)			**100.0%**	**0.63 [0.18 , 2.18]**

Heterogeneity: Chi² = 1.82, df = 2 (P = 0.40); I² = 0%
Test for overall effect: Z = 0.73 (P = 0.47)
Test for subgroup differences: Not applicable

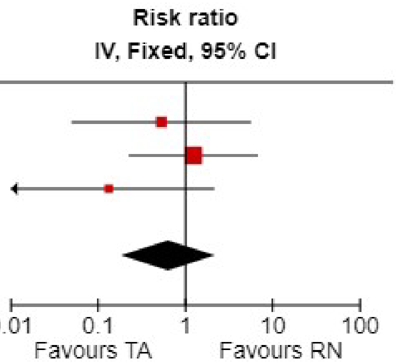


Figure 53 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Almadalal 2022	-0.3285040669720361	0.19408668603825305	0.72 [0.49 , 1.05]

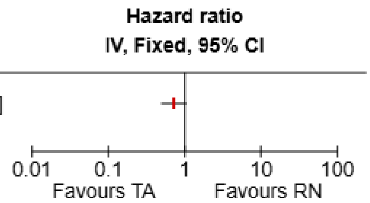


Figure 54 Mortality ≤5 years

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
Takaki 2010	2.889303	1.442302	35.1%	17.98 [1.06 , 303.74]
Takaki 2014	2.228477	1.06148	64.9%	9.29 [1.16 , 74.36]
Total (95% CI)			**100.0%**	**11.71 [2.19 , 62.57]**

Heterogeneity: Chi² = 0.14, df = 1 (P = 0.71); I² = 0%
Test for overall effect: Z = 2.88 (P = 0.004)
Test for subgroup differences: Not applicable

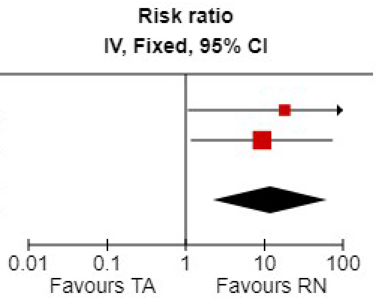


Figure 55 Cancer-specific survival ≤5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Xing 2018	-0.11332868530700327	0.26996949981814666	0.89 [0.53 , 1.52]

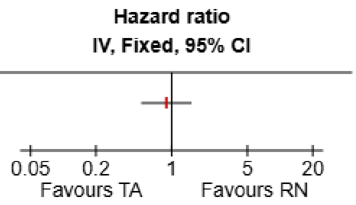


Figure 56 Cancer-specific mortality ≤5 years

Study or Subgroup	log[RR]	SE	Weight	Risk ratio IV, Fixed, 95% CI
Takaki 2010	Not estimable	Not estimable		Not estimable
Takaki 2014	1.696449	1.611277	44.1%	5.45 [0.23 , 128.32]
Shapiro 2020	-1.575862	1.432094	55.9%	0.21 [0.01 , 3.42]
Total (95% CI)			**100.0%**	**0.88 [0.11 , 7.14]**

Heterogeneity: Chi² = 2.30, df = 1 (P = 0.13); I² = 57%
Test for overall effect: Z = 0.12 (P = 0.90)
Test for subgroup differences: Not applicable

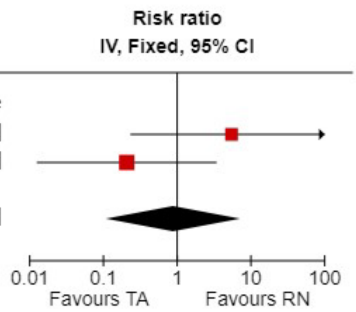


Figure 57 Renal function impairment: Change in eGFR ≤5 years (mL/min/1.73 m2, higher is better)

Study or Subgroup	MD	SE	Weight	Mean difference IV, Random, 95% CI
Lucas 2008	7.2	7.32359	8.5%	7.20 [-7.15 , 21.55]
Foyil 2008	11.29	1.975087	21.7%	11.29 [7.42 , 15.16]
Deklaj 2010	13.4	9.35361	6.0%	13.40 [-4.93 , 31.73]
Takaki 2012	14.3	2.048193	21.5%	14.30 [10.29 , 18.31]
Takaki 2014	22.4	9.895991	5.5%	22.40 [3.00 , 41.80]
Cooper 2015	-1.53	3.171319	18.2%	-1.53 [-7.75 , 4.69]
Danzig 2015	6.31	2.982702	18.7%	6.31 [0.46 , 12.16]
Total (95% CI)			**100.0%**	**9.06 [3.91 , 14.21]**

Heterogeneity: Tau² = 27.94; Chi² = 21.42, df = 6 (P = 0.002); I² = 72%
Test for overall effect: Z = 3.45 (P = 0.0006)
Test for subgroup differences: Not applicable

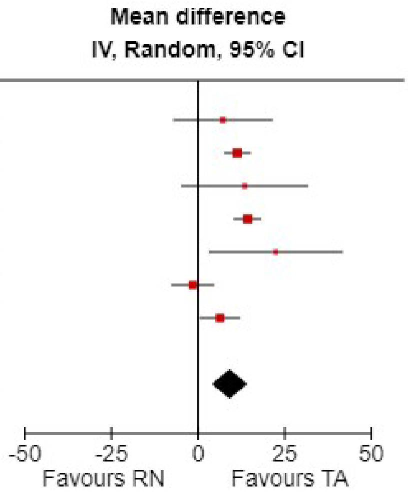
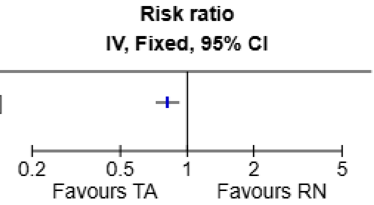


Figure 58 Cardiovascular events

Study or Subgroup	Thermal ablation Events	Thermal ablation Total	Radical nephrectomy Events	Radical nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Xing 2018	270	733	331	733	0.82 [0.72 , 0.92]



Active surveillance versus partial nephrectomy non-randomised evidence

Figure 59 Metastasis ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Yasuda 2022	2	26	50	842	1.30 [0.33 , 5.04]

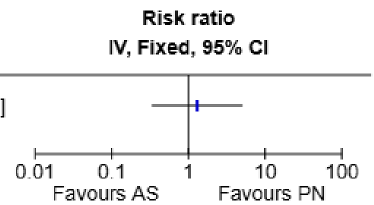


Figure 60 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Guo 2019	0.916291	0.0826	2.50 [2.13 , 2.94]

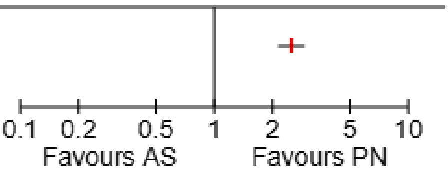


Figure 61 Mortality ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Yasuda 2022	10	26	381	842	0.85 [0.52 , 1.39]

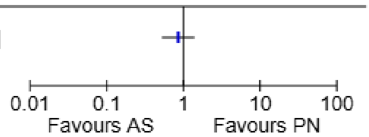
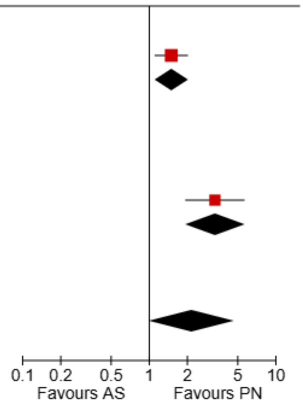


Figure 62 Cancer-specific survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
4.4.1 Systematic review				
Guo 2019[a]	0.400478	0.155102	54.1%	1.49 [1.10 , 2.02]
Subtotal			**54.1%**	**1.49 [1.10 , 2.02]**
Test for overall effect: Z = 2.58 (P = 0.010)				
Heterogeneity: Not applicable				
4.4.2 Single study				
Palumbo 2020	1.1939224684724346	0.27574810559933743	45.9%	3.30 [1.92 , 5.67]
Subtotal			**45.9%**	**3.30 [1.92 , 5.67]**
Test for overall effect: Z = 4.33 (P < 0.0001)				
Heterogeneity: Not applicable				
Total (Wald[b])			**100.0%**	**2.15 [0.99 , 4.66]**

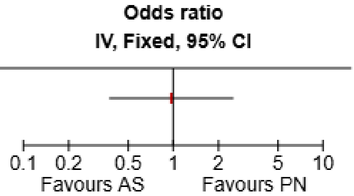


Test for overall effect: Z = 1.93 (P = 0.05)
Test for subgroup differences: Chi² = 6.29, df = 1 (P = 0.01), I² = 84.1%
Heterogeneity: Tau² (DL[c]) = 0.26; Chi² = 6.29, df = 1 (P = 0.01); I² = 84%

Footnotes
[a]Guo 2019 is a systematic review where the included studies could not be disaggregated.
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.

Figure 63 New onset eGFR <45 mL/min/1.73 m2

Study or Subgroup	log[OR]	SE	Odds ratio IV, Fixed, 95% CI
Alam 2019	-0.030459207484708574	0.48841076712970427	0.97 [0.37 , 2.53]



Active surveillance versus radical nephrectomy non-randomised evidence

Figure 64 Metastasis ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Radical nephrectomy Events	Radical nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Lane 2010	0	105	1	146	0.46 [0.02 , 11.24]

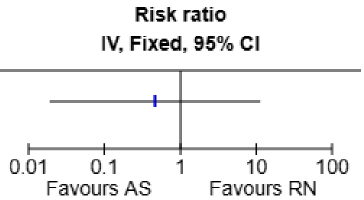


Figure 65 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
Lane 2010	0.2876820724517809	0.2626628410761835	62.7%	1.33 [0.80 , 2.23]
Tang 2017	0.10536051565782628	0.3405677546249648	37.3%	1.11 [0.57 , 2.17]
Total (95% CI)			**100.0%**	**1.25 [0.83 , 1.87]**

Heterogeneity: Chi² = 0.18, df = 1 (P = 0.67); I² = 0%
Test for overall effect: Z = 1.06 (P = 0.29)
Test for subgroup differences: Not applicable

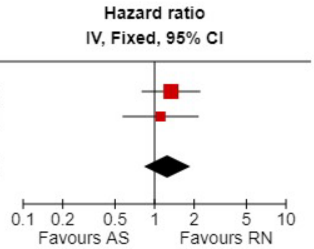


Figure 66 Mortality ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Radical nephrectomy Events	Radical nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Patel 2012	12	71	8	41	0.87 [0.39 , 1.94]

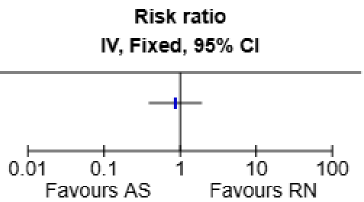


Figure 67 Cancer-specific survival >5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Xing 2018	0.0769610411361284	0.14008109706701818	1.08 [0.82 , 1.42]

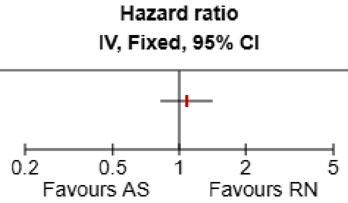


Figure 68 Cancer-specific mortality ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Radical nephrectomy Events	Radical nephrectomy Total	Weight	Risk ratio IV, Random, 95% CI
Lane 2010	6	105	7	146	65.1%	1.19 [0.41 , 3.44]
Patel 2012	1	71	3	41	34.9%	0.19 [0.02 , 1.79]
Total (95% CI)		**176**		**187**	**100.0%**	**0.63 [0.11 , 3.46]**
Total events:	7		10			

Heterogeneity: Tau² = 0.87; Chi² = 2.09, df = 1 (P = 0.15); I² = 52%
Test for overall effect: Z = 0.53 (P = 0.60)
Test for subgroup differences: Not applicable

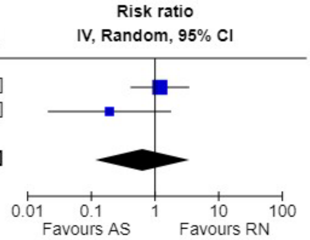
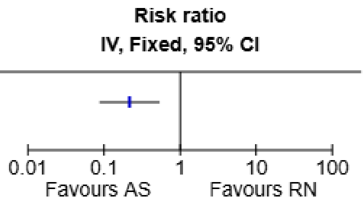


Figure 69 Renal function impairment: New onset eGFR <60 ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Radical nephrectomy Events	Radical nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Lane 2010	5	105	32	146	0.22 [0.09 , 0.54]



SABR versus partial nephrectomy non-randomised evidence

Figure 70 Local recurrence ≤5 years

Study or Subgroup	SABR Events	SABR Total	Partial nephrectomy Events	Partial nephrectomy Total	Risk ratio IV, Fixed, 95% CI
Staehler 2022	1	35	0	35	3.00 [0.13 , 71.22]

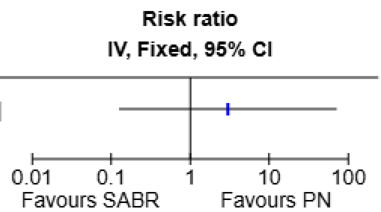


Figure 71 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
Uhlig 2020	1.2378743560016174	0.22556598597978317	54.5%	3.45 [2.22 , 5.37]
Staehler 2022	-0.3920420877760237	0.5404849965425877	45.5%	0.68 [0.23 , 1.95]
Total (95% CI)			**100.0%**	**1.64 [0.33 , 8.07]**

Heterogeneity: Tau² = 1.16; Chi² = 7.75, df = 1 (P = 0.005); I² = 87%
Test for overall effect: Z = 0.61 (P = 0.54)
Test for subgroup differences: Not applicable

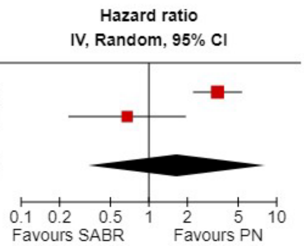
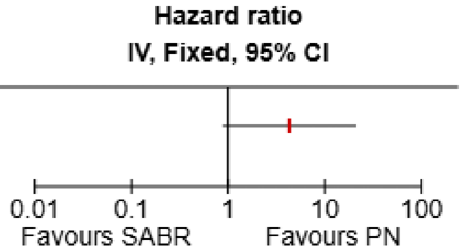


Figure 72: Cancer-specific mortality

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
de Angelis 2024	1.458615	0.80886	4.30 [0.88 , 20.99]



Active surveillance versus thermal ablation non-randomised evidence

Figure 73 Metastasis ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Thermal ablation Events	Thermal ablation Total	Weight	Risk ratio IV, Fixed, 95% CI
Umari 2022	1	75	1	59	22.6%	0.79 [0.05 , 12.31]
Yasuda 2022	2	26	8	102	77.4%	0.98 [0.22 , 4.35]
Total (95% CI)		**101**		**161**	**100.0%**	**0.93 [0.25 , 3.45]**
Total events:	3		9			

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)
Test for subgroup differences: Not applicable

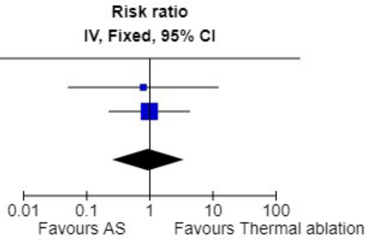
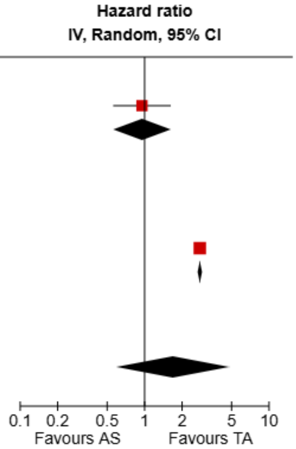


Figure 74 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
7.2.1 Systematic review				
Guo 2019[a]	-0.04879016416943205	0.27189848238113185	46.8%	0.95 [0.56 , 1.62]
Subtotal			**46.8%**	**0.95 [0.56 , 1.62]**
Test for overall effect: Z = 0.18 (P = 0.86)				
Heterogeneity: Not applicable				
7.2.2 Single study				
Grant 2020	1.0216512475319814	0.02097949219602256	53.2%	2.78 [2.67 , 2.89]
Subtotal			**53.2%**	**2.78 [2.67 , 2.89]**
Test for overall effect: Z = 48.70 (P < 0.00001)				
Heterogeneity: Not applicable				
Total (Wald[b])			**100.0%**	**1.68 [0.59 , 4.80]**

Test for overall effect: Z = 0.97 (P = 0.33)
Test for subgroup differences: Chi² = 15.41, df = 1 (P < 0.0001), I² = 93.5%
Heterogeneity: Tau² (DL[c]) = 0.54; Chi² = 15.41, df = 1 (P < 0.0001); I² = 94%



Footnotes
[a]Guo 2019 is a systematic review where the included studies could not be disaggregated.
[b]CI calculated by Wald-type method.
[c]Tau² calculated by DerSimonian and Laird method.

Figure 75 Mortality ≤5 years

Study or Subgroup	Active surveillance Events	Active surveillance Total	Thermal ablation Events	Thermal ablation Total	Risk ratio IV, Fixed, 95% CI
Yasuda 2022	10	26	28	102	1.40 [0.78 , 2.50]

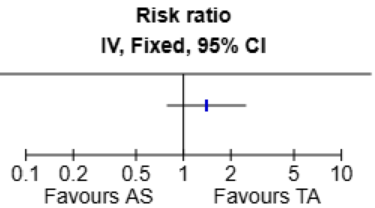
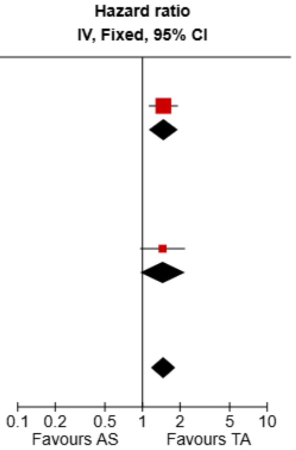


Figure 76 Cancer-specific survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Fixed, 95% CI
7.4.1 Systematic review				
Guo 2019[a]	0.38566248081198456	0.13709248113361194	70.4%	1.47 [1.12 , 1.92]
Subtotal			**70.4%**	**1.47 [1.12 , 1.92]**
Test for overall effect: Z = 2.81 (P = 0.005)				
Heterogeneity: Not applicable				
7.4.2 Single study				
Xing 2018	0.371564	0.211596	29.6%	1.45 [0.96 , 2.20]
Subtotal			**29.6%**	**1.45 [0.96 , 2.20]**
Test for overall effect: Z = 1.76 (P = 0.08)				
Heterogeneity: Not applicable				
Total			**100.0%**	**1.46 [1.17 , 1.83]**



Test for overall effect: Z = 3.32 (P = 0.0009)
Test for subgroup differences: Chi² = 0.00, df = 1 (P = 0.96), I² = 0%
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² = 0%

Footnotes
[a]Guo 2019 is a systematic review where the included studies could not be disaggregated.

SABR versus thermal ablation non-randomised evidence

Figure 77 Overall survival >5 years – cryoablation

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Uhlig 2020	0.916290731874155	0.2133324976351262	2.50 [1.65 , 3.80]

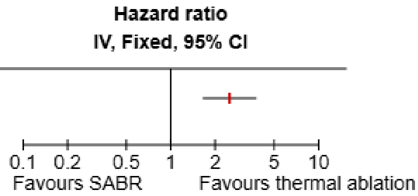
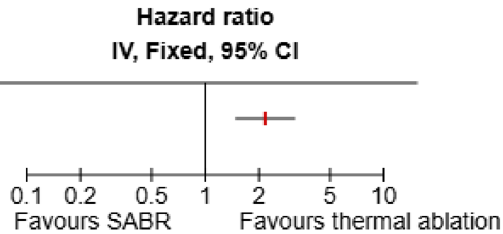


Figure 78 Overall survival >5 years – radiofrequency ablation

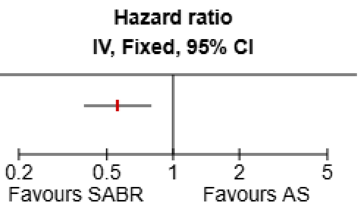
Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Uhlig 2020	0.774727	0.197378	2.17 [1.47 , 3.19]



SABR versus active surveillance non-randomised evidence

Figure 79 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Hazard ratio IV, Fixed, 95% CI
Grant 2020	-0.579818495252942	0.18007632076390964	0.56 [0.39 , 0.80]

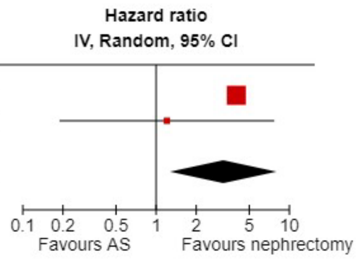


Active surveillance versus nephrectomy non-randomised evidence

Figure 80 Overall survival ≤5 years

Study or Subgroup	log[HR]	SE	Weight	Hazard ratio IV, Random, 95% CI
Grant 2020	1.3862943611198906	0.020419433291692095	81.1%	4.00 [3.84 , 4.16]
Cheung 2023	0.18632957819149348	0.9468781470288576	18.9%	1.20 [0.19 , 7.71]
Total (95% CI)			**100.0%**	**3.19 [1.27 , 8.01]**

Heterogeneity: Tau² = 0.27; Chi² = 1.61, df = 1 (P = 0.21); I² = 38%
Test for overall effect: Z = 2.47 (P = 0.01)
Test for subgroup differences: Not applicable



Appendix F – GRADE tables

Thermal ablation versus partial nephrectomy

Table 22 Clinical evidence profile for thermal ablation versus partial nephrectomy RCT evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Postoperative severe adverse events - Clavien-Dindo I											
1[1] (n=50)	randomised trials	very serious[a]	serious[b]	not serious	very serious[c]	none	2/25 (8.0%)	3/25 (12.0%)	RR 0.67 (0.12 to 3.65)	40 fewer per 1,000 (from 106 fewer to 318 more)	Not estimable as no events in either arm
Postoperative severe adverse events - Clavien-Dindo 2											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[1] (n=50)	randomised trials	very serious[a]	serious[b]	not serious	very serious[c]	none	1/25 (4.0%)	4/25 (16.0%)	RR 0.25 (0.03 to 2.08)	120 fewer per 1,000 (from 155 fewer to 173 more)	Very low
Postoperative severe adverse events - Clavien-Dindo 3-5											
1[1] (n=50)	randomised trials	very serious[a]	serious[b]	not serious	very serious[d]	none	0/25 (0.0%)	0/25 (0.0%)	not estimable	not estimable	Very low
Renal functional impairment: Change in eGFR at 6 months (mL/min/1.73 m^2)											
1[1] (n=50)	randomised trials	very serious[a]	serious[b]	not serious	very serious[c]	none	25	25	-	MD 0.8 higher (6.46 lower to 8.06 higher)	Very low

Explanations

1. Neves et al. (2023)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded twice for imprecision as fewer than 420 participants contributing to this outcome, and zero events in both arms meaning that a 95% confidence interval cannot be produced or evaluated.

Table 23 Clinical evidence profile for thermal ablation versus partial nephrectomy non-randomised evidence – Recurrence outcomes

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Disease-free survival ≤5 years											
4[1] (n=2363)	non-randomised studies	very serious[a]	not serious	not serious	not serious	none	NR	NR	HR 1.96 (1.25 to 3.07)	NR	Low
Disease-free survival >5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[2] (n=74)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	NR	NR	HR 0.85 (0.23 to 3.15)	NR	Very low
Recurrence ≤5 years											
10[3] (n=2983)	non-randomised studies	very serious[a]	very serious[d]	not serious	not serious	none	NR	NR	OR 2.13 (1.07 to 4.22)	NR	Very low
Local recurrence-free survival ≤5 years											
4[4] (n=2420)	non-randomised studies	very serious[a]	not serious	not serious	not serious	none	NR	NR	HR 2.57 (1.50 to 4.40)	NR	Low
Local recurrence-free survival >5 years											
2[5] (n=1901)	non-randomised studies	very serious[a]	very serious[d]	not serious	serious[e]	none	NR	NR	HR 0.69 (0.14 to 3.38)	NR	Very low
Local recurrence ≤5 years											
21[6] (n=5883)	non-randomised studies	very serious[a]	very serious[d]	not serious	not serious	publication bias strongly suspected[f]	NR	NR	OR 3.24 (1.74 to 6.03)	NR	Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Local recurrence >5 years											
3[7] (n=1005)	non-randomised studies	very serious[a]	very serious[d]	not serious	serious[e]	none	NR	NR	OR 3.07 (0.48 to 19.70)	46 more per 1000 (from 12 fewer to 303 more)	Very low
Metastasis-free survival ≤5 years											
2[8] (n=204)	non-randomised studies	serious[g]	not serious	not serious	very serious[h]	none	NR	NR	HR 0.83 (0.45 to 1.54)	NR	Very low
Metastasis-free survival >5 years											
2[5] (n=1798)	non-randomised studies	very serious[a]	not serious	not serious	serious[e]	none	NR	NR	HR 0.44 (0.15 to 1.35)	NR	Very low
Metastasis ≤5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
12[9] (n=2510)	non-randomised studies	very serious[a]	not serious	not serious	serious[e]	none	32/850 (3.8%)	76/1660 (4.6%)	RR 1.28 (0.77 to 2.14)	13 more per 1,000 (from 11 fewer to 55 more)	Very low
Metastasis >5 years											
1[10] (n=816)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[e]	none	4/151 (2.6%)	15/665 (2.3%)	RR 1.17 (0.40 to 3.49)	4 more per 1,000 (from 14 fewer to 54 more)	Very low

Explanations

1. Fossati 2015, Lehrer 2023, Millan 2022, Pantelidou 2016
2. Olweny 2012
3. Almadalal 2022, Anglickis 2019, Bird 2009, Caputo 2017, Long 2017, Qiu 2023, Rembeyo 2019, Tanagho 2013, Uemura 2021, Yasuda 2022
4. Aikawa 2023, Fraisse 2019, Millan 2022, Pedraza-Sanchez 2023

5. Andrews 2019, Chan 2022
6. Almadalal 2022, Attawettayanon 2023, Beksac 2022, Cazalas 2023, Desai 2005, Emara 2014, Fossati 2015, Guillotreau 2012, Haber 2011, Klatte 2011, Lucas 2008, Mues 2012, Pandolfo 2023, Park 2018, Qiu 2023, Shapiro 2020, Stern 007, Takaki 2010, Thompson 2015, Turna 2009, Yasuda 2022
7. Bianchi 2021, Olweny 2012, Park 2019
8. Aikawa 2023, Bhindi 2018
9. Attawettayanon 2023, Cazalas 2023, Haber 2011, Mason 2018, Mues 2012, Pandolfo 2023, Pedraza-Sanchez 2023, Shapiro 2020, Turna 2009, Takaki 2010, Yasuda 2022, Yamanoi 2024
10. Bianchi 2021

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded once for imprecision as fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded twice for inconsistency as I^2 >60%

e. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

f. Funnel plot visually examined. Distribution of studies in this meta-analysis are skewed, with an absence of studies with large standard error favouring thermal ablation (bottom left of plot). This is especially apparent for studies reporting on cryotherapy. Several studies (Yasuda 2022, Thompson 2015, Almadalal 2022) lie outside of the 95% confidence interval line. Publication bias may be partially due to English language limitation in protocol. No statistical test for publication bias has been carried out.

g. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

h. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

Table 24 Clinical evidence profile for thermal ablation versus partial nephrectomy non-randomised evidence – Survival outcomes

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Overall survival ≤5 years											
10[1] (n=19959)	non-randomised studies	very serious[a]	not serious	not serious	not serious	none	NR	NR	HR 1.89 (1.53 to 2.34)	NR	Low
Overall survival >5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
4[2] (n=14433)	non-randomised studies	very serious[a]	very serious[b]	not serious	not serious	none	NR	NR	HR 1.69 (1.22 to 2.35)	NR	Very low
Mortality ≤5 years											
13[3] (n=3521)	non-randomised studies	very serious[a]	very serious[b]	not serious	serious[c]	none	157/1159 (13.5%)	527/2362 (22.3%)	RR 1.50 (0.94 to 2.38)	112 more per 1,000 (from 13 fewer to 308 more)	Very low
Mortality >5 years											
1[4] (n=115)	non-randomised studies	very serious[a]	serious[d]	not serious	very serious[e]	none	2/62 (3.2%)	0/53 (0.0%)	RR 4.29 (0.21 to 87.34)	Not calculable – 0 events in control arm	Very low
Cancer-specific survival ≤5 years											
6[5] (n=25430)	non-randomised studies	very serious[a]	not serious	not serious	not serious	none	NR	NR	HR 1.64 (1.28 to 2.10)	NR	Low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Cancer-specific survival >5 years											
2[6] (n=1679)	non-randomised studies	very serious[a]	not serious	not serious	serious[c]	none	NR	NR	HR 1.29 (0.38 to 4.39)	NR	Very low
Cancer-specific mortality ≤5 years											
8[7] (n=1508)	non-randomised studies	very serious[a]	not serious	not serious	serious[c]	none	10/719 (1.4%)	9/789 (1.1%)	RR 1.00 (0.32 to 3.12)	0 fewer per 1,000 (from 8 fewer to 24 more)	Very low
Cancer-specific mortality >5 years											
1[8] (n=931)	non-randomised studies	very serious[a]	serious[d]	not serious	not serious	none	4/213 (1.9%)	4/718 (0.6%)	RR 4.40 (1.11 to 17.41)	19 more per 1,000 (from 1 more to 91 more)	Very low

Explanations

1. Aikawa 2023, Alam 2019, Bhindi 2018, Lehrer 2023, Millan 2022, Pedraza-Sanchez 2023, Takaki 2012, Thompson 2015, Uhlig 2020, Yang 2024
2. Andrews 2019, Chan 2022, Kitley 2019, Olweny 2012
3. Almadalal 2022, Kawaguchi 2022, Long 2017, Mues 2012, Qiu 2023, Pandolfo 2023, Rembeyo 2019, Rusinek 2022, Takaki 2010, Turna 2009, Uemura 202, Yamanoi 2024, Yasuda 2022
4. Park 2019
5. Aikawa 2023, Alam 2019, Bhindi 2019, Palumbo 2020, Pecoraro 2019, Yang 2024
6. Andrews 2019, Olweny 2012
7. Fraisse 2019, Long 2017, Pedraza-Sanchez 2023, Rembeyo 2019, Shapiro 2020, Takaki 2010, Turna 2009, Yamanoi 2024
8. Bianchi 2021

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded twice for inconsistency as I^2 >60%

c. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

d. Downgraded once for inconsistency due to single study contributing to GRADE profile

e. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

Table 25 Clinical evidence profile for thermal ablation versus partial nephrectomy non-randomised evidence – Complications and duration of stay

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Postoperative severe adverse events - Clavien-Dindo I-V											
31[1] (n=5414)	non-randomised studies	very serious[a]	very serious[b]	not serious	not serious	none	NR	NR	RR 0.76 (0.60 to 0.96)	NR	Very low
Postoperative severe adverse events - Clavien-Dindo I-II											
12[2] (n=2257)	non-randomised studies	very serious[a]	very serious[b]	not serious	serious[c]	none	NR	NR	RR 0.88 (0.73 to 1.07)	NR	Very low
Postoperative severe adverse events - Clavien-Dindo III-V											
36[3] (n=6896)	non-randomised studies	very serious[a]	not serious	not serious	serious[c]	none	NR	NR	RR 0.83 (0.63 to 1.09)	NR	Very low
Duration of hospital stay (days)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
17[4] (n=16926)	non-randomised studies	very serious[a]	very serious[b]	not serious	not serious	none	NR	NR	-	MD 2.7 lower (3.68 lower to 1.73 lower)	Very low
Duration of hospital stay (days) – sensitivity analysis for minimally invasive surgery											
7[5] (n= 15280)	non-randomised studies	very serious[a]	very serious[b]	not serious	not serious	none	NR	NR	-	MD 1.84 lower (2.95 lower to 0.74 lower)	Very low

Explanations

1. Acosta Ruiz 2021, Aikawa 2023, Bhindi 2018, Caputo 2017, Chan 2022, Desai 2005, Emara 2014, Fossati 2015, Garcia 2021, Guillotreau 2012, Haramis 2012, Junker 2022, Kiriluk 2011, Klatte 2011, Ko 2008, Long 2017, Lucignani 2023, Mues 2012, Pandolfo 2023, Pantelidou 2016, Panumatrassamee 2013, Pedraza-Sanchez 2023, Qiu 2023, Rembeyo 2019, Shapiro 2020, Stern 2007, Tanagho 2013, Yamanoi 2024, Yanagisawa 2018, Yanagisawa 2020
2. Chan 2022, Emara 2014, Junker 2022, Kiriluk 2011, Mues 2012, Pandolfo 2023, Pantelidou 2016, Panumatrassamee 2013,

Pedraza-Sanchez 2023, Qiu 2023, Rusinek 2022, Tanagho 2013
3. Aikawa et al. (2023), Anglickis et al. (2019), Attawettayanon et al. (2023), Caputo et al. (2017), Cazalas et al. (2023), Chan et al. (2022), Desai et al. (2005), Emara et al. (2014), Fossati et al. (2015), Garcia et al. (2021), Guillotreau et al. (2012), Haramis et al. (2012), Junker et al. (2022), Kawaguchi et al. (2022), Kim et al. (2015), Klatte et al. (2011), Ko et al. (2008), Long et al. (2017), Lucignani et al. (2023), Mues et al. (2012), Pandolfo et al. (2023), Panumatrassamee et al. (2013), Pantelidou et al. (2016), Park et al. (2018), Park et al. (2019), Pedraza-Sanchez et al. (2023), Qiu et al. (2023), Rembeyo et al. (2019), Rusinek et al. (2022), Shapiro et al. (2020), Stern et al. (2007), Tanagho et al. (2013), Tanagisawa et al. (2018), Yamanoi et al. (2024), Yanagisawa et al. (2020), Yasuda et al. (2022)
4. Bird et al. (2009), Desai et al. (2005), Fossati et al. (2015), Garci et al. (2021), Haber et al. (2011), Jasinski et al. (2024), Kim et al. (2015), Ko et al. (2008), Lehrer et al. (2023), Long et al. (2017), Pandolfo et al. (2023), Park et al. (2018), Pedraza-Sanchez et al. (2023), Turna et al. (2009), Weinberg et al. (2015), Yanagisawa et al. (2018), Yanagisawa et al. (2020)
5. Bird et al. (2009), Haber et al. (2011), Lehrer et al. (2023), Pandolfo et al. (2023), Turna et al. (2009), Weinberg et al. (2015), Yanagisawa et al. (2020)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded twice for inconsistency as I^2 >60%

c. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

Table 26 Clinical evidence profile for thermal ablation versus partial nephrectomy non-randomised evidence – Renal functional outcomes

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Renal function impairment: Change in eGFR ≤5 years mL/min/1.73 m2											
25[1] (n=3611)	non-randomised studies	serious[a]	serious[b]	not serious	Serious[c]	none	NR	NR	-	MD 0.99 higher (0.7 lower to 2.68 higher)	Very low
Renal function impairment: New onset eGFR <60 mL/min/1.73 m2											
5[2] (n=859)	non-randomised studies	very serious[d]	serious[b]	not serious	serious[c]	none	62/399 (15.5%)	59/460 (12.8%)	RR 1.17 (0.82 to 1.69)	23 more per 1,000 (from 23 fewer to 85 more)	Very low
Renal function impairment: New onset eGFR <45 mL/min/1.73 m2											
1[3] (n=258)	non-randomised studies	very serious[d]	Serious[e]	not serious	very serious[f]	none	NR	NR	OR 1.72 (0.39 to 7.56)	NR	Very low
Renal function impairment: New onset eGFR <30 mL/min/1.73 m2											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
1[4] (n=106)	non-randomised studies	very serious[d]	Serious[e]	not serious	very serious[f]	none	NR	NR	RR 1.50 (0.26 to 8.62)	NR	Very low
Renal function impairment: New onset eGFR <15 mL/min/1.73 m2											
7[5] (n=1159)	non-randomised studies	very serious[d]	not serious	not serious	serious[c]	none	NR	NR	RR 1.21 (0.57 to 2.57)	NR	Very low
Quality of life at 14 days (EORTC questionnaire)											
1[6] (n=165)	non-randomised studies	serious[a]	Serious[e]	not serious	Serious[g]	none	NR	NR	-	MD 9.6 lower (15.95 lower to 3.25 lower)	Very low
Quality of life at 90 days (EORTC questionnaire)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[6] (n=165)	non-randomised studies	serious[a]	Serious[e]	not serious	very serious[f]	none	NR	NR	-	MD 0.26 higher (6.14 lower to 6.66 higher)	Very low

Explanations

1. Acosta Ruiz et al. (2021), Bertolo et al. (2019), Cazalas et al. (2023), Cooper et al. (2015), Danxig et al. (2015), Deklaj et al. (2010), Duus et al. (2023), Faddegon et al. (2013), Foyil et al. (2008), Guillotreau et al. (2012), Kawaguchi et al. (2022), Kiriluk et al. (2011), Klatte et al. (2011), Long et al. (2017), Lucas et al. (2008), Mitchell et al. (2011), Mues et al. (2012), Pandolfo et al. (2023), Pascal et al. (2011), Pedraza-Sanchez et al. (2023), Takaki et al. (2010), Takaki et al. (2014), Tanagho et al. (2013), Turna et al. (2009), Youn et al. (2013)
2. Beksac et al. (2022), Pandolfo et al. (2023), Park et al. (2018), Rembeyo et al. (2019), Ryoo et al. (2022)
3. Alam et al. (2019)
4. Ryoo et al. (2022)
5. Beksac et al. (2022), Guillotreau et al. (2012), Lucas et al. (2008), Mues et al. (2012), Pascal et al. (2011), Ryoo et al. (2022), Turna et al. (2009)
6. Junker et al. (2022)

a. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

b. Downgraded once for inconsistency as I^2 between 41 and 60%

c. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

d. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

e. Downgraded once for inconsistency due to single study contributing to GRADE profile

f. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

g. Downgraded once for imprecision as fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

Table 27 Clinical evidence profile for thermal ablation versus partial nephrectomy non-randomised evidence – Quality of life

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Quality of life at 14 days (EORTC questionnaire)											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[1] (n=165)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	NR	NR	-	MD 9.6 lower (15.95 lower to 3.25 lower)	Very low
Quality of life at 90 days (EORTC questionnaire)											
1[1] (n=165)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[d]	none	NR	NR	-	MD 0.26 higher (6.14 lower to 6.66 higher)	Very low

Explanations

1. Junker et al. (2022)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded once for imprecision due to fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

Thermal ablation versus radical nephrectomy

Table 28 Clinical evidence profile for thermal ablation versus radical nephrectomy non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Thermal ablation**	**Radical nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Disease-free survival ≤5 years											
1[1] (n=1107)	non-randomised studies	very serious[a]	serious[b]	not serious	not serious	none	NR	NR	HR 5.67 (3.23 to 9.95)	NR	Very low
Recurrence ≤5 years											
1[2] (n=60)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[c]	none	NR	NR	RR 0.93 (0.19 to 4.66)	7 fewer (83 fewer to 377 more)	Very low
Local recurrence ≤5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Radical nephrectomy	Relative (95% CI)	Absolute (95% CI)	
2[3] (n=311)	non-randomised studies	very serious[a]	not serious	not serious	serious[d]	none	NR	NR	RR 8.31 (1.24 to 55.51)	NR	Very low
Metastasis ≤5 years											
3[4] (=426)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[c]	none	NR	NR	RR 0.63 (0.18 to 2.18)	NR	Very low
Overall survival ≤5 years											
1[1] (n=1107)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[e]	none	NR	NR	HR 0.72 (0.49 to 1.05)	90 fewer per 1000 (from 164 fewer to 16 more)	Very low
Mortality ≤5 years											
2[5] (n=175)	non-randomised studies	very serious[a]	not serious	not serious	serious[d]	none	NR	NR	RR 11.71 (2.19 to 62.57)	NR	Very low
Cancer-specific survival ≤5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Thermal ablation	Radical nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[6] (n=1466)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[f]	none	NR	NR	HR 0.89 (0.53 to 1.52)	NR	Very low
Cancer-specific mortality ≤5 years											
3[4] (n=426)	non-randomised studies	very serious[a]	serious[g]	not serious	very serious[c]	none	NR	NR	RR 0.88 (0.11 to 7.14)	NR	Very low
Renal function impairment: Change in eGFR ≤5 years mL/min/1.73 m^2											
7[7] (n=390)	non-randomised studies	serious[h]	very serious[i]	not serious	serious[d]	none	NR	NR	-	MD 9.06 higher (3.91 higher to 14.21 higher)	Very low
Cardiovascular events											
1[6] (n=1466)	non-randomised studies	serious[h]	serious[b]	not serious	not serious	none	270/733 (36.8%)	331/733 (45.2%)	RR 0.82 (0.72 to 0.92)	81 fewer per 1,000 (from 126 fewer to 36 fewer)	Low

Explanations

1. Almadalal et al. (2022)
2. Takaki et al. (2014)
3. Shapiro et al. (2020), Takaki et al. (2014)
4. Shapiro et al. (2020), Takaki et al. (2010), Takaki et al. (2014)
5. Takaki et al. (2010), Takaki et al. (2014)
6. Xing et al. (2018)
7. Cooper et al. (2015), Danzig et al. (2015), Deklaj et al. (2010), Foyil et al. (2008), Lucas et al. (2008), Takaki et al. (2010), Takaki et al. (2014)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded once for imprecision as fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

e. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 1300 participants contributing to this outcome

f. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

g. Downgraded once for inconsistency as I^2 between 41 and 60%

h. Downgraded once for risk of bias as >50% of weight from studies at moderate or high risk of bias for this outcome

i. Downgraded twice for inconsistency as I^2 >60%

Active surveillance versus partial nephrectomy

Table 29 Clinical evidence profile for active surveillance versus partial nephrectomy non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active surveillance	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Metastasis ≤5 years											
1[1] (n=868)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	2/26 (7.7%)	50/842 (5.9%)	RR 1.30 (0.33 to 5.04)	18 more per 1,000 (from 40 fewer to 240 more)	Very low
Overall survival ≤5 years											
5[d,2] (n=3517)	non-randomised studies	very serious[a]	very serious[e]	not serious	not serious	none	NR	NR	HR 2.50 (2.13 to 2.94)	NR	Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active surveillance	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Mortality ≤5 years											
1[1] (n=868)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	10/26 (38.5%)	381/842 (45.2%)	RR 0.85 (0.52 to 1.39)	68 fewer per 1,000 (from 217 fewer to 176 more)	Very low
Cancer-specific survival ≤5 years											
6[d,3] (n=6629)	non-randomised studies	very serious[a]	very serious[e]	not serious	serious[c]	none	NR	NR	HR 2.15 (0.99 to 4.66)	NR	Very low
Renal function impairment: New onset eGFR <45 mL/min/1.73 m^2											
1[4] (n=570)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	NR	NR	OR 0.97 (0.37 to 2.53)	NR	Very low

Explanations

1. Yasuda et al. (2022)
2. Alam et al. (2019), Miller et al. (2018), Patel et al. (2012), Patel et al. (2015), Tang et al. (2017)
3. Alam et al. (2019), Miller et al. (2018), Palumbo et al. (2020), Patel et al. (2012), Patel et al. (2015), Tang et al. (2017)
4. Alam et al. (2019)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

d. Guo 2019 result is made up of 5 studies reported by the systematic review (Patel 2012, Patel 2015, Tang 2017, Miller 2018, Alam 2019)

e. Result presented in Guo 2019 as single statistic without forest plot.

Active surveillance versus radical nephrectomy

Table 30 Clinical evidence profile for active surveillance versus radical nephrectomy non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Active surveillance**	**Radical nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Metastasis ≤5 years											
1[1] (n=251)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[c]	none	0/105 (0.0%)	1/146 (0.7%)	RR 0.46 (0.02 to 11.24)	4 fewer per 1,000 (from 7 fewer to 70 more)	Very low
Overall survival ≤5 years											
2[2] (n=335)	non-randomised studies	very serious[a]	not serious	not serious	very serious[d]	none	NR	NR	HR 1.25 (0.83 to 1.87)	NR	Very low
Mortality ≤5 years											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active surveillance	Radical nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[3] (n=112)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[c]	none	12/71 (16.9%)	8/41 (19.5%)	RR 0.87 (0.39 to 1.94)	25 fewer per 1,000 (from 119 fewer to 183 more)	Very low
Cancer-specific survival >5 years											
1[4] (n=3348)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[e]	none	NR	NR	HR 1.08 (0.82 to 1.42)	NR	Very low
Cancer-specific mortality ≤5 years											
2[5] (n=363)	non-randomised studies	very serious[a]	serious[f]	not serious	very serious[c]	none	7/176 (4.0%)	10/187 (5.3%)	RR 0.63 (0.11 to 3.46)	20 fewer per 1,000 (from 48 fewer to 132 more)	Very low
Renal function impairment: New onset eGFR <60 mL/min/1.73 m^2											

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active surveillance	Radical nephrectomy	Relative (95% CI)	Absolute (95% CI)	
1[1] (n=251)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[g]	none	5/105 (4.8%)	32/146 (21.9%)	RR 0.22 (0.09 to 0.54)	171 fewer per 1,000 (from 199 fewer to 101 fewer)	Very low

Explanations

1. Lane et al. (2010)
2. Lane et al. (2010), Tang et al. (2017)
3. Patel et al. (2012)
4. Xing et al. (2018)
5. Lane et al. (2010), Patel et al. (2012)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 1300 participants contributing to this outcome

e. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

f. Downgraded once for inconsistency due to I^2 between 41 and 60%

g. Downgraded once for imprecision due to fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

SABR versus partial nephrectomy

Table 31 Clinical evidence profile for SABR versus partial nephrectomy non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SABR**	**Partial nephrectomy**	**Relative (95% CI)**	**Absolute (95% CI)**	
Local recurrence ≤5 years											
1[1] (n=70)	non-randomised studies	serious[a]	serious[b]	not serious	very serious[c]	none	1/35 (2.9%)	0/35 (0.0%)	RR 3.00 (0.13 to 71.22)	NR	Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SABR	Partial nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Overall survival ≤5 years											
2[2] (n=388)	non-randomised studies	very serious[d]	very serious[e]	not serious	very serious[f]	none	NR	NR	HR 1.64 (0.33 to 8.07)	NR	Very low
Cancer-specific mortality											
1[3] (n=184)	non-randomised studies	very serious[d]	serious[b]	not serious	very serious[c]	none	NR	NR	HR 4.30 (0.88 to 20.99)	NR	Very low

Explanations

1. Staehler et al. (2022)
2. Staehler et al. (2022), Uhlig et al. (2020)
3. de Angelis et al. (2024)

a. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Downgraded twice for risk of bias due to >50% of weight from outcomes at high risk of bias

e. Downgraded twice for inconsistency as I^2 >60%

f. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 1300 participants contributing to this outcome

Active surveillance versus thermal ablation

Table 32 Clinical evidence profile for active surveillance versus thermal ablation non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Active surveillance**	**Thermal ablation**	**Relative (95% CI)**	**Absolute (95% CI)**	
Metastasis ≤5 years											
2[1] (n=262)	non-randomised studies	very serious[a]	not serious	not serious	very serious[c]	none	3/101 (3.0%)	9/161 (5.6%)	RR 0.93 (0.25 to 3.45)	4 fewer per 1,000 (from 42 fewer to 137 more)	Very low

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active surveillance	Thermal ablation	Relative (95% CI)	Absolute (95% CI)	
Overall survival ≤5 years											
3[d,2] (n=35907)	non-randomised studies	Serious[e]	very serious[f]	not serious	serious[g]	none	NR	NR	HR 1.68 (0.59 to 4.80)	NR	Very low
Mortality ≤5 years											
1[3] (n=128)	non-randomised studies	very serious[a]	serious[b]	not serious	very serious[c]	none	10/26 (38.5%)	28/102 (27.5%)	RR 1.40 (0.78 to 2.50)	110 more per 1,000 (from 60 fewer to 412 more)	Very low
Cancer-specific survival ≤5 years											
4[h,4] (n=3624)	non-randomised studies	very serious[a]	not serious	not serious	very serious[i]	none	NR	NR	HR 1.46 (1.17 to 1.83)	NR	Very low

Explanations

1. Umari et al. (2022), Yasuda et al. (2022)
2. Alam et al. (2019), Grant et al. (2020), Miller et al. (2018)
3. Yasuda et al. (2022)
4. Alam et al. (2019), Larcher et al. (2015), Miller et al. (2018), Xing et al. (2018)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 420 participants contributing to this outcome (for outcomes other than overall survival)

d. Guo 2019 result is made up of 2 studies reported by the systematic review (Miller 2018, Alam 2019)

e. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

f. Downgraded twice for inconsistency as I^2 >60%

g. Downgraded once for imprecision as 95% confidence interval includes the line of no effect

h. Guo 2019 result is made up of 3 studies reported by the systematic review (Larcher 2015, Miller 2018, Alam 2019)

i. Cannot be fully assessed as individual results for studies included in Guo 2019 are not available, only a summary result is available. A forest plot from Guo 2019 displaying thermal ablation and partial nephrectomy arms being combined (described as nephron sparing interventions) and compared against active surveillance has moderate heterogeneity (I^2 = 54%).

SABR versus thermal ablation

Table 33 Clinical evidence profile for SABR versus thermal ablation non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SABR	Thermal ablation	Relative (95% CI)	Absolute (95% CI)	
Overall survival >5 years - cryotherapy											
1[1] (n=318)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	NR	NR	HR 2.50 (1.65 to 3.80)	NR	Very low
Overall survival >5 years – radiofrequency ablation											
1[1] (n=318)	non-randomised studies	very serious[a]	serious[b]	not serious	serious[c]	none	NR	NR	HR 2.17 (1.47 to 3.19)	NR	Very low

Explanations

1. Uhlig et al. (2020)

a. Downgraded twice for risk of bias due to >50% of weight from studies at high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded once for imprecision as fewer than 1300 participants contributing to this outcome

SABR versus active surveillance

Table 34 Clinical evidence profile for SABR versus active surveillance non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**SABR**	**Active Surveillance**	**Relative (95% CI)**	**Absolute (95% CI)**	
Overall survival ≤5 year											
1[1] (n=18345)	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	NR	NR	HR 0.56 (0.39 to 0.80)	NR	Low

Explanations

1. Grant et al. (2020)

a. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

Active surveillance versus nephrectomy

Table 35 Clinical evidence profile for active surveillance versus nephrectomy non-randomised evidence

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Active Surveillance	Nephrectomy	Relative (95% CI)	Absolute (95% CI)	
Overall survival ≤5 years											
2[1] (n=183706)	non-randomised studies	serious[a]	not serious	not serious	not serious	none	NR	NR	HR 3.19 (1.27 to 8.01)	NR	Moderate
Overall survival ≤5 years – Sensitivity analysis by confirmed RCC											
1[2] (confirmed RCC) (n=183539)	non-randomised studies	serious[a]	serious[b]	not serious	not serious	none	NR	NR	HR 4.00 (3.84 to 4.16)	NR	Moderate
1[3] (not confirmed RCC) (n=167)	non-randomised studies	serious[a]	serious[b]	not serious	very serious[c]	none	NR	NR	HR 1.20 (0.19 to 7.71)	NR	Very low

Explanations

1. Cheung et al. (2023), Grant et al. (2020)
2. Grant et al. (2020)
3. Cheung et al. (2023)

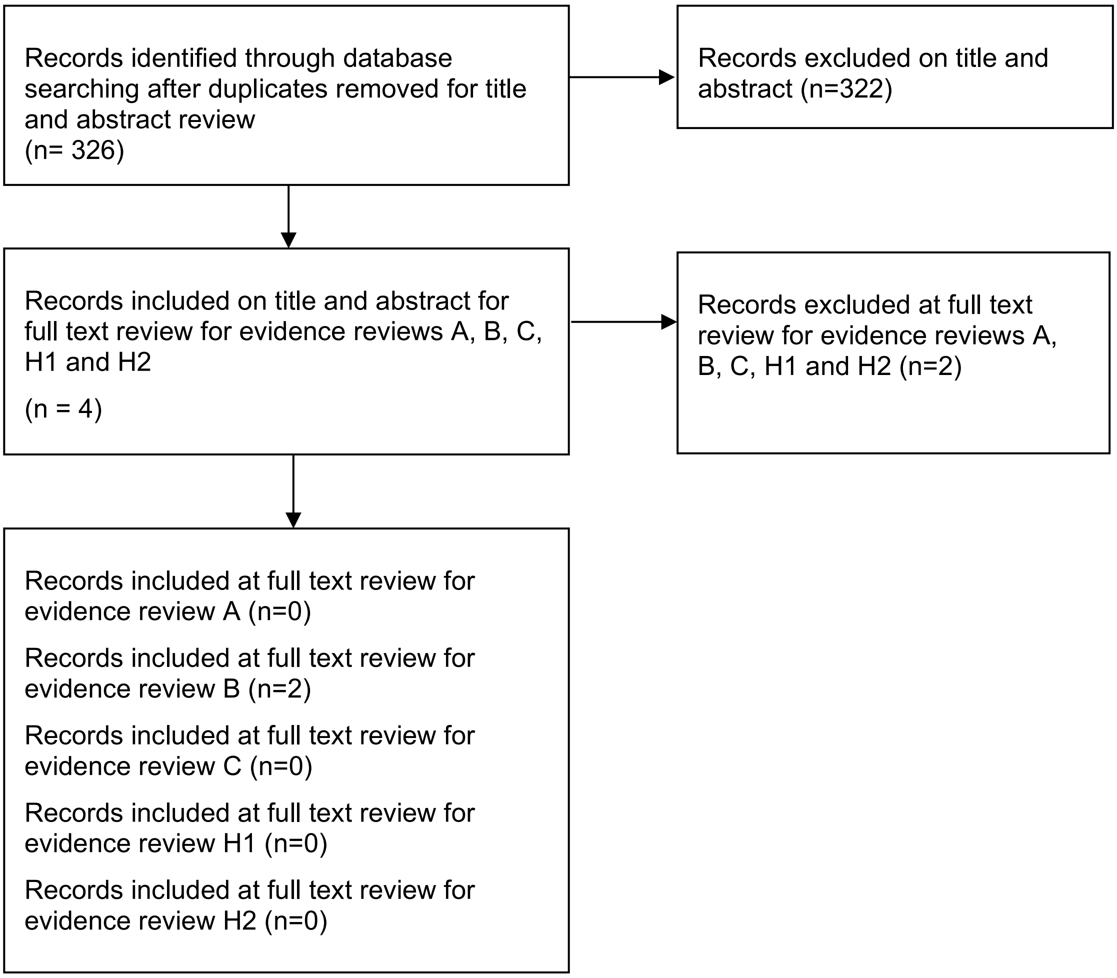
a. Downgraded once for risk of bias due to >50% of weight from studies at moderate or high risk of bias for this outcome

b. Downgraded once for inconsistency due to single study contributing to GRADE profile

c. Downgraded twice for imprecision as 95% confidence interval includes the line of no effect and fewer than 1300 participants contributing to this outcome

Appendix G – Economic evidence study selection

Figure 81: Economic evidence study selection



1 # Appendix H – Economic evidence tables

2 ## Table 36: Economic evidence table

Study	Study type	Setting	Interventions	Population	Methods of analysis	Base-case results	Sensitivity analyses	Additional comments
Health Technology Wales	Economic analysis: Cost-utility analysis Study design: Partitioned survival model Time horizon: lifetime	Setting: UK Perspective: NHS and PSS	SABR Observation	Population: people with primary renal cancer who cannot be managed using surgery or thermal ablation techniques Baseline age: 74 years	Discount rate: 3.5% Efficacy data: Overall survival data was taken from a national cancer registry [Grant et al. (2020)] for both arms. Progression free survival was based on a naïve comparison, with data for SABR sourced from a pooled retrospective analysis [Siva et al. (2018)] and data for observation from an analysis of registry data [Metcalf et al. (2021)]. Cost data: SABR costs were estimated using costs provided from a cancer centre in Wales, based on a lung cancer treatment which experts	Costs: Observation £6,701 SABR £9,096 Incremental £2,395 QALYs: Observation 4.82 SABR 6.83 Incremental 2.02 ICER: £1,188 The key driver of the results of the analysis is	Deterministic scenario analyses found that the results were not sensitive to individual parameter variations, with the ICER remaining below £4,000 per QALY in all scenarios. Probabilistic sensitivity analysis found that at the threshold of £20,000 per QALY, SABR had a 100%	Progression-free survival was based on a naïve comparison, and was also from a different source to the overall survival data, resulting in the implication that PFS for observation is better than for SABR. Additionally a correction was made in the model to account for PFS being predicted as higher than OS, given the disparate data sources.

Study	Study type	Setting	Interventions	Population	Methods of analysis	Base-case results	Sensitivity analyses	Additional comments
					advised was similar in costing to SABR for kidney cancer. Follow-up costs were not included in the analysis as they were considered to be equivalent between arms. Utility data: QoL values were sourced from a published UK cost-utility analysis [Rossi et al. (2021)]	the improved effectiveness of SABR compared with observation, driven by the improvement in OS reported by Grant et al.	probability of being cost-effective compared with observation.	

1

Table 37: Applicability and quality checklist for economic evaluations – Health Technology Wales (2022)

Study identification **Health Technology Wales (2022) Evidence Appraisal Report: Stereotactic ablative radiotherapy to treat people with primary kidney cancer**		
Category	**Rating**	**Comments**
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	The study population is fully in line with a subgroup of the population in the review question
1.2 Are the interventions appropriate for the review question?	Yes	Interventions are appropriate for the subgroup included in the study
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	
1.4 Is the perspective for costs appropriate for the review question?	Yes	
1.5 Is the perspective for outcomes appropriate for the review question?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Yes	
1.8 OVERALL JUDGEMENT	**DIRECTLY APPLICABLE**	Directly applicable to the subgroup of people whose cancer cannot be managed with surgery or thermal ablation.
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all	Yes	

Study identification Health Technology Wales (2022) Evidence Appraisal Report: Stereotactic ablative radiotherapy to treat people with primary kidney cancer		
Category	**Rating**	**Comments**
important differences in costs and outcomes?		
2.3 Are all important and relevant outcomes included?	Partly	No mention of adverse events
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Grant paper identified via clinical review. Unclear how Metcalf study identified but uses registry data so likely to be appropriate source for baseline estimates
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	Unclear how Metcalf study identified. HTW study itself notes limitations of using separate sources for baseline and relative effects. Indirectly explored via sensitivity analysis.
2.6 Are all important and relevant costs included?	Partly	No mention of adverse events
2.7 Are the estimates of resource use from the best available source?	Yes	
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	N/A	
2.12 OVERALL ASSESSMENT	**POTENTIALLY SERIOUS LIMITATIONS**	

Table 38: Applicability and quality checklist for economic evaluations – Xia et al. (2025)

Study identification **Xia et al. (2025) Cost-effectiveness analysis of microwave ablation versus robot-assisted partial nephrectomy for patients with small renal masses in Australia**		
Category	**Rating**	**Comments**
Applicability		
1.1 Is the study population appropriate for the review question?	Yes	
1.2 Are the interventions appropriate for the review question?	Yes	
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	Australian healthcare system
1.4 Is the perspective for costs appropriate for the review question?	Yes	Australian direct healthcare costs
1.5 Is the perspective for outcomes appropriate for the review question?	Partly	Australian healthcare system perspective
1.6 Are all future costs and outcomes discounted appropriately?	Partly	3% discount rate for costs and outcomes
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.5 above).	Yes	
1.8 OVERALL JUDGEMENT	**PARTIALLY APPLICABLE**	Partially applicable as cost and discounting perspectives are from the Australian healthcare system not UK sources.
Limitations		
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all	Yes	

Study identification Xia et al. (2025) Cost-effectiveness analysis of microwave ablation versus robot-assisted partial nephrectomy for patients with small renal masses in Australia		
Category	**Rating**	**Comments**
important differences in costs and outcomes?		
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Unclear	Unclear how transition probabilities were estimated from the underpinning clinical study (Chlorogiannis 2024), as the study reported no statistical difference in recurrence-free survival or metastasis-free survival. There are also concerns with how the survival rates in the clinical study were reported, and thus concerns over which numbers were used for the economic analysis.
2.5 Are the estimates of relative intervention effects from the best available source?	Unclear	Unclear how transition probabilities were estimated from the underpinning clinical study (Chlorogiannis 2024), as the study reported no statistical difference in recurrence-free survival or metastasis-free survival. There are also concerns with how the survival rates in the clinical study were reported, and thus concerns over which numbers were used for the economic analysis.
2.6 Are all important and relevant costs included?	Yes	
2.7 Are the estimates of resource use from the best available source?	Yes	
2.8 Are the unit costs of resources from the best available source?	Yes	
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	
2.11 Has no potential financial conflict of interest been declared?	Yes	No conflicts reported.

Study identification Xia et al. (2025) Cost-effectiveness analysis of microwave ablation versus robot-assisted partial nephrectomy for patients with small renal masses in Australia		
Category	**Rating**	**Comments**
2.12 OVERALL ASSESSMENT	**VERY SERIOUS LIMITATIONS**	Underpinning clinical study was excluded from the clinical review as it did not report HR outcomes. It was unclear how the underpinning clinical study was used to generate transition probabilities and there are concerns with the reported numbers in that study and how they were used in the economic analysis.

Appendix I – Health economic model

No original economic modelling was conducted for this review question. A cost analysis was conducted to aid in decision making for this review question, see the accompanying cost analysis report for further details.

Appendix J – Excluded studies

Effectiveness studies

References excluded at full text (n = 103)

Study	Reason
Abdel Raheem, Ali, Chang, Ki Don, Alenzi, Mohammed Jayed et al. (2019) Robot-Assisted Partial Nephrectomy for Totally Endophytic Renal Tumors: Step by Step Standardized Surgical Technique and Long-Term Outcomes with a Median 59-Month Follow-Up. Journal of laparoendoscopic & advanced surgical techniques. Part A 29(1): 1-11	- Exclude RQC- Study included only patients T1-T2
Abdollah, Firas, Sun, Maxine, Thuret, Rodolphe et al. (2011) Mortality and morbidity after cytoreductive nephrectomy for metastatic renal cell carcinoma: a population-based study. Annals of surgical oncology 18(10): 2988-96	- Comparator in study does not match that specified in protocol *Compares radical nephrectomy Versus. cytoreductive nephrectomy.Unclear about the use of SACT*
Abedali, Zain A, Monn, M Francesca, Huddleston, Patrick et al. (2020) Robotic and open partial nephrectomy for intermediate and high complexity tumors: a matched-pairs comparison of surgical outcomes at a single institution. Scandinavian journal of urology 54(4): 313-317	- Exclude - For RQC Proportion of patients stage T3 < 90%
Abu-Ghanem, Yasmin, Fernandez-Pello, Sergio, Bex, Axel et al. (2020) Limitations of Available Studies Prevent Reliable Comparison Between Tumour Ablation and Partial Nephrectomy for Patients with Localised Renal Masses: A Systematic Review from the European Association of Urology Renal Cell Cancer Guideline Panel. European urology oncology 3(4): 433-452	- Data not reported in an extractable format
Abu-Ghanem, Yasmin, van Thienen, Johannes V, Blank, Christian et al. (2022) Cytoreductive nephrectomy and exposure to sunitinib - a post hoc analysis of the Immediate Surgery or Surgery After	- Study does not contain a relevant outcome *No additional outcomes to reported*

Study	Reason
Sunitinib Malate in Treating Patients With Metastatic Kidney Cancer (SURTIME) trial. BJU international 130(1): 68-75	
Acosta Ruiz, Vanessa, Ladjevardi, Sam, Brekkan, Einar et al. (2019) Periprocedural outcome after laparoscopic partial nephrectomy versus radiofrequency ablation for T1 renal tumors: a modified R.E.N.A.L nephrometry score adjusted comparison. Acta radiologica (Stockholm, Sweden : 1987) 60(2): 260-268	- Study published before included SR/s for the outcome/s reported
Aeppli, S., Engeler, D.S., Fischer, S. et al. (2022) Incidence and outcome of patients with renal cell carcinoma treated with partial or radical nephrectomy in the Cantons St Gallen and Appenzell 2009-2018. Swiss Medical Weekly 152(2324): w30175	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Ahn, Thomas, Ellis, Robert J, White, Victoria M et al. (2018) Predictors of new-onset chronic kidney disease in patients managed surgically for T1a renal cell carcinoma: An Australian population-based analysis. Journal of surgical oncology 117(7): 1597-1610	- Primary study covered fully by an included systematic review
Alasker, Ahmed, Alnafisah, Turki Rashed, Alghafees, Mohammad et al. (2023) Preserving Renal Function without Compromising Oncological Outcomes: A Comparative Study of Partial and Total Nephrectomies in T3 Stage Renal Cell Carcinoma. Journal of kidney cancer and VHL 10(4): 28-32	- Comparator in study does not match that specified in protocol *Compared PN versus RN in T3a RCC: not relevant for RQC*
Ali, Muhammad, Kwon, Young Suk, Koo, Kendrick et al. (2025) Salvage stereotactic ablative body radiotherapy after thermal ablation of primary kidney cancer. BJU international 135(1): 110-116	- Study did not compare the interventions of interest
Alnimer, Yanal, Qasrawi, Ayman, Yan, Donglin et al. (2021) Prognostic Impact of Cytoreductive Nephrectomy in Patients with Metastatic Renal Cell Carcinoma: Data from a Large Population-Based Database. Urology journal 19(2): 111-119	- Exclude - Outcome was measured using a measure out of scope

Study	Reason
Alper, Isik and Yuksel, Esra (2016) Comparison of Acute and Chronic Pain after Open Nephrectomy versus Laparoscopic Nephrectomy: A Prospective Clinical Trial. Medicine 95(16): e3433	- There is no information on cT or pT stage
Alshyarba, M.H.M., Alamri, A., Assiri, J.M.M. et al. (2020) Treatment and overall survival in renal cell carcinoma. Bahrain Medical Bulletin 42(2): 113-115	- Data not reported in an extractable format *Kaplan-Meier for overall survival*
Althaus, Adam B, Chang, Peter, Mao, Jialin et al. (2020) Patient-Reported Quality of Life and Convalescence After Minimally Invasive Kidney Cancer Surgery. Urology 144: 123-129	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Alvim, Ricardo, Tin, Amy, Nogueira, Lucas et al. (2021) A comparison of oncologic and functional outcomes in patients with pt3a renal cell carcinoma treated with partial and radical nephrectomy. International braz j urol : official journal of the Brazilian Society of Urology 47(4): 777-783	- Comparator in study does not match that specified in protocol *Compared RN with PN in T3a tumours - not relevant for RQC*
Alzamzami, M, Geirbely, A, Ahmed, MB et al. (2023) A Literature Review of Perioperative Outcomes of Robotic Radical Nephrectomy (RRN) Versus Laparoscopic Radical Nephrectomy (LRN) for Renal Cell Carcinoma (RCC). Cureus 15(11): e49077	- Exclude - For RQC Proportion of patients stage T3 < 90%
Amin, C., Wallen, E., Pruthi, R.S. et al. (2008) Preoperative Tyrosine Kinase Inhibition as an Adjunct to Debulking Nephrectomy. Urology 72(4): 864-868	- Study does not contain a relevant intervention *Irrelevant nephrectomy type. Study observes the patients undergone laparoscopic and radical nephrectomy*
Andrade, Hiury S, Zargar, Homayoun, Akca, Oktay et al. (2017) Is Robotic Partial Nephrectomy Safe for T3a Renal Cell Carcinoma? Experience of a High-Volume Center. Journal of endourology 31(2): 153-157	- Comparator in study does not match that specified in protocol *Compares RN and PN in T3a RCC - not relevant for RQC*
Andrews, Jack R, Lohse, Christine M, Boorjian, Stephen A et al. (2022) Outcomes following cytoreductive nephrectomy without immediate postoperative systemic therapy	- Comparator in study does not match that specified in protocol *None of the participants had SACT*

Study	Reason
for patients with synchronous metastatic renal cell carcinoma. Urologic oncology 40(4): 166e1-166e8	
Anele, Uzoma A, Marchioni, Michele, Yang, Bo et al. (2019) Robotic versus laparoscopic radical nephrectomy: a large multi-institutional analysis (ROSULA Collaborative Group). World journal of urology 37(11): 2439-2450	- Exclude - For RQC Proportion of patients stage T3 < 90%
Ansari, Jawaher, Farrag, Ashraf, Ali, Arwa et al. (2021) Concurrent use of nivolumab and radiotherapy for patients with metastatic non-small cell lung cancer and renal cell carcinoma with oligometastatic disease progression on nivolumab. Molecular and clinical oncology 15(4): 214	- Study does not contain a relevant outcome
Antonelli, Alessandro, Palumbo, Carlotta, Sandri, Marco et al. (2020) Renal Function Impairment Below Safety Limits Correlates With Cancer-specific Mortality in Localized Renal Cell Carcinoma: Results From a Single-center Study. Clinical genitourinary cancer 18(4): e360-e367	- Study does not contain a relevant outcome
Antonelli, Alessandro, Veccia, Alessandro, Pavan, Nicola et al. (2019) Outcomes of Partial and Radical Nephrectomy in Octogenarians - A Multicenter International Study (Resurge). Urology 129: 139-145	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Aron, Monish, Koenig, Phillipe, Kaouk, Jihad H et al. (2008) Robotic and laparoscopic partial nephrectomy: a matched-pair comparison from a high-volume centre. BJU international 102(1): 86-92	- There is no information on cT or pT stage
Artsitas, Sotirios, Artsitas, Dimitrios, Segkou, Ioanna et al. (2022) Considering "Trifecta" as a Single Outcome when Comparing Robotic With Open Partial Nephrectomy: A Mathematical Model of Volume Conservation and Systematic Review. In vivo (Athens, Greece) 36(6): 2558-2578	- Exclude - assessed outcome is out of scope

Study	Reason
Bacic, Janine, Liu, Tao, Thompson, R Houston et al. (2020) Emulating Target Clinical Trials of Radical Nephrectomy With or Without Lymph Node Dissection for Renal Cell Carcinoma. Urology 140: 98-106	- Comparator in study does not match that specified in protocol *LND versus no LND*
Badrigilan, S., Meola, A., Chang, S.D. et al. (2023) Stereotactic radiosurgery with immune checkpoint inhibitors for brain metastases: a meta-analysis study. British Journal of Neurosurgery 37(6): 1533-1543	- Exclude - wrong population
Baio, Raffaele, Molisso, Giovanni, Caruana, Christian et al. (2023) "Could Patient Age and Gender, along with Mass Size, Be Predictive Factors for Benign Kidney Tumors?": A Retrospective Analysis of 307 Consecutive Single Renal Masses Treated with Partial or Radical Nephrectomy. Bioengineering (Basel, Switzerland) 10(7)	- Study does not contain a relevant outcome
Bamias, Aristotle, Tzannis, Kimon, Papatsoris, Athanasios et al. (2014) Prognostic significance of cytoreductive nephrectomy in patients with synchronous metastases from renal cell carcinoma treated with first-line sunitinib: a European multiinstitutional study. Clinical genitourinary cancer 12(5): 373-83	- Mixed population of SACT pre/post non-pharmacological regimens *No information available to interpret if the SACT was given before or after CN*
Baudo, A., Incesu, R.-B., Morra, S. et al. (2023) Other-Cause Mortality, According to Partial vs. Radical Nephrectomy: Age and Stage Analyses. Clinical Genitourinary Cancer	- Study does not contain a relevant outcome
Bayrak, Omer, Seckiner, Ilker, Erturhan, Sakip et al. (2014) Comparison of the complications and the cost of open and laparoscopic radical nephrectomy in renal tumors larger than 7 centimeters. Urology journal 11(1): 1222-7	- Exclude - For RQC Proportion of patients stage T3 < 90%
Bazzi, Wassim M, Sjoberg, Daniel D, Feuerstein, Michael A et al. (2015) Long-term survival rates after resection for locally advanced kidney cancer: Memorial Sloan Kettering Cancer Center 1989 to 2012	- Comparator in study does not match that specified in protocol

Study	Reason
experience. The Journal of urology 193(6): 1911-6	
Bekema, Hendrika J, MacLennan, Steven, Imamura, Mari et al. (2013) Systematic review of adrenalectomy and lymph node dissection in locally advanced renal cell carcinoma. European urology 64(5): 799-810	- Comparator in study does not match that specified in protocol
Beksac, Alp T, Okhawere, Kennedy E, Abou Zeinab, Mahmoud et al. (2022) Robotic partial nephrectomy for management of renal mass in patients with a solitary kidney: can we expand the indication to T2 and T3 disease?. Minerva urology and nephrology 74(2): 203-208	- Exclude - For RQC Proportion of patients stage T3 < 90%
Benichou, Ygal, Audenet, Francois, Bensalah, Karim et al. (2023) Partial nephrectomy in solitary kidneys: comparison between open surgery and robotic-assisted laparoscopy on perioperative and functional outcomes (UroCCR-54 study). World journal of urology 41(2): 315-324	- Exclude - For RQC Proportion of patients stage T3 < 90%
Bianchi, Lorenzo, Chessa, Francesco, Piazza, Pietro et al. (2022) Percutaneous ablation or minimally invasive partial nephrectomy for cT1a renal masses? A propensity score-matched analysis. International journal of urology : official journal of the Japanese Urological Association 29(3): 222-228	- Secondary publication of an included study that does not provide any additional relevant information
Binsaleh, Saleh, Madbouly, Khaled, Matsumoto, Edward D et al. (2015) A Prospective Randomized Study of Pfannenstiel Versus Expanded Port Site Incision for Intact Specimen Extraction in Laparoscopic Radical Nephrectomy. Journal of endourology 29(8): 913-8	- Exclude - Intervention is out of scope
Blom, Jan H M, van Poppel, Hein, Marechal, Jean M et al. (2009) Radical nephrectomy with and without lymph-node dissection: final results of European Organization for Research and Treatment of	- Comparator in study does not match that specified in protocol *Lymphadenectomy vs no lymphadenectomy*

Study	Reason
Cancer (EORTC) randomized phase 3 trial 30881. European urology 55(1): 28-34	
Bosse, Dominick, Lin, Xun, Simantov, Ronit et al. (2019) Response of Primary Renal Cell Carcinoma to Systemic Therapy. European urology 76(6): 852-860	- Not a relevant study design *Pooled Analysis*
Boylu, U., Basatac, C., Yildirim, U. et al. (2015) Comparison of surgical, functional, and oncological outcomes of open and robot-assisted partial nephrectomy. Journal of Minimal Access Surgery 11(1): 72-77	- Exclude - For RQC Proportion of patients stage T3 < 90%
Bravi, C.A., on behalf of the Junior ERUS/Young Academic Urologist Working Group on Robot-Assisted, Surgery, Dell'Oglio, P. et al. (2024) Surgical Experience and Functional Outcomes after Laparoscopic and Robot-Assisted Partial Nephrectomy: Results from a Multi-Institutional Collaboration. Journal of Clinical Medicine 13(19): 6016	- Exclude - RQC Patients with localised tumour
Breda, Alberto; Anterasian, Christine; Belldegrun, Arie (2010) Management and outcomes of tumor recurrence after focal ablation renal therapy. Journal of endourology 24(5): 749-52	- More recent systematic review included that covers the same topic
Britton, Cameron J, Sharma, Vidit, Lohse, Christine M et al. (2022) Progression of Chronic Kidney Disease Following Radical and Partial Nephrectomy. Urology 169: 125-133	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Brown, Janet E, Royle, Kara-Louise, Gregory, Walter et al. (2023) Temporary treatment cessation versus continuation of first-line tyrosine kinase inhibitor in patients with advanced clear cell renal cell carcinoma (STAR): an open-label, non-inferiority, randomised, controlled, phase 2/3 trial. The Lancet. Oncology 24(3): 213-227	- Study does not contain a relevant intervention
Buckland, Benjamin, Tree, Kevin, Best, Oliver et al. (2024) Robotic versus Laparoscopic Partial Nephrectomy: A	- Exclude - RQC Patients with localised tumour

Study	Reason
Systematic Review and Meta-Analysis of Randomised Trials. Surgical technology international 45	
Burgess, Neil A, Koo, Brendan C, Calvert, Robert C et al. (2007) Randomized trial of laparoscopic v open nephrectomy. Journal of endourology 21(6): 610-3	- There is no information on cT or pT stage
Cacciamani, Giovanni E, Medina, Luis G, Gill, Tania et al. (2018) Impact of Surgical Factors on Robotic Partial Nephrectomy Outcomes: Comprehensive Systematic Review and Meta-Analysis. The Journal of urology 200(2): 258-274	- Exclude - For RQC Proportion of patients stage T3 < 90%
Cai, Yi; Li, Han-Zhong; Zhang, Yu-Shi (2018) Comparison of Partial and Radical Laparascopic Nephrectomy: Long-Term Outcomes for Clinical T1b Renal Cell Carcinoma. Urology journal 15(2): 16-20	- Non-OECD country
Calpin, Gavin G, Ryan, Fintan R, McHugh, Fiachra T et al. (2023) Comparing the outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a network meta-analysis. BJU international 132(4): 353-364	- Exclude - For RQC Proportion of patients stage T3 < 90%
Calpin, GG, Ryan, FR, McHugh, FT et al. (2023) Comparing the Outcomes of Open, Laparoscopic & Robotic Partial Nephrectomy: A Network Meta-Analysis. BJU international	- Duplicate reference
Campi, Riccardo, Berni, Alessandro, Amparore, Daniele et al. (2022) Impact of frailty on perioperative and oncologic outcomes in patients undergoing surgery or ablation for renal cancer: a systematic review. Minerva urology and nephrology 74(2): 146-160	- More recent systematic review included that covers the same topic
Cao, Dalong, Huang, Yongqiang, Zhang, Chuankai et al. (2019) Adverse Effect of Lymph Node Dissection in Metastatic Renal Cell Cancer Patients Treated with Cytoreductive Nephrectomy: A	- Study did not compare the interventions of interest

Study	Reason
Contemporary Analysis of Survival. Journal of Cancer 10(19): 4639-4646	
Capitanio, U., Larcher, A., Cianflone, F. et al. (2020) Hypertension and Cardiovascular Morbidity Following Surgery for Kidney Cancer. European Urology Oncology 3(2): 209-215	- Primary study covered fully by an included systematic review
Capitanio, Umberto, Zini, Laurent, Perrotte, Paul et al. (2008) Cytoreductive partial nephrectomy does not undermine cancer control in metastatic renal cell carcinoma: a population-based study. Urology 72(5): 1090-5	- Study does not contain a relevant intervention *Compares partial nephrectomy with radical nephrectomy*
Carbonara, Umberto, Ditonno, Francesco, Beksac, Alp T et al. (2025) Percutaneous Cryotherapy and Radiofrequency Ablation of Renal Masses: Multicenter Comparative Analysis with Minimum 3-Year Follow-up. International braz j urol : official journal of the Brazilian Society of Urology 51(2)	- Compares two types of ablation
Carvalho, Filipe L F, Zheng, Chaoyi, Witmer, Kenneth et al. (2019) Complications associated with perioperative use of tyrosine kinase inhibitor in cytoreductive nephrectomy. Scientific reports 9(1): 15272	- Study does not contain a relevant intervention *Compares nephrectomy followed by SACT vs. nephrectomy alone.- study evaluates the effect of preoperative SACT. It's unclear whether SACT was given before or after the surgery.*
Castilho, Tiago Mendonca Lopez, Lemos, Gustavo Caserta, Cha, Jonathan Doyun et al. (2020) Transition from open partial nephrectomy directly to robotic surgery: experience of a single surgeon to achieve "TRIFECTA". International braz j urol : official journal of the Brazilian Society of Urology 46(5): 814-821	- Exclude - Study with a single arm
Cerrato, Clara, Meagher, Margaret F, Autorino, Riccardo et al. (2023) Partial versus radical nephrectomy for complex renal mass: multicenter comparative analysis of functional outcomes (Rosula collaborative group). Minerva urology and nephrology 75(4): 425-433	- Study does not contain a relevant outcome *Outcomes presented for T1, T2 and T3 combined*

Study	Reason
Chan, Vinson Wai-Shun, Tan, Wei Shen, Leow, Jeffrey J et al. (2021) Delayed surgery for localised and metastatic renal cell carcinoma: a systematic review and meta-analysis for the COVID-19 pandemic. World journal of urology 39(12): 4295-4303	- Exclude - Result reported in the most updated MA
Chanbour, Hani, Chen, Jeffrey W, Bendfeldt, Gabriel A et al. (2024) Impact of Targeted Systemic Therapy and Radiotherapy on Patients Undergoing Spine Surgery for Metastatic Renal Cell Carcinoma. International journal of spine surgery 18(3): 343-352	- Exclude - Intervention is out of scope *Spinal surgery*
Chang, Ki Don, Abdel Raheem, Ali, Kim, Kwang Hyun et al. (2018) Functional and oncological outcomes of open, laparoscopic and robot-assisted partial nephrectomy: a multicentre comparative matched-pair analyses with a median of 5 years' follow-up. BJU international 122(4): 618-626	- Exclude RQC- Study included only patients T1-T2
Chang, Xiaofeng, Liu, Tieshi, Zhang, Fan et al. (2015) Radiofrequency ablation versus partial nephrectomy for clinical T1a renal-cell carcinoma: long-term clinical and oncologic outcomes based on a propensity score analysis. Journal of endourology 29(5): 518-25	- Non-OECD country
Chang, Xiaofeng, Zhang, Fan, Liu, Tieshi et al. (2015) Radio frequency ablation versus partial nephrectomy for clinical T1b renal cell carcinoma: long-term clinical and oncologic outcomes. The Journal of urology 193(2): 430-5	- Non-OECD country
Chang, Ying-Hsu, Chang, Su-Wei, Liu, Chung-Yi et al. (2018) Demographic characteristics and complications of open and minimally invasive surgeries for renal cell carcinoma: a population-based case-control study in Taiwan. Therapeutics and clinical risk management 14: 1235-1241	- Non-OECD country
Chapin, Brian F, Delacroix, Scott E Jr, Culp, Stephen H et al. (2011) Safety of presurgical targeted therapy in the setting of	- Comparator in study does not match that specified in protocol

Study	Reason
metastatic renal cell carcinoma. European urology 60(5): 964-71	*Study compares SACT followed by CN with immediate CN. Results section indicates that both groups received SACT post surgery as well.*
Chapman, Terence N, Sharma, Satish, Zhang, Shaozeng et al. (2008) Laparoscopic lymph node dissection in clinically node-negative patients undergoing laparoscopic nephrectomy for renal carcinoma. Urology 71(2): 287-91	- Comparator in study does not match that specified in protocol *LND vs no LND*
Chen, Bo, Li, Jinze, Huang, Yin et al. (2023) The role of cytoreductive nephrectomy in metastatic renal cell carcinoma in the targeted therapy and immunological therapy era: a systematic review and meta-analysis. International journal of surgery (London, England) 109(4): 982-994	- Exclude - error in the paper
Chen, Yonghui, Wu, Xiaorong, Zhou, Jiale et al. (2022) Thermal ablation assisted laparoscopic partial nephrectomy for clinical T1b renal tumors. Minimally invasive therapy & allied technologies : MITAT : official journal of the Society for Minimally Invasive Therapy 31(2): 179-184	- Non-OECD country
Cheung, Douglas C and Finelli, Antonio (2017) Active Surveillance in Small Renal Masses in the Elderly: A Literature Review. European urology focus 3(45): 340-351	- More recent systematic review included that covers the same topic
Cheung, Patrick, Patel, Samir, North, Scott A et al. (2021) Stereotactic Radiotherapy for Oligoprogression in Metastatic Renal Cell Cancer Patients Receiving Tyrosine Kinase Inhibitor Therapy: A Phase 2 Prospective Multicenter Study. European urology 80(6): 693-700	- Not a relevant study design
Chiancone, Francesco, Fabiano, Marco, Meccariello, Clemente et al. (2021) Laparoscopic versus open partial nephrectomy for the management of highly complex renal tumors with PADUA score 10: A single center analysis. Urologia 88(4): 343-347	- Exclude RQC- Study included only patients T1-T2

Study	Reason
Chiou, Jiun-Kai, Chang, Li-Wen, Li, Jian-Ri et al. (2023) Metastasectomy Improves Overall Survival in Metastatic Renal Cell Carcinoma: A Retrospective Cohort Study. Anticancer research 43(7): 3193-3201	- Mixed population of SACT pre/post non-pharmacological regimens *All participants received SACT. Not sufficient information to know the timeline of SACT.Compares patients undergone metastasectomy vs. non-metastasectomy.*
Chlorogiannis, David-Dimitris, Kratiras, Zisis, Efthymiou, Evgenia et al. (2024) Percutaneous Microwave Ablation Versus Robot-Assisted Partial Nephrectomy for Stage I Renal Cell Carcinoma: A Propensity-Matched Cohort Study Focusing Upon Long-Term Follow-Up of Oncologic Outcomes. Cardiovascular and interventional radiology 47(5): 573-582	- Data not reported in an extractable format
Cho, C L, Ho, K L, Chu, S S M et al. (2011) Robot-assisted versus standard laparoscopic partial nephrectomy: comparison of perioperative outcomes from a single institution. Hong Kong medical journal = Xianggang yi xue za zhi 17(1): 33-8	- Non-OECD country - Not a relevant study design *Consecutive case series*
Choi, Chang Il, Kang, Minyong, Sung, Hyun Hwan et al. (2018) Oncologic Outcomes of Cytoreductive Nephrectomy in Synchronous Metastatic Renal-Cell Carcinoma: A Single-Center Experience. Clinical genitourinary cancer 16(6): e1189-e1199	- Mixed population of SACT pre/post non-pharmacological regimens *All participants received SACT. Not sufficient information to know the timeline of SACT.*
Choi, J.D., Park, J.W., Lee, H.W. et al. (2013) A comparison of surgical and functional outcomes of robot-assisted versus pure laparoscopic partial nephrectomy. Journal of the Society of Laparoendoscopic Surgeons 17(2): 292-299	- Exclude RQC- Study included only patients T1-T2
Choi, J.E., You, J.H., Kim, D.K. et al. (2015) Comparison of perioperative outcomes between robotic and laparoscopic partial nephrectomy: A systematic review and meta-analysis. European Urology 67(5): 891-901	- Exclude - RQC Patients with localised tumour
Choi, Se Young, Ha, Moon Soo, Lee, Jeong Woo et al. (2023) Shifting role of cytoreductive nephrectomy according to	- Mixed population of SACT pre/post non-pharmacological regimens

Study	Reason
type of systemic therapy: A nationwide cohort study. Asian journal of surgery 46(1): 328-336	*All participants received SACT. Not sufficient information to know the timeline of SACT.*
Choi, Se Young, Jung, Han, You, Dalsan et al. (2019) Robot-assisted partial nephrectomy is associated with early recovery of renal function: Comparison of open, laparoscopic, and robot-assisted partial nephrectomy using DTPA renal scintigraphy. Journal of surgical oncology 119(7): 1016-1023	- There is no information on cT or pT stage
Chung, Doo Yong, Kang, Dong Hyuk, Kim, Jong Won et al. (2020) Comparison of oncologic outcomes between partial nephrectomy and radical nephrectomy in patients who were upstaged from cT1 renal tumor to pT3a renal cell carcinoma: an updated systematic review and meta-analysis. Therapeutic advances in urology 12: 1756287220981508	- Comparator in study does not match that specified in protocol *PN vs RN for upstaged pT3 tumour*
Chung, Jae-Seung, Son, Nak Hoon, Lee, Sang Eun et al. (2018) Partial versus Radical Nephrectomy for T1-T2 Renal Cell Carcinoma in Patients with Chronic Kidney Disease Stage III: a Multiinstitutional Analysis of Kidney Function and Survival Rate. Journal of Korean medical science 33(43): e277	- More recent systematic review included that covers the same topic *already included by Ochoa but also reports HR in people with CKD 30 ≤ eGFR < 60 in table 2 Looks like Ochoa only included new onset CKD which is why they've only used the stage i-iii values - can exclude*
Cinar, O., Bolat, M.S., Cicek, M.C. et al. (2020) Experiences of Laparoscopic Partial Nephrectomy for T1a Kidney Tumours: Results of Two Hundred and Fifteen Patients. Bulletin of Urooncology 19(3): 130-135	- Exclude RQC- Study included only patients T1-T2
Colombo, Jose R Jr, Haber, Georges-Pascal, Jelovsek, John E et al. (2008) Seven years after laparoscopic radical nephrectomy: oncologic and renal functional outcomes. Urology 71(6): 1149-54	- Exclude - For RQC Proportion of patients stage T3 < 90%
Correa, Rohann J M, Louie, Alexander V, Zaorsky, Nicholas G et al. (2019) The Emerging Role of Stereotactic Ablative Radiotherapy for Primary Renal Cell	- More recent systematic review included that covers the same topic

Study	Reason
Carcinoma: A Systematic Review and Meta-Analysis. European urology focus 5(6): 958-969	
Cotta, Brittney H, Meagher, Margaret F, Patil, Dattatraya et al. (2021) Elevated preoperative C-reactive protein is associated with renal functional decline and non-cancer mortality in surgically treated renal cell carcinoma: analysis from the INternational Marker Consortium for Renal Cancer (INMARC). BJU international 127(3): 311-317	- Primary study covered fully by an included systematic review
Crocerossa, Fabio, Autorino, Riccardo, Derweesh, Ithaar et al. (2023) Management of renal cell carcinoma in transplant kidney: a systematic review and meta-analysis. Minerva urology and nephrology 75(1): 1-16	- Does not contain a population of people with kidney cancer *Transplanted kidneys only*
Crocerossa, Fabio, Carbonara, Umberto, Cantiello, Francesco et al. (2021) Robot-assisted Radical Nephrectomy: A Systematic Review and Meta-analysis of Comparative Studies. European urology 80(4): 428-439	- Exclude - For RQC Proportion of patients stage T3 < 90%
Culp, Stephen H, Tannir, Nizar M, Abel, E Jason et al. (2010) Can we better select patients with metastatic renal cell carcinoma for cytoreductive nephrectomy?. Cancer 116(14): 3378-88	- Mixed population of SACT pre/post non-pharmacological regimens *All participants received SACT. Not sufficient information to know the timeline of SACT received before or after CN.*
Dabestani, Saeed, Marconi, Lorenzo, Hofmann, Fabian et al. (2014) Local treatments for metastases of renal cell carcinoma: a systematic review. The Lancet. Oncology 15(12): e549-61	- Mixed population of SACT pre/post non-pharmacological regimens
Dahm, P., Ergun, O., Uhlig, A. et al. (2024) Cytoreductive nephrectomy in metastatic renal cell carcinoma. Cochrane Database of Systematic Reviews 2024(6): cd013773	- Systematic review used as source of primary studies
Dahm, Philipp, Ergun, Onuralp, Uhlig, Annemarie et al. (2024) Cytoreductive nephrectomy in metastatic renal cell carcinoma. The Cochrane database of systematic reviews 6: cd013773	- Duplicate reference

Study	Reason
Danzig, Matthew R, Ghandour, Rashed A, Chang, Peter et al. (2015) Active Surveillance is Superior to Radical Nephrectomy and Equivalent to Partial Nephrectomy for Preserving Renal Function in Patients with Small Renal Masses: Results from the DISSRM Registry. The Journal of urology 194(4): 903-9	- Primary study covered fully by an included systematic review
Dariane, Charles; Timsit, Marc-Olivier; Mejean, Arnaud (2018) Position of cytoreductive nephrectomy in the setting of metastatic renal cell carcinoma patients: does the CARMENA trial lead to a paradigm shift?. Bulletin du cancer 105suppl3: 229-s234	- Systematic review used as source of primary studies
Das, Manoj K, Rohith, Gorrepati, Mandal, Swarnendu et al. (2024) Intraoperative ultrasonography (IOUS)-guided vs conventional laparoscopic nephrectomy: a randomised control trial. BJU international 133(1): 71-78	- Exclude - Intervention is out of scope
Dash, A., Vickers, A.J., Schachter, L.R. et al. (2006) Comparison of outcomes in elective partial vs radical nephrectomy for clear cell renal cell carcinoma of 4-7 cm. BJU International 97(5): 939-945	- For RQA. Study published before 2016 (search date for disease-free survival)
de Bruijn, Roderick, Wimalasingham, Akhila, Szabados, Bernadett et al. (2020) Deferred Cytoreductive Nephrectomy Following Presurgical Vascular Endothelial Growth Factor Receptor-targeted Therapy in Patients with Primary Metastatic Clear Cell Renal Cell Carcinoma: A Pooled Analysis of Prospective Trial Data. European urology oncology 3(2): 168-173	- Systematic review used as source of primary studies
De Gobbi, Alberto, Biasoni, Davide, Catanzaro, Mario et al. (2018) Surgery of locally advanced and metastatic kidney cancer after tyrosine kinase inhibitors therapy: single institute experience. Tumori 104(5): 388-393	- Not a relevant study design *observational study*
de Saint Aubert, N, Audenet, F, Mccaig, F et al. (2018) Nephron sparing surgery in	- Primary study covered fully by an included systematic review

Study	Reason
tumours greater than 7cm. Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie 28(6): 336-343	
Deka, H., Medam, N.M., Ginil Kumar, P. et al. (2024) Comparison of Trifecta and Pentafecta Outcomes across 3 Surgical Modalities of Partial Nephrectomy (PN) - Open, Lap, and Robotic. Journal of Kidney Cancer and VHL 11(3): 27	- Exclude - For RQC Proportion of patients stage T3 < 90%
Deng, Huan, Fan, Yan, Yuan, Feifei et al. (2021) Partial nephrectomy provides equivalent oncologic outcomes and better renal function preservation than radical nephrectomy for pathological T3a renal cell carcinoma: A meta-analysis. International braz j urol : official journal of the Brazilian Society of Urology 47(1): 46-60	- Comparator in study does not match that specified in protocol *Compares RN vs PN for T3 tumours*
Deng, Wen, Chen, Luyao, Wang, Yibing et al. (2019) Cryoablation versus Partial Nephrectomy for Clinical Stage T1 Renal Masses: A Systematic Review and Meta-Analysis. Journal of Cancer 10(5): 1226-1236	- More recent systematic review included that covers the same topic
Deng, Wen, Zhou, Zhengtao, Zhong, Jian et al. (2020) Retroperitoneal laparoscopic partial versus radical nephrectomy for large (>= 4 cm) and anatomically complex renal tumors: A propensity score matching study. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 46(7): 1360-1365	- Non-OECD country
Dengina, N., Mitin, T., Gamayunov, S. et al. (2019) Stereotactic body radiation therapy in combination with systemic therapy for metastatic renal cell carcinoma: A prospective multicentre study. ESMO Open 4(5): e000535	- Not a relevant study design
Desideri, I, Francolini, G, Scotti, V et al. (2019) Benefit of ablative versus palliative-only radiotherapy in combination with nivolumab in patients affected by metastatic	- Does not contain a population of people with kidney cancer *Mix of non-small cell lung cancer and RCC. No separate results for participants with*

Study	Reason
kidney and lung cancer. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 21(7): 933-938	*RCC reported.No comparator groupParticipants received RT and SACT simultaneously. Or RT given at least 60 days after the last does of SACT.*
Dillenburg, Wolfgang, Poulakis, Vassilis, Skriapas, Konstantinos et al. (2006) Retroperitoneoscopic versus open surgical radical nephrectomy for large renal cell carcinoma in clinical stage cT2 or cT3a: quality of life, pain and reconvalescence. European urology 49(2): 314-3	- Exclude - For RQC Proportion of patients stage T3 < 90%
Dong, Bao Nan, Song, Jie, Yang, Wen Li et al. (2024) Comparison of Outcomes Between Partial and Radical Laparoscopic Nephrectomy for Localized Renal Tumors Larger Than Four Centimeters: A Systematic Review and Meta-Analysis. World journal of oncology 15(4): 625-639	- Systematic review with case control studies
Dong, Hanzhi, Cao, Yuan, Jian, Yan et al. (2023) Patients with metastatic renal cell carcinoma who receive immune-targeted therapy may derive survival benefit from nephrectomy. BMC cancer 23(1): 943	- Study does not contain a relevant intervention *Compares SACT vs. non pharma (nephrectomy). Only 40% of the patients in the nephrectomy arm underwent CN with rest of them arm receiving radical nephrectomy. No subgroup data available.*
Dong, Lin, Liang, Wang You, Ya, Lu et al. (2022) A Systematic Review and Meta-Analysis of Minimally Invasive Partial Nephrectomy Versus Focal Therapy for Small Renal Masses. Frontiers in oncology 12: 732714	- Does not contain a population of people with kidney cancer *SR focussing on small renal masses*
Dragomir, Alice, Nazha, Sara, Wood, Lori A et al. (2020) Outcomes of complete metastasectomy in metastatic renal cell carcinoma patients: The Canadian Kidney Cancer information system experience. Urologic oncology 38(10): 799e1-799e10	- Study does not contain a relevant intervention *compares mastectomy Vs. no mastectomy. No information regarding the use of SACT prior or during the mastectomy is given. Baseline data reports percentage of patients used SCAT during follow-up, which can not be used to determine the timeline of SCAT*
El-Ghazaly, Tarek H; Mason, Ross J; Rendon, Ricardo A (2014) Oncological	- There is no information on cT or pT stage

Study	Reason
outcomes of partial nephrectomy for tumours larger than 4 cm: A systematic review. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 8(12): 61-6	
Ellis, E.E. and Messing, E. (2021) Active Surveillance of Small Renal Masses: A Systematic Review. Kidney Cancer 5(3): 139-152	- More recent systematic review included that covers the same topic
Ellison, Jonathan S, Montgomery, Jeffrey S, Wolf, J Stuart Jr et al. (2012) A matched comparison of perioperative outcomes of a single laparoscopic surgeon versus a multisurgeon robot-assisted cohort for partial nephrectomy. The Journal of urology 188(1): 45-50	- Exclude - For RQC Proportion of patients stage T3 < 90%
Enikeev, Dmitry, Morozov, Andrey, Bazarkin, Andrey et al. (2023) Thermal ablation vs. active surveillance for renal masses: a systematic review and network meta-analysis. Minerva urology and nephrology 75(2): 154-162	- More recent systematic review included that covers the same topic *Reports unadjusted outcomes only*
Ergun, Muslum, Sagir, Suleyman, Akyuz, Osman et al. (2024) Evolving Approach in Nephron-Sparing Surgery: Has Anything Changed from Open Surgery to Laparoscopy?. Archivos espanoles de urologia 77(7): 726-731	- Exclude - RQC Patients with localised tumour
Faddegon, Stephen, Ju, Tom, Olweny, Ephrem O et al. (2013) A comparison of long term renal functional outcomes following partial nephrectomy and radiofrequency ablation. The Canadian journal of urology 20(3): 6785-9	- Study published before included SR/s for the outcome/s reported
Faiena, Izak, Salmasi, Amirali, Lenis, Andrew T et al. (2018) Overall survival in patients with metastatic renal cell carcinoma and clinical N1 disease undergoing cytoreductive nephrectomy and lymph node dissection. Urologic oncology 36(2): 79e19-79e26	- Study does not contain a relevant intervention *Compares lymphadenectomy vs. No lymphadenectomy. All had previously received CN, no information of background use of SACT given. No additional sub-group analysis*

Study	Reason
Fallah, Jaleh, Gittleman, Haley, Weinstock, Chana et al. (2024) Cytoreductive nephrectomy in the era of immune checkpoint inhibitors: a US Food and Drug Administration pooled analysis. Journal of the National Cancer Institute 116(7): 1043-1050	- Exclude - Intervention is out of scope *Pooled analysis of trials comparing pharmaceuticals only.*
Feder, Marc T, Patel, Manoj B, Melman, Arnold et al. (2008) Comparison of open and laparoscopic nephrectomy in obese and nonobese patients: outcomes stratified by body mass index. The Journal of urology 180(1): 79-83	- Exclude - For RQC Proportion of patients stage T3 < 90%
Feuerstein, Michael A, Kent, Matthew, Bazzi, Wassim M et al. (2014) Analysis of lymph node dissection in patients with >=7-cm renal tumors. World journal of urology 32(6): 1531-6	- Comparator in study does not match that specified in protocol - Study did not compare the interventions of interest
Feuerstein, Michael A, Kent, Matthew, Bernstein, Melanie et al. (2014) Lymph node dissection during cytoreductive nephrectomy: a retrospective analysis. International journal of urology : official journal of the Japanese Urological Association 21(9): 874-9	- Study does not contain a relevant intervention *Compares lymphadenectomy vs. No lymphadenectomy. All had previously received CN, no information of background use of SACT given.*
Ficarra, V., Crestani, A., Inferrera, A. et al. (2018) Positive surgical margins after partial nephrectomy: A systematic review and meta-analysis of comparative studies. Kidney Cancer 2(2): 133-145	- Exclude - assessed outcome is out of scope
Ficarra, Vincenzo, Minervini, Andrea, Antonelli, Alessandro et al. (2014) A multicentre matched-pair analysis comparing robot-assisted versus open partial nephrectomy. BJU international 113(6): 936-41	- Exclude RQC- Study included only patients T1-T2
Figaroa, Orlane, Zondervan, Patricia, Kessels, Rob et al. (2024) PrimerX: A Bayesian Multistage Cohort Embedded Randomised Trial to Evaluate the Role of Deferred Local Therapy of the Primary Tumour in Combination with Immune Checkpoint Inhibitor-based First-line	- Comparator in study does not match that specified in protocol *People in the comparator group were allowed to receive deferred CN if primary tumour was progressing*

Study	Reason
Therapy in Metastatic Renal Cell Carcinoma Patients. European urology open science 70: 28-35	
Fossati, Nicola, Larcher, Alessandro, Gadda, Giulio M et al. (2015) Minimally Invasive Partial Nephrectomy Versus Laparoscopic Cryoablation for Patients Newly Diagnosed with a Single Small Renal Mass. European urology focus 1(1): 66-72	- Primary study covered fully by an included systematic review
Franzese, Ciro, Marini, Beatrice, Baldaccini, Davide et al. (2023) The impact of stereotactic ablative radiotherapy on oligoprogressive metastases from renal cell carcinoma. Journal of cancer research and clinical oncology 149(8): 4411-4417	- 6b SABR exclude *All patients received active SCAT during SABR*
Franzese, Ciro, Marvaso, Giulia, Francolini, Giulio et al. (2021) The role of stereotactic body radiation therapy and its integration with systemic therapies in metastatic kidney cancer: a multicenter study on behalf of the AIRO (Italian Association of Radiotherapy and Clinical Oncology) genitourinary study group. Clinical & experimental metastasis 38(6): 527-537	- 6b SABR exclude
Gandi, C., Totaro, A., Bientinesi, R. et al. (2022) Purely Off-Clamp Partial Nephrectomy: Robotic Approach Better than Open Using a Pentafecta Outcome with Propensity Score Matching. Journal of Clinical Medicine 11(21): 6241	- Exclude - For RQC Proportion of patients stage T3 < 90%
Gao, HuiYu, Zhou, Lin, Zhang, JiaBin et al. (2024) Comparative efficacy of cryoablation versus robot-assisted partial nephrectomy in the treatment of cT1 renal tumors: a systematic review and meta-analysis. BMC cancer 24(1): 1150	- Systematic review used as source of primary studies
Gao, X., Hu, L., Pan, Y. et al. (2018) Surgical outcomes of nephrectomy for elderly patients with renal cell carcinoma. Pakistan Journal of Medical Sciences 34(2): 288-293	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*

Study	Reason
Garcia-Perdomo, Herney A; Zapata-Copete, James A; Castillo-Cobaleda, Diego F (2018) Role of cytoreductive nephrectomy in the targeted therapy era: A systematic review and meta-analysis. Investigative and clinical urology 59(1): 2-9	- Exclude - Result reported in the most updated MA
Garg, Harshit, Das, Bhabatosh, Bansal, Amit et al. (2022) Trifecta and Pentafecta Outcomes in Laparoscopic and Robotic Nephron-Sparing Surgery for Highly Complex Renal Tumors: A Propensity Score-Matched Cohort Analysis. Journal of endourology 36(8): 1050-1056	- Exclude RQC- Study included only patients T1-T2
Garg, Harshit, Tiwari, Deviprasad, Nayak, Brusabhanu et al. (2020) A comparative analysis of various surgical approaches of nephron-sparing surgery and correlation of histopathological grade with RENAL nephrometry score in renal cell carcinoma. Journal of minimal access surgery 16(2): 144-151	- Exclude RQC- Study included only patients T1-T2
Garisto, Juan, Bertolo, Riccardo, Dagenais, Julien et al. (2018) Robotic versus open partial nephrectomy for highly complex renal masses: Comparison of perioperative, functional, and oncological outcomes. Urologic oncology 36(10): 471e1-471e9	- Exclude RQC- Study included only patients T1-T2
Ge, Si, Wang, Zuoping, Li, Yunxiang et al. (2025) Is Ablation Suitable For Small Renal Masses? A Meta-Analysis. Academic radiology 32(1): 218-235	- Systematic review used as source of primary studies
Gebbia, Vittorio, Girlando, Andrea, DI Grazia, Alfio et al. (2020) Stereotactic Radiotherapy for the Treatment of Patients With Oligo-progressive Metastatic Renal Cell Carcinoma Receiving Vascular Endothelial Growth Factor Receptor Tyrosine Kinase Inhibitor: Data From the Real World. Anticancer research 40(12): 7037-7043	- 6b SABR exclude *All participants received concomitant SACT*
Gershman, Boris, Moreira, Daniel M, Thompson, R Houston et al. (2018) Perioperative Morbidity of Lymph Node	- Comparator in study does not match that specified in protocol

Study	Reason
Dissection for Renal Cell Carcinoma: A Propensity Score-based Analysis. European urology 73(3): 469-475	
Gershman, Boris, Thompson, R Houston, Boorjian, Stephen A et al. (2018) Radical Nephrectomy with or without Lymph Node Dissection for High Risk Nonmetastatic Renal Cell Carcinoma: A Multi-Institutional Analysis. The Journal of urology 199(5): 1143-1148	- Exclude - For RQC Proportion of patients stage T3 < 90% - Comparator in study does not match that specified in protocol *LND vs no LND*
Gershman, Boris, Thompson, R Houston, Moreira, Daniel M et al. (2017) Lymph Node Dissection is Not Associated with Improved Survival among Patients Undergoing Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma: A Propensity Score Based Analysis. The Journal of urology 197(3pt1): 574-579	- Mixed population of SACT pre/post non-pharmacological regimens - Study does not contain a relevant intervention *Compares CN with lymphadenectomy vs. CN without lymphadenectomy.Mixed population with pre and post non-pharmacological treatment.*
Gershman, Boris, Thompson, R Houston, Moreira, Daniel M et al. (2017) Radical Nephrectomy With or Without Lymph Node Dissection for Nonmetastatic Renal Cell Carcinoma: A Propensity Score-based Analysis. European urology 71(4): 560-567	- Comparator in study does not match that specified in protocol *LND vs no LND*
Ghani, Khurshid R, Sukumar, Shyam, Sammon, Jesse D et al. (2014) Practice patterns and outcomes of open and minimally invasive partial nephrectomy since the introduction of robotic partial nephrectomy: results from the nationwide inpatient sample. The Journal of urology 191(4): 907-12	- There is no information on cT or pT stage
Gill, Inderbir S, Matin, Surena F, Desai, Mihir M et al. (2003) Comparative analysis of laparoscopic versus open partial nephrectomy for renal tumors in 200 patients. The Journal of urology 170(1): 64-8	- Exclude - For RQC Proportion of patients stage T3 < 90%
Golombos, D.M., Chughtai, B., Trinh, Q.-D. et al. (2017) Adoption of technology and its impact on nephrectomy outcomes, a U.S.	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
population-based analysis (2008-2012). Journal of Endourology 31(1): 91-99	
Golombos, David M, Chughtai, Bilal, Trinh, Quoc-Dien et al. (2017) Minimally invasive vs open nephrectomy in the modern era: does approach matter?. World journal of urology 35(10): 1557-1568	- Exclude - For RQC Proportion of patients stage T3 < 90% *Reported as stage 3*
Gonzalez-Ruiz de Leon, C., Pellejero-Perez, P., Quintas-Blanco, A. et al. (2017) Beneficio de la nefrectomia en el tratamiento del carcinoma de celulas renales metastasico, Benefit of on nephrectomy for treating metastatic renal cell carcinoma. Actas urologicas espanolas 41(5): 338-342	- Exclude - non-English paper
Graham, Jeffrey, Wells, J Connor, Donskov, Frede et al. (2019) Cytoreductive Nephrectomy in Metastatic Papillary Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium. European urology oncology 2(6): 643-648	- Exclude - Result reported in the most updated MA
Green, Harshani; Taylor, Alexandra; Khoo, Vincent (2023) Beyond the Knife in Renal Cell Carcinoma: A Systematic Review-To Ablate or Not to Ablate?. Cancers 15(13)	- More recent systematic review included that covers the same topic
Grimaud, L.W., Chen, F.V., Chang, J. et al. (2021) Comparison of Perioperative Outcomes for Radical Nephrectomy Based on Surgical Approach for Masses Greater Than 10 cm. Journal of Endourology 35(12): 1785-1792	- Exclude - For RQC Proportion of patients stage T3 < 90% *Study excluded cT3b-4 disease*
Grimm, Marc-Oliver, Oya, Mototsugu, Choueiri, Toni K et al. (2024) Impact of Prior Cytoreductive Nephrectomy on Efficacy in Patients with Synchronous Metastatic Renal Cell Carcinoma Treated with Avelumab plus Axitinib or Sunitinib: Post Hoc Analysis from the JAVELIN Renal 101 Phase 3 Trial. European urology 85(1): 8-12	- Not a relevant study design
Grivas, Nikolaos, Kalampokis, Nikolaos, Larcher, Alessandro et al. (2019) Robot-	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
assisted versus open partial nephrectomy: comparison of outcomes. A systematic review. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 71(2): 113-120	
Gross, Evan E, Li, Mingjia, Yin, Ming et al. (2023) A multicenter study assessing survival in patients with metastatic renal cell carcinoma receiving immune checkpoint inhibitor therapy with and without cytoreductive nephrectomy. Urologic oncology 41(1): 51e25-51e31	- Mixed population of SACT pre/post non-pharmacological regimens
Gu, Liangyou, Liu, Kan, Shen, Donglai et al. (2020) Comparison of Robot-Assisted and Laparoscopic Partial Nephrectomy for Completely Endophytic Renal Tumors: A High-Volume Center Experience. Journal of endourology 34(5): 581-587	- Exclude RQC- Study included only patients T1-T2
Gu, Liangyou, Ma, Xin, Gao, Yu et al. (2017) Robotic versus Open Level I-II Inferior Vena Cava Thrombectomy: A Matched Group Comparative Analysis. The Journal of urology 198(6): 1241-1246	- Non-OECD country
Gu, Liangyou, Ma, Xin, Wang, Baojun et al. (2018) Laparoscopic vs robot-assisted partial nephrectomy for renal tumours of >4 cm: a propensity score-based analysis. BJU international 122(3): 449-455	- Exclude - For RQC Proportion of patients stage T3 < 90%
Guan, Wei, Bai, Jian, Liu, Jihong et al. (2012) Microwave ablation versus partial nephrectomy for small renal tumors: intermediate-term results. Journal of surgical oncology 106(3): 316-21	- Non-OECD country
Guglielmetti, Giuliano B, Dos Anjos, Gabriel C, Sawczyn, Guilherme et al. (2022) A Prospective, Randomized Trial Comparing the Outcomes of Open vs Laparoscopic Partial Nephrectomy. The Journal of urology 208(2): 259-267	- Exclude - For RQC Proportion of patients stage T3 < 90%
Guillotreau, Julien, Haber, Georges-Pascal, Autorino, Riccardo et al. (2012) Robotic partial nephrectomy versus laparoscopic	- Primary study covered fully by an included systematic review

Study	Reason
cryoablation for the small renal mass. European urology 61(5): 899-904	
Guner, E. and Sahin, S. (2019) Comparison of robotic and laparoscopic partial nephrectomy in robotic surgery era. Bulletin of Urooncology 18(4): 154-157	- There is no information on cT or pT stage
Guo, Run-Qi, Peng, Jin-Zhao, Sun, Jie et al. (2024) Comparing Oncologic Outcomes of Heat-Based Thermal Ablation and Cryoablation in Patients With T1a Renal Cell Carcinoma: A Population-Based Cohort Study From the SEER Database. Korean journal of radiology 25(12): 1061-1069	- Compares two types of ablation
Gupta, K., Omil-Lima, D., Sheyn, D. et al. (2021) Temporal improvements in renal surgery outcomes across surgical approaches. International Urology and Nephrology 53(7): 1311-1316	- Study does not contain a relevant outcome
Haber, Georges-Pascal, White, Wesley M, Crouzet, Sebastien et al. (2010) Robotic versus laparoscopic partial nephrectomy: single-surgeon matched cohort study of 150 patients. Urology 76(3): 754-8	- Not a relevant study design *Consecutive case series*
Hahn, Andrew W, Kotecha, Ritesh R, Viscuse, Paul V et al. (2023) Cytoreductive Nephrectomy for Patients with Metastatic Sarcomatoid and/or Rhabdoid Renal Cell Carcinoma Treated with Immune Checkpoint Therapy. European urology focus 9(5): 734-741	- Mixed population of SACT pre/post non-pharmacological regimens
Hakam, Nizar, Heidar, Nassib Abou, El-Asmar, Jose et al. (2023) Comparative analysis of partial versus radical nephrectomy for renal cell carcinoma: Is oncologic safety compromised during nephron sparing in higher stage disease?. Urology annals 15(2): 226-231	- Non-OECD country
Hall, Mary E, Bhindi, Bimal, Luckenbaugh, Amy N et al. (2021) Association between cytoreductive nephrectomy and survival among patients with metastatic renal cell carcinoma receiving modern therapies: a	- Mixed population of SACT pre/post non-pharmacological regimens

Study	Reason
systematic review and meta-analysis examining effect modification according to systemic therapy approach. Cancer causes & control : CCC 32(7): 675-680	
Haramis, Georgios, Graversen, Joseph A, Mues, Adam C et al. (2012) Retrospective comparison of laparoscopic partial nephrectomy versus laparoscopic renal cryoablation for small (<3.5 cm) cortical renal masses. Journal of laparoendoscopic & advanced surgical techniques. Part A 22(2): 152-7	- Primary study covered fully by an included systematic review
Harke, N.N., Mandel, P., Witt, J.H. et al. (2018) Are there limits of robotic partial nephrectomy? TRIFECTA outcomes of open and robotic partial nephrectomy for completely endophytic renal tumors. Journal of Surgical Oncology 118(1): 206-211	- Not a relevant study design *Consecutive case series*
Harryman, O.A., Davenport, K., Keoghane, S. et al. (2009) A Comparative Study of Quality of Life Issues Relating to Open Versus Laparoscopic Nephrectomy: A Prospective Pragmatic Study. Journal of Urology 181(3): 998-1003	- There is no information on cT or pT stage
Harshman, Lauren C, Yu, R James, Allen, Genevera I et al. (2013) Surgical outcomes and complications associated with presurgical tyrosine kinase inhibition for advanced renal cell carcinoma (RCC). Urologic oncology 31(3): 379-85	- Not a relevant study design *Reports case series*
Hatayama, Tomoya, Tasaka, Ryo, Mochizuki, Hideki et al. (2022) Comparison of surgical outcomes and split renal function between laparoscopic and robot-assisted partial nephrectomy: a propensity score-matched analysis. International urology and nephrology 54(4): 805-811	- There is no information on cT or pT stage
He, Liru, Liu, Yang, Han, Hui et al. (2020) Survival Outcomes After Adding Stereotactic Body Radiotherapy to Metastatic Renal Cell Carcinoma Patients Treated With Tyrosine Kinase Inhibitors.	- 6b SABR exclude *SABR and SACT given concomitantly*

Study	Reason
American journal of clinical oncology 43(1): 58-63	
Health Technology, Wales (2022) Stereotactic ablative radiotherapy (SABR) for the treatment of renal cell carcinoma.	- Systematic review used as source of primary studies
Heng, Daniel Y C, Wells, J Connor, Rini, Brian I et al. (2014) Cytoreductive nephrectomy in patients with synchronous metastases from renal cell carcinoma: results from the International Metastatic Renal Cell Carcinoma Database Consortium. European urology 66(4): 704-10	- Mixed population of SACT pre/post non-pharmacological regimens *Unclear if participants received SACT before or during or after the CN*
Hoeh, Benedikt, Wenzel, Mike, Eckart, Olivia et al. (2023) Comparison of peri- and intraoperative outcomes of open vs robotic-assisted partial nephrectomy for renal cell carcinoma: a propensity-matched analysis. World journal of surgical oncology 21(1): 189	- Exclude - For RQC Proportion of patients stage T3 < 90%
Hong, Xuwei, Li, Fei, Tang, Kaiqiang et al. (2016) Prognostic value of cytoreductive nephrectomy combined with targeted therapy for metastatic renal cell carcinoma: a meta-analysis. International urology and nephrology 48(6): 967-75	- Exclude - Result reported in the most updated MA
Hori, Shunta, Sakamoto, Keiichi, Onishi, Kenta et al. (2023) Perioperative outcomes of open and robot-assisted partial nephrectomy in patients with renal tumors of moderate to high complexity. Asian journal of surgery 46(6): 2310-2318	- Exclude - RQC Patients with localised tumour
Hsieh, Po-Yen, Hung, Sheng-Chun, Li, Jian-Ri et al. (2021) The effect of metastasectomy on overall survival in metastatic renal cell carcinoma: A systematic review and meta-analysis. Urologic oncology 39(7): 422-430	- Non-OECD country
Hu, Xu, Wang, Yaohui, Shao, Yanxiang et al. (2023) Radical versus partial nephrectomy for T1 non-clear cell renal cell carcinoma. European journal of surgical	- SEER database overlap

Study	Reason
oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 49(8): 1519-1523	
Huang, Jiwei, Zhang, Jin, Wang, Yanqing et al. (2016) Comparing Zero Ischemia Laparoscopic Radio Frequency Ablation Assisted Tumor Enucleation and Laparoscopic Partial Nephrectomy for Clinical T1a Renal Tumor: A Randomized Clinical Trial. The Journal of urology 195(6): 1677-83	- Study does not contain a relevant intervention *Radio frequency ablation group also had tumour enucleation*
Huang, Ryan S, Chow, Ronald, Benour, Ali et al. (2025) Comparative efficacy and safety of ablative therapies in the management of primary localised renal cell carcinoma: a systematic review and meta-analysis. The Lancet. Oncology	- Data not reported in an extractable format
Hutchinson, Ryan, Singla, Nirmish, Krabbe, Laura-Maria et al. (2017) Increased use of antihypertensive medications after partial nephrectomy vs. radical nephrectomy. Urologic oncology 35(11): 660e17-660e25	- Primary study covered fully by an included systematic review
Iisager, Laura, Ahrenfeldt, Johanne, Donskov, Frede et al. (2024) Multicenter randomized trial of deferred cytoreductive nephrectomy in synchronous metastatic renal cell carcinoma receiving checkpoint inhibitors: the NORDIC-SUN-Trial. BMC cancer 24(1): 260	- study protocol
Ingels, A, Bensalah, K, Beauval, J B et al. (2022) Comparison of open and robotic-assisted partial nephrectomy approaches using multicentric data (UroCCR-47 study). Scientific reports 12(1): 18981	- Exclude - For RQC Proportion of patients stage T3 < 90%
Ingrosso, Gianluca, Becherini, Carlotta, Francolini, Giulio et al. (2021) Stereotactic body radiotherapy (SBRT) in combination with drugs in metastatic kidney cancer: A systematic review. Critical reviews in oncology/hematology 159: 103242	- Systematic review used as source of primary studies

Study	Reason
Izol, Volkan, Gokalp, Fatih, Sozen, Sinan et al. (2021) Factors affecting long-term renal functions after partial vs radical nephrectomy for clinical T1 renal masses: A Multicentre Study of the Urooncology Association, Turkey. International journal of clinical practice 75(5): e13960	- More recent systematic review included that covers the same topic *'requirement of dialysis' could mean eGFR <15see rec 1.1.3 within NG107also from Ochoa:"Due to the heterogeneity of defining CKD across studies, we pooled the studies for stages III-V or IV-V as determined by the EGFR or by renal replacement therapy and kidney transplant"Not included in Ochoa most likely because data not reported as HR/OR - to exclude*
Jang, Hoon Ah, Kim, Jin Wook, Byun, Seok Soo et al. (2016) Oncologic and Functional Outcomes after Partial Nephrectomy Versus Radical Nephrectomy in T1b Renal Cell Carcinoma: A Multicenter, Matched Case-Control Study in Korean Patients. Cancer research and treatment 48(2): 612-20	- Primary study covered fully by an included systematic review
Jang, Hyeon Jun, Song, Wan, Suh, Yoon Seok et al. (2014) Comparison of perioperative outcomes of robotic versus laparoscopic partial nephrectomy for complex renal tumors (RENAL nephrometry score of 7 or higher). Korean journal of urology 55(12): 808-13	- There is no information on cT or pT stage
Janisch, Florian, Hillemacher, Tobias, Fuehner, Constantin et al. (2020) The impact of cytoreductive nephrectomy on survival outcomes in patients treated with tyrosine kinase inhibitors for metastatic renal cell carcinoma in a real-world cohort. Urologic oncology 38(9): 739e9-739e15	- Data not reported in an extractable format *Reports OS, PFS and CSS as median months*
Jelley, C.R., Kurukulaarachchi, K.A.S.H., Forster, L. et al. (2017) Comparison of open and robotic nephron sparing surgery: a single centre experience. Journal of Clinical Urology 10(1): 28-35	- Exclude RQC- Study included only patients T1-T2
Jeon, Hwang Gyun, Jeong, In Gab, Lee, Jeong Woo et al. (2009) Prognostic factors for chronic kidney disease after curative surgery in patients with small renal tumors. Urology 74(5): 1064-8	- Primary study covered fully by an included systematic review

Study	Reason
Jeong, In Gab, Khandwala, Yash S, Kim, Jae Heon et al. (2017) Association of Robotic-Assisted vs Laparoscopic Radical Nephrectomy With Perioperative Outcomes and Health Care Costs, 2003 to 2015. JAMA 318(16): 1561-1568	- There is no information on cT or pT stage
Jeong, Seung-Hwan, Kim, Jung Kwon, Park, Juhyun et al. (2016) Pathological T3a Upstaging of Clinical T1 Renal Cell Carcinoma: Outcomes According to Surgical Technique and Predictors of Upstaging. PloS one 11(11): e0166183	- Comparator in study does not match that specified in protocol
Ji, B., Li, D., Fu, S. et al. (2020) Propensity-score matched comparison of partial versus radical nephrectomy for T1N0M0 sarcomatoid renal cell carcinoma. Translational Andrology and Urology 9(2): 250-257	- SEER database overlap
Ji, Changwei, Zhao, Xiaozhi, Zhang, Shiwei et al. (2016) Laparoscopic Radiofrequency Ablation versus Partial Nephrectomy for cT1a Renal Tumors: Long-Term Outcome of 179 Patients. Urologia internationalis 96(3): 345-53	- Non-OECD country
Jiang, Jianping, Zheng, Xiangyi, Qin, Jie et al. (2009) Health-related quality of life after hand-assisted laparoscopic and open radical nephrectomies of renal cell carcinoma. International urology and nephrology 41(1): 23-7	- Exclude - For RQC Proportion of patients stage T3 < 90%
Jiang, Yu-Li, Peng, Cheng-Xia, Wang, Heng-Zi et al. (2019) Comparison of the long-term follow-up and perioperative outcomes of partial nephrectomy and radical nephrectomy for 4 cm to 7 cm renal cell carcinoma: a systematic review and meta-analysis. BMC urology 19(1): 48	- Systematic review used as source of primary studies
Jiang, Yu-Li, Yu, Dong-Dong, Xu, Yang et al. (2023) Comparison of perioperative outcomes of robotic vs. laparoscopic partial nephrectomy for renal tumors with a RENAL nephrometry score >=7: A meta-analysis. Frontiers in surgery 10: 1138974	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
Jin, Seok-Joon, Park, Jun-Young, Kim, Doo-Hwan et al. (2017) Comparison of postoperative pain between laparoscopic and robot-assisted partial nephrectomies for renal tumors: A propensity score matching analysis. Medicine 96(29): e7581	- Exclude - For RQC Proportion of patients stage T3 < 90%
Jokimaki, A., Hietala, H., Lemma, J. et al. (2023) Previous radiotherapy improves treatment responses and causes a trend toward longer time to progression among patients with immune checkpoint inhibitor-related adverse events. Cancer Immunology, Immunotherapy 72(10): 3337-3347	- 6b SABR exclude *Protocol relevant outcomes are not reported for RCC subgroup*
Jones, J.O., Ince, W.H.J., Welsh, S.J. et al. (2022) Activity of Immunotherapy Regimens on Primary Renal Tumours: A Systematic Review. Kidney Cancer 6(4): 221-236	- Systematic review used as source of primary studies
Joslyn, Sue A; Sirintrapun, S Joseph; Konety, Badrinath R (2005) Impact of lymphadenectomy and nodal burden in renal cell carcinoma: retrospective analysis of the National Surveillance, Epidemiology, and End Results database. Urology 65(4): 675-80	- There is no information on cT or pT stage
Junker, Theresa, Duus, Louise, Rasmussen, Benjamin S B et al. (2022) Quality of life and complications after nephron-sparing treatment of renal cell carcinoma stage T1-a systematic review. Systematic reviews 11(1): 4	- Systematic review used as source of primary studies
Kalogirou, Charis, Fender, Hendrik, Muck, Patricia et al. (2017) Long-Term Outcome of Nephron-Sparing Surgery Compared to Radical Nephrectomy for Renal Cell Carcinoma >=4 cm - A Matched-Pair Single Institution Analysis. Urologia internationalis 98(2): 138-147	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Kandi, Maryam, Richard, Patrick O, Violette, Philippe D et al. (2024) Complications and blood loss after invasive treatments for small renal masses: A systematic review. Canadian Urological Association journal =	- Comparator in study does not match that specified in protocol

Study	Reason
Journal de l'Association des urologues du Canada	
Kaneko, Gou, Miyajima, Akira, Kikuchi, Eiji et al. (2012) The benefit of laparoscopic partial nephrectomy in high body mass index patients. Japanese journal of clinical oncology 42(7): 619-24	- Exclude RQC- Study included only patients T1-T2
Kapoor, A., Wong, E.C.L., Fang, W. et al. (2019) Upfront cytoreductive nephrectomy vs. Upfront systemic therapy in metastatic kidney cancer. Canadian Urological Association Journal 13(11): e377-e381	- Data not reported in an extractable format *Protocol relevant outcomes reported as median, no time to event data*
Kato, Daiki, Nakane, Keita, Enomoto, Torai et al. (2021) The utility of laparoscopic partial nephrectomy with renal function preservation, regardless of warm ischemia time, compared with laparoscopic radical nephrectomy. Asian journal of endoscopic surgery 14(3): 386-393	- Data not reported in an extractable format
Kato, Renpei, Naito, Sei, Numakura, Kazuyuki et al. (2022) Significance of upfront cytoreductive nephrectomy stratified by IMDC risk for metastatic renal cell carcinoma in targeted therapy era - a multi-institutional retrospective study. International journal of clinical oncology 27(3): 563-573	- Mixed population of SACT pre/post non-pharmacological regimens
Katsanos, K, Mailli, L, Krokidis, M et al. (2014) Systematic review and meta-analysis of thermal ablation versus surgical nephrectomy for small renal tumours. Cardiovascular and interventional radiology 37(2): 427-37	- More recent systematic review included that covers the same topic
Katsimperis, Stamatios, Tzelves, Lazaros, Bellos, Themistoklis et al. (2022) Cytoreductive nephrectomy for synchronous metastatic renal cell carcinoma. Is there enough evidence?. Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 94(4): 476-485	- Systematic review used as source of primary studies

Study	Reason
Kawase, Kota, Enomoto, Torai, Kawase, Makoto et al. (2022) The Impact of Postoperative Renal Function Recovery after Laparoscopic and Robot-Assisted Partial Nephrectomy in Patients with Renal Cell Carcinoma. Medicina (Kaunas, Lithuania) 58(4)	- Exclude - For RQC Proportion of patients stage T3 < 90%
Khalifeh, Ali, Autorino, Riccardo, Hillyer, Shahab P et al. (2013) Comparative outcomes and assessment of trifecta in 500 robotic and laparoscopic partial nephrectomy cases: a single surgeon experience. The Journal of urology 189(4): 1236-42	- Exclude - For RQC Proportion of patients stage T3 < 90%
Khalil, M.I., Ubeda, J., Soehner, T. et al. (2019) Contemporary Perioperative Morbidity and Mortality Rates of Minimally Invasive vs Open Partial Nephrectomy in Obese Patients with Kidney Cancer. Journal of Endourology 33(11): 920-927	- There is no information on cT or pT stage
Khan, M.M.A., Patel, R.A., Jain, N. et al. (2019) Prospective analysis of laparoscopic versus open radical nephrectomy for renal tumours more than 7 cm. Journal of Minimal Access Surgery 15(1): 14-18	- Non-OECD country - There is no information on cT or pT stage
Kim, Jeong Ho, Park, Yong Hyun, Kim, Yong June et al. (2015) Perioperative and long-term renal functional outcomes of robotic versus laparoscopic partial nephrectomy: a multicenter matched-pair comparison. World journal of urology 33(10): 1579-84	- There is no information on cT or pT stage
Kim, Jung Kwon, Lee, Hakmin, Oh, Jong Jin et al. (2019) Comparison of robotic and open partial nephrectomy for highly complex renal tumors (RENAL nephrometry score >=10). PloS one 14(1): e0210413	- Exclude - For RQC Proportion of patients stage T3 < 90%
Kim, Na Young, Lee, Hye Sun, Park, Jin Ha et al. (2022) Influence of age on gender-related differences in acute kidney injury after minimally invasive radical or partial nephrectomy. Surgical endoscopy 36(5): 2962-2972	- Study does not contain a relevant outcome

Study	Reason
Kim, Simon P, Thompson, R Houston, Boorjian, Stephen A et al. (2012) Comparative effectiveness for survival and renal function of partial and radical nephrectomy for localized renal tumors: a systematic review and meta-analysis. The Journal of urology 188(1): 51-7	- Systematic review used as source of primary studies
Kim, Sung Han, Jeong, Kyung-Chae, Joung, Jae Young et al. (2018) Prognostic significance of nephrectomy in metastatic renal cell carcinoma treated with systemic cytokine or targeted therapy: A 16-year retrospective analysis. Scientific reports 8(1): 2974	- Study does not contain a relevant intervention *Mixed population, receiving radical nephrectomy and CN*
Kim, Sung Han, Lee, Eun-Sik, Kim, Hyeon Hoe et al. (2015) A propensity-matched comparison of perioperative complications and of chronic kidney disease between robot-assisted laparoscopic partial nephrectomy and radiofrequency ablative therapy. Asian journal of surgery 38(3): 126-33	- Primary study covered fully by an included systematic review
Kim, Sung Han, Park, Boram, Hwang, Eu Chang et al. (2021) A Retrospective, Multicenter, Long-Term Follow-Up Analysis of the Prognostic Characteristics of Recurring Non-Metastatic Renal Cell Carcinoma After Partial or Radical Nephrectomy. Frontiers in oncology 11: 653002	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Kizilay, Fuat, Turna, Burak, Apaydin, Erdal et al. (2019) Comparison of long-term outcomes of laparoscopic and robot-assisted laparoscopic partial nephrectomy. The Kaohsiung journal of medical sciences 35(4): 238-243	- Comparator in study does not match that specified in protocol
Klatte, Tobias, Berni, Alessandro, Serni, Sergio et al. (2021) Intermediate- and long-term oncological outcomes of active surveillance for localized renal masses: a systematic review and quantitative analysis. BJU international 128(2): 131-143	- More recent systematic review included that covers the same topic *Single arm studies*

Study	Reason
Klatte, Tobias, Fife, Kate, Welsh, Sarah J et al. (2018) Prognostic effect of cytoreductive nephrectomy in synchronous metastatic renal cell carcinoma: a comparative study using inverse probability of treatment weighting. World journal of urology 36(3): 417-425	- Mixed population of SACT pre/post non-pharmacological regimens
Klatte, Tobias, Grubmuller, Bernhard, Waldert, Matthias et al. (2011) Laparoscopic cryoablation versus partial nephrectomy for the treatment of small renal masses: systematic review and cumulative analysis of observational studies. European urology 60(3): 435-43	- Review article but not a systematic review
Klatte, Tobias; Shariat, Shahrokh F; Remzi, Mesut (2014) Systematic review and meta-analysis of perioperative and oncologic outcomes of laparoscopic cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal tumors. The Journal of urology 191(5): 1209-17	- More recent systematic review included that covers the same topic
Kobayashi, Satoshi, Mutaguchi, Jun, Kashiwagi, Eiji et al. (2021) Clinical advantages of robot-assisted partial nephrectomy versus laparoscopic partial nephrectomy in terms of global and split renal functions: A propensity score-matched comparative analysis. International journal of urology : official journal of the Japanese Urological Association 28(6): 630-636	- Exclude - For RQC Proportion of patients stage T3 < 90%
Kokorovic, Andrea and Rendon, Ricardo A (2019) Cytoreductive nephrectomy in metastatic kidney cancer: what do we do now?. Current opinion in supportive and palliative care 13(3): 255-261	- Review article but not a systematic review
Komninos, Christos, Shin, Tae Young, Tuliao, Patrick et al. (2014) R-LESS partial nephrectomy trifecta outcome is inferior to multiport robotic partial nephrectomy: comparative analysis. European urology 66(3): 512-7	- There is no information on cT or pT stage
Koo, Kyo Chul, Kim, Jong Chan, Cho, Kang Su et al. (2016) Oncological outcomes after	- Not a relevant study design *Consecutive case series*

Study	Reason
partial vs radical nephrectomy in renal cell carcinomas of <=7 cm with presumed renal sinus fat invasion on preoperative imaging. BJU international 117(1): 87-93	
Kopp, Ryan P, Mehrazin, Reza, Palazzi, Kerrin L et al. (2014) Survival outcomes after radical and partial nephrectomy for clinical T2 renal tumours categorised by R.E.N.A.L. nephrometry score. BJU international 114(5): 708-18	- Secondary publication of an included study that does not provide any additional relevant information
Kowalewski, Karl-Friedrich, Muller, Dennis, Kirchner, Marietta et al. (2021) Robotic-Assisted Versus Conventional Open Partial Nephrectomy (Robocop): A Propensity Score-Matched Analysis of 249 Patients. Urologia internationalis 105(56): 490-498	- There is no information on cT or pT stage
Krabbe, Laura-Maria, Haddad, Ahmed Q, Westerman, Mary E et al. (2014) Surgical management of metastatic renal cell carcinoma in the era of targeted therapies. World journal of urology 32(3): 615-22	- Review article but not a systematic review
Kroeze, Stephanie G C, Fritz, Corinna, Schaule, Jana et al. (2021) Stereotactic radiotherapy combined with immunotherapy or targeted therapy for metastatic renal cell carcinoma. BJU international 127(6): 703-711	- Mixed population of SACT pre/post non-pharmacological regimens *76% of the participants received SACT before SRT, no subgroup results reported*
Kunath, Frank, Schmidt, Stefanie, Krabbe, Laura-Maria et al. (2017) Partial nephrectomy versus radical nephrectomy for clinical localised renal masses. The Cochrane database of systematic reviews 5: cd012045	- Systematic review used as source of primary studies
Kunkle, David A; Egleston, Brian L; Uzzo, Robert G (2008) Excise, ablate or observe: the small renal mass dilemma--a meta-analysis and review. The Journal of urology 179(4): 1227-4	- More recent systematic review included that covers the same topic
Kwak, Cheol, Park, Yong Hyun, Jeong, Chang Wook et al. (2007) No role of adjuvant systemic therapy after complete	- Comparator in study does not match that specified in protocol

Study	Reason
metastasectomy in metastatic renal cell carcinoma?. Urologic oncology 25(4): 310-6	*All included participants had undergone complete metastasectomy. Compares SACT vs. No SACT population.*
Kwak, Cheol, Park, Yong Hyun, Jeong, Chang Wook et al. (2007) Metastasectomy without systemic therapy in metastatic renal cell carcinoma: comparison with conservative treatment. Urologia internationalis 79(2): 145-51	- Study does not contain a relevant intervention *None of the participants received SACT at anytime point. Study compares metastasectomy vs. no metastasectomy after nephrectomy*
La Vecchia, Maria, Federico, Manuela, Aiello, Dario et al. (2024) The Role of Stereotactic Body Radiotherapy (SBRT) in Oligoprogressive Renal Cell Carcinoma (RCC) Treated with ICIs-TKIs: A Retrospective Multicentric Study. Journal of personalized medicine 14(10)	- Comparator in study does not match that specified in protocol *There isn't a defined comparator group. Outcomes were reported for some patients before SBRT but these outcomes did not meet the protocol criteria and these patients did go on to have SBRT also.*
Laganosky, D., Filson, C.P., Patil, D. et al. (2020) Survival benefit with extended lymphadenectomy for advanced renal malignancy: A population-based analysis. Asian Journal of Urology 7(1): 29-36	- Comparator in study does not match that specified in protocol
Lai, G.-S., Li, J.-R., Wang, S.-S. et al. (2020) Survival analysis of pathological T3a upstaging in clinical T1 renal cell carcinoma. In Vivo 34(2): 799-805	- Non-OECD country
Lai, Gu-Shun, Li, Jian-Ri, Wang, Shian-Shiang et al. (2024) Outcome benefits of upfront cytoreductive nephrectomy for patients with metastatic renal cell carcinoma: An analysis of the TriNetX database. PloS one 19(3): e0299102	- Non-OECD country
Lai, T.C.T.; Ma, W.K.; Yiu, M.K. (2016) Partial nephrectomy for t1 renal cancer can achieve an equivalent oncological outcome to radical nephrectomy with better renal preservation: The way to go. Hong Kong Medical Journal 22(1): 39-45	- Primary study covered fully by an included systematic review
Lam, Jing Kai Jackie; Tan, Sher Yin; Chong, Kian Tai (2020) Is partial nephrectomy worth performing compared to radical nephrectomy for small, localised	- Data not reported in an extractable format *reports CKD at 5 years but it was published within the search dates of Ochoa-Arvizo - do we include Lam?To exclude - Looking at this paper they have not reported the N at*

Study	Reason
renal cortical tumours in geriatric patients?. Singapore medical journal 61(4): 190-193	*5yrs which is likely why it wasn't included in Ochoa*
Larcher, A, Sun, M, Dell'Oglio, P et al. (2017) Mortality, morbidity and healthcare expenditures after local tumour ablation or partial nephrectomy for T1A kidney cancer. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 43(4): 815-822	- Data not reported in an extractable format *Insufficient data reported to assess study methodology*
Larcher, Alessandro, Meskawi, Malek, Valdivieso, Roger et al. (2016) Comparison of renal function detriments after local tumor ablation or partial nephrectomy for renal cell carcinoma. World journal of urology 34(3): 383-9	- Data not reported in an extractable format *Insufficient information reported to assess study*
Laru, Lauri, Ronkainen, Hanna, Ohtonen, Pasi et al. (2021) Nephrectomy improves the survival of metastatic renal cell cancer patients with moderate to good performance status-results from a Finnish nation-wide population-based study from 2005 to 2010. World journal of surgical oncology 19(1): 190	- Comparator in study does not match that specified in protocol *Study compares CN vs. metastasectomy. Does not report about the SACT status*
Lasorsa, Francesco, Bignante, Gabriele, Orsini, Angelo et al. (2024) Partial nephrectomy in elderly patients: a systematic review and analysis of comparative outcomes. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 50(10): 108578	- Systematic review used as source of primary studies
Le Guevelou, Jennifer, Sargos, Paul, Siva, Shankar et al. (2023) The Emerging Role of Extracranial Stereotactic Ablative Radiotherapy for Metastatic Renal Cell Carcinoma: A Systematic Review. European urology focus 9(1): 114-124	- Systematic review used as source of primary studies
Lee, H., Lee, M., Lee, S.E. et al. (2018) Outcomes of pathologic stage T3a renal cell carcinoma up-staged from small renal	- Study does not contain a relevant intervention

Study	Reason
tumor: Emphasis on partial nephrectomy. BMC Cancer 18(1): 427	
Lee, Nora G; Zampini, Anna; Tuerk, Ingolf (2012) Single surgeon's experience with laparoscopic versus robotic partial nephrectomy: perioperative outcomes/complications and influence of tumor characteristics on choice of therapy. The Canadian journal of urology 19(5): 6465-70	- Exclude RQC- Study included only patients T1-T2
Lee, Sangchul, Oh, Jongjin, Hong, Seong Kyu et al. (2011) Open versus robot-assisted partial nephrectomy: effect on clinical outcome. Journal of endourology 25(7): 1181-5	- There is no information on cT or pT stage
Lee, Sangchul; Ryu, Hoyoung; Lee, Jeong Woo (2021) Open Partial Nephrectomy vs. Robot-assisted Partial Nephrectomy for a Renal Tumor Larger than 4 cm: a Propensity Score Matching Analysis. Journal of Korean medical science 36(20): e135	- Exclude - For RQC Proportion of patients stage T3 < 90%
Lenis, A.T., Salmasi, A.H., Donin, N.M. et al. (2018) Trends in usage of cytoreductive partial nephrectomy and effect on overall survival in patients with metastatic renal cell carcinoma. Urologic Oncology: Seminars and Original Investigations 36(2): 78e21-78e28	- Comparator in study does not match that specified in protocol *Compares partial CN Vs. radical CN*
Lesnyak, O., Stroy, O., Banyra, O. et al. (2020) Assessment of the effectiveness of radiofrequency ablation as a technique for destroying small renal tumors in patients older than 70. Central European Journal of Urology 73(4): 1-7	- Non-OECD country
Li, G, Luo, Q, Lang, Z et al. (2018) Histopathologic analysis of stage pT1b kidney neoplasms for optimal surgical margins of nephron-sparing surgery. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico 20(9): 1196-1201	- Study does not contain a relevant outcome

Study	Reason
Li, Jingdong, Zhang, Yanping, Teng, Zhihai et al. (2019) Partial nephrectomy versus radical nephrectomy for cT2 or greater renal tumors: a systematic review and meta-analysis. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 71(5): 435-444	- Systematic review used as source of primary studies
Li, Jinze, Peng, Lei, Cao, Dehong et al. (2020) Comparison of Perioperative Outcomes of Robot-Assisted vs. Laparoscopic Radical Nephrectomy: A Systematic Review and Meta-Analysis. Frontiers in oncology 10: 551052	- Exclude - For RQC Proportion of patients stage T3 < 90%
Li, Kun-Peng, Chen, Si-Yu, Wan, Shun et al. (2024) Percutaneous ablation versus robotic-assisted partial nephrectomy for cT1 renal cell carcinoma: an evidence-based analysis of comparative outcomes. Journal of robotic surgery 18(1): 301	- Systematic review used as source of primary studies
Li, Kun-Peng, Chen, Si-Yu, Wang, Chen-Yang et al. (2023) The impact of cytoreductive nephrectomy on survival outcomes in patients with metastatic renal cell carcinoma receiving immunotherapy: An evidence-based analysis of comparative outcomes. Frontiers in immunology 14: 1132466	- Exclude - wrong population
Li, Kun-Peng, Chen, Si-Yu, Wang, Chen-Yang et al. (2023) Comparison between minimally invasive partial nephrectomy and open partial nephrectomy for complex renal tumors: a systematic review and meta-analysis. International journal of surgery (London, England) 109(6): 1769-1782	- Exclude - For RQC Proportion of patients stage T3 < 90%
Li, Kun-Peng, Wan, Shun, Chen, Si-Yu et al. (2024) Perioperative, functional and oncologic outcomes of percutaneous ablation versus minimally invasive partial nephrectomy for clinical T1 renal tumors: outcomes from a pooled analysis. Journal of robotic surgery 18(1): 306	- Systematic review used as source of primary studies
Li, Kun-Peng, Wan, Shun, Wang, Chen-Yang et al. (2023) Perioperative, functional,	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
and oncologic outcomes of robot-assisted versus open partial nephrectomy for complex renal tumors (RENAL score >= 7): an evidence-based analysis. Journal of robotic surgery 17(4): 1247-1258	
Li, Pin, Peng, Cheng, Gu, Liangyou et al. (2019) Radical Nephrectomy with or without Lymph Node Dissection for pT3 Renal Cell Carcinoma: A Propensity Score-based Analysis. Journal of Cancer 10(10): 2369-2375	- Non-OECD country - Comparator in study does not match that specified in protocol
Li, Wentao, Cheng, Yanlei, Cheng, Yi et al. (2014) Clinical efficacy of radical nephrectomy versus nephron-sparing surgery on localized renal cell carcinoma. European journal of medical research 19: 58	- Systematic review used as source of primary studies
Liao, Xinyang, Qiu, Shi, Wang, Wanyu et al. (2019) Partial nephrectomy vs cryoablation for T1a renal cell carcinoma: A comparison of survival benefit stratified by tumour size. Cancer epidemiology 59: 221-226	- Non-OECD country
Liek, Elisabeth, Elsebach, Klaus, Gobel, Hubert et al. (2018) The Overall Survival Benefit for Patients with T1 Renal Cell Carcinoma after Nephron-Sparing Surgery Depends on Gender and Age. Urologia internationalis 100(3): 309-316	- Data not reported in an extractable format *Overall survival reported as Kaplan-Meier and P values*
Lin, J., Song, A.J., Hoffman-Censits, J. et al. (2020) A Pilot Study of Radiation Therapy in Combination with Pembrolizumab in Patients with Metastatic Renal Cell Cancer. American Journal of Clinical Oncology: Cancer Clinical Trials 43(2): 82-86	- Not a relevant study design *Reports a part of RCT. Reported subgroup irrelevant to the protocol*
Lin, Pengxiu, Wu, Minhong, Gu, Hongyong et al. (2021) Comparison of outcomes between laparoscopic and robot-assisted partial nephrectomy for complex renal tumors: RENAL score >=7 or maximum tumor size >4 cm. Minerva urology and nephrology 73(2): 154-164	- Exclude RQC- Study included only patients T1-T2

Study	Reason
Lin, Wenhao, Yang, Zhenggang, Yan, Ling et al. (2023) Comparison of partial nephrectomy and radical nephrectomy for cystic renal cell carcinoma: a SEER-based and retrospective study. Scientific reports 13(1): 8052	- SEER database overlap
Liu, Changfu, Cao, Fei, Xing, Wenge et al. (2019) Efficacy of cryoablation combined with sorafenib for the treatment of advanced renal cell carcinoma. International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group 36(1): 220-228	- Study does not contain a relevant intervention *SACT given along with cryotherapy*
Liu, Gang, Ma, Yulei, Wang, Shouhua et al. (2017) Laparoscopic Versus Open Radical Nephrectomy for Renal Cell Carcinoma: a Systematic Review and Meta-Analysis. Translational oncology 10(4): 501-510	- Exclude - For RQC Proportion of patients stage T3 < 90%
Liu, H.; Gao, C.; Yu, H. (2016) Safety and effectiveness of percutaneous radiofrequency ablation in early stage renal cell carcinoma. Oncology Letters 12(6): 4618-4622	- Non-OECD country
Liu, Hui, Kong, Qing-Fang, Li, Jian et al. (2021) A meta-analysis for comparison of partial nephrectomy vs. radical nephrectomy in patients with pT3a renal cell carcinoma. Translational andrology and urology 10(3): 1170-1178	- Comparator in study does not match that specified in protocol *PN vs RN for T3 tumour*
Liu, Ning, Huang, Daoguang, Cheng, Xiangming et al. (2017) Percutaneous radiofrequency ablation for renal cell carcinoma vs. partial nephrectomy: Comparison of long-term oncologic outcomes in both clear cell and non-clear cell of the most common subtype. Urologic oncology 35(8): 530e1-530e6	- Non-OECD country
Liu, Wing K, Lam, J M, Butters, T et al. (2020) Cytoreductive nephrectomy in metastatic renal cell carcinoma: outcome of patients treated with a multidisciplinary,	- Mixed population of SACT pre/post non-pharmacological regimens

Study	Reason
algorithm-driven approach. World journal of urology 38(12): 3199-3205	
Liu, X-H, Song, J, Ma, W-M et al. (2024) Comparison of perioperative outcomes between robot-assisted partial nephrectomy and laparoscopic partial nephrectomy in obese patients. European review for medical and pharmacological sciences 28(10): 3583-3589	- Exclude - RQC Patients with localised tumour
Liu, Y., Zhang, Z., Han, H. et al. (2021) Survival After Combining Stereotactic Body Radiation Therapy and Tyrosine Kinase Inhibitors in Patients With Metastatic Renal Cell Carcinoma. Frontiers in Oncology 11: 607595	- Study does not contain a relevant outcome
Liu, Yang, Long, Wen, Zhang, Zhiling et al. (2021) Metastasis-directed stereotactic body radiotherapy for oligometastatic renal cell carcinoma: extent of tumor burden eradicated by radiotherapy. World journal of urology 39(11): 4183-4190	- Mixed population of SACT pre/post non-pharmacological regimens - 6b SABR exclude
Liu, Yang, Zhang, Zhiling, Liu, Ruiqi et al. (2021) Stereotactic body radiotherapy in combination with non-frontline PD-1 inhibitors and targeted agents in metastatic renal cell carcinoma. Radiation oncology (London, England) 16(1): 211	- 6b SABR exclude *doesn't separate out SABR given before vs after SACT*
Liu, Ying, Wang, Li, Bao, Er-Hao et al. (2024) Perioperative, functional, and oncological outcomes after cryoablation or partial nephrectomy for small renal masses in solitary kidneys: a systematic review and meta-analysis. BMC urology 24(1): 19	- Systematic review used as source of primary studies
Liu, Z., Wang, P., Xia, D. et al. (2013) Comparison between laparoscopic and open partial nephrectomy: Surgical, oncologic, and functional outcomes. Kaohsiung Journal of Medical Sciences 29(11): 624-628	- Non-OECD country - Exclude RQC- Study included only patients T1-T2
Liu, Zhenhua, Yang, Zhenyu, Li, Jibin et al. (2023) Partial versus radical nephrectomy for the treatment of pT3aN0M0 renal cell	- Comparator in study does not match that specified in protocol

Study	Reason
carcinoma: A propensity score analysis. Asian journal of surgery 46(9): 3607-3613	*For RQC - comparison RN vs PN in T3 tumours which is not applicable for this question*
Ljungberg, Borje, Sundqvist, Pernilla, Lindblad, Per et al. (2020) Survival advantage of upfront cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma compared with systemic and palliative treatments in a real-world setting. Scandinavian journal of urology 54(6): 487-492	- Comparator in study does not match that specified in protocol *Compares SACT alone with upfront CN.*
Long, Jean-Alexandre, Yakoubi, Rachid, Lee, Byron et al. (2012) Robotic versus laparoscopic partial nephrectomy for complex tumors: comparison of perioperative outcomes. European urology 61(6): 1257-62	- Exclude - RQC Patients with localised tumour
Loo Gan, Chun, Huang, Jiaming, Pan, Elizabeth et al. (2023) Real-world Practice Patterns and Safety of Concurrent Radiotherapy and Cabozantinib in Metastatic Renal Cell Carcinoma: Results from the International Metastatic Renal Cell Carcinoma Database Consortium. European urology oncology 6(2): 204-211	- 6b SABR exclude - Mixed population of SACT pre/post non-pharmacological regimens
Lounova, Veronika, Student, Vladimir Jr, Purova, Dana et al. (2024) Frequency of benign tumors after partial nephrectomy and the association between malignant tumor findings and preoperative clinical parameters. BMC urology 24(1): 175	- Study did not compare the interventions of interest *Reporting results for benign and malignant tumours and not for the two different surgical techniques for nephrectomy*
Love, Harrison, Yong, Courtney, Slaven, James E et al. (2024) Outcomes of open versus robotic partial nephrectomy: a 20-year single institution experience. Journal of robotic surgery 18(1): 315	- Exclude - For RQC Proportion of patients stage T3 < 90%
Lucas, Steven M, Mellon, Matthew J, Erntsberger, Luke et al. (2012) A comparison of robotic, laparoscopic and open partial nephrectomy. JSLS : Journal of the Society of Laparoendoscopic Surgeons 16(4): 581-7	- Comparator in study does not match that specified in protocol

Study	Reason
Luciani, Lorenzo G, Chiodini, Stefano, Mattevi, Daniele et al. (2017) Robotic-assisted partial nephrectomy provides better operative outcomes as compared to the laparoscopic and open approaches: results from a prospective cohort study. Journal of robotic surgery 11(3): 333-339	- Exclude - For RQC Proportion of patients stage T3 < 90%
Luo, X., Yi, M., Hu, Q. et al. (2019) Is cytoreductive nephrectomy necessary for metastatic renal cell carcinoma: A systematic review and meta-analysis. International Journal of Clinical and Experimental Medicine 12(6): 7029-7037	- Exclude - Result reported in the most updated MA
Luo, X, Li, J-X, Liu, Y-T et al. (2019) Influence of lymph node dissection in patients undergoing radical nephrectomy for non-metastatic renal cell carcinoma: a systematic review and meta-analysis. European review for medical and pharmacological sciences 23(14): 6079-6090	- Exclude - For RQC Proportion of patients stage T3 < 90%
Luo, You, Chen, San-San, Bai, Liang et al. (2017) Nephron Sparing Surgery Has Better Oncologic Outcomes Than Extirpative Nephrectomy in T1a but Not in T1b or T2 Stage Renal Cell Carcinoma. Medical science monitor : international medical journal of experimental and clinical research 23: 3480-3488	- SEER database overlap
Lv, ZongYing, Chen, GuiYuan, Chen, XiaoBin et al. (2023) Open versus robot-assisted partial nephrectomy for highly complex renal masses: a meta-analysis of perioperitive and functional outcomes. Journal of robotic surgery 17(5): 1955-1965	- Exclude - For RQC Proportion of patients stage T3 < 90%
Ma, Ming-Wei, Li, Hong-Zhen, Gao, Xian-Shu et al. (2022) Outcomes of High-Dose Stereotactic Ablative Radiotherapy to All/Multiple Sites for Oligometastatic Renal Cell Cancer Patients. Current oncology (Toronto, Ont.) 29(10): 7832-7841	- Mixed population of SACT pre/post non-pharmacological regimens - 6b SABR exclude
MacLennan, Steven, Imamura, Mari, Lapitan, Marie C et al. (2012) Systematic	- Systematic review used as source of primary studies

Study	Reason
review of oncological outcomes following surgical management of localised renal cancer. European urology 61(5): 972-93	
MacLennan, Steven, Imamura, Mari, Lapitan, Marie C et al. (2012) Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. European urology 62(6): 1097-117	- Systematic review used as source of primary studies
Maisel, Franziska, Smolle, Maria A, Mollnar, Stefanie et al. (2022) Benefit of Metastasectomy in Renal Cell Carcinoma: A Propensity Score Analysis. Clinical genitourinary cancer 20(4): 344-353	- Comparator in study does not match that specified in protocol - Study does not contain a relevant intervention
Malaeb, B.S., Sherwood, J.B., Taylor, G.D. et al. (2005) Hand-assisted laparoscopic nephrectomy for renal masses >9.5 cm: Series comparison with open radical nephrectomy. Urologic Oncology: Seminars and Original Investigations 23(5): 323-327	- Exclude - For RQC Proportion of patients stage T3 < 90%
Manikandan, R; Srinivasan, V; Rane, A (2004) Which is the real gold standard for small-volume renal tumors? Radical nephrectomy versus nephron-sparing surgery. Journal of endourology 18(1): 39-44	- More recent systematic review included that covers the same topic
Marchioni, M., Bandini, M., Pompe, R.S. et al. (2018) The impact of lymph node dissection and positive lymph nodes on cancer-specific mortality in contemporary pT2-3 non-metastatic renal cell carcinoma treated with radical nephrectomy. BJU International 121(3): 383-392	- Comparator in study does not match that specified in protocol *LND vs no LND*
Marchioni, Michele, Cheaib, Joseph G, Takagi, Toshio et al. (2021) Active surveillance for small renal masses in elderly patients does not increase overall mortality rates compared to primary intervention: a propensity score weighted analysis. Minerva urology and nephrology 73(6): 781-788	- Comparator in study does not match that specified in protocol *Ablation and partial nephrectomy groups combined in results vs active surveillance*

Study	Reason
Marchioni, Michele, Preisser, Felix, Bandini, Marco et al. (2019) Comparison of Partial Versus Radical Nephrectomy Effect on Other-cause Mortality, Cancer-specific Mortality, and 30-day Mortality in Patients Older Than 75 Years. European urology focus 5(3): 467-473	- Study does not contain a relevant outcome
Margulis, Vitaly, Tamboli, Pheroze, Jacobsohn, Kenneth M et al. (2007) Oncological efficacy and safety of nephron-sparing surgery for selected patients with locally advanced renal cell carcinoma. BJU international 100(6): 1235-9	- Comparator in study does not match that specified in protocol *Compares Rn vs PN in locally advanced RCC - not applicable for RQC*
Maric, P., Jovanovic, M., Milovic, N. et al. (2017) Complications of radical and partial nephrectomy for renal cell carcinoma up to 7 cm. Vojnosanitetski Pregled 74(7): 639-643	- Data not reported in an extractable format *Severe complications (Clavien-Dindo ≥III) were only reported in a graphDuration of hospital stay was reported as median and range*
Mason, Ross J, Atwell, Thomas D, Lohse, Christine et al. (2017) Renal functional outcomes in patients undergoing percutaneous cryoablation or partial nephrectomy for a solitary renal mass. BJU international 120(4): 544-549	- Study does not contain a relevant outcome
Massari, Francesco, Di Nunno, Vincenzo, Gatto, Lidia et al. (2018) Should CARMENA Really Change our Attitude Towards Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma? A Systematic Review and Meta-Analysis Evaluating Cytoreductive Nephrectomy in the Era of Targeted Therapy. Targeted oncology 13(6): 705-714	- Mixed population of SACT pre/post non-pharmacological regimens
Masson-Lecomte, Alexandra, Bensalah, Karim, Seringe, Elise et al. (2013) A prospective comparison of surgical and pathological outcomes obtained after robot-assisted or pure laparoscopic partial nephrectomy in moderate to complex renal tumours: results from a French multicentre collaborative study. BJU international 111(2): 256-63	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
Masson-Lecomte, Alexandra, Yates, David R, Hupertan, Vincent et al. (2013) A prospective comparison of the pathologic and surgical outcomes obtained after elective treatment of renal cell carcinoma by open or robot-assisted partial nephrectomy. Urologic oncology 31(6): 924-9	- There is no information on cT or pT stage
Mastroianni, R., Chiacchio, G., Perpepaj, L. et al. (2024) Comparison of Perioperative, Functional, and Oncologic Outcomes of Open vs. Robot-Assisted Off-Clamp Partial Nephrectomy: A Propensity Scored Match Analysis. Sensors (Basel, Switzerland) 24(9)	- Exclude RQC- Study included only patients T1-T2
Mathieu, Romain, Pignot, Geraldine, Ingles, Alexandre et al. (2015) Nephrectomy improves overall survival in patients with metastatic renal cell carcinoma in cases of favorable MSKCC or ECOG prognostic features. Urologic oncology 33(8): 339e9-15	- Mixed population of SACT pre/post non-pharmacological regimens
May, D.N., Hill, H., Matrana, M.R. et al. (2021) A Contemporary Analysis of the 30-day Morbidity and Mortality Associated With Cytoreductive Nephrectomy. Urology 147: 186-191	- Comparator in study does not match that specified in protocol
Mearini, Luigi, Nunzi, Elisabetta, Vianello, Alberto et al. (2016) Margin and complication rates in clampless partial nephrectomy: a comparison of open, laparoscopic and robotic surgeries. Journal of robotic surgery 10(2): 135-44	- There is no information on cT or pT stage
Mehra, Ketan, Manikandan, Ramanitharan, Dorairajan, Lalgudi Narayanan et al. (2019) Trifecta Outcomes in Open, Laparoscopy or Robotic Partial Nephrectomy: Does the Surgical Approach Matter?. Journal of kidney cancer and VHL 6(1): 8-12	- Non-OECD country - There is no information on cT or pT stage
Mennitto, A, Verzoni, E, Cognetti, F et al. (2021) Radical metastasectomy followed by sorafenib versus observation in patients withclear cell renal cell carcinoma: extended follow -up of efficacy results from the randomized phase II RESORT trial. Expert	- Comparator in study does not match that specified in protocol *Compares patients with metastatic rcc treated with sorafenib vs. observation-alone after the radical surgery of metastases*

Study	Reason
review of clinical pharmacology 14(2): 261-268	
Mershon, J Patrick; Tuong, Mei N; Schenkman, Noah S (2020) Thermal ablation of the small renal mass: a critical analysis of current literature. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 72(2): 123-134	- More recent systematic review included that covers the same topic
Metcalf, Meredith R, Cheaib, Joseph G, Biles, Michael J et al. (2021) Outcomes of Active Surveillance for Young Patients with Small Renal Masses: Prospective Data from the DISSRM Registry. The Journal of urology 205(5): 1286-1293	- Comparator in study does not match that specified in protocol *Surgery and cryoablation combined*
Metcalf, Meredith R, Pena, Vanessa N, Cheaib, Joseph G et al. (2022) Disparities in the Treatment and Survival of Metastatic Renal Cell Carcinoma. Urology 165: 89-97	- Mixed population of SACT pre/post non-pharmacological regimens
Michalak, M., Kopczynska, A., Antczak, A. et al. (2024) Outcomes of treatment, laboratory results, adverse effects, and tolerability of cancer treatment in patients with metastatic renal cell carcinoma treated with ipilimumab and nivolumab after cytoreductive nephrectomy. Nowotwory 74(6): 344	- Data not reported in an extractable format *Data for PFS was reported as mean and range only*
Michalak, M., Tomczak, P., Milecki, T. et al. (2024) Outcomes of treatment, laboratory results, adverse effects, and tolerability of cancer treatment in patients with metastatic renal-cell carcinoma treated with sunitinib after cytoreductive nephrectomy. Nowotwory 74(2): 105	- Exclude - assessed outcome is out of scope
Miller, Brady L, Mankowski Gettle, Lori, Van Roo, Jason R et al. (2018) Comparative Analysis of Surgery, Thermal Ablation, and Active Surveillance for Renal Oncocytic Neoplasms. Urology 112: 92-97	- Does not contain a population of people with kidney cancer
Miller, Jacob A, Balagamwala, Ehsan H, Angelov, Lilyana et al. (2016) Spine stereotactic radiosurgery with concurrent tyrosine kinase inhibitors for metastatic	- Conference abstract

Study	Reason
renal cell carcinoma. Journal of neurosurgery. Spine 25(6): 766-774	
Minervini, Andrea, Vittori, Gianni, Antonelli, Alessandro et al. (2014) Open versus robotic-assisted partial nephrectomy: a multicenter comparison study of perioperative results and complications. World journal of urology 32(1): 287-93	- Exclude - For RQC Proportion of patients stage T3 < 90%
Mir, Maria Carmen, Derweesh, Ithaar, Porpiglia, Francesco et al. (2017) Partial Nephrectomy Versus Radical Nephrectomy for Clinical T1b and T2 Renal Tumors: A Systematic Review and Meta-analysis of Comparative Studies. European urology 71(4): 606-617	- Systematic review used as source of primary studies
Mitchell, Christopher R, Atwell, Thomas D, Weisbrod, Adam J et al. (2011) Renal function outcomes in patients treated with partial nephrectomy versus percutaneous ablation for renal tumors in a solitary kidney. The Journal of urology 186(5): 1786-90	- Study does not contain a relevant outcome *eGFR during postop period only*
Mittal, Abhenil, Al-Ezzi, Esmail, Li, Xuan et al. (2023) The role of cytoreductive nephrectomy and systemic therapy in the management of tumour thrombus in patients with metastatic renal cell carcinoma. British journal of cancer 128(10): 1888-1896	- Mixed population of SACT pre/post non-pharmacological regimens
Miyake, Hideaki, Hinata, Nobuyuki, Imai, Satoshi et al. (2015) Partial nephrectomy for hilar tumors: comparison of conventional open and robot-assisted approaches. International journal of clinical oncology 20(4): 808-13	- There is no information on cT or pT stage
Mo, Cheng-Qiang, Yu, Zhou, Tan, Wu-Lin et al. (2014) Comparison between laparoscopic partial nephrectomy and laparoscopic ablation therapy: a meta-analysis. Minimally invasive therapy & allied technologies : MITAT : official journal of the Society for Minimally Invasive Therapy 23(6): 317-25	- More recent systematic review included that covers the same topic

Study	Reason
Monda, S.; Lara, P.N.; Gulati, S. (2024) Post-Metastasectomy Adjuvant Therapy in Patients with Renal Cell Carcinoma: A Systematic Review. Kidney Cancer 8(1): 115	- Comparator in study does not match that specified in protocol
Mori, Keiichiro, Quhal, Fahad, Yanagisawa, Takafumi et al. (2022) The effect of immune checkpoint inhibitor combination therapies in metastatic renal cell carcinoma patients with and without previous cytoreductive nephrectomy: A systematic review and meta-analysis. International immunopharmacology 108: 108720	- Mixed population of SACT pre/post non-pharmacological regimens
Morkos, John, Porosnicu Rodriguez, Kori A, Zhou, Alice et al. (2020) Percutaneous Cryoablation for Stage 1 Renal Cell Carcinoma: Outcomes from a 10-year Prospective Study and Comparison with Matched Cohorts from the National Cancer Database. Radiology 296(2): 452-459	- Secondary publication of an included study that does not provide any additional relevant information
Muhlbauer, Julia, de Gilde, Johannes, Mueller-Steinhardt, Michael et al. (2020) Perioperative Blood Transfusion Is a Predictor of Acute and Chronic Renal Function Deterioration after Partial and Radical Nephrectomy for Renal Cell Carcinoma. Urologia internationalis 104(910): 775-780	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Muhlbauer, Julia, Kowalewski, Karl-Friedrich, Walach, Margarete T et al. (2020) Partial nephrectomy preserves renal function without increasing the risk of complications compared with radical nephrectomy for renal cell carcinomas of stages pT2-3a. International journal of urology : official journal of the Japanese Urological Association 27(10): 906-913	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Nakada, S Y, Fadden, P, Jarrard, D F et al. (2001) Hand-assisted laparoscopic radical nephrectomy: comparison to open radical nephrectomy. Urology 58(4): 517-20	- Exclude - RQC Patients with localised tumour
Nandanan, N., Veccia, A., Antonelli, A. et al. (2020) Outcomes and predictors of benign	- Study does not contain a relevant outcome

Study	Reason
histology in patients undergoing robotic partial or radical nephrectomy for renal masses: A multicenter study. Central European Journal of Urology 73(1): 33-38	
Nason, Gregory J, Walsh, Leon G, Redmond, Ciaran E et al. (2015) Comparative effectiveness of adrenal sparing radical nephrectomy and non-adrenal sparing radical nephrectomy in clear cell renal cell carcinoma: Observational study of survival outcomes. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 9(910): e583-8	- Comparator in study does not match that specified in protocol
Nayak, J.G., Patel, P., Saarela, O. et al. (2016) Pathological Upstaging of Clinical T1 to Pathological T3a Renal Cell Carcinoma: A Multi-institutional Analysis of Short-term Outcomes. Urology 94: 154-160	- Primary study covered fully by an included systematic review
Nguyen, D.P., Vertosick, E.A., Corradi, R.B. et al. (2016) Histological subtype of renal cell carcinoma significantly affects survival in the era of partial nephrectomy. Urologic Oncology: Seminars and Original Investigations 34(6): e1-259	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Nian, Xinwen, Ye, Huamao, Zhang, Wei et al. (2022) Propensity-matched pair analysis of safety and efficacy between laparoscopic and open radical nephrectomy for the treatment of large renal masses (>10 cm): a retrospective cohort study. Translational andrology and urology 11(8): 1148-1156	- Exclude RQC- Study included only patients T1-T2
Nicaise, Edouard, Feldman, Adam S, Gusev, Andrew et al. (2024) A contemporary comparison of laparoscopic versus open partial nephrectomy for renal cell carcinoma. BMC urology 24(1): 58	- Exclude RQC- Study included only patients T1-T2
Nowak, Lukasz, Janczak, Dawid, Laszkiewicz, Jan et al. (2024) Clinical and Oncological Outcomes Following Percutaneous Cryoablation vs. Partial Nephrectomy for Clinical T1 Renal	- Systematic review used as source of primary studies

Study	Reason
Tumours: Systematic Review and Meta-Analysis. Cancers 16(6)	
Nunez Bragayrac, Luciano, Hoffmeyer, Jan, Abbotoy, Daniel et al. (2016) Minimally invasive cytoreductive nephrectomy: a multi-institutional experience. World journal of urology 34(12): 1651-1656	- Comparator in study does not match that specified in protocol *No information about SACT*
O'Malley, Rebecca L, Berger, Aaron D, Kanofsky, Jamie A et al. (2007) A matched-cohort comparison of laparoscopic cryoablation and laparoscopic partial nephrectomy for treating renal masses. BJU international 99(2): 395-8	- Study published before included SR/s for the outcome/s reported
Ocak, Birol, Sahin, Ahmet Bilgehan, Erturk, Ismail et al. (2024) Can Cytoreductive Nephrectomy Improve Outcomes of Nivolumab Treatment in Patients with Metastatic Clear-Cell Renal Carcinoma?. Current oncology (Toronto, Ont.) 31(9): 5195-5205	- Data not reported in an extractable format *Only median (95% CI) OS has been reported. Other data is time to treatment discontinuation for systemic treatments which is out of scope for this review.*
Oh, Jong Jin, Byun, Seoksoo, Hong, Sung Kyu et al. (2014) Comparison of robotic and open partial nephrectomy: Single-surgeon matched cohort study. Canadian Urological Association journal = Journal de l'Association des urologues du Canada 8(78): e471-5	- Exclude - For RQC Proportion of patients stage T3 < 90%
Ohno, Y., Nakashima, J., Ohori, M. et al. (2014) Clinical variables for predicting metastatic renal cell carcinoma patients who might not benefit from cytoreductive nephrectomy: Neutrophil-to-lymphocyte ratio and performance status. International Journal of Clinical Oncology 19(1): 139-145	- Mixed population of SACT pre/post non-pharmacological regimens *Unclear about the SACT treatment or any other treatment in no CN group*
Okita, Kazutaka, Hatakeyama, Shingo, Naito, Sei et al. (2021) External validation of the REMARCC model for the selection of cytoreductive nephrectomy in patients with primary metastatic renal cell carcinoma: A multicenter retrospective study. Urologic oncology 39(12): 836e11-836e17	- Comparator in study does not match that specified in protocol *Study compares CN vs SACT. Combines upfront and deferred CN participants into one CN arm. No subgroup results reported*

Study	Reason
Olweny, Ephrem O, Park, Samuel K, Tan, Yung K et al. (2012) Radiofrequency ablation versus partial nephrectomy in patients with solitary clinical T1a renal cell carcinoma: comparable oncologic outcomes at a minimum of 5 years of follow-up. European urology 61(6): 1156-61	- Primary study covered fully by an included systematic review
Onal, Cem, Oymak, Ezgi, Guler, Ozan Cem et al. (2023) Stereotactic body radiotherapy and tyrosine kinase inhibitors in patients with oligometastatic renal cell carcinoma: a multi-institutional study. Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al] 199(5): 456-464	- 6b SABR exclude - Mixed population of SACT pre/post non-pharmacological regimens
Onishi, Takehisa, Nishikawa, Kouhei, Hasegawa, Yoshihiro et al. (2007) Assessment of health-related quality of life after radiofrequency ablation or laparoscopic surgery for small renal cell carcinoma: a prospective study with medical outcomes Study 36-Item Health Survey (SF-36). Japanese journal of clinical oncology 37(10): 750-4	- Study does not contain a relevant outcome *HRQoL reported as SF36*
Ontario, Health (2023) Robotic-assisted partial nephrectomy for kidney cancer.	- Exclude - wrong population *Population too broad*
Pahouja, Gaurav, Sweigert, Sarah E, Sweigert, Patrick J et al. (2022) Does size matter? Comparing robotic versus open radical nephrectomy for very large renal masses. Urologic oncology 40(10): 456e1-456e7	- Exclude - For RQC Proportion of patients stage T3 < 90%
Palacios, Diego Aguilar, Zabor, Emily C, Munoz-Lopez, Carlos et al. (2021) Does Reduced Renal Function Predispose to Cancer-specific Mortality from Renal Cell Carcinoma?. European urology 79(6): 774-780	- Data not reported in an extractable format *No denominators for recurrence data*
Palumbo, Carlotta, Mistretta, Francesco A, Knipper, Sophie et al. (2020) Contemporary Cytoreductive Nephrectomy Provides Survival Benefit in Clear-cell Metastatic	- Mixed population of SACT pre/post non-pharmacological regimens

Study	Reason
Renal Cell Carcinoma. Clinical genitourinary cancer 18(6): e730-e738	
Pan, Xiu-Wu, Cui, Xin-Ming, Huang, Hai et al. (2015) Radiofrequency ablation versus partial nephrectomy for treatment of renal masses: A systematic review and meta-analysis. The Kaohsiung journal of medical sciences 31(12): 649-58	- More recent systematic review included that covers the same topic
Panian, Justine, Saidian, Ava, Hakimi, Kevin et al. (2023) Pathological Outcomes of Patients With Advanced Renal Cell Carcinoma Who Receive Nephrectomy Following Immunotherapy. The oncologist	- Not a relevant study design
Panumatrassamee, Kamol, Autorino, Riccardo, Laydner, Humberto et al. (2013) Robotic versus laparoscopic partial nephrectomy for tumor in a solitary kidney: a single institution comparative analysis. International journal of urology : official journal of the Japanese Urological Association 20(5): 484-91	- Exclude - For RQC Proportion of patients stage T3 < 90%
Papadopoulou, Ariadni, Campain, Nicholas, Abu-Ghanem, Yasmin et al. (2024) Not-so-simple nephrectomy: Comparative analysis of radical and simple nephrectomy in a high-volume tertiary referral center. International journal of urology : official journal of the Japanese Urological Association 31(2): 160-168	- Comparator in study does not match that specified in protocol *Comparator is people who had simple nephrectomy; people who had partial nephrectomy were excluded.*
Patel, Hiten D, Kates, Max, Pierorazio, Phillip M et al. (2014) Survival after diagnosis of localized T1a kidney cancer: current population-based practice of surgery and nonsurgical management. Urology 83(1): 126-32	- Study does not contain a relevant intervention *Not clearly active surveillance*
Patel, Hiten D, Riffon, Mark F, Joice, Gregory A et al. (2016) A Prospective, Comparative Study of Quality of Life among Patients with Small Renal Masses Choosing Active Surveillance and Primary Intervention. The Journal of urology 196(5): 1356-1362	- Study does not contain a relevant outcome *QoL reported as SF12*

Study	Reason
Patel, Sunil H, Uzzo, Robert G, Larcher, Alessandro et al. (2020) Oncologic and Functional Outcomes of Radical and Partial Nephrectomy in pT3a Pathologically Upstaged Renal Cell Carcinoma: A Multi-institutional Analysis. Clinical genitourinary cancer 18(6): e723-e729	- Comparator in study does not match that specified in protocol *PN vs RN*
Patton, Michael W, Salevitz, Daniel A, Tyson, Mark D 2nd et al. (2016) Robot-assisted partial nephrectomy for complex renal masses. Journal of robotic surgery 10(1): 27-31	- There is no information on cT or pT stage
Pecoraro, A., Roussel, E., Amparore, D. et al. (2023) New-onset Chronic Kidney Disease After Surgery for Localised Renal Masses in Patients with Two Kidneys and Preserved Renal Function: A Contemporary Multicentre Study. European Urology Open Science 52: 100-108	- Data not reported in an extractable format *No information on participant split between I and C, or baseline characteristics by intervention.*
Pecoraro, A, Amparore, D, Manfredi, M et al. (2022) Partial vs. radical nephrectomy in non-metastatic pT3a kidney cancer patients: a population-based study. Minerva urology and nephrology 74(4): 445-451	- Comparator in study does not match that specified in protocol *Compares PN vs RN in T3 tumours. Not applicable for RQC*
Peng, B, Zheng, J-H, Xu, D-F et al. (2006) Retroperitoneal laparoscopic nephrectomy and open nephrectomy for radical treatment of renal cell carcinoma: a comparison of clinical outcomes. Academic journal of second military medical university 27(11): 1167-1169	- Study not reported in English
Peng, Ding, He, Zhi-Song, Li, Xue-Song et al. (2017) Partial nephrectomy for T3aN0M0 renal cell carcinoma: shall we step forward?. International braz j urol : official journal of the Brazilian Society of Urology 43(5): 849-856	- Non-OECD country - Comparator in study does not match that specified in protocol *Compares PN vs RN in T3 tumours. Not applicable for RQ C*
Peng, Jonathan; Lalani, Aly-Khan; Swaminath, Anand (2021) Cytoreductive stereotactic body radiotherapy (SBRT) and combination SBRT with immune checkpoint inhibitors in metastatic renal cell carcinoma. Canadian Urological Association journal =	- Systematic review with single arm studies included only

Study	Reason
Journal de l'Association des urologues du Canada 15(8): 281-286	
Petrelli, Fausto, Coinu, Andrea, Vavassori, Ivano et al. (2016) Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma Treated With Targeted Therapies: A Systematic Review With a Meta-Analysis. Clinical genitourinary cancer 14(6): 465-472	- Exclude - Result reported in the most updated MA
Petros, Firas G, Venkatesan, Aradhana M, Kaya, Diana et al. (2019) Conditional survival of patients with small renal masses undergoing active surveillance. BJU international 123(3): 447-455	- Data not reported in an extractable format *Insufficient information about comparator arm to include*
Peyronnet, Benoit, Seisen, Thomas, Oger, Emmanuel et al. (2016) Comparison of 1800 Robotic and Open Partial Nephrectomies for Renal Tumors. Annals of surgical oncology 23(13): 4277-4283	- There is no information on cT or pT stage
Piening, A., Al-Hammadi, N., Dombrowski, J. et al. (2023) Survival in Metastatic Renal Cell Carcinoma Treated With Immunotherapy and Stereotactic Radiation Therapy or Immunotherapy Alone: A National Cancer Database Analysis. Advances in Radiation Oncology 8(5): 101238	- Mixed population of SACT pre/post non-pharmacological regimens *Combines participants receiving SACT and conventional radiotherapy in a single arm and compares it to SRT*
Pierorazio, Phillip M, Johnson, Michael H, Ball, Mark W et al. (2015) Five-year analysis of a multi-institutional prospective clinical trial of delayed intervention and surveillance for small renal masses: the DISSRM registry. European urology 68(3): 408-15	- Comparator in study does not match that specified in protocol *Does not separate ablation and nephrectomy in comparator group*
Pierorazio, Phillip M, Johnson, Michael H, Patel, Hiten D et al. (2016) Management of Renal Masses and Localized Renal Cancer: Systematic Review and Meta-Analysis. The Journal of urology 196(4): 989-99	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*
Pignot, Geraldine, Margue, Gaelle, Bigot, Pierre et al. (2025) The effect of tumor downsizing on surgical complexity during	- Study did not compare the interventions of interest

Study	Reason
nephrectomy after immune checkpoint inhibitors for metastatic renal cell carcinoma. World journal of urology 43(1): 54	
Pignot, Geraldine, Mejean, Arnaud, Bernhard, Jean-Christophe et al. (2015) The use of partial nephrectomy: results from a contemporary national prospective multicenter study. World journal of urology 33(1): 33-40	- Does not contain a population of people with kidney cancer *population has kidney cancer but >10% of participants have stage 3 or higher*
Pignot, Geraldine, Thiery-Vuillemin, Antoine, Albiges, Laurence et al. (2022) Oncological Outcomes of Delayed Nephrectomy After Optimal Response to Immune Checkpoint Inhibitors for Metastatic Renal Cell Carcinoma. European urology oncology 5(5): 577-584	- Comparator in study does not match that specified in protocol - Study does not contain a relevant intervention
Poinas, G, Long, JA, Rébillard, X et al. (2018) [Place of partial nephrectomy assisted by robot: Review of the literature at the time of a request for a specific nomenclature]. Progres en urologie : journal de l'Association francaise d'urologie et de la Societe francaise d'urologie 28(16): 890-899	- Study not reported in English
Posa, A., Lancellotta, V., Paoletti, F. et al. (2022) The Role of Focal Approach as Alternative to Nephron-Sparing Surgery in the Treatment of Stage I Cancer in Renal Graft: Results of a Systematic Review. Turk Onkoloji Dergisi 37(3): 351-360	- More recent systematic review included that covers the same topic *kidney graft patients only*
Prata, F., Ragusa, A., Tedesco, F. et al. (2024) Trifecta Outcomes of Robot-Assisted Partial Nephrectomy Using the New HugoTM RAS System Versus Laparoscopic Partial Nephrectomy. Journal of Clinical Medicine 13(7): 2138	- Exclude - For RQC Proportion of patients stage T3 < 90%
Prins, Fieke M, Kerkmeijer, Linda G W, Pronk, Anne A et al. (2017) Renal Cell Carcinoma: Alternative Nephron-Sparing Treatment Options for Small Renal Masses, a Systematic Review. Journal of endourology 31(10): 963-975	- More recent systematic review included that covers the same topic

Study	Reason
Procopio, Giuseppe, Apollonio, Giulia, Cognetti, Francesco et al. (2019) Sorafenib Versus Observation Following Radical Metastasectomy for Clear-cell Renal Cell Carcinoma: Results from the Phase 2 Randomized Open-label RESORT Study. European urology oncology 2(6): 699-707	- Comparator in study does not match that specified in protocol *Compares patients with metastatic rcc treated with sorafenib vs. observation-alone after the radical surgery of metastases*
Pyrgidis, N., Schulz, G.B., Stief, C. et al. (2024) Surgical Trends and Complications in Partial and Radical Nephrectomy: Results from the GRAND Study. Cancers 16(1): 97	- Data not reported in an extractable format *no info on tumour stage (see highlighted text on page 9)study reports length of hospital stay (table 3)we could include and downgrade for applicability To exclude - as there is no information on tumour characteristics*
Qi, Nienie, Wu, Pengjie, Chen, Jinchao et al. (2017) Cytoreductive nephrectomy with thrombectomy before targeted therapy improves survival for metastatic renal cell carcinoma with venous tumor thrombus: a single-center experience. World journal of surgical oncology 15(1): 4	- Study does not contain a relevant intervention
Qu, Hongchen; Wang, Kai; Hu, Bin (2023) Meta analysis of clinical prognosis of radiofrequency ablation versus partial nephrectomy in the treatment of early renal cell carcinoma. Frontiers in oncology 13: 1105877	- Systematic review used as source of primary studies *Sources insufficient*
Qu, Hongchen; Wang, Kai; Hu, Bin (2024) Meta-analysis of clinical outcomes of robot-assisted partial nephrectomy and classical open partial nephrectomy. International journal of surgery (London, England) 110(10): 6268-6281	- Exclude - RQC Patients with localised tumour
Raman, Jay D, Raj, Ganesh V, Lucas, Steven M et al. (2010) Renal functional outcomes for tumours in a solitary kidney managed by ablative or extirpative techniques. BJU international 105(4): 496-500	- Study published before included SR/s for the outcome/s reported
Reese, Stephen W, Eismann, Lennert, White, Charlie et al. (2023) Surgical outcomes of cytoreductive nephrectomy in patients receiving systemic immunotherapy	- Comparator in study does not match that specified in protocol

Study	Reason
for advanced renal cell carcinoma. Urologic oncology	
Reifsnyder, Jennifer E, Ramasamy, Ranjith, Ng, Casey K et al. (2012) Laparoscopic and open partial nephrectomy: complication comparison using the Clavien system. JSLS : Journal of the Society of Laparoendoscopic Surgeons 16(1): 38-44	- There is no information on cT or pT stage
Ricciardulli, Stefano, Ding, Qiang, Zhang, Xu et al. (2015) Evaluation of laparoscopic vs robotic partial nephrectomy using the margin, ischemia and complications score system: a retrospective single center analysis. Archivio italiano di urologia, andrologia : organo ufficiale [di] Societa italiana di ecografia urologica e nefrologica 87(1): 49-55	- Exclude RQC- Study included only patients T1-T2
Richey, S L, Culp, S H, Jonasch, E et al. (2011) Outcome of patients with metastatic renal cell carcinoma treated with targeted therapy without cytoreductive nephrectomy. Annals of oncology : official journal of the European Society for Medical Oncology 22(5): 1048-1053	- Comparator in study does not match that specified in protocol *Compares targeted therapy with chemotherapy and other types of SACT*
Rim, C.H., Cho, W.K., Lee, J.H. et al. (2022) Role of Local Treatment for Oligometastasis: A Comparability-Based Meta-Analysis. Cancer Research and Treatment 54(4): 953-969	- Exclude - wrong population - Exclude - Intervention is out of scope
Rini, Brian I and Campbell, Steven C (2007) The evolving role of surgery for advanced renal cell carcinoma in the era of molecular targeted therapy. The Journal of urology 177(6): 1978-84	- Review article but not a systematic review
Rivero, J Ricardo, De La Cerda, Jose 3rd, Wang, Hanzhang et al. (2018) Partial Nephrectomy versus Thermal Ablation for Clinical Stage T1 Renal Masses: Systematic Review and Meta-Analysis of More than 3,900 Patients. Journal of vascular and interventional radiology : JVIR 29(1): 18-29	- More recent systematic review included that covers the same topic

Study	Reason
Roaldsen, Marius, Lohne, Vetle, Stenberg, Thor Allan et al. (2024) Comparing open and robot-assisted partial nephrectomy - a single institution report. BMC urology 24(1): 197	- Exclude RQC- Study included only patients T1-T2
Roussel, Eduard, Laenen, Annouschka, Bhindi, Bimal et al. (2023) Predicting short- and long-term renal function following partial and radical nephrectomy. Urologic oncology 41(2): 110e1-110e6	- Study does not contain a relevant outcome
Roussel, Eduard, Verbiest, Annelies, Milenkovic, Uros et al. (2020) Too good for CARMENA: criteria associated with long systemic therapy free intervals post cytoreductive nephrectomy for metastatic clear cell renal cell carcinoma. Scandinavian journal of urology 54(6): 493-499	- Study does not contain a relevant outcome
Russo, P. (2009) Radical nephrectomy with and without lymph node dissection: Final results of European Organization for Research and Treatment of Cancer (EORTC) randomized phase 3 trial 30881. Blom JH, van Poppel H, Marechal JM, Jacqmin D, Schroder FH, de Prijck L, Sylvester R, EORTC Genitourinary Tract Cancer Group, St. Franciscus Gasthuis, Rotterdam, The Netherlands. Urologic Oncology: Seminars and Original Investigations 27(1): 102	- Conference abstract
Russo, P., Blum, K.A., Weng, S. et al. (2022) Outcomes for Atypical Tumor Recurrences Following Minimally Invasive Kidney Cancer Operations. European Urology Open Science 40: 125-132	- Does not contain a population of people with kidney cancer *All participants were treated for recurrence after partial or radical nephrectomy*
Saeed, S., Shah, S.R., Najeebullah et al. (2024) THE ROLE OF NEPHRON-SPARING SURGERY IN THE MANAGEMENT OF SMALL RENAL MASSES COMPARING THE ONCOLOGICAL OUTCOMES, RENAL FUNCTION PRESERVATION, AND COMPLICATION RATES OF PARTIAL NEPHRECTOMY VERSUS RADICAL	- Non-OECD country

Study	Reason
NEPHRECTOMY. Journal of Population Therapeutics and Clinical Pharmacology 31(9): 981	
Sandbergen, Laura, Spriensma, Alette S, de la Rosette, Jean J et al. (2020) Health-related quality of life in localized renal masses: A matter of sparing nephrons or minimizing the incision?. Urologic oncology 38(2): 43e1-43e11	- Study does not contain a relevant outcome *QoL as SF-36*
Schernuk, Jordan, Garcia Marchinena, Patricio A, Carminatti, Tomas et al. (2023) Renal Cell Carcinoma with Venous Extension: Safety of Laparoscopic Surgery for Thrombus Levels I-IIIa. Journal of endourology 37(7): 786-792	- Comparator in study does not match that specified in protocol
Schiff, Jonathan D, Palese, Michael, Vaughan, E Darracott Jr et al. (2005) Laparoscopic vs open partial nephrectomy in consecutive patients: the Cornell experience. BJU international 96(6): 811-4	- There is no information on cT or pT stage
Scosyrev, Emil, Messing, Edward M, Sylvester, Richard et al. (2014) Renal function after nephron-sparing surgery versus radical nephrectomy: results from EORTC randomized trial 30904. European urology 65(2): 372-7	- Secondary publication of an included study that does not provide any additional relevant information
Scosyrev, Emil, Wu, Kevin, Levey, Helen R et al. (2014) Overall Survival after Partial Versus Radical Nephrectomy for a Small Renal Mass: Systematic Review of Observational Studies. Urology practice 1(1): 27-34	- More recent systematic review included that covers the same topic
Selim, A.M., Zaghloul, A.S., Aboulkassem, H.A. et al. (2020) Minimally invasive approach in surgical management of renal neoplasms national cancer institute experience. Open Access Macedonian Journal of Medical Sciences 8(b): 1071-1076	- Study does not contain a relevant intervention *Laparoscopic & robotic compared to open nephrectomy irrespective of being partial or radical*
Shah, Paras H, Leibovich, Bradley C, Van Houten, Holly et al. (2019) Association of Partial versus Radical Nephrectomy with	- Primary study covered fully by an included systematic review

Study	Reason
Subsequent Hypertension Risk Following Renal Tumor Resection. The Journal of urology 202(1): 69-75	
Shah, Paras H, Moreira, Daniel M, Patel, Vinay R et al. (2017) Partial Nephrectomy is Associated with Higher Risk of Relapse Compared with Radical Nephrectomy for Clinical Stage T1 Renal Cell Carcinoma Pathologically Up Staged to T3a. The Journal of urology 198(2): 289-296	- Comparator in study does not match that specified in protocol *Compares RN and PN for upstaged T3 tumours.*
Sharma, Gopal, Sharma, Aditya Prakash, Tyagi, Shantanu et al. (2022) Robot-assisted partial nephrectomy for moderate to highly complex renal masses. A systematic review and meta-analysis. Indian journal of urology : IJU : journal of the Urological Society of India 38(3): 174-183	- Exclude - For RQC Proportion of patients stage T3 < 90%
Shaw, Greg L, Hussain, Mahreen, Nair, Rajesh et al. (2012) Performing cytoreductive nephrectomy following targeted sunitinib therapy for metastatic renal cell carcinoma: a surgical perspective. Urologia internationalis 89(1): 83-8	- Comparator in study does not match that specified in protocol
Shchukin, D.V., Lesovoy, V.N., Garagatiy, I.A. et al. (2017) Comparative analysis of oncologic outcomes of radical nephrectomy and nephron-sparing surgery in patients with intravenous extension of tumor into the renal vein. New Armenian Medical Journal 11(2): 58-62	- Non-OECD country - Comparator in study does not match that specified in protocol *Comparing RN vs PN in locally advanced tumours*
Shemshaki, Hamidreza, Al-Mamari, Said Abdallah, Al-Hooti, Qais et al. (2022) Comparison of cytoreductive partial versus radical nephrectomy in metastatic renal cell carcinoma: To be on the horns of a dilemma. Urologia 89(2): 160-166	- Exclude - Intervention is out of scope
Shen, Zhonghua, Xie, Linguo, Xie, Wanqin et al. (2016) The comparison of perioperative outcomes of robot-assisted and open partial nephrectomy: a systematic review and meta-analysis. World journal of surgical oncology 14(1): 220	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
Shi, Xu, Feng, Dechao, Li, Dengxiong et al. (2021) The Role of Lymph Node Dissection for Non-Metastatic Renal Cell Carcinoma: An Updated Systematic Review and Meta-Analysis. Frontiers in oncology 11: 790381	- Exclude - For RQC Proportion of patients stage T3 < 90%
Shinohara, N, Harabayashi, T, Sato, S et al. (2001) Impact of nephron-sparing surgery on quality of life in patients with localized renal cell carcinoma. European urology 39(1): 114-9	- Data not reported in an extractable format
Shirotake, Suguru, Miyama, Y U, Baba, Yasutaka et al. (2022) Impact of Cytoreductive Nephrectomy Following Nivolumab Plus Ipilimumab Therapy for Patients With Advanced Renal Cell Carcinoma. Anticancer research 42(5): 2727-2735	- Study does not contain a relevant outcome - Not a relevant study design
Shvero, Asaf, Nativ, Ofer, Abu-Ghanem, Yasmin et al. (2018) Oncologic Outcomes of Partial Nephrectomy for Stage T3a Renal Cell Cancer. Clinical genitourinary cancer 16(3): e613-e617	- Comparator in study does not match that specified in protocol *Compared PN vs RN in locally advanced tumours*
Sidoti Abate, Marie Angela, Menold, Hanna Saskia, Neuberger, Manuel et al. (2024) Quality-of-life outcomes of the ROBOtic-assisted versus Conventional Open Partial nephrectomy (ROBOCOP) II trial. BJU international 134(3): 434-441	- Exclude - For RQC Proportion of patients stage T3 < 90%
Simhan, J., Smaldone, M.C., Tsai, K.J. et al. (2012) Perioperative outcomes of robotic and open partial nephrectomy for moderately and highly complex renal lesions. Journal of Urology 187(6): 2000-2004	- There is no information on cT or pT stage
Simone, Giuseppe, Tuderti, Gabriele, Anceschi, Umberto et al. (2017) Oncological outcomes of minimally invasive partial versus minimally invasive radical nephrectomy for cT1-2/N0/M0 clear cell renal cell carcinoma: a propensity score-matched analysis. World journal of urology 35(5): 789-794	- Data not reported in an extractable format

Study	Reason
Siva, Shankar, Ali, Muhammad, Correa, Rohann J M et al. (2022) 5-year outcomes after stereotactic ablative body radiotherapy for primary renal cell carcinoma: an individual patient data meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney). The Lancet. Oncology 23(12): 1508-1516	- Review article but not a systematic review
Siva, Shankar, Louie, Alexander V, Kotecha, Rupesh et al. (2024) Stereotactic body radiotherapy for primary renal cell carcinoma: a systematic review and practice guideline from the International Society of Stereotactic Radiosurgery (ISRS). The Lancet. Oncology 25(1): e18-e28	- Not a relevant study design *Single arm studies only*
Siva, Shankar, Pham, Daniel, Gill, Suki et al. (2012) A systematic review of stereotactic radiotherapy ablation for primary renal cell carcinoma. BJU international 110(11ptb): e737-43	- More recent systematic review included that covers the same topic
Soisrithong, C., Sirisreetreerux, P., Sangkum, P. et al. (2021) Comparative outcomes and predictive assessment of trifecta in open, laparoscopic, and robotic-assisted partial nephrectomy cases with renal cell carcinoma: A 10-year experience at ramathibodi hospital. Research and Reports in Urology 13: 425-435	- Non-OECD country - There is no information on cT or pT stage
Song, Y., Du, C.-X., Zhang, W. et al. (2016) Impact of cytoreductive nephrectomy on survival in patients with metastatic renal cell carcinoma treated by targeted therapy. Chinese Medical Journal 129(5): 530-535	- Data not reported in an extractable format *OS data reported as median and range*
Soomro, Naeem, Lecouturier, Jan, Stocken, Deborah D et al. (2017) Surveillance versus ablation for incidentally diagnosed small renal tumours: the SURAB feasibility RCT. Health technology assessment (Winchester, England) 21(81): 1-68	- Study does not contain a relevant outcome
Spaas, M, Sundahl, N, Rottey, S et al. (2021) Immuno-radiotherapy in solid tumors: preliminary results of the	- Conference abstract

Study	Reason
randomized phase 2 CHEERS trial. Radiotherapy and oncology 161: S490-S491	
Spaas, Mathieu, Sundahl, Nora, Kruse, Vibeke et al. (2023) Checkpoint Inhibitors in Combination With Stereotactic Body Radiotherapy in Patients With Advanced Solid Tumors: The CHEERS Phase 2 Randomized Clinical Trial. JAMA oncology 9(9): 1205-1213	- 6b SABR exclude
Spiess, Philippe E and Fishman, Mayer N (2010) Cytoreductive nephrectomy vs medical therapy as initial treatment: a rational approach to the sequence question in metastatic renal cell carcinoma. Cancer control : journal of the Moffitt Cancer Center 17(4): 269-78	- Review article but not a systematic review
Sprenkle, Preston C, Power, Nicholas, Ghoneim, Tarek et al. (2012) Comparison of open and minimally invasive partial nephrectomy for renal tumors 4-7 centimeters. European urology 61(3): 593-9	- Exclude - For RQC Proportion of patients stage T3 < 90%
Stellato, M., Santini, D., Verzoni, E. et al. (2021) Impact of Previous Nephrectomy on Clinical Outcome of Metastatic Renal Carcinoma Treated With Immune-Oncology: A Real-World Study on Behalf of Meet-URO Group (MeetUro-7b). Frontiers in Oncology 11: 682449	- Not a relevant study design - Study does not contain a relevant intervention *Mixed CN and radical nephrectomy population*
Stenman, M, Sinclair, G, Paavola, P et al. (2018) Overall survival after stereotactic radiotherapy or surgical metastasectomy in oligometastatic renal cell carcinoma patients treated at two Swedish centres 2005-2014. Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology 127(3): 501-506	- Comparator in study does not match that specified in protocol *Compares SRT with metastasectomy. Mixed SACT population*
Stern, Joshua M, Svatek, Robert, Park, Sangtae et al. (2007) Intermediate comparison of partial nephrectomy and radiofrequency ablation for clinical T1a	- Primary study covered fully by an included systematic review

Study	Reason
renal tumours. BJU international 100(2): 287-90	
Steward, James E, Kern, Sean Q, Cheng, Liang et al. (2021) Clear cell papillary renal cell carcinoma: Characteristics and survival outcomes from a large single institutional series. Urologic oncology 39(6): 370e21-370e25	- Not a relevant study design
Stewart, Grant D, Ang, W Jensen, Laird, Alexander et al. (2012) The operative safety and oncological outcomes of laparoscopic nephrectomy for T3 renal cell cancer. BJU international 110(6): 884-90	- Not a relevant study design *Non-comparative study*
Stroup, Sean P, Palazzi, Kerrin, Kopp, Ryan P et al. (2012) RENAL nephrometry score is associated with operative approach for partial nephrectomy and urine leak. Urology 80(1): 151-6	- Exclude - For RQC Proportion of patients stage T3 < 90%
Su, Jia-Rui, Zhu, Ding-Jun, Liang, Wu et al. (2012) Investigation on the indication of ipsilateral adrenalectomy in radical nephrectomy: a meta-analysis. Chinese medical journal 125(21): 3885-90	- Comparator in study does not match that specified in protocol *Adrenalectomy vs no adrenalectomy*
Suk-Ouichai, Chalairat, Tanaka, Hajime, Wang, Yanbo et al. (2019) Renal Cancer Surgery in Patients without Preexisting Chronic Kidney Disease-Is There a Survival Benefit for Partial Nephrectomy?. The Journal of urology 201(6): 1088-1096	- Data not reported in an extractable format *Stage of kidney cancer was not reported*
Sun, M, Abdollah, F, Shariat, S F et al. (2012) Propensity-score matched comparison of complications, blood transfusions, length of stay, and in-hospital mortality between open and laparoscopic partial nephrectomy: a national series. European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology 38(1): 80-7	- There is no information on cT or pT stage
Sun, Maxine, Becker, Andreas, Tian, Zhe et al. (2014) Management of localized kidney cancer: calculating cancer-specific mortality	- Study does not contain a relevant intervention *Non-surgical management is unclear*

Study	Reason
and competing risks of death for surgery and nonsurgical management. European urology 65(1): 235-41	
Sun, Zi-Jun, Liu, Feng, Wei, Hai-Bin et al. (2023) Laparoscopic partial versus radical nephrectomy for localized renal cell carcinoma over 4 cm. Journal of cancer research and clinical oncology 149(20): 17837-17848	- Non-OECD country
Takagi, T., Kondo, T., Iizuka, J. et al. (2016) Comparison of survival rates in stage 1 renal cell carcinoma between partial nephrectomy and radical nephrectomy patients according to age distribution: A propensity score matching study. BJU International 117(6): e52-e59	- For RQ 3a Study published before 2016 (search date for overall survival)
Takagi, Toshio, Kondo, Tsunenori, Omae, Kenji et al. (2016) Comparison of progression to end-stage renal disease requiring dialysis after partial or radical nephrectomy for renal cell carcinoma in patients with severe chronic kidney disease. International urology and nephrology 48(9): 1421-7	- Study does not contain a relevant outcome
Takahara, K., Fukaya, K., Nukaya, T. et al. (2022) Perioperative and long-term functional outcomes of robot-assisted versus open partial nephrectomy: A single-center retrospective study of a Japanese cohort. Annals of Medicine and Surgery 75: 103482	- There is no information on cT or pT stage
Talenfeld, Adam D, Gennarelli, Renee L, Elkin, Elena B et al. (2018) Percutaneous Ablation Versus Partial and Radical Nephrectomy for T1a Renal Cancer: A Population-Based Analysis. Annals of internal medicine 169(2): 69-77	- Secondary publication of an included study that does not provide any additional relevant information *SEER database - covered by other included studies*
Tam, Andrew W, Kutikov, Alexander, Winoker, Jared S et al. (2022) Propensity-score matched oncological outcomes and patterns of recurrence following open and minimally-invasive partial nephrectomy for	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
renal cell carcinoma. Urologic oncology 40(3): 111e19-111e25	
Tan, H.-J., Wolf Jr., J.S., Ye, Z. et al. (2011) Population-level comparative effectiveness of laparoscopic versus open radical nephrectomy for patients with kidney cancer. Cancer 117(18): 4184-4193	- Exclude - RQC Patients with localised tumour
Tan, Jo-Lynn, Frydenberg, Mark, Grummet, Jeremy et al. (2018) Comparison of perioperative, renal and oncologic outcomes in robotic-assisted versus open partial nephrectomy. ANZ journal of surgery 88(3): e194-e199	- Exclude - For RQC Proportion of patients stage T3 < 90%
Tang, Amber B, Lamaina, Margherita, Childers, Christopher P et al. (2021) Perioperative and Long-Term Outcomes of Robot-Assisted Partial Nephrectomy: A Systematic Review. The American surgeon 87(1): 21-29	- Exclude - For RQC Proportion of patients stage T3 < 90%
Tang, Kun, Yao, Weimin, Li, Heng et al. (2014) Laparoscopic renal cryoablation versus laparoscopic partial nephrectomy for the treatment of small renal masses: a systematic review and meta-analysis of comparative studies. Journal of laparoendoscopic & advanced surgical techniques. Part A 24(6): 403-10	- More recent systematic review included that covers the same topic
Tarkowska, M., Glowacka-Mrotek, I., Peterson, D. et al. (2023) Quality of life at 3 to 5 years after surgical treatment of renal cell carcinoma - a pilot cross-sectional study. Nowotwory 73(4): 201-212	- Study does not contain a relevant outcome *Quality of life was measured with the WHOQOL-BREF questionnaire*
Tatsugami, Katsunori, Shinohara, Nobuo, Kondo, Tsunenori et al. (2015) Role of cytoreductive nephrectomy for Japanese patients with primary renal cell carcinoma in the cytokine and targeted therapy era. International journal of urology : official journal of the Japanese Urological Association 22(8): 736-40	- Mixed population of SACT pre/post non-pharmacological regimens
Teishima, J., Hara, T., Tobe, T. et al. (2023) The impact of primary region resection on	- Study does not contain a relevant outcome

Study	Reason
the therapeutic outcome of combination regimens for metastatic renal cell carcinoma. Oncology Letters 26(5): 470	
Teishima, Jun, Goto, Keisuke, Sekino, Yohei et al. (2022) Prognostic model of upfront cytoreductive nephrectomy in patients with metastatic renal cell carcinoma treated with immune checkpoint inhibitors and/or targeted agents. International urology and nephrology 54(6): 1225-1232	- Data not reported in an extractable format
Teishima, Jun, Ohara, Shinya, Shinmei, Shunsuke et al. (2018) Normalization of C-reactive protein levels following cytoreductive nephrectomy in patients with metastatic renal cell carcinoma treated with tyrosine kinase inhibitors is associated with improved overall survival. Urologic oncology 36(7): 339e9-339e15	- Comparator in study does not match that specified in protocol
Thaidumrong, T. and Duangkae, S. (2018) Comparison of the outcomes of laparoscopic and open nephrectomy in Rajavithi hospital. Journal of the Medical Association of Thailand 101(2supplement2): 103-s108	- Non-OECD country - Exclude - For RQC Proportion of patients stage T3 < 90%
Thompson, R Houston, Atwell, Tom, Schmit, Grant et al. (2015) Comparison of partial nephrectomy and percutaneous ablation for cT1 renal masses. European urology 67(2): 252-9	- Primary study covered fully by an included systematic review
Tian, J., Zeng, X., Wan, J. et al. (2022) Partial and Radical Nephrectomy Provides Equivalent Oncologic Outcomes in pT3a Renal Cell Carcinoma: A Population-Based Study. Frontiers in Oncology 11: 819098	- Comparator in study does not match that specified in protocol *Compares RN vs PN for upstaged T3 tumours*
Tobert, Conrad M; Riedinger, Christopher B; Lane, Brian R (2014) Do we know (or just believe) that partial nephrectomy leads to better survival than radical nephrectomy for renal cancer?. World journal of urology 32(3): 573-9	- Review article but not a systematic review
Tsai, Sheng-Han, Tseng, Ping-Tao, Sherer, Benjamin A et al. (2019) Open versus	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
robotic partial nephrectomy: Systematic review and meta-analysis of contemporary studies. The international journal of medical robotics + computer assisted surgery : MRCAS 15(1): e1963	
Uhlig, A., Hahn, O., Strauss, A. et al. (2018) Treatment for Localized T1a Clear Cell Renal Cell Carcinoma: Survival Benefit for Cryosurgery and Thermal Ablation Compared to Deferred Therapy. CardioVascular and Interventional Radiology 41(2): 277-283	- Secondary publication of an included study that does not provide any additional relevant information *NCDB database - more recent studies from this database included*
Uhlig, Johannes, Kokabi, Nima, Xing, Minzhi et al. (2018) Ablation versus Resection for Stage 1A Renal Cell Carcinoma: National Variation in Clinical Management and Selected Outcomes. Radiology 288(3): 889-897	- Secondary publication of an included study that does not provide any additional relevant information
Uhlig, Johannes, Strauss, Arne, Rucker, Gerta et al. (2019) Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. European radiology 29(3): 1293-1307	- More recent systematic review included that covers the same topic
Uprety, Dipesh, Bista, Amir, Smith, Angela L et al. (2018) Cytoreductive Nephrectomy in Elderly Patients with Metastatic Renal Cell Carcinoma in the Targeted Therapy Era. Anticancer research 38(5): 3013-3018	- Study does not contain a relevant intervention *No information about SACT* - Not a relevant study design *Case-control*
Van Poppel, Hein, Becker, Frank, Cadeddu, Jeffrey A et al. (2011) Treatment of localised renal cell carcinoma. European urology 60(4): 662-72	- Review article but not a systematic review
Vartolomei, Liliana, Cotrus, Andrei, Stanciu, Camelia et al. (2022) Quality of Life and Psychological Distress among Patients with Small Renal Masses. Journal of clinical medicine 11(14)	- Systematic review used as source of primary studies
Veccia, Alessandro, Dell'oglio, Paolo, Antonelli, Alessandro et al. (2020) Robotic partial nephrectomy versus radical	- Data not reported in an extractable format *Data was not reported by stage of kidney cancer*

Study	Reason
nephrectomy in elderly patients with large renal masses. Minerva urologica e nefrologica = The Italian journal of urology and nephrology 72(1): 99-108	
Veltri, Andrea, Gazzera, Carlo, Busso, Marco et al. (2014) T1a as the sole selection criterion for RFA of renal masses: randomized controlled trials versus surgery should not be postponed. Cardiovascular and interventional radiology 37(5): 1292-8	- Not a relevant study design *Noncomparative study*
Venkatramani, Vivek, Koru-Sengul, Tulay, Miao, Feng et al. (2018) A comparison of overall survival and perioperative outcomes between partial and radical nephrectomy for cT1b and cT2 renal cell carcinoma-Analysis of a national cancer registry. Urologic oncology 36(3): 90e9-90e14	- Superceded by Ristau
Verbiest, A., De Meerleer, G., Albersen, M. et al. (2018) Non-surgical ablative treatment of distant extracranial metastases for renal cell carcinoma: A systematic review. Kidney Cancer 2(1): 57-67	- Systematic review used as source of primary studies
Verbiest, A., Roussel, E., Tosco, L. et al. (2020) Long-Term Outcomes in Clear-Cell Renal Cell Carcinoma Patients Treated with Complete Metastasectomy. Kidney Cancer 4(4): 177-183	- Mixed population of SACT pre/post non-pharmacological regimens
Verzoni, Elena, Ratta, Raffaele, Grassi, Paolo et al. (2018) TARIBO trial: targeted therapy with or without nephrectomy in metastatic renal cell carcinoma: liquid biopsy for biomarkers discovery. Tumori 104(5): 401-405	- Not a relevant study design *Protocol for TARIBO trial. On going trial.*
Veys, Ralf, Abdollah, Firas, Briganti, Alberto et al. (2018) Oncological and functional efficacy of nephron-sparing surgery versus radical nephrectomy in renal cell carcinoma stages >=cT1b: a single institution, matched analysis. Central European journal of urology 71(1): 48-57	- Exclude - wrong population
Vilaseca, Antoni, Guglielmetti, Giuliano, Vertosick, Emily A et al. (2020) Value of	- Comparator in study does not match that specified in protocol

Study	Reason
Partial Nephrectomy for Renal Cortical Tumors of cT2 or Greater Stage: A Risk-benefit Analysis of Renal Function Preservation Versus Increased Postoperative Morbidity. European urology oncology 3(3): 365-371	*Compares RN vs PN in locally advanced RCC*
Vitruk, Iurii, Voylenko, Oleg, Stakhovsky, Oleksandr et al. (2023) Advantages of organ-sparing treatment approaches in metastatic kidney cancer. Journal of cancer research and clinical oncology 149(7): 3131-3137	- Comparator in study does not match that specified in protocol *Compares complete CN and partial CN. Inclusion criteria indicates all participants received SACT*
Wang, Agnes J and Bhayani, Sam B (2009) Robotic partial nephrectomy versus laparoscopic partial nephrectomy for renal cell carcinoma: single-surgeon analysis of >100 consecutive procedures. Urology 73(2): 306-10	- There is no information on cT or pT stage
Wang, Dong, Xiao, Zejun, Shou, Jianzhong et al. (2019) Comparison of Laparoscopy and Open Radical Nephrectomy of Renal Cell Cancer. Open medicine (Warsaw, Poland) 14: 392-397	- Exclude - For RQC Proportion of patients stage T3 < 90%
Wang, Li, Li, Kun-Peng, Yin, Shan et al. (2023) Oncologic and perioperative outcomes of laparoscopic versus open radical nephrectomy for the treatment of renal tumor (> 7 cm): a systematic review and pooled analysis of comparative outcomes. World journal of surgical oncology 21(1): 35	- Exclude - For RQC Proportion of patients stage T3 < 90%
Wang, Luke L, Yuen, Kit L, Saitta, Cesare et al. (2024) Comparison of outcomes of radical and partial nephrectomy for sarcomatoid renal cell carcinoma: analysis of the national cancer database. World journal of urology 42(1): 508	- Patients with sarcomatoid RCC and pT3 > 10% (61%)
Wang, Shangqian, Qin, Chao, Peng, Zhihang et al. (2014) Radiofrequency ablation versus partial nephrectomy for the treatment of clinical stage 1 renal masses: a systematic review and meta-analysis. Chinese medical journal 127(13): 2497-503	- More recent systematic review included that covers the same topic

Study	Reason
Wang, Yubin, Ma, Xin, Huang, Qingbo et al. (2016) Comparison of robot-assisted and laparoscopic partial nephrectomy for complex renal tumours with a RENAL nephrometry score >=7: peri-operative and oncological outcomes. BJU international 117(1): 126-30	- Non-OECD country - Exclude - For RQC Proportion of patients stage T3 < 90%
Wang, Yubin, Shao, Jinkai, Ma, Xin et al. (2017) Robotic and open partial nephrectomy for complex renal tumors: a matched-pair comparison with a long-term follow-up. World journal of urology 35(1): 73-80	- Non-OECD country - Exclude - For RQC Proportion of patients stage T3 < 90%
Wang, Zheng, Wang, Ganggang, Xia, Qinghua et al. (2016) Partial nephrectomy vs. radical nephrectomy for renal tumors: A meta-analysis of renal function and cardiovascular outcomes. Urologic oncology 34(12): 533e11-533e19	- More recent systematic review included that covers the same topic
Webb, C.M., Kamel, M., Eltahawy, E. et al. (2015) A comparative study of open, laparoscopic and robotic partial nephrectomy in obese patients. Urology Annals 7(2): 231-234	- There is no information on cT or pT stage
Wei, Xiyi, Ren, Xiaohan, Ding, Yichao et al. (2019) Comparative outcomes of radio frequency ablation versus partial nephrectomy for T1 renal tumors: a systematic review. Translational andrology and urology 8(6): 601-608	- More recent systematic review included that covers the same topic
Weight, Christopher J, Lythgoe, Casey, Unnikrishnan, Raman et al. (2011) Partial nephrectomy does not compromise survival in patients with pathologic upstaging to pT2/pT3 or high-grade renal tumors compared with radical nephrectomy. Urology 77(5): 1142-6	- Comparator in study does not match that specified in protocol *RN vs PN in upstaged T2/T3 tumours. Not applicable for RQC*
Wen, Zhi, Wang, Li, Huang, Jing et al. (2023) Perioperative, functional, and oncologic outcomes after ablation or partial nephrectomy for solitary renal tumors: a systematic review and meta-analysis of	- Systematic review used as source of primary studies *Solitary kidney only*

Study	Reason
comparative trials. Frontiers in oncology 13: 1202587	
Whitson, Jared M; Harris, Catherine R; Meng, Maxwell V (2012) Population-based comparative effectiveness of nephron-sparing surgery vs ablation for small renal masses. BJU international 110(10): 1438-1443	- Secondary publication of an included study that does not provide any additional relevant information *SEER database - more fully covered in another included study*
Wong, Ruby; Patel, Bijendra; Biyani, Chandra Shekhar (2023) Perioperative outcomes between laparoscopic versus open versus robotic partial nephrectomy: Current Review. Urologia: 3915603231211975	- Exclude - For RQC Proportion of patients stage T3 < 90%
Wu, Jing, Chang, Joshua, Bai, Harrison X et al. (2019) A Comparison of Cryoablation with Heat-Based Thermal Ablation for Treatment of Clinical T1a Renal Cell Carcinoma: A National Cancer Database Study. Journal of vascular and interventional radiology : JVIR 30(7): 1027-1033e3	- Comparator in study does not match that specified in protocol *Compares cryoablation with thermal ablation*
Wu, Xiaorong, Chen, Wei, Huang, Jiwei et al. (2020) Zero ischemia laparoscopic microwave ablation assisted enucleation vs. laparoscopic partial nephrectomy in clinical T1a renal tumor: a randomized clinical trial. Translational cancer research 9(1): 194-202	- Study does not contain a relevant intervention *Microwave ablation group also had tumour enucleation*
Wu, Z., Li, M., Liu, B. et al. (2014) Robotic versus open partial nephrectomy: A systematic review and meta-analysis. PLoS ONE 9(4): e94878	- There is no information on cT or pT stage
Wu, Zhenjie, Li, Mingmin, Qu, Le et al. (2014) A propensity-score matched comparison of perioperative and early renal functional outcomes of robotic versus open partial nephrectomy. PloS one 9(4): e94195	- Non-OECD country - There is no information on cT or pT stage
Wu, Zhenjie, Li, Mingmin, Song, Shangqing et al. (2015) Propensity-score matched analysis comparing robot-assisted with laparoscopic partial nephrectomy. BJU international 115(3): 437-45	- Non-OECD country - There is no information on cT or pT stage

Study	Reason
Xia, Leilei, Wang, Xianjin, Xu, Tianyuan et al. (2017) Systematic Review and Meta-Analysis of Comparative Studies Reporting Perioperative Outcomes of Robot-Assisted Partial Nephrectomy Versus Open Partial Nephrectomy. Journal of endourology 31(9): 893-909	- Exclude - For RQC Proportion of patients stage T3 < 90%
Xiao, W.-J., Zhu, Y., Dai, B. et al. (2015) Assessment of survival of patients with metastatic clear cell renal cell carcinoma after radical cytoreductive nephrectomy versus no surgery: a seer analysis. International braz j urol : official journal of the Brazilian Society of Urology 41(2): 288-295	- Mixed population of SACT pre/post non-pharmacological regimens
Xiaobing, Wu, Wentao, Gong, Guangxiang, Liu et al. (2017) Comparison of radiofrequency ablation and partial nephrectomy for tumor in a solitary kidney. BMC urology 17(1): 79	- Non-OECD country
Xu, Haozhe, Xing, Zhuo, Ai, Kai et al. (2024) Patients with high nuclear grade pT1-ccRCC are more suitable for radical nephrectomy than partial nephrectomy: a multicenter retrospective study using propensity score. World journal of surgical oncology 22(1): 24	- Non-OECD country
Xu, L. and Fan, W. (2020) Efficacy of sorafenib combined with radiofrequency ablation in renal cancer and its effects on immunity and inflammation in patients. Journal of B.U.ON. 25(1): 514-519	- Mixed population of SACT pre/post non-pharmacological regimens *No information about SACT in the arm treated with radiofrequency ablation* - Study does not contain a relevant outcome
Yan, Shuai, Yang, Wei, Zhu, Cheng-Mei et al. (2019) Comparison among cryoablation, radiofrequency ablation, and partial nephrectomy for renal cell carcinomas sized smaller than 2 cm or sized 2-4 cm: A population-based study. Medicine 98(21): e15610	- Non-OECD country
Yang, Chao and Liao, Zhaolin (2018) Comparison of Radical Nephrectomy and Partial Nephrectomy for T1 Renal Cell	- Systematic review used as source of primary studies

Study	Reason
Carcinoma: A Meta-Analysis. Urologia internationalis 101(2): 175-183	
Yang, Chia-Min, Chung, Hsiao-Jen, Huang, Yi-Hsiu et al. (2014) Standardized analysis of laparoscopic and robotic-assisted partial nephrectomy complications with Clavien classification. Journal of the Chinese Medical Association : JCMA 77(12): 637-41	- Non-OECD country - There is no information on cT or pT stage
Yang, Chuance, Wang, Zhenlong, Huang, Shanlong et al. (2018) Retroperitoneal Laparoscopic Partial Nephrectomy Versus Radical Nephrectomy for Clinical T1 Renal Hilar Tumor: Comparison of Perioperative Characteristics and Short-Term Functional and Oncologic Outcomes. Journal of laparoendoscopic & advanced surgical techniques. Part A 28(10): 1183-1187	- Non-OECD country
Yang, F.; Zhou, Q.; Xing, N. (2020) Comparison of survival and renal function between partial and radical laparoscopic nephrectomy for T1b renal cell carcinoma. Journal of Cancer Research and Clinical Oncology 146(1): 261-272	- Non-OECD country
Yang, Quancheng, Meng, Fanzheng, Li, Kai et al. (2015) Safety and Efficacy of Thermal Ablation for Small Renal Masses in Solitary Kidney: Evidence from Meta-Analysis of Comparative Studies. PloS one 10(6): e0131290	- More recent systematic review included that covers the same topic
Yang, Yong (2020) Partial Versus Radical Nephrectomy in Patients with Renal Cell Carcinoma: A Systematic Review and Meta-analysis. Urology journal 17(2): 109-117	- More recent systematic review included that covers the same topic
Yang, Yue, Chen, Shouzhen, Chen, Fan et al. (2015) Outcome of radiofrequency ablation over partial nephrectomy for small renal mass (<4 cm): a systematic review and meta-analysis. International journal of clinical and experimental medicine 8(11): 20670-4	- More recent systematic review included that covers the same topic
Yin, Xiaotao, Cui, Liang, Li, Fanglong et al. (2015) Radiofrequency Ablation Versus	- More recent systematic review included that covers the same topic

Study	Reason
Partial Nephrectomy in Treating Small Renal Tumors: A Systematic Review and Meta-Analysis. Medicine 94(50): e2255	
Yoo, Sangjun, You, Dalsan, Jeong, In Gab et al. (2017) Preserving Renal Function through Partial Nephrectomy Depends on Tumor Complexity in T1b Renal Tumors. Journal of Korean medical science 32(3): 495-501	- Primary study covered fully by an included systematic review
Yoon, Young Eun, Lee, Hyung Ho, Kim, Ki Hong et al. (2018) Focal therapy versus robot-assisted partial nephrectomy in the management of clinical T1 renal masses: A systematic review and meta-analysis. Medicine 97(45): e13102	- Study does not contain a relevant intervention
Yoshida, Kazuhiko, Oida, Nao, Kondo, Tsunenori et al. (2024) Surgical and functional outcomes of repeat robot-assisted laparoscopic partial nephrectomy compared with repeat open partial nephrectomy. International journal of urology : official journal of the Japanese Urological Association 31(4): 355-361	- Exclude RQC- Study included only patients T1-T2
You, Dalsan, Jeong, In Gab, Song, Cheryn et al. (2015) Analysis of pre-operative variables for identifying patients who might benefit from upfront cytoreductive nephrectomy for metastatic renal cell carcinoma in the targeted therapy era. Japanese journal of clinical oncology 45(1): 96-102	- Data not reported in an extractable format
Youn, C.S., Park, J.M., Lee, J.Y. et al. (2013) Comparison of laparoscopic ra diofrequency a blation and open partial nephrectomy in patients with a small renal mass. Korean Journal of Urology 54(9): 603-608	- Primary study covered fully by an included systematic review
Yu, Jie, Liang, Ping, Yu, Xiao-ling et al. (2014) US-guided percutaneous microwave ablation versus open radical nephrectomy for small renal cell carcinoma: intermediate-term results. Radiology 270(3): 880-7	- Non-OECD country

Study	Reason
Yu, Kun, Liu, Meiping, Xie, Zhenguo et al. (2020) Comparison of efficacy and long-term survival of laparoscopic radical nephrectomy with partial nephrectomy in the treatment of patients with early renal cell carcinoma Running title: laparoscopic radical nephrectomy. Journal of B.U.ON. : official journal of the Balkan Union of Oncology 25(2): 1155-1160	- Non-OECD country
Zaid, Harras B, Parker, William P, Safdar, Nida S et al. (2017) Outcomes Following Complete Surgical Metastasectomy for Patients with Metastatic Renal Cell Carcinoma: A Systematic Review and Meta-Analysis. The Journal of urology 197(1): 44-49	- Mixed population of SACT pre/post non-pharmacological regimens
Zaorsky, Nicholas G, Lehrer, Eric J, Kothari, Gargi et al. (2019) Stereotactic ablative radiation therapy for oligometastatic renal cell carcinoma (SABR ORCA): a meta-analysis of 28 studies. European urology oncology 2(5): 515-523	- Exclude - wrong population - Study did not compare the interventions of interest
Zargar, Homayoun, Bhayani, Sam, Allaf, Mohamad E et al. (2014) Comparison of perioperative outcomes of robot-assisted partial nephrectomy and open partial nephrectomy in patients with a solitary kidney. Journal of endourology 28(10): 1224-30	- Exclude - For RQC Proportion of patients stage T3 < 90%
Zeng, Zhiqiang, Ge, Si, Li, Yunxiang et al. (2024) Perioperative and Oncological Outcomes of Partial Versus Radical Nephrectomy for Complex Renal Tumors (RENAL Score >= 7): Systematic Review and Meta-Analysis. Annals of surgical oncology 31(7): 4762-4772	- Systematic review used as source of primary studies
Zhang, Fan, Hu, Jiang-Sheng, Zhang, Kai-Yu et al. (2023) Perioperative, functional, and oncologic outcomes of laparoscopic partial nephrectomy versus open partial nephrectomy for complex renal tumors: a systematic review and meta-analysis. Frontiers in oncology 13: 1283935	- Exclude - For RQC Proportion of patients stage T3 < 90%

Study	Reason
Zhang, M., Zhao, Z., Duan, X. et al. (2018) Partial versus radical nephrectomy for T1b-2N0M0 renal tumors: A propensity score matching study based on the SEER database. PLoS ONE 13(2): e0193530	- SEER database overlap
Zhang, Y., Hu, J., Xie, Y. et al. (2022) Selection of Optimal Candidates for Cytoreductive Nephrectomy in Patients with Metastatic Clear Cell Renal Cell Carcinoma: A Predictive Model Based on SEER Database. Frontiers in Oncology 12: 814512	- Mixed population of SACT pre/post non-pharmacological regimens
Zhang, Yu, Bi, Hai, Yan, Ye et al. (2023) Comparative analysis of surgical and oncologic outcomes of robotic, laparoscopic and open radical nephrectomy with venous thrombectomy: a propensity-matched cohort study. International journal of clinical oncology 28(1): 145-154	- Non-OECD country
Zhang, Yuanyuan, Schoenhals, Jonathan, Christie, Alana et al. (2019) Stereotactic Ablative Radiation Therapy (SAbR) Used to Defer Systemic Therapy in Oligometastatic Renal Cell Cancer. International journal of radiation oncology, biology, physics 105(2): 367-375	- Not a relevant study design - Mixed population of SACT pre/post non-pharmacological regimens
Zhang, Yucong, Long, Gongwei, Shang, Haojie et al. (2021) Comparison of the oncological, perioperative and functional outcomes of partial nephrectomy versus radical nephrectomy for clinical T1b renal cell carcinoma: A systematic review and meta-analysis of retrospective studies. Asian journal of urology 8(1): 117-125	- Systematic review used as source of primary studies
Zhang, Zhao, Wu, Hongliang, Yang, Tong et al. (2020) Metastatic renal cell carcinoma patients of T4 stage who are in status of N1 stage or older than 76 years cannot benefit from cytoreductive nephrectomy. BMC cancer 20(1): 844	- Mixed population of SACT pre/post non-pharmacological regimens *No information regarding SACT in both arms*
Zhao, Kaidong, Kim, Eric H, Vetter, Joel M et al. (2020) Laparoscopic cytoreductive nephrectomy is associated with significantly	- Exclude - Outcome was measured using a measure out of scope *OS reported in median months*

Study	Reason
improved survival compared with open cytoreductive nephrectomy or targeted therapy alone. Molecular and clinical oncology 13(6): 71	
Zhao, Z., Wu, W., Duan, X. et al. (2019) The value of cytoreductive nephrectomy on the survival of metastatic renal carcinoma patients based on the number of site-specific metastases. PLoS ONE 14(4): e0215861	- Mixed population of SACT pre/post non-pharmacological regimens *No information about the treatment received by non CN arm reported. The sequence of SACT reported is also not reported.*
Zhou, Minerva, Mills, Abigail, Noda, Christopher et al. (2018) SEER study of ablation versus partial nephrectomy in cT1A renal cell carcinoma. Future oncology (London, England) 14(17): 1711-1719	- Secondary publication of an included study that does not provide any additional relevant information *SEER database - more fully covered in another included study*
Zhuang, W, Chen, J, Li, Y et al. (2019) The effect of cytoreductive partial nephrectomy in elderly patients with metastatic renal cell carcinoma : a systematic review. ResearchSquare	- Exclude - Outcome was measured using a measure out of scope
Zini, Laurent, Perrotte, Paul, Jeldres, Claudio et al. (2008) Nephrectomy improves the survival of patients with locally advanced renal cell carcinoma. BJU international 102(11): 1610-4	- Comparator in study does not match that specified in protocol *Nephrectomy vs no surgery*

Economic studies

HE excluded at full text (n=2)

Study	Reason for exclusion
Health Improvement Scotland (2011) Evidence Note: Is radiofrequency ablation treatment a clinically and cost effective treatment to be offered to people with renal cancer in NHS Scotland? Is radiofrequency ablation treatment a clinically and cost effective treatment to be offered to people with renal cancer in NHSScotland? (york.ac.uk)	-Based on a US health economics study with a quasi-societal perspective and US costs.

Study	Reason for exclusion
Iossa, Vincenzo, Pandolfo, Savio Domenico, Buonopane, Roberto et al. (2025) Robot-assisted partial nephrectomy vs. percutaneous cryoablation for T1a renal tumors: a single-center retrospective analysis of outcomes and costs. International urology and nephrology 57(4): 1097-1104	- Exclude - cost analysis only, did not have a QoL outcome

Appendix K– Research recommendations – full details

K1.1 Research recommendation

What is the clinical and cost effectiveness of stereotactic ablative radiotherapy compared to surgical interventions, thermal ablation and active surveillance, for localised renal cell carcinoma?

K1.1.1 Why this is important

There is limited evidence currently available about the effectiveness of stereotactic ablative radiotherapy (SABR) for localised RCC, compared with other non-pharmacological interventions. Additional research could support the existing recommendations and provide more information about its effectiveness, particularly in comparison to thermal ablation.

K1.1.2 Rationale for research recommendation

Table 39: Rationale for research recommendation

Importance to 'patients' or the population	There is uncertainty about the relative effectiveness and safety of SABR in relation to other treatments for localised RCC. Understanding for whom SABR is best used would be clinically valuable.
Relevance to NICE guidance	SABR has been considered in this guideline and there is a low volume of evidence about effectiveness and safety compared with other treatments.
Relevance to the NHS	The outcome would affect the types of treatment for localised RCC provided by the NHS
National priorities	Low
Current evidence base	Minimal data
Equality considerations	None known

K1.1.3 Modified PICO table

Table 40: Modified PICO table

Population	Adults with histologically confirmed or suspected localised renal cell carcinoma (RCC)
Intervention	Stereotactic ablative radiotherapy (SABR), any dose or fractionation.

Comparator	• Surgery (partial or radical nephrectomy) • Thermal ablation • Active surveillance
Outcome	• Recurrence (disease-free survival; metastasis-free survival; local recurrence-free survival) • Survival (cancer-specific survival) • Intraoperative and postoperative adverse events (using the Common Terminology Criteria for Adverse Events) • Renal function (eGFR) • Cardiovascular events • Duration of hospital stay • Quality of life using a validated tool • Cost effectiveness
Study design	Prospective or retrospective cohort study The effects of confounding should be minimised (for example by using propensity score matching or adjusting for confounders in the analysis)
Timeframe	Long term for recurrence and survival outcomes
Additional information	None