NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of minimally invasive radical hysterectomy for early stage cervical cancer

Cervical cancer develops in the lower part of the womb (uterus) where it joins the top of the vagina (an area called the cervix). Early stage cervical cancer is confined to the cervix or has only spread to the top of the vagina. In a radical hysterectomy the cervix and the uterus along with other structures connected to them are removed with the aim of completely removing the cancer. In this procedure, the surgery is done through the abdomen using a tube with a camera on the end (laparoscope) with or without the assistance of a robot – this is known as “keyhole” or minimally invasive surgery.

Contents

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2019 and updated in January 2020.

Procedure name

- Minimally invasive radical hysterectomy for early stage cervical cancer

Specialist societies

- Royal College of Obstetricians and Gynaecologists
- British Society of Gynaecological Endoscopy
- British Gynaecological Cancer Society

Description of the procedure

Indications and current treatment

Cervical cancer is the second most common cancer in women under 35 years in the UK. The most common symptoms are abnormal vaginal bleeding or discharge, and discomfort during intercourse.

The International Federation of Gynecology and Obstetrics (FIGO) system is used to stage cervical cancer from 1 to 4. Early stage cervical cancer includes stage 1 (cancer confined to the cervix) to stage 2a (tumour has spread down into the top of the vagina).

Radical hysterectomy (also known as Wertheim's hysterectomy) is the most common surgical treatment for cervical cancer and is conventionally done through an incision in the abdomen or through the vagina. It includes removing the uterus and supporting ligaments, cervix, upper vagina, the pelvic lymph nodes and sometimes the para-aortic lymph nodes.

Radiotherapy may be used, with or without surgery, and is usually combined with chemotherapy. More advanced cervical cancer is generally treated with radiotherapy and chemotherapy.

What the procedure involves

Minimally invasive radical hysterectomy for early stage cervical cancer is done using general anaesthesia. A uterine manipulator is inserted through the vagina and attached to the uterus and cervix. The abdomen is insufflated with carbon dioxide, and several small incisions are made to provide access for the laparoscope and surgical instruments. A robot may be used to assist with the procedure. A hysterectomy is done by dividing the round ligaments, accessing the broad ligaments, dividing the uterine vessels and mobilising the uterus out of its peritoneal coverings by dividing the uterosacral ligaments. If the ovaries are to be left in position, the utero-ovarian ligaments are transected. The pelvic lymph nodes and sometimes the para-aortic lymph nodes are removed through 1 of the abdominal incisions or through the vagina. The upper vagina, cervix and uterus are removed through the vagina.

The technique is distinct from laparoscopically assisted vaginal hysterectomy, which combines laparoscopic division of the infundibulopelvic ligaments and the uterine vessels, before a vaginal hysterectomy is done.

A nerve-sparing radical hysterectomy is a modified technique that preserves pelvic nerves to prevent bladder dysfunction.

The aim is to remove all the cancer. The suggested benefits of the laparoscopic approach are shorter length of stay in hospital, shorter recovery period and minimal abdominal scarring.

Efficacy summary

Overall survival

In a randomised controlled trial (RCT) of 631 patients with FIGO stage 1A1, 1A2 or 1B1 cervical cancer, 3-year overall survival was 94% in patients who had minimally invasive surgery (laparoscopic radical hysterectomy [LRH] or robot-assisted radical hysterectomy [RRH]). It was 99% in those who had open radical hysterectomy (ORH) (hazard ratio [HR] for death from any cause 6.00, 95% confidence interval [CI] 1.77 to 20.30).[1]

In a non-randomised comparative study of 2,461 patients with FIGO stage 1A2 or 1B1 cervical cancer, the risk of death within 4 years of diagnosis was 9% in patients who had minimally invasive surgery (LRH or RRH) compared with 5% of patients who had ORH (HR 1.65, 95% CI 1.22 to 2.22, p=0.002).[2]

In a systematic review of 2,922 patients with cervical cancer treated with LRH or ORH, there was no statistically significant difference in 5-year overall survival between LRH and ORH (HR −0.02, 95% CI −0.14 to 0.10, p=0.73).[9]

In a non-randomised comparative study of 593 patients with FIGO stage 1B2 to 2A2 cervical cancer, 5-year overall survival was 94% for patients who had LRH and 92% for those who had ORH (p=0.788).[3]

In a non-randomised comparative study of 678 patients with stage 1A2 to 2A cervical cancer treated with LRH or ORH, there were no statistically significant differences between the groups in overall survival (HR=0.61, 95% CI 0.32 to 1.15, p=0.122). Mortality was 5% in the LRH group and 9% in the ORH group (median follow-up 47 months).[6]

In a non-randomised comparative study of 1,863 patients with FIGO stage 1A2 to 2A2 cervical cancer, 5-year overall survival was 94% for patients who had LRH and 90% for those who had ORH (p=0.260).[7]

In a non-randomised comparative study of 6,335 patients with cervical cancer, Kaplan−Meier analysis showed a statistically significant better overall survival in patients who had LRH compared with those who had ORH (adjusted HR for all-cause mortality 0.61, 95% CI 0.53 to 0.70, p<0.001).[4]

In a non-randomised comparative study of 188 patients, overall survival was 93% in the minimally invasive surgery group (LRH or RRH) compared with 81% in the ORH group (p=0.03), with a median follow up of 112 months.[5]

In a non-randomised comparative study of 929 patients with stage 1A2, 1B or 1B1 cervical cancer, overall survival was statistically significantly lower in the minimally invasive surgery group compared with the open surgery group (93% compared with 97% at 4.5 years, p=0.007).[18]

In a non-randomised comparative study of 958 patients, all-cause mortality was 8% (39/473) in the minimally invasive surgery group (mean follow-up 5.3 years) and 10% (46/485) in the open surgery group (mean follow-up 6.7 years) (p=0.04). For patients with stage 1B disease, after adjusting for patient and surgeon factors, minimally invasive surgery was associated with increased risks of all-cause death (HR 2.20, 95% CI 1.15 to 4.19) compared with open surgery. For patients with stage 1A disease, there were no statistically significant associations.[15]

Disease-free survival

In the RCT of 631 patients, 3-year disease-free survival was 91% in patients who had minimally invasive surgery and 97% in those who had ORH (HR for disease recurrence or death from cervical cancer 3.74, 95% CI 1.63 to 8.58). Disease-

free survival at 4.5 years was 86% in the minimally invasive group and 97% in the ORH group (a difference of −10.6 percentage points, 95% CI, −16.4 to −4.7; p=0.87 for non-inferiority).[1]

In the non-randomised comparative study of 593 patients, 5-year progression-free survival was 79% for patients who had LRH and 90% for those who had ORH (p<0.001). Multivariate analysis identified laparoscopic surgery as an independent poor prognostic factor for progression-free survival (adjusted HR 2.88, 95% CI 1.71 to 4.86, p<0.001).[3]

In the systematic review of 2,922 patients, there was no statistically significant difference in 5-year disease-free survival between LRH and ORH (HR 0.01, 95% CI -0.10 to 0.11, p=0.91).[9]

In the non-randomised comparative study of 678 patients, there were no statistically significant differences between the groups in progression-free survival (HR=0.77, 95% CI 0.47 to 1.25, p=0.285). [6]

In the non-randomised comparative study of 1,863 patients, 5-year disease-free survival was 94% for patients who had LRH and 89% for those who had ORH (p=0.292).[7]

Survival by tumour size

In the non-randomised comparative study of 678 patients, for a tumour diameter bigger than 4 cm there was a statistically significantly shorter overall survival for patients who had LRH compared with ORH (HR=3.36, 95% CI 1.16 to 9.68, p=0.017). Conversely for tumour diameter 4 cm or less, overall survival of patients in the LRH group was statistically significantly longer than the ORH group (HR=0.37, 95% CI 0.16 to 0.84, p=0.013). There were no statistically significant differences in progression-free survival: for tumours bigger than 4 cm, HR=0.78, 95% CI 0.45 to 1.35 and for tumours 4 cm or smaller, HR=1.20, 95% 0.40 to 3.60, p=0.756.[6]

In a non-randomised study of 2,461 patients, the risk of death within 4 years after diagnosis was statistically significantly higher in patients who had MIS compared with ORH (9.1% compared with 5.3%, HR=1.65, 95% CI 1.22 to 2.22, p=0.002). A subgroup analysis showed that there was a statistically significant increased risk in patients who had a tumour sized 2 cm or above (HR=1.66, 95% 1.19 to 2.30). There was also an increased risk for patients with a tumour smaller than 2 cm but it did not reach statistical significance (HR=1.46, 95% 0.70 to 3.02).[2]

In a non-randomised comparative study of 593 patients who had LRH or ORH, for patients with a tumour 2 cm or smaller, there were no statistically significant differences in 5-year overall survival or progression-free survival between the groups. For patients with a tumour sized between 2 and 4 cm, those who had

LRH had a statistically significant lower 5-year progression-free survival than those who had ORH (72% compared with 87%, p=0.044). Overall survival was 88% and 92% respectively, p=0.907.[3]

In a matched cohort study of 565 patients, patients who had LRH had a statistically significantly lower 3-year progression-free survival than those who had ORH (85% compared with 92%, p=0.036). 5-year overall survival was similar in the 2 groups (97% compared with 95%, p=0.4). For patients with a tumour 2 cm or smaller there was no statistically significant difference in 3-year progression (90% compared with 93%, p=0.8) or 5-year overall survival (99% compared with 96%, p=0.6).[16]

In a cohort study of 779 patients who had a radical hysterectomy by any approach, mortality was 0.6% (3/452) for patients who had a tumour smaller than 2 cm and 3.1% (8/256) for patients who had a tumour sized 2 cm or above (p<0.01).[17]

Recurrence

In the RCT of 631 patients, there were 27 recurrences in the 319 patients who had minimally invasive surgery and 7 recurrences in the 312 patients who had ORH, with a median follow up of 2.5 years.[1]

In the non-randomised comparative study of 593 patients, recurrence rates were 16% in the LRH group and 11% in the ORH group.[3]

In the non-randomised comparative study of 188 patients, recurrence rates were 15% in the minimally invasive surgery group compared with 14% in the ORH group (p=0.64), with a median follow up of 112 months.[5]

In the non-randomised comparative study of 678 patients, recurrence rates were 10% in the LRH group and 13% in the ORH group (median follow up 47 months).[6]

In the non-randomised comparative study of 1,863 patients, recurrence rates were 4% (35/1,007; 14 local, 21 metastasis) in the LRH group (mean follow up 52 months) and 5% (35/740; 16 local, 19 metastasis) in the ORH group (mean follow up 69 months, p=0.269).[7]

In a systematic review of 2,197 patients with cervical cancer treated with LRH, RRH or ORH, there was no statistically significant difference in recurrence between RRH and LRH (odds ratio [OR] 0.96, 95% CI 0.50 to 1.87, p=0.91) or between RRH and ORH (OR 0.85, 95% CI 0.58 to 1.27, p=0.43).[8]

In the systematic review of 2,922 patients with cervical cancer treated with LRH or ORH, there was no statistically significant difference in recurrence between LRH and ORH (OR 0.82, 95% CI 0.61 to 1.11, p=0.20).[9]

In the non-randomised comparative study of 958 patients, minimally invasive surgery was associated with increased risks of recurrence (HR 1.97, 95% CI 1.10 to 3.50) after adjusting for patient and surgeon factors in patients with stage IB disease compared with open surgery.[15]

Length of hospital stay

In the RCT of 631 patients, the median length of hospital stay was 3 days in the minimally invasive surgery group compared with 5 days in the ORH group (p value not reported).[1]

In the non-randomised comparative study of 1,863 patients, the hospital stay was statistically significantly shorter in the LRH group compared with ORH (19 days compared with 30 days, p<0.05).[7]

In the systematic review of 2,197 patients, the hospital stay was statistically significantly shorter in the RRH group compared with ORH (weighted mean difference −2.71, p<0.01; 6 studies).[8]

In the systematic review of 2,922 patients, the hospital stay was statistically significantly shorter in the LRH group compared with ORH (weighted mean difference −4.36, 95% CI −5.38 to −3.34, p<0.00001; 16 studies).[9]

Postoperative adjuvant therapy

The rate of postoperative adjuvant therapy was similar between the 2 treatment groups in the RCT of 631 patients. Of the patients in the minimally invasive group, 25% had radiotherapy, and in the open group 23% had radiotherapy (p=0.56). In the minimally invasive group, 23% of patients had chemotherapy, and in the open group, 21% had chemotherapy (p=0.67).[1]

In the non-randomised comparative study of 2,461 patients, similar rates of adjuvant radiotherapy and adjuvant chemotherapy were given. In the minimally invasive group, 22% of patients had radiotherapy compared with 21% in the open group and 17% and 14% of patients respectively had adjuvant chemotherapy.[2]

There was a statistically significantly lower rate of postoperative adjuvant therapy in the LRH group compared with the ORH group in the non-randomised comparative study of 6,335 patients (adjusted OR 0.63, 95% 0.57 to 0.69, p<0.001).[4]

Safety summary

Overall complications

Intraoperative complications were reported in 12% of patients who had minimally invasive surgery and 10% of patients who had open surgery in the RCT of 631 patients (p=0.45). Early postoperative complications (less than 6 weeks after surgery) were reported in 43% and 40% of patients respectively (p=0.49). [1]

The rate of intraoperative complications was similar between LRH and ORH in the non-randomised comparative study of 1,863 patients (8% [87/1,071] compared with 11% [85/792], p=0.068). The rate of postoperative complications was statistically significantly lower in the LRH group compared with the ORH group (34% [362/1,071] compared with 40% [318/792], p=0.007).[7]

There was a statistically significantly lower rate of intraoperative complications in the LRH group compared with the ORH group in the non-randomised comparative study of 6,335 patients (adjusted OR 0.80, 95% 0.72 to 0.90, p=0.008). The adjusted OR for postoperative complications was 0.87, 95% 0.80 to 0.95, p=0.002.[4]

There was a statistically significantly lower rate of intraoperative complications in the RRH group compared with the ORH group in the systematic review of 2,197 patients (OR 0.52, p=0.04). The rate of postoperative complications was similar between the groups (OR 0.74, p=0.24).[8]

There was a statistically significantly lower rate of postoperative complications in the LRH group compared with the ORH group in the systematic review of 2,922 patients (OR 0.75, 95% CI 0.62 to 0.91, p=0.003; 18 studies, I^2=60%). The rate of intraoperative complications was similar between the groups (OR 1.48, 95% CI 0.75 to 2.91, p=0.25; 10 studies, I^2=0%).[9]

Death

Perioperative death was reported in 1 patient who had minimally invasive surgery and 3 patients who had open surgery in the non-randomised comparative study of 2,461 patients.[2]

Conversions to open surgery

Conversion to laparotomy was reported in 2% (2/90) of patients who had LRH in the non-randomised comparative study of 188 patients. Both were necessary because of ureteral damage.[5]

Vaginal cuff dehiscence

Vaginal cuff dehiscence was reported in 7% (6/90) of patients who had LRH in the non-randomised comparative study of 188 patients.[5]

Ureteric, bladder or bowel injury

Ureter injury was reported in 2% (5/279) of patients who had minimally invasive surgery and 2% (4/257) of patients who had open surgery in the RCT of 631 patients (p=0.83). Bladder injury was reported in 3% (7/279) and 1% (2/257) of patients respectively (p=0.11) and bowel injury was reported in 1% (2/279) and less than 1% (1/257) of patients respectively (p=0.61).[1]

Ureteric injury was reported in 2% (2/90) of patients who had LRH and 1% (1/76) of patients who had ORH in the non-randomised comparative study of 188 patients. In the same study, urinoma and intestinal perforation were each reported in 1 patient who had LRH.[5]

Injury to the urinary or gastrointestinal tract was reported in 4% (43/1,071) of patients who had LRH and 3% (24/792) of patients who had ORH in the non-randomised comparative study of 1,863 patients.[7] Intraoperative bowel or urinary injury did not differ statistically significantly between LRH and ORH in the systematic review of 2,922 patients (OR 1.50, 95% CI 0.99 to 2.26, p=0.06; 17 studies, I^2=0%).[9]

Urinary complications

Urinary tract infection was reported in 3% (3/90) of patients who had LRH and 8% (6/76) of patients who had ORH in the non-randomised comparative study of 188 patients. In the same study, acute urine retention was reported in 3% (3/90) of patients who had LRH, 14% (3/22) of patients who had RRH and 1% (1/76) of patients who had ORH.[5]

Urinary retention was reported in 24% (257/1,071) of patients who had LRH and 28% (222/792) of patients who had ORH in the non-randomised comparative study of 1,863 patients (p=0.06).[7]

Bowel complications

Acute colonic pseudo-obstruction after RRH for cervical cancer was described in a case report.[13]

Ileus was reported in 1% (1/90) of patients who had LRH and 5% (4/76) of patients who had ORH in the non-randomised comparative study of 188 patients.[5]

Vascular injury

Vascular injury was reported in 1% (4/279) of patients who had minimally invasive surgery and 1% (3/257) of patients who had open surgery in the RCT of 631 patients (p=0.79).[1]

'Obturator vein lesion' was reported in 1 patient who had LRH in the non-randomised comparative study of 188 patients. 'Cava vein lesion', 'internal iliac vein lesion' and 'external iliac vein lesion' were each reported in 1 patient in the ORH group.[5]

Vessel injury was reported in 3% (28/1,071) of patients who had LRH and 8% (61/792) of patients who had ORH in the non-randomised comparative study of 1,863 patients (p<0.001).[7]

Nerve injury

Nerve injury was reported in 2% (6/279) of patients who had minimally invasive surgery and less than 1% (1/257) of patients who had open surgery in the RCT of 631 patients (p=0.06).[1]

Lymphocele or lymphocyst

Lymphocele was reported in 1 patient who had RRH in the non-randomised comparative study of 188 patients.[5]

Haematoma

Pelvic haematoma was reported in 1 patient who had LRH and abdominal wall haematoma was reported in 1 patient who had ORH in the non-randomised comparative study of 188 patients.[5]

Blood transfusions

Blood transfusion was reported in 2% (5/279) of patients who had minimally invasive surgery and 5% (12/257) of patients who had open surgery in the RCT of 631 patients (p=0.06).[1]

There was a statistically significant lower rate of blood transfusions in the LRH group compared with the ORH group in the non-randomised comparative study of 6,335 patients (adjusted OR 0.30, 95% 0.28 to 0.33, p<0.001).[4]

Blood transfusions were reported in 3% (3/90) of patients in the LRH group and 22% (17/76) of patients in the ORH group in the non-randomised comparative study of 188 patients (p value not reported).[5]

Surgical site complications

Surgical site infection was reported in 2% (5/279) of patients who had minimally invasive surgery and 2% (4/257) of patients who had open surgery in the RCT of 631 patients. Wound complications were reported in 1% (4/279) and 6% (16/257) of patients respectively ($p<0.05$).[1]

There was a statistically significant lower rate of surgical site complications in the LRH group compared with the ORH group in the non-randomised comparative study of 6,335 patients (adjusted OR 0.75, 95% 0.66 to 0.86, $p<0.001$).[4]

Wound dehiscence was reported in 1% (7/1,071) of patients who had LRH and 4% (32/792) of patients who had ORH in the non-randomised comparative study of 1,863 patients ($p<0.001$).[7]

Port-site metastasis

Port-site metastasis has been reported after LRH and after RRH; a study published in 2010 stated that there had been 25 reported cases of laparoscopic port-site metastasis in patients with cervical cancer.[10,11]

Vaginal vault complications

Vaginal vault complications were reported in 4% (11/279) of patients who had minimally invasive surgery and 1% (2/257) of patients who had open surgery in the RCT of 631 patients.[1]

Other

Cerebral oedema after RRH and lower extremity compartment syndrome after LRH were each described in a case report.[12, 14]

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, specialist advisers described the following anecdotal adverse event: recognition of early recurrences. They considered that the following was a theoretical adverse event: manipulating the cervix with cancer present.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to minimally invasive radical hysterectomy for early stage cervical cancer. The following databases were searched, covering the period from their start to 24 October 2019: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with early stage cervical cancer
Intervention/test	Minimally invasive radical hysterectomy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base

List of studies included in the IP overview

This IP overview is based on over 20,000 patients from 1 RCT (2 publications), 8 non-randomised comparative studies, 1 cohort study, 2 systematic reviews, 5 case reports and a report from the National Cancer Registration and Analysis Service.[1–19]

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) are listed in the appendix.

Table 2 Summary of key efficacy and safety findings on minimally invasive radical hysterectomy for early stage cervical cancer

Study 1a Ramirez P (2018), 1b Obermair A (2019)

Details

Study type	**Randomised controlled trial**
Country	US, Argentina, Australia, Brazil, Bulgaria, China, Colombia, Italy, Republic of Korea, Mexico, Peru and Puerto Rico
Recruitment period	2008 to 2017
Study population and number	**n=631** Randomly assigned to: 319 MIS, 312 open surgery Patients with FIGO stage 1A1 (lymphovascular invasion), 1A2 or 1B1 cervical carcinoma
Age	Mean 46 years
Patient selection criteria	Inclusion criteria: • FIGO stage 1A1, 1A2, 1B1 • Histological subtype: squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma • No node involvement • Eastern Cooperative Oncology Group performance status score of 0 or 1 Exclusion criteria: • Uterine size >12cm in length • History of abdominal or pelvic radiotherapy • Evidence of metastatic disease on positron-emission tomography-computed tomography, magnetic resonance imagining or computed tomography • If considered by the investigator to be unable to have surgery, or unable to withstand lithotomy and the steep Trendelenburg position
Technique	MIS group included laparoscopic (84%) or robot-assisted radical hysterectomy. Type II or III radical hysterectomy. Adjuvant radiotherapy or chemotherapy were offered according to the practice of each centre.
Follow up	**Median follow up 2.5 years (range 0 to 6.3 years)**
Conflict of interest/source of funding	Funding: • Departmental research fund in the Department of Gynaecologic Oncology and Reproductive Medicine, University of Texas Anderson Cancer Center. • Grant from Medtronic One author reported grants from Clovis and AbbVie and grants and personal fees from AstraZeneca, Janssen, and Genentech/Roche outside the submitted work. One author reported grants and personal fees from Novadaq/Stryker, personal fees from Johnson and Johnson, and grants from Navidea outside the submitted work. One author reported grants, personal fees and other support from Surgical Performance PTY LTD outside the submitted work. In addition, they have a patent, Surgical Performance in class 09 (International Trademark No. 1196847) licensed to Surgical Performance IP (QLD) Pty Ltd.

Analysis

Follow-up issues: The trial was permanently closed before the full sample size had been recruited, because of sufficiently strong evidence that there was an imbalance in deaths between the MIS and open surgery groups. Because of early termination only 60% of patients had reached the 4.5-year time point for follow up of the primary outcome. All sites were instructed to submit any missing follow-up data at this point. Drop out from the randomised treatment arms is shown below:

Drop out after randomisation	MIS	Open
Did not have surgery they were assigned to	30	38
Withdrew from surgery	12	19
Surgery aborted	16	11
Switched treatment group before surgery	2	8
N received treatment assigned:	**259**	**236**
Assigned to MIS and had MIS	• LRH: 84.4% • RRH: 15.6%	Not applicable

Of 631 patients randomised, 536 (85%) met the inclusion criteria for the analysis of adverse events (Obermair et al., 2019).

Study design issues: Multicentre, randomised controlled trial. Randomisation was done with a web-based system, using the method of minimisation with equal assignment to treatment groups. The choice of laparoscopic or robot-assisted was at the surgeon's discretion. the primary objective to evaluate the hypothesis that laparoscopic or robot-assisted radical hysterectomy (minimally invasive surgery) was not inferior to open abdominal radical hysterectomy (open surgery) with respect to the percentage of patients who were disease-free at 4.5 years after surgery. Although the study was terminated early, data was available to provide a high degree of power (84%). An independent recurrence adjudication committee reviewed all recurrences to ensure these were because of disease and verify the location of recurrence. Intention-to-treat analysis and per protocol analysis were done.

Study population issues: The treatment groups were balanced with respect to baseline characteristics. Most patients included had FIGO stage 1B1 cervical cancer (92%).

Other issues: Results of the trial cannot be generalised to patients with 'low risk' cervical cancer (tumour size less than 2 cm, no lymphovascular invasion, depth of invasion less than 10 mm and no lymph node involvement) because the trial was not powered to assess outcomes in patients with these clinical presentations.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **Total: 631**. **319 (50.6%) MIS (including both LRH and RRH) and 312 (49.4%) open surgery.**

Operative data

	MIS n=319	Open n=312
Surgery, n (%)		
1A1	5 (1.6)	5 (1.6)
1A2	21 (6.6)	20 (6.4)
1B1	293 (91.8)	287 (92)
Median length of hospital stay. Days (range)	3 (0-72)	5 (0-69)
Conversion n (%)	10 (3.5)	0
Tumour grade III (%)	21	21.6
Tumour size ≥2cm (%)	42.3	42.9
Parametrial invasion (%)	6.5	3.9
Lymph node involvement (%)	12.4	13.1
Lymphovascular invasion (%)	24.1	28.7
Superficially invasive tumours (%)	28.5	21.6

Postoperative adjuvant treatment:

	MIS n (%)	**Open n (%)**	**p**
Radiotherapy	81 (25.4)	73 (23.4)	0.56
Chemotherapy	72(22.6)	66 (21.2)	0.67

Total deaths (n)
- MIS: 19
- Open: 3

Recurrence (n)
- MIS: 27
- Open: 7

4.5-year disease-free survival (%)
- MIS: 86.0
- Open: 96.5, (difference −10.6 percentage points (95% CI, −16.4 to −4.7) p=0.87 for non-inferiority

Results were consistent between LRH and RRH.

3-year disease-free survival (%)
- MIS: 91.0
- Open: 97.1

HR for disease recurrence or death from cervical cancer: 3.74 95% CI (1.63 to 8.58)

Overall survival at 3 years (%)
- MIS: 93.8
- Open: 99.0, HR: 6.00 95% CI (1.77 to 20.30)

Death rate from cervical cancer at 3 years (%)
- MIS: 4.4
- Open: 0.6, HR: 6.56 95% CI (1.48 to 29.00)

Locoregional recurrence-free survival at 3 years (%)
- MIS: 94.3
- Open: 98.3, HR: 4.26 95% CI (1.44 to 12.6)

Safety

Adverse events reported in Obermair et al. (2019), n=536

Adverse event	MIS n=279	ORH n=257	p
Any adverse event	59%	53%	0.17
Intraoperative adverse event	12%	10%	0.45
Postoperative adverse event	54%	48%	0.14
Early postoperative (up to 6 weeks after surgery)	43%	40%	0.49
Delayed postoperative (3 to 6 months after surgery)	25%	20%	0.18
Major adverse event*	18%	16%	0.54
Serious adverse event#	14%	12%	0.43

* CTCAE grade 3 or above, or a serious adverse event as defined below

an adverse event that needed inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability or incapacity, was life-threatening, or resulted in death.

Intraoperative complications (patients who experienced the given complication at least once)

	MIS, n (%)	ORH, n (%)	p
Blood transfusion	5 (1.8)	12 (4.7)	0.06
Ureter injury	5 (1.8)	4 (1.6)	0.83
Vascular injury	4 (1.4)	3 (1.2)	0.79
Bladder injury	7 (2.5)	2 (0.8)	0.11
Nerve injury	6 (2.2)	1 (0.4)	0.06
Bowel injury	2 (0.7)	1 (0.4)	0.61
Uterus rupture	3 (1.1)	0 (0)	0.24
Vaginal laceration	2 (0.7)	0 (0)	0.39
Other	5 (1.8)	3 (1.2)	0.55

Postoperative complications (patients who experienced the give complication at least once)

	MIS, n (%)	ORH, n (%)
Adverse events by organ system		
Any urinary adverse event	63 (22.6)	46 (17.9)
Any gastrointestinal adverse event	44 (15.8)	36 (14.0)
Any pulmonary adverse event	5 (1.8)	3 (1.2)
Any cardiac adverse event*	2 (0.7)	10 (3.9)
Any sepsis adverse event	2 (0.7)	2 (0.8)
Any other adverse event	95 (34.1)	86 (33.5)
Individual adverse events		
Pain	19 (6.8)	24 (9.3)
Anaemia	16 (5.7)	16 (6.2)
Delay to bladder function	13 (4.7)	13 (5.0)
Vaginal vault complications*	11 (3.9)	2 (0.8)
Genitourinary fistula or stricture	10 (3.6)	7 (2.7)
Nausea	8 (2.9)	9 (3.5)
Neuropathy	7 (2.5)	2 (0.8)
Febrile morbidity	6 (2.2)	2 (0.8)
Surgical site infection	5 (1.8)	4 (1.6)
Wound complications*	4 (1.4)	16 (6.2)
Obstruction	3 (1.1)	1 (0.4)

Anxiety	2 (0.7)	3 (1.2)
Acute renal injury	1 (0.4)	1 (0.4)
Gastrointestinal fistula	1 (0.4)	0 (0)
Deep vein thrombosis/pulmonary embolism	1 (0.4)	0 (0)
Lymphoedema	1 (0.4)	2 (0.8)
Incisional or port site hernia	0 (0)	1 (0.4)
Ileus	0 (0)	2 (0.8)
Lymphocele formation	0 (0)	3 (1.2)

* p<0.05

Abbreviations used: CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; MIS, minimally invasive surgery; RRH, robotic radical hysterectomy; CI confidence interval. HR, hazard ratio

Study 2 Melamed A (2018)

Details

Study type	**Non-randomised comparative study**
Country	US
Recruitment period	2000 to 2013
Study population and number	**n=2,461 (247 LRH, 978 RRH, 1,236 open)** Patients with FIGO stage 1A2 or 1B1 cervical carcinoma
Age	Not reported
Patient selection criteria	Inclusion criteria: diagnosed with FIGO stage 1A2 or 1B1 squamous cell carcinoma, adeno-squamous carcinoma or adenocarcinoma of the cervix, who had a diagnosis between 2010-2013 and who had had radical hysterectomy as the primary treatment. Exclusion criteria: • Surgical approach unknown • Pre-existing cancer diagnosis • Lack of pathological confirmation of cancer • Had had neoadjuvant chemotherapy or radiotherapy • Those who did not have pelvic lymphadenectomy • Lymphadenectomy status unknown The factors impacting choice of technique is not recorded.
Technique	1,225 (49.8%) patients had MIS (including both LRH and RRH) and 1,236 (50.2%) patients had open surgery. Of those who had MIS, 247 (20.1%) patients had LRH and 978 (79.8%) patients had RRH. Data regarding rationale for use of adjuvant therapy is not included.
Follow up	**Median follow up in propensity score weighted cohort was 45 months.**
Conflict of interest/source of funding	Supported by grants from the National Cancer Institute, the National Institute of Child Health and Human Development, the American Association of Obstetricians and Gynaecologists Foundation, the Foundation for Womens Cancer, the Jean Donovan Estate and the Phebe Novakovic Fund. One author received consulting fees from Clovis Oncology and Tesaro. One author reported holding patents licensed to Corcept Therapeutics on methods and compositions related to glucorticoid-receptor antagonists and breast cancer, for which they receive royalties Also, a pending patent licensed to Corcept Therapeutics on methods and compositions related to glucorticoid-receptor antagonists and breast cancer, for which they receive royalties.

Analysis

Follow-up issues: Follow-up data not fully reported; no losses to follow up reported. Deaths reported for MIS or open surgery only (n=94 and 70 respectively), but not for LRH or RRH specifically.

Study design issues: Cohort study using data from the National Cancer Database and data from STEER database to support survival analysis. Factors impacting choice of technique were not reported. Inverse Probability of Treatment Weighting was used to adjust for pretreatment differences in characteristics between MIS or open surgery. The characteristics included year of diagnosis, age, race or ethnic group, facility type (academic or non-academic), geographic region, rural or urban status, ZIP Code-level income and education levels, presence of coexisting conditions, stage of disease, histologic type, tumour grade and tumour size.

The primary outcome of interest was the time to death, as recorded by the cancer registrar and ascertained through the end of 2016. Additional outcomes included the 4-year survival rate, death within 90 days after surgery, number of lymph nodes evaluated, frequency of positive lymph nodes, parametrial involvement, and positive surgical margins. In the

primary intention-to-treat analysis, all the patients who started with a laparoscopic or robot-assisted approach were categorised as having had minimally invasive surgery, even when conversion to open surgery occurred.

Most analysis completed compared MIS with open surgery. Only propensity score weighted results were reported. Results were reported jointly for 1A2 and 1B1 cervical carcinoma. Sensitivity analysis was conducted to assess robustness of findings and a quasi-experimental interrupted time series analysis was conducted to test whether findings from the patient level analysis could be because of a causal effect of MIS.

Study population issues: The study included patients who were diagnosed in Commission on Cancer accredited centres, which account for approximately 70% of newly diagnosed cancer cases in the US. This means patients not diagnosed in these centres have not been included in the analysis.

Of 2,793 patients who were identified on the National Cancer Database with stage 1A2 or 1B1 cervical cancer, who had radical hysterectomy in 2010-2013, 332 (11.5%) were excluded based on the criteria listed above. Most exclusions were because the surgical approach was ‘unknown’ (n=168, 50.6%), because of pre-existing cancer diagnosis (n=98, 29.5%) or did not have lymphadenectomy / the lymphadenectomy status was unknown (n=46, 13.9%).

Women having MIS were more likely to be of white ethnicity, have private health insurance, live in areas with higher levels of education and income and to have smaller, lower grade tumours and adenocarcinomas. This difference was adjusted for using inverse probability of treatment weighting.

For the time series analysis, data from the Surveillance, Epidemiology and End Results (SEER) 18-registry database was also used to include data before 2004 because this was not available for the National Cancer Database. SEER includes data covering 28% of the US population.

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>
Number of patients analysed: Total: 2,461. 1225 (49.8%) MIS (including both LRH and RRH) and 1,236 (50.2%) open surgery.

Operative data (propensity score weighted)
<table>
<tr><th></th><th>MIS n=1225</th><th>Open n=1236</th><th>p</th></tr>
<tr><td>Surgery, n (%)</td><td></td><td></td><td>-</td></tr>
<tr><td>1A2</td><td>155 (11.6)</td><td>157 (11.7)</td><td>0.94</td></tr>
<tr><td>1B1</td><td>1179 (88.4)</td><td>1183 (88.3)</td><td></td></tr>
<tr><td>Parametrial invasion % (95% CI)</td><td>11% (9.1 to 13.2)</td><td>9.5% (7.7 to 11.6)</td><td></td></tr>
<tr><td>Rate of positive margins (95% CI)</td><td>5% (3.7 to 6.6)</td><td>4.4% (3.2 to 6.0)</td><td></td></tr>
<tr><td>Lymph node involvement (95% CI)</td><td>10.7% (8.9 to 12.9)</td><td>8.9% (7.2 to 11.0)</td><td></td></tr>
<tr><td>Lymphovascular space invasion (95% CI)</td><td>31.9% (28.9 to 35)</td><td>28% (25.1 to 31)</td><td></td></tr>
</table>
Adjuvant treatment:
Radiotherapy:
• MIS=22.1% (95% CI 19.5 to 24.9)
• Open=20.9% (95% CI 18.4 to 23.7)
Chemotherapy:
• MIS=16.8% (95% CI 14.5 to 19.4)
• Open=13.6% (95% CI 11.6 to 16.0)

Deaths
• MIS: 94
• Open: 70

Survival
The risk of death within 4 years after diagnosis:
• MIS: 9.1%
• Open: 5.3%, p=0.002 by log rank test; HR=1.65 (95% CI 1.22 to 2.22)
Equates to having 65% higher risk of death within 4 years post diagnosis among women having MIS compared with those underdoing open surgery.

Exploratory subgroup analysis – HR for death (all cause mortality) with MIS
RRH vs open: HR=1.61 (95% CI 1.18 to 2.21), LRH vs open: HR=1.50 (95% CI 0.97 to 2.31)
Tumour size <2 cm: HR=1.46 (95% CI 0.70 to 3.02)
Tumour size ≥2 cm: HR=1.66 (95% CI 1.19 to 2.30)

Interrupted time series analysis results:
Before MIS in the US (2000-2006) = non-significant trend toward longer survival, measured by 4-year relative survival (0.3% 95% CI -0.1 to 0.6)

After MIS used in the US (2006 – 2010) = statistically significant (p=0.01) trend toward decline in survival rate, measured by 4-year relative survival (0.8% 95% CI 0.3 to 1.4)
</td><td>
Perioperative death:
• MIS, n=1
• Open, n=3
</td></tr>
<tr><td colspan="2">Abbreviations used: CI confidence interval; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; LRH, laparoscopic radical hysterectomy; MIS, minimally invasive surgery; RRH, robotic radical hysterectomy</td></tr>
</table>

Study 3 Kim SI (2019a)

Details

Study type	**Non-randomised comparative study**
Country	Republic of Korea
Recruitment period	2000 to 2018
Study population and number	**n=593 (158 laparoscopic radical hysterectomy, 435 open radical hysterectomy)** Patients with cervical cancer FIGO stage 1B2 to 2A2
Age	For the 349 patients with FIGO stage 1BI disease and preoperative MRI: mean 51 years (53 years in laparoscopic group, 50 years in open group, p=0.012)
Patient selection criteria	Patients with FIGO stage 1B1 to 2A2 disease who had primary surgical treatment. Patients were only included if they had Type C radical hysterectomy according to Querleu and Morrow's classification. Patients with the following characteristics were excluded: fertility-sparing surgery, total mesometrial resection or vaginal total hysterectomy; neoadjuvant chemotherapy before surgery; histological types other than squamous cell carcinoma, usual type adenocarcinoma or adenosquamous carcinoma; insufficient clinical or pathological data.
Technique	Minimally invasive group: laparoscopic surgery (13 patients who had robot-assisted surgery were excluded) Open group: traditional laparotomy Adjuvant radiation therapy was offered to patients when 1 or more pathological risk factors were present (involvement of parametrium, resection margin, or lymph node). In patients with node-negative, margin-negative, parametrium-negative disease, adjuvant radiation therapy was offered selectively according to the presence of intermediate risk factors (lymphovascular space invasion, stromal invasion, and tumour size).
Follow up	**Median 115 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Losses to follow up were not described. The authors noted there was a statistically significant difference in the observation period between the 2 groups because of a high rate of laparoscopic surgery within the last 5 years.

Study design issues: Retrospective, single-centre, non-randomised comparative study. Patients were identified from a cancer registry. The main aim of the study was to compare survival outcomes by surgery type. Survival status was obtained from Statistics Korea, a service of the South Korean government, using the patients' resident registration numbers. Overall survival was defined as the time interval between the date of initial diagnosis and the date of cancer-related death or the end of the study. Progression-free survival was defined as the time interval between the date of initial diagnosis and the date of disease progression, based on the Response Evaluation Criteria in Solid Tumours version 1.1. A separate analysis was done for patients with FIGO stage 1B1 and preoperative MRI (n=349).

Study population issues: There were statistically significant differences between the groups with regard to parametrial involvement (6.3% in laparoscopic group compared with 15.4% in open group, p=0.004) and surgery on para-aortic lymph nodes (12.7% compared with 21.1%, p=0.02). Concurrent chemoradiation therapy was the most common type of adjuvant treatment in both groups and was more common in the open surgery group than the laparoscopic group (40.9% compared with 28.5%, p=0.006).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **593 (158 Laparoscopic, 435 open)**

During a median length of observation of 114.8 months, 74 (12.5%) patients had disease recurrence and 68 (11.5%) died.

5-year overall survival

- Laparoscopic=94.4%
- Open=92.3%, p=0.788

5-year progression-free survival

- Laparoscopic=78.5%
- Open=89.7%, p<0.001

Recurrence rates

- Laparoscopic=15.8%
- Open=11.3%

Multivariate analysis identified laparoscopic surgery as an independent poor prognostic factor for progression-free survival (adjusted HR 2.88, 95% CI 1.71 to 4.86, p<0.001). Non-squamous cell carcinoma histological type (adjusted HR 2.05, 95% CI 1.16 to 3.64, p=0.014) and resection margin involvement (adjusted HR 2.32, 95% CI 1.02 to 5.28, p=0.045) were also poor prognostic factors, whereas preoperative conisation was a favourable prognostic factor for progression-free survival (adjusted HR 0.32, 95% CI 0.15 to 0.69, p=0.004).

Patients with FIGO stage 1B1 and preoperative MRI (n=349, 103 laparoscopic, 246 open)

During a median length of observation of 106.0 months, 40 (11.5%) patients had disease recurrence and 35 (10.0%) died.

	5-year overall survival			5-year progression-free survival		
	Laparoscopic	Open	p	Laparoscopic	Open	p
All patients (n=349)	94.4%	92.7%	0.848	83.5%	89.6%	0.093
Cervical mass size ≤2 cm	96.2%	96.5%	0.570	92.4%	93.5%	0.749
Cervical mass size >2 cm and ≤4 cm	91.5%	87.6%	0.907	72.1%	86.9%	0.044

Multivariate analysis identified laparoscopic surgery as an independent poor prognostic factor for progression-free survival (adjusted HR 2.28, 95% CI 1.04 to 4.99, p=0.04). Non-squamous cell carcinoma histological type (adjusted HR 2.41, 95% CI 1.14 to 5.06, p=0.02) and parametrial involvement (adjusted HR 2.83, 95% CI 1.16 to 6.92, p=0.02) were also poor prognostic factors, whereas preoperative conisation was a favourable prognostic factor for progression-free survival (adjusted HR 0.34, 95% CI 0.14 to 0.86, p=0.02). Cervical mass size >2 cm on MRI showed a trend towards worse progression-free survival (adjusted HR 2.02, 95% CI 0.97 to 4.20, p=0.06).

For those patients with FIGO stage 1B1 disease and cervical mass ≤2 cm on preoperative MRI (n=207), the surgical approach did not affect progression-free survival (adjusted HR 1.15, 95% CI 0.28 to 4,72, p=0.85).

Abbreviations used: CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio

Study 4 Kim JH (2019)

Details

Study type	**Non-randomised comparative study**
Country	Korea
Recruitment period	2011 to 2014
Study population and number	**n=6,335 (3,100 laparoscopic radical hysterectomy, 3,235 open radical hysterectomy)** Patients with cervical cancer
Age	20% of patients were 39 years or younger, 33% were between 40 and 49, 27% were between 50 and 59, and 20% were 60 years or older.
Patient selection criteria	Women 18 years and older who had radical hysterectomy for cervical cancer.
Technique	Laparoscopic radical hysterectomy. No robotic procedures were included.
Follow up	**Not reported**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: Death was deemed to have occurred when patients did not use any medical services for 12 consecutive months after discharge.

Study design issues: The Korean Health Insurance Review and Assessment Service database was used to identify patients. This database captures inpatient and outpatient data on disease and services for all citizens in Korea. The database was searched to identify charges for laparoscopic materials to identify patients who had laparoscopic surgery. The primary outcome was overall survival. The inverse probability of treatment weighting method based on propensity scoring was applied to balance the observed confounders.

Study population issues: When patients were stratified according to the surgical approach, there were statistically significant differences between the groups with regard to age, year of diagnosis, insurance status, comorbidities, the extent of lymphadenectomy, and hospital region. After propensity score balancing, there was no statistically significant difference in these variables between the 2 groups. Patients who were younger, had a more recent year of diagnosis, were hospitalised in a metropolitan area and had a Medicare insurance status were more likely to have laparoscopic surgery ($p<0.05$ for all). Patients with more medical comorbidities who were hospitalised at a small hospital or clinic were less likely to have laparoscopic surgery ($p<0.05$).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **6,335 (3,100 laparoscopic, 3,235 open)**

All-cause mortality

	Unadjusted		Adjusted by IPTW		Adjusted by IPTW and postoperative adjuvant therapy	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Total	0.52 (0.43 to 0.63)	<0.001	0.61 (0.53 to 0.70)	<0.001	0.74 (0.64 to 0.85)	<0.001
With adjuvant therapy	0.74 (0.56 to 0.90)	0.005	0.85 (0.72 to 0.99)	0.046	-	-
Without adjuvant therapy	0.48 (0.34 to 0.67)	<0.001	0.52 (0.41 to 0.66)	<0.001	-	-

Kaplan-Meier analysis showed a statistically significant better overall survival in the MIS group.

Safety

Comparison of morbidity

	Unadjusted		Adjusted by IPTW	
	OR (95% CI)	p	OR (95% CI)	p
Intraoperative complications	0.73 (0.63 to 0.86)	<0.001	0.80 (0.72 to 0.90)	0.008
Postoperative complications	0.97 (0.87 to 1.07)	0.525	0.87 (0.80 to 0.95)	0.002
Surgical site complications	0.73 (0.60 to 0.88)	0.001	0.75 (0.66 to 0.86)	<0.001
Medical complications	0.88 (0.79 to 0.98)	0.018	0.99 (0.90 to 1.08)	0.739
Blood transfusions	0.28 (0.25 to 0.31)	<0.001	0.30 (0.28 to 0.33)	<0.001
Postoperative adjuvant therapy	0.59 (0.52 to 0.67)	<0.001	0.63 (0.57 to 0.69)	<0.001
Radiation only	0.92 (0.76 to 1.11)	0.387	0.87 (0.76 to 0.99)	0.042
Chemotherapy only	0.48 (0.41 to 0.56)	<0.001	0.55 (0.49 to 0.61)	<0.001
Concurrent chemoradiation	0.44 (0.39 to 0.49)	<0.001	0.47 (0.43 to 0.51)	<0.001

Abbreviations used: CI, confidence interval; HR, hazard ratio; IPTW, inverse probability of treatment weighting; MIS, minimally invasive surgery; OR, odds ratio

Study 5 Gil-Moreno A (2019)

Details

Study type	**Non-randomised comparative study**
Country	Spain
Recruitment period	1999 to 2016
Study population and number	**n=188 (90 LRH, 22 RRH, 76 ORH)** Patients with FIGO stage 1A2-1B1-2A1 cervical cancer
Age	Mean 48 years
Patient selection criteria	All patients who were clinically diagnosed with FIGO stage 1A2-1B1-2A1 cervical cancer and had radical hysterectomy were included. A total of 5 patients with stages 1B2-2A2 (n=3) and 2B (n=2) were also included because of specific characteristics and preferences of these patients after agreement by the gynaecology-oncology multidisciplinary team committee. Pregnant women in whom radical hysterectomy was done at the time of caesarean section and those patients who had previous chemotherapy or pelvic radiotherapy were excluded from the study. The choice of technique depended on the patient's characteristics together with the surgeon's and patient's preferences. General exclusion criteria for the laparoscopic or robotic approach included severe cardiorespiratory disease preventing a Trendelenburg position, an enlarged uterus over 12 pregnancy weeks in size, body mass index of 40kg/m^2 or higher and age 80 years or older. Over time, the laparoscopic approach was adopted as the standard of care.
Technique	A nerve-sparing technique was used in all procedures done after October 2006 (n=75). Patients with FIGO stage 1A2 or 1B1 and tumour size ≤2 cm had proximal or modified radical hysterectomy (Piver type 2) or type B1. Patients with FIGO stage 1B1 with a tumour mass <2 cm after physical examination but with a larger mass on MRI and those with a tumour mass bigger than 2 cm and up to 4 cm had a distal radical hysterectomy technique (Piver type 3) or type C1. After surgery, patients with 1 or more high-risk factors were referred for adjuvant chemoradiotherapy. Patients with more than 2 intermediate risk factors were referred for adjuvant radiation therapy.
Follow up	**Median 112 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were reviewed at weeks 1, 2 and 4 after discharge. For the first 2 years, patients had 3-monthly follow ups, then 6-monthly for the next 3 years and yearly follow ups thereafter. A total of 3 (1.6%) patients were lost to follow up (2 in the LRH group and 1 in the ORH group).

Study design issues: Prospective, single-centre, non-randomised comparative study. Overall survival was calculated from the date of surgery to the date of death or last follow up. Recurrence-free survival was calculated from the date of surgery to the date of the first recurrence or last follow up in patients without relapse. Patients who died of causes other than cervical cancer were censored at the time of their death. Data on patients who were alive were censored at the last follow-up visit.

Study population issues: There were statistically significant differences between the groups with regard to median body mass index (26 in LRH, 26.5 in ORH and 22.2 in RRH, p=0.008) and histological grade (RRH had a higher proportion of G1 than the other groups, p=0.0057). Of the 188 patients, 6% had FIGO stage 1A2 disease, 32% had stage 1B1 ≤2 cm, 52% had stage 1B1 >2 cm, 7% had stage 2A1, 1% had stage 2B and 2% had stage 1B2-2A2. The final pathological examination revealed 16 tumours (8.5%) larger than 4 cm and 15 (8.0%) with microscopic paracervical involvement, with no differences between the groups.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **188 (90 LRH, 22 RRH, 76 ORH)**

Operative data

	LRH n=90	RRH n=22	ORH n=76	p
Surgery, n (%) *B1*	21 (23.3)	7 (31.8)	2 (2.6)	-
C1	18 (20)	15 (68.1)	12 (15.8)	
Type 2	19 (21.1)	0	24 (31.6)	
Type 3	32 (35.5)	0	38 (50)	
Ovarian preservation, n (%)	38 (42.2)	9 (40.9)	24 (31.6)	0.087
Sentinel node, n (%)	63 (70)	14 (63.6)	44 (57.8)	0.075
Extracted pelvic nodes, median (SD)	19 (8 to 51)	19 (8 to 37)	20 (5 to 52)	0.08
Positive pelvic nodes, n (%)	10 (11.1)	2 (9.1)	12 (15.8)	0.57
Mean total parametrial volume, cm^3 (SD)	21.9 (9.7)	14.8 (8.4)	18.3 (10.5)	0.006
Operative time (min), mean (SD)	289 (47.8)	235.3 (61.7)	244.9 (41.6)	<0.0001
Blood loss (ml), mean (SD)	291.6 (190.6)	121.8 (116.4)	502.6 (318.4)	<0.0001

Adjuvant treatment was indicated in 33.3% (30/90) of patients in the LRH group, 27.3% (6/22) of patients in the RRH group and 57.9% (44/76) of patients in the open group.

Survival
There were no differences in disease-free survival rates or cancer-specific mortality rates between the 3 groups.

Recurrence rates:
- MIS=15.1%
- ORH=14.4%, p=0.64

Overall survival
- MIS=92.8%
- ORH=81.3%, p=0.03

Of the 188 patients, 156 (83.0%) were alive and free of disease at the time of the study.

Safety

Morbidity data

	Intraoperative complications (n=34)	≤30-day complications* (n=37)
LRH n=90	2 ureteral sections (1 suture, 1 ureterneocystostomy) 1 obturator vein lesion (bipolar coagulation and compression) 1 intestinal perforation (suture) 3 blood transfusions 2 conversions to laparotomy (because of ureteral sections) 1 anaphylactic shock secondary to isosulfan blue injection for sentinel lymph node identification	*Grade II: n=8* 3 urinary infections 3 acute urine retention 1 ileum 1 pelvic haematoma *Grade IIIb: n=7* 6 vaginal cuff dehiscences (vaginal suture) 1 urinoma secondary to sutured ureter (laparotomy/ ureteroneocystostomy)
RRH n=22	1 vesical lesion (suture and prolonged urinary catheter)	*Grade II: n=3* 3 acute urine retention *Grade IIIa: n=1* 1 lymphocele (percutaneous drainage)
ORH n=76	2 vesical lesions (suture and prolonged urinary catheter) 1 ureteral section (ureteroneocystostomy) 1 cava vein lesion (suture) 1 left internal iliac vein lesion (Tissucol and compression) 1 external iliac vein lesion (suture) 17 blood transfusions	*Grade II: n=14* 6 urinary infections 1 acute urine retention 2 abdominal wall infection 1 abdominal wall haematoma 4 ileum *Grade IIIb: n=3* 2 abdominal evisceration (suture) 1 vesical-vaginal fistula (surgical correction) *Grade V: n=1* Secondary to external iliac vein lesion, progressive multiorgan dysfunction, and intravascular disseminated coagulation

* Clavien-Dindo scoring system

Abbreviations used: FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; MIS, minimally invasive surgery; ORH, open radical hysterectomy; RRH, robotic radical hysterectomy; SD, standard deviation

Study 6 Hu TWY (2019)

Details

Study type	**Non-randomised comparative study**
Country	China
Recruitment period	2013 to 2015
Study population and number	**n=678** (255 laparoscopic radical hysterectomy [LRH], 423 open radical hysterectomy [ORH]) Adult patients with cervical cancer stage 1A2 to 2A
Age	• LRH: median 44 years (range 21 to 69) • ORH: median 42 years (range 23 to 77), p=0.095
Patient selection criteria	Adult patients with cervical cancer, FIGO stage 1A2, 1B, or 2A, who had LRH or ORH (Piver-Rutledge type 3 radical hysterectomy and lymphadenectomy). Patients were excluded if they had incomplete medical records or irregular follow-up.
Technique	LRH or ORH Neoadjuvant chemotherapy was offered to patients who had a large tumour or if the primary surgery was considered to be challenging. Postoperative radiochemotherapy was offered if the postoperative pathological results showed: negative lymph nodes with sizeable primary tumour, deep stromal invasion or lymphovascular space invasion; positive pelvic nodes or positive surgical margin or positive parametrium; positive para-aortic lymph nodes with no distant metastasis.
Follow-up	**Median 47 months (range 1 to 60)**
Conflict of interest/source of funding	None

Analysis

Study design issues: Retrospective single centre cohort study. The surgical approach was determined by the surgeon's preference and the patient's decision. The primary outcome of interest was overall survival, which was derived from the date of operation to the date of death or the last follow-up. Progression-free survival was derived from the date of operation to the date of first tumour recurrence.

Study population issues: Patients in the LRH group had a higher median BMI than those in the ORH group (22.3 kg/m^2 compared with 21.6 kg/m^2, p=0.002). A statistically significant higher proportion of patients in the LRH group had a tumour smaller than 4 cm in diameter (91.8% compared with 79.0% in the ORH group, p<0.001). There were also statistically significant differences in FIGO stage: in the LRH group, 11.4% of tumours were stage 1A2, 72.2% were stage 1B and 16.4% were stage 2A compared with 7.3%, 55.3% and 37.4% respectively in the ORH group, p<0.001. Deep stromal invasion was reported in 40.0% of patients in the LRH group compared with 55.1% of patients in the ORH group (p<0.001) and vaginal invasion was present in 16.1% and 9.4% of patients respectively (p=0.014).

Key efficacy and safety findings

Efficacy

Survival – all patients

There were no statistically significant differences between the groups in overall survival (HR=0.61, 95% CI 0.32 to 1.15, p=0.122) and progression-free survival (HR=0.77, 95% CI 0.47 to 1.25, p=0.285)

Recurrence rate (median follow-up 47 months, range 1 to 60)

- LRH=10.4%
- ORH=12.6%

Death rate (median follow-up 47 months, range 1 to 60)

- LRH=5.0%
- ORH=9.2%

Survival by tumour size

In patients with a tumour diameter >4 cm, the LRH group had a statistically significantly shorter overall survival than the ORH group (HR=3.36, 95% CI 1.16 to 9.68, p=0.017)

Conversely, in patients with a tumour diameter ≤4 cm, overall survival in the LRH group was statistically significantly longer than the ORH group (HR=0.37, 95% CI 0.16 to 0.84, p=0.013)

There were no statistically significant differences in progression-free survival: for tumours >4 cm, HR=0.78, 95% CI 0.45 to 1.35 and for tumours ≤4 cm, HR=1.20, 95% 0.40 to 3.60, p=0.756

Univariate Cox regression analysis of independent variables of LRH compared with ORH

Variables	Overall survival		Progression-free survival	
	HR (95% CI)	p	HR (95% CI)	p
Age, years	1.02 (0.97 to 1.05)	0.283	1.02 (1.0 to 1.04)	0.241
Length of hospital stay, days	1.06 (1.01 to 1.11)	0.017	1.02 (0.97 to 1.07)	0.392
Operative time, minutes	1.0 (0.99 to 1.0)	0.20	1.0 (1.0 to 1.0)	0.039
Estimated blood loss, ml	1.0 (1.0 to 1.0)	0.029	1.0 (1.0 to 1.0)	0.068
Surgical method (ARH versus LRH)	0.61 (0.32 to 1.15)	0.127	0.77 (0.47 to 1.25)	0.287
Neoadjuvant chemotherapy	1.64 (0.84 to 3.22)	0.148	1.21 (0.66 to 2.20)	0.538
Tumour diameter (<4 versus ≥4 cm)	2.26 (1.22 to 4.22)	0.01	1.95 (1.16 to 3.28)	0.012
FIGO stage (1 versus 2)	3.86 (2.16 to 6.88)	<0.001	2.73 (1.73 to 4.29)	<0.001
Histology (squamous versus others)	2.16 (1.16 to 4.02)	0.016	1.82 (1.08 to 3.07)	0.024
Deep stromal invasion	5.39 (2.52 to 11.51)	<0.001	3.51 (2.06 to 5.96)	<0.001
Vaginal invasion	2.78 (1.49 to 5.17)	0.001	2.21 (1.30 to 3.76)	0.003
Parametrial invasion	7.51 (4.03 to 14.01)	<0.001	6.65 (3.95 to 11.20)	<0.001
Positive surgical margins	0.05 (0.0 to 0.29)	0.591	3.34 (1.05 to 10.63)	0.041
Lymphovascular space invasion	4.49 (2.34 to 8.63)	<0.001	2.62 (1.64 to 4.18)	<0.001
Pelvic lymph node invasion	5.40 (3.06 to 9.52)	<0.001	5.22 (3.31 to 8.23)	<0.001
Paraaortic lymph node invasion	7.12 (2.29 to 22.11)	0.001	7.32 (2.67 to 20.08)	<0.001
Postoperative radiochemotherapy	2.24 (1.01 to 5.0)	0.049	2.88 (1.43 to 5.77)	0.003

Multivariate Cox regression analysis of independent variables of LRH compared with ORH

Variables	Overall survival		Progression-free survival	
	HR (95% CI)	p	HR (95% CI)	p
Length of hospital stay, days	1.04 (0.92 to 1.19)	0.513	0.99 (0.86 to 1.12)	0.978
Estimated blood loss, ml	1.0 (0.99 to 1.0)	0.948	1.0 (1.0 to 1.0)	0.477
Surgical method (ARH versus LRH)	1.33 (1.14 to 13.10)	0.806	2.77 (0.51 to 14.89)	0.236
Neoadjuvant chemotherapy	0.66 (0.17 to 2.53)	0.541	0.60 (0.18 to 1.98)	0.402
Tumour diameter (<4 versus ≥4 cm)	0.28 (0.03 to 2.26)	0.230	0.46 (0.09 to 2.36)	0.352
FIGO stage (1 versus 2)	14.31 (1.54 to 133.06)	0.019	10.48 (2.01 to 54.66)	0.005
Histology (squamous versus others)	6.55 (1.83 to 23.48)	0.004	5.25 (1.71 to 16.09)	0.004
Deep stromal invasion	2.51 (0.42 to 14.81)	0.311	2.98 (0.56 to 15.73)	0.201
Vaginal invasion	0.90 (0.21 to 3.83)	0.883	1.08 (0.34 to 3.45)	0.902
Parametrial invasion	4.33 (1.15 to 16.34)	0.03	5.16 (2.02 to 13.19)	0.001
Positive surgical margins	0.0 (0.0 to 0.0)	0.983	2.57 (0.34 to 19.51)	0.362
Lymphovascular space invasion	0.72 (0.19 to 2.83)	0.642	0.48 (0.14 to 1.62)	0.235
Pelvic lymph node invasion	4.49 (1.04 to 19.34)	0.044	6.60 (1.87 to 23.29)	0.003
Paraaortic lymph node invasion	1.99 (0.38 to 10.6)	0.419	1.79 (0.46 to 6.90)	0.398
Postoperative radiochemotherapy	0.74 (0.14 to 4.09)	0.733	2.51 (0.28 to 22.13)	0.408

Abbreviations used: CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; LRH, laparoscopic radical hysterectomy; ORH, open radical hysterectomy

Study 7 He H (2017)

Details

Study type	**Non-randomised comparative study**
Country	China (6 hospitals)
Recruitment period	2007 to 2014
Study population and number	**n=1,863** (1,071 LRH, 792 ORH) Patients with FIGO stage 1A2 to 2A2 cervical cancer
Age	Mean 46 years
Patient selection criteria	Patients with FIGO stage 1A2 to 2A2 cervical cancer, not previously treated.
Technique	Radical or modified radical hysterectomy combined with a pelvic or para-aortic lymph node dissection. Patients with stage 1A2 cervical cancer had a modified radical hysterectomy (LRH 6.5% [70/1,071] and ORH 8.3% [66/792]). Of the 1,071 LRH procedures, 22% were nerve-sparing. After surgery, patients with high-risk intermediate factors were recommended for adjuvant treatment (radiotherapy or chemoradiotherapy).
Follow up	• **LRH=mean 52 months (range 13 to 95)** • **ORH=mean 69 months (range 14 to 101)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients were followed up through letters, telephone interviews and email.

Study design issues: Retrospective, multicentre, non-randomised comparative study. The choice of surgical technique was based on the patient's preference. The aims of the study were to compare the long-term survival outcomes, complications, pelvic floor function and sexual function between LRH and ORH in early stage cervical cancer, and to analyse the risk factors for the prognosis of LRH.

Study population issues: There was a statistically significant lower proportion of patients with deep stromal invasion in the LRH group compared with the ORH group (27% compared with 39%, $p<0.001$). Other baseline clinical and pathological characteristics were similar between the groups.

Other issues: There were differences between the centres with regard to laparoscopic equipment and surgical techniques.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **1,863 (1,071 LRH, 792 ORH)**

Surgical outcomes

	LRH (n=1,071)	ORH (n=792)	p value
Operating time (minutes)	257.0±68.8	238.2±56.1	<0.05
Estimated blood loss (ml)	358.0±314.2	703.8±430.7	<0.05
Return of bowel movement (days)	2.5±0.9	2.9±0.8	<0.05
Removal of Foley catheter (days)	14.8±6.9	18.1±9.0	<0.05
Postoperative hospital stay (days)	19.4±15.8	29.6±21.1	<0.05

Extent of surgical excision

	LRH (n=1,071)	ORH (n=792)	p value
Length of left parametrial resection (cm)	2.5±0.8	2.7±0.7	0.719
Length of right parametrial resection (cm)	2.6±0.3	2.7±0.2	0.652
Length of vaginal tissue resection (cm)	2.4±0.7	2.2±0.7	0.437
Number of lymph nodes removed	21.1±8.4	20.4±8.4	0.233

Recurrence

- LRH=3.5% (35/1,007) (14 local, 21 metastasis)
- ORH=4.7% (35/740) (16 local, 19 metastasis), p=0.269

5-year overall survival

- LRH=94.0%
- ORH=90.2%, p=0.260

5-year disease-free survival

- LRH=93.9%
- ORH=89.1%, p=0.292

Univariate analysis showed that tumour size>4 cm (p<0.001), FIGO stage 1B2 and 2A2 (p<0.001), cervical stromal invasion >1/2 (p<0.001), lymphovascular space invasion (p=0.011) and lymph node metastasis (p<0.001) were associated with a decreased 5-year overall survival.

In multivariate analysis, non-squamous (p=0.045), FIGO stage 1B2 and 2A2 (p<0.001) and lymphovascular space invasion were associated with a decreased 5-year overall survival. FIGO stage 1B2 and 2A2 (p<0.001), positive lymphovascular space invasion and lymph node metastasis (p=0.013) were associated with a decreased 5-year disease-free survival.

Safety

Intra- and postoperative complications

	LRH (n=1,071)	ORH (n=792)	p value
Intraoperative complications	87 (8.1%)	85 (10.7%)	0.068
Organ injury (urinary tract and gastrointestinal tract)	43 (4.0%)	24 (3.0%)	0.297
Vessel injury	28 (2.6%)	61 (7.7%)	<0.001
Postoperative complications	362 (33.8%)	318 (40.2%)	0.007
Urinary retention	257 (24.0%)	222 (28.0%)	0.06
Wound dehiscence	7 (0.7%)	32 (4.0%)	<0.001
Febrile morbidity	78 (7.3%)	56 (7.1%)	0.925

Proportion of patients with urinary incontinence at 12-month follow up (based on ICIQ–FLUTS scores) – patients with baseline and follow-up data

	LRH (n=573)	ORH (n=198)	p value
Total, n (%)	191 (33.3%)	71 (35.9%)	Not significant
Mild	128 (22.3%)	47 (23.7%)	Not significant
Moderate	44 (7.7%)	16 (8.1%)	
Severe	12 (2.1%)	5 (2.5%)	
Serious	7 (1.2%)	3 (1.5%)	

Proportion of patients with urinary incontinence at 12-month follow up (based on ICIQ–FLUTS scores) – nerve-sparing LRH

	Nerve-sparing LRH (n=236)	ORH (n=198)	p value
Total, n (%)	67 (28.4%)	71 (35.9%)	0.004
Mild	43 (18.2%)	47 (23.7%)	0.980
Moderate	15 (6.4%)	16 (8.1%)	
Severe	5 (2.1%)	5 (2.5%)	
Serious	4 (1.7%)	3 (1.5%)	

Sexual dysfunction (FSFI score<26.55)

	LRH (n=573)	ORH (n=198)	p value
Baseline	161 (28.1%)	52 (26.3%)	0.574
12 months	313 (54.7%)	113 (57.1%)	0.361

Sexual dysfunction (FSFI score<26.55) – nerve-sparing LRH

	Nerve-sparing LRH (n=236)	ORH (n=198)	p value
Baseline	27.5%	25.7%	0.493
12 months	47.1%	56.1%	0.001

Abbreviations used: FIGO, International Federation of Gynecology and Obstetrics; FSFI, Female Sexual Function Index; ICIQ-FLUTS; International Consultation on Incontinence Questionnaire–Female Lower Urinary Tract Symptoms; LRH, laparoscopic radical hysterectomy; ORH, open radical hysterectomy

Study 8 Zhang S (2019)

Details

Study type	**Systematic review and meta-analysis**
Country	France, Italy, Sweden, US, Korea, Norway
Recruitment period	Search date: published 'up to 2018' (no start date given)
Study population and number	**n=2,197** (373 LRH; 932 RRH; 892 open surgery); 13 studies in meta-analysis Differs by study but FIGO scores included range from 1A2 to 2B2, with 1 study including up to stage IVA.
Age	Not reported
Patient selection criteria	Inclusion criteria for meta-analysis: prospective and retrospective cohorts assessing surgical outcomes of RRH; comparing interested surgical outcomes of RRH with LRH or open surgery. Studies were quality assessed using the methodological index for non-randomised studies (MINORS) using the 8-item method and a cut off score of 12/16 points was needed for inclusion (indicating higher study design quality). Excluded studies: case reports, reviews, letters, editorials, studies lacking control groups. Studies reporting outcomes for patients with benign lesions or gynaecologic malignancy other than cervical cancer. Overlapped studies. Where it was not possible to extract the interested outcomes data.
Technique	LRH, RRH and open surgery for cervical cancer.
Follow up	**Overall follow up not reported. Median follow up in 16 studies ranged from 11.6 months to 59 months**
Conflict of interest/source of funding	Authors report having received no funding and no conflicts of interest to disclose.

Analysis

Study design issues: Systematic review and meta-analysis. Studies were quality assessed for inclusion using a validated tool for non-randomised interventional studies (MINORS tool). Of the 26 articles assessed, 13 were deemed suitable for meta-analysis (4 compared RRH with open surgery, 6 compared RRH with LRH and 3 compared RRH, LRH and open surgery). No RCTs were identified. Although 3 studies compared RRH, LRH and open surgery, results for LRH compared with open surgery are not reported and no explanation is given for this. Study follow-up periods varied substantially, as did the number of centres involved in each study (1-5 centres). There was statistically significant heterogeneity between the studies regarding operation time, intraoperative blood loss, overall postoperative outcomes, retrieved lymph nodes, and length of hospital stay. The authors note that these parameters are influenced by the surgeon's skills, patient's conditions and perioperative care protocol. These factors will impact bias in the results of the metanalysis. Potential publication bias was detected for 2 of the studies included using funnel plot analysis; 1 study comparing RRH with LRH and 1 comparing RRH with open surgery. Long-term survival rates could not be calculated because of limited data.

Study population issues: FIGO stage included varied between studies and an overall proportion of patients represented by FIGO stage is not provided, nor per study. The sample size varied between studies (range 52 to 461 patients).

Key efficacy and safety findings

Efficacy

Operative data

RRH vs LRH

	No. of studies	Weighted mean difference (WMD) or Odds Ratio (OR)	P value	Heterogeneity p, I^2
Operation time (mins)	9	WMD:18.10	0.28	<0.01, 93%
Intraoperative estimated blood loss (ml)	8	WMD: -22.5	0.46	<0.01, 89%
Transfusion (%)	5	OR: 0.53	0.29	0.50, 0%
Conversion (%)	3	OR: 0.66	0.68	0.24, 30%
Hospital stay (days)	9	WMD: -024	0.67	<0.1, 87%
Retrieved lymph nodes (n)	9	WMD: 2.46	0.10	<0.1, 67%

Pooled data for recurrence: OR=0.96 (95% CI 0.50 to 1.87, p=0.91; I^2=0%; 7 studies)

RRH vs open surgery

	No. of studies	WMD or OR	P value	Heterogeneity p, I^2
Operation time (mins)	6	WMD: 36.07	0.02	<0.01, 95%
Intra-operative estimated blood loss (mL)	5	WMD: -322.59	<0.01	<0.01, 98%
Transfusion (%)	6	OR: 0.19	<0.01	0.17, 36%
Hospital stay (days)	6	WMD: -2.71	<0.01	<0.1, 78%
Retrieved lymph nodes (n)	6	WMD: -3.43	0.12	<0.1, 89%

Pooled data for recurrence: OR=0.85 (95% CI 0.58 to 1.27, p=0.43; I^2=0%; 5 studies)

Safety

RRH vs LRH

	No. of studies	OR	p	Heterogeneity p, I^2
Overall intra-operative complications (%)	7	1.17	0.32	0.52, 0%
Overall postoperative complications (%)	9	0.66	0.13	0.17, 31%

RRH vs open surgery

	No. of studies	OR	p	Heterogeneity p, I^2
Overall intra-operative complications (%)	5	0.52	0.04	0.37, 6%
Overall postoperative complications (%)	7	0.74	0.24	0.01, 65%

Abbreviations used: CI confidence interval; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; OR, odds ratio; RRH, robotic radical hysterectomy; WMD: weighted mean difference

Study 9 Cao T (2015)

Details

Study type	**Systematic review and meta-analysis**
Country	Not reported for individual studies
Recruitment period	Search date: April 2015
Study population and number	**n=2,922 (1,230 LRH and 1,692 ORH; 22 studies)** Patients with biopsy-proven cervical cancer
Age	Not reported
Patient selection criteria	All available randomised controlled trials, non-randomised controlled designs, and retrospective comparative studies were included. Patients had biopsy-proven cervical cancer and had a radical hysterectomy. Editorials, letters to the editor, review articles, case reports, and animal experiment studies were excluded.
Technique	No details reported.
Follow up	**Mean or median follow-up ranged from 7 months to 92 months in the LRH group and from 23 weeks to 106 months in the ORH group.**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The follow-up time varied between the studies. The review does not discuss completeness of follow up.

Study design issues: The review was done according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis and Meta-analysis of Observational Studies in Epidemiology recommendations. The main outcomes were 5-year disease-free survival, 5-year overall survival, and recurrence rate. The studies included 1 small randomised controlled trial, 15 retrospective studies and 6 prospective studies. The quality of the included studies was generally low. A sensitivity analysis was done for high-quality studies and funnel plots were used to screen for potential publication bias. The authors concluded there was no obvious publication bias.

Study population issues: Five studies included patients with stage 1B1 or below disease. Only 2 studies included patients with stage 2B disease. One study defined stage 1B1 as a tumour size less than 2 cm. One study included cervical cancer tumours diagnosed as FIGO stage 1B to 2A with a tumour diameter of 3 cm or greater. In 1 study, patients had neoadjuvant chemotherapy before radical surgery.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **2,922 (1,230 LRH and 1,692 ORH)**

Prognostic factors showed no statistically significant difference

Results of meta-analysis

Outcome	Number of studies	Number of patients		WMD/OR/HR (95% CI)	p	Study heterogeneity			
		LRH	ORH			X^2	df	I^2 (%)	p
5-year disease-free survival*	10	791	1,031	0.01 (-0.10 to 0.11)	0.91	4.78	9	0	0.85
5-year overall survival*	6	656	847	-0.02 (-0.14 to 0.10)	0.73	4.28	5	0	0.51
Recurrence rate*	13	924	1,350	0.82 (0.61 to 1.11)	0.20	3.37	12	0	0.99
Pelvic lymph nodes removed	16	813	1,220	-1.44 (-4.14 to 1.27)	0.3	247.4	15	94	<0.00001
Para-aortic lymph nodes removed	2	73	78	-1.79 (-6.39 to 2.82)	0.45	18.41	1	95	<0.0001
Operation time (minutes)	17	841	1,383	18.76 (2.13 to 35.39)	0.03	184.2	16	91	<0.00001
Length of stay (days)	16	1,054	1,437	-4.36 (-5.38 to -3.34)	<0.00001	141.3	15	89	<0.00001
Blood loss (ml)	17	1,089	1,481	-193.6 (-236.8 to -150.4)	<0.00001	80.44	16	80	<0.00001

* prognostic factors were not statistically significantly different, including Stage 2B or above (only 2 studies included Stage 2B or above and showed no differences; others included cases below Stage 2B), Grade G3 (OR=1.44; 95% CI 0.70 to 2.96, p=0.32), non–squamous cancer histology (OR=0.98; 95% CI 0.78 to 1.23, p=0.84), positive lymph node rate (OR=1.08; 95% CI 0.83 to 1.41, p=0.57), positive lymphovascular space invasion (OR=1.26; 95% CI 0.68 to 2.33, p=0.47), tumour size ≥4 cm (OR=1.27; 95% CI 0.62 to 2.62, p=0.52), positive parametrial margin rate (OR=1.12; 95% CI 0.71 to 1.78, p=0.62), and positive vaginal margin rate (OR=2.79; 95% CI 0.88 to 8.82, p=0.08).

Sensitivity analysis

Outcome	Number of studies	Number of patients		WMD/OR/HR (95% CI)	p	Study heterogeneity			
		LRH	ORH			X^2	df	I^2 (%)	p
5-year disease-free survival*	6	608	686	0.02 (-0.11 to 0.15)	0.77	4.00	5	0	0.55
5-year overall survival*	4	503	576	-0.01 (-0.15 to 0.14)	0.93	2.81	3	0	0.42
Recurrence rate*	7	613	895	0.80 (0.53 to 1.22)	0.30	2.14	6	0	0.91
Pelvic lymph nodes removed	10	494	793	-0.99 (-6.07 to 4.10)	0.70	148.9	9	94	<0.00001
Operation time (minutes)	12	656	1,053	20.89 (0.53 to 41.25)	0.04	155.0	11	93	<0.00001
Length of stay (days)	11	757	1,056	-3.98 (-4.99 to -2.98)	<0.00001	73.90	10	86	<0.00001
Blood loss (ml)	12	792	1,100	-179.8 (-225.4 to -134.3)	0.70	148.9	9	94	<0.00001

* prognostic factors were not statistically significantly different

Safety

Results of meta-analysis

Outcome	Number of studies	Number of patients		WMD/OR/HR (95% CI)	p	Study heterogeneity			
		LRH	ORH			X^2	df	I^2 (%)	p
Intraoperative bowel or urinary injury	17	1,083	1,282	1.50 (0.99 to 2.26)	0.06	6.79	16	0	0.98
Perioperative complication	4	315	555	0.56 (0.36 to 0.90)	0.02	2.50	3	0	0.47
Postoperative complication	18	1,078	1,451	0.75 (0.62 to 0.91)	0.003	40.31	16	60	0.0007
Intraoperative complication	10	523	661	1.48 (0.75 to 2.91)	0.25	8.31	9	0	0.50
Bladder recovery (days)	3	61	119	-2.48 (-5.16 to 0.19)	0.07	17.46	2	89	0.0002
Anorectal recovery (days)	4	104	123	-0.80 (-1.16 to -0.44)	<0.00001	4.65	2	57	0.1

Sensitivity analysis

Outcome	Number of studies	Number of patients		WMD/OR/HR (95% CI)	p	Study heterogeneity			
		LRH	ORH			X^2	df	I^2 (%)	p
Intraoperative bowel or urinary injury	13	802	889	1.49 (0.93 to 2.37)	0.10	5.77	12	0	0.93
Perioperative complication	2	146	255	0.66 (0.32 to 1.73)	0.26	1.52	1	34	0.22
Postoperative complication	12	781	1,070	0.78 (0.63 to 0.97)	0.02	37.14	11	70	0.0001
Intraoperative complication	4	159	175	0.79 (0.28 to 2.20)	0.65	3.04	3	1	0.38
Anorectal recovery (days)	2	73	78	-0.65 (-0.93 to -0.36)	<0.00001	0.62	1	0	0.43

Abbreviations used: df, degrees of freedom; FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; LRH, laparoscopic radical hysterectomy; OR, odds ratio; ORH, open radical hysterectomy; WMD, weighted mean difference

Study 10 Goel V (2018)

Details

Study type	**Case report**
Country	India
Recruitment period	2016
Study population and number	**n=1** Patient with isolated port-site metastasis after laparoscopic radical hysterectomy for cervical cancer stage 1B1
Age	50 years
Patient selection criteria	Not applicable
Technique	Laparoscopic type III radical hysterectomy, followed by adjuvant radiation.
Follow up	**4 months**
Conflict of interest/source of funding	None

Isolated port-site metastasis

10 months after completion of treatment, the patient presented with abdominal pain and a lump in the anterior wall at the periumbilical area. Metastatic carcinoma was diagnosed, and the tumour was removed laparoscopically. A defect created in the rectus sheath was repaired with prolene mesh. Other sites of metastasis were ruled out.

At last follow up, 4 months after surgery to remove metastasis, the patient was asymptomatic and disease free.

Study 11 Sert B (2010)

Details

Study type	**Case report and review**
Country	Norway
Recruitment period	2007
Study population and number	**n=1** Patient with robotic port-site and pelvic recurrences after robot-assisted LRH for stage 1B1 cervical cancer
Age	60 years
Patient selection criteria	Not applicable
Technique	Robot-assisted laparoscopic radical hysterectomy, bilateral pelvic lymph node dissection and bilateral salpingo-oophorectomy.
Follow up	**15 months**
Conflict of interest/source of funding	Not reported

Port-site metastasis and pelvic recurrence

The patient had a robot-assisted laparoscopic radical hysterectomy, bilateral pelvic lymph node dissection and bilateral salpingo-oophorectomy for stage 1B1 cervical cancer (a middle and highly differentiated endocervical type adenocarcinoma). All of the margins were free, and the 13 pelvic lymph nodes were reported without metastases. 18 months later, the patient had a cystoscopy for urinary symptoms and a metastatic lesion was found on the bladder wall. A CT also suggested robotic port-site metastases. A diagnostic laparoscopy revealed metastatic adenocarcinoma from the previous cervical adenocarcinoma. The patient had chemoradiation therapy. Fifteen months after treatment, the patient was alive without recurrence.

Review

The authors note that there have been 25 reported cases of laparoscopic port-site metastasis in patients with cervical cancer (median age 44 years, range 31 to 74). Most of these patients (80%) had squamous cell carcinoma and 67% of patients had early stage 1-2 disease at the time of laparoscopy. The median time to the development of port-site metastases was 5 months (range 1 to 48). In 45% of the patients, they were documented as isolated to a port-site.

Study 12 Lawrenz B (2011)

Details

Study type	**Case report**
Country	Germany
Recruitment period	Not reported
Study population and number	**n=1** Patient with lower extremity compartment syndrome after laparoscopic radical hysterectomy for cervical cancer
Age	30 years
Patient selection criteria	Not applicable
Technique	Laparoscopic radical hysterectomy (Piver II/III) with pelvic lymphadenectomy of the internal iliac, the external iliac and the obturator fossa lymphatic tissue.
Follow up	**None**
Conflict of interest/source of funding	None

Compartment syndrome

About 6 hours after the laparoscopic radical hysterectomy, the patient developed pain in the lower left extremity with tingling and loss of sensibility to touch. The anterior tibial compartment appeared swollen and tender to touch and pressure (10/10 on a pain scale). Compartment syndrome was diagnosed, and an incision was made to access the compartment. Management followed the usual surgical approach of gradual closure of the cutaneous suture over several days. The patient needed an 11-day hospital stay; at which time the lower extremity wound was completely closed.

Study 13 Orfanelli T (2017)

Details

Study type	**Case report**
Country	US
Recruitment period	Not reported
Study population and number	**n=1** Patient with acute colonic pseudo-obstruction after robotic-assisted radical hysterectomy for cervical cancer
Age	40 years
Patient selection criteria	Not applicable
Technique	Robotic-assisted radical hysterectomy
Follow up	**None**
Conflict of interest/source of funding	None

Acute colonic pseudo-obstruction (Ogilvie's syndrome)

The patient had stage 1B1 cervical adenocarcinoma, positive for lymphovascular invasion. She had a robotic-assisted laparoscopic radical hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and cystoscopy. The final pathology was without evidence of tumour on the organs removed and all 17 lymph nodes were negative for disease. On postoperative day 2, she had increasing abdominal pain, nausea and absent flatus. An abdominal X-ray showed diffuse gaseous distention of the large and small bowel consistent with ileus, which was treated conservatively. Two days later, a CT scan pneumatosis in the caecum and ascending colon with caecal dilation up to 11 cm in the absence of an apparent occlusive lesion. Acute colonic pseudo-obstruction was diagnosed. The patient had a neostigmine challenge, followed by insertion of a rectal tube. At 48 hours after a second dose of neostigmine, she had a normal bowel movement and was tolerating a low-residue mechanical soft diet. She was discharged home on postoperative day 10.

Study 14 Barr C (2013)

Details

Study type	**Case report**
Country	UK
Recruitment period	
Study population and number	**n=1** Patient with cerebral oedema after a robotic assisted radical hysterectomy for stage 1B1 cervical cancer
Age	51 years
Patient selection criteria	Not applicable
Technique	Robotic assisted radical hysterectomy.
Follow up	
Conflict of interest/source of funding	Not reported

Cerebral oedema

The procedure was prolonged because of difficulties dissecting the left parametrium and left vaginal fornix with persistent bleeding from the left vaginal vault. The patient was electively sedated and ventilated for the first 24 hours after the operation. Extubation was difficult because of patient agitation but was achieved on day 2. Agitation persisted and a head CT scan was done, which appeared normal. A presumptive diagnosis of cerebral oedema was made, and the patient had supportive treatment on the intensive care unit. She was discharged home on day 11 with no long-term sequelae.

The authors note that this complication happened early in the learning curve of this procedure and adjustments for robotics compared with standard laparoscopy were subsequently made.

Study 15 Cusimano M (2019)

Details

Study type	**Non-randomised comparative study**
Country	Canada
Recruitment period	2006 to 2017
Study population and number	**n=958** (473 minimally invasive radical hysterectomy [MIS], 485 open radical hysterectomy [ORH]) Adult women with cervical cancer
Age	Mean 46 years
Patient selection criteria	The study included all adult women (aged 18 years or over) in Ontario, Canada, diagnosed with cervical cancer who had primary radical hysterectomy within 9 months of diagnosis. Exclusion criteria: non-Ontario residents, atypical histology, radiation or chemotherapy after diagnosis but before hysterectomy, not treated by a gynaecological oncologist, prior malignancy, missing data.
Technique	MIS included laparoscopic (90%) or robotic (10%) radical hysterectomy. The proportion of minimally invasive procedures increased from 5% in 2006 to 65% in 2017. Radical hysterectomy included resection of the parametrium/uterosacral ligaments, resection of the upper 2 to 3 cm of the vagina, and pelvic lymphadenectomy.
Follow-up	**Mean 6 years**
Conflict of interest/source of funding	None

Analysis

Study design issues: Population based retrospective cohort study. Patients were identified from the Ontario Cancer Registry, which contains records for all incident cancers in the province. The primary outcome was all-cause death. Secondary outcomes were cervical cancer-specific death and recurrence (defined as health service utilisation suggesting treatment of recurrent disease by surgery, radiation, chemotherapy of palliative care 6 months or more after hysterectomy). Data on all cause death and recurrence were available to March 2018 but data on cause of death was only available to December 2015.

Study population issues: Patients who had MIS were younger with fewer comorbidities, less likely to live in rural areas, more likely to have high-risk features (stage II+) and more likely to have had a high-volume surgeon for both technique and cervical cancer. Patients who had MIS were less likely to have adjuvant therapy (25% compared with 33%). None of these differences were statistically significant. Pathological stage (used as a surrogate for clinical stage) was 1A in 26% (244/958) of patients, 1B in 56% (534/958), 2+ in 13% (124/958), and unknown in 6% (56/958) of patients. All patients were assumed to have FIGO early stage disease.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **958 (473 MIS, 485 ORH)**

All-cause death – all patients

- MIS=8.2% (39/473) (mean follow-up 5.3 years)
- ORH=9.5% (46/485) (mean follow-up 6.7 years)

p=0.04

Recurrence – all patients

- MIS=12.1% (57/473) (mean follow-up 5.0 years)
- ORH=10.9% (53/485) (mean follow-up 6.2 years)

p=0.04

Outcomes for patients with stage IB disease: unadjusted 5-year cumulative incidence (95% confidence interval [CI])

	MIS	ORH	p
All-cause death	12.5% (8.5 to 18.3)	5.4% (3.1 to 9.4)	0.019
Cervical cancer specific death	9.3% (4.9 to 15.4)	3.3% (1.2 to 7.0)	0.003
Recurrence	16.2% (11.6 to 21.4)	8.4% (5.3 to 12.3)	0.008

After adjusting for patient and surgeon factors, MIS was associated with increased risks of all-cause death (hazard ratio [HR] 2.20, 95% CI 1.15 to 4.19) and recurrence (HR 1.97, 95% CI 1.10 to 3.50) compared with ORH in patients with stage IB disease.

For patients with stage 1A disease, there were no statistically significant associations: death HR 0.73 (95% CI 0.13 to 4.01), recurrence HR 0.34 (95% CI 0.10 to 1.10).

For patients with stage 2+ disease, there were no statistically significant associations: death HR 0.92 (95% CI 0.33 to 2.53), recurrence HR 1.07 (95% CI 0.49 to 2.37).

For patients with unknown stage, there were no statistically significant associations: death HR 0.22 (95% CI 0.04 to 1.22), recurrence HR 0.79 (95% CI 0.21 to 2.94).

Abbreviations used: CI, confidence interval; HR, hazard ratio; MIS, minimally invasive surgery; ORH, open radical hysterectomy

Study 16 Kim SI (2019b)

Details

Study type	**Non-randomised comparative study**
Country	Republic of Korea (2 centres)
Recruitment period	2000 to 2018
Study population and number	**n=565** (222 LRH, 343 ORH) Patients with FIGO stage 1B cervical cancer
Age	Mean 49 years
Patient selection criteria	Inclusion criteria: patients who were diagnosed and treated for stage 1B cervical cancer according to the 2014 FIGO staging system; primary Type C radical hysterectomy according to Querleu and Morrow's classification. Exclusion criteria: patients who had neoadjuvant chemoradiotherapy before surgery; histological types other than squamous cell carcinoma, usual type adenocarcinoma, or adenosquamous carcinoma; insufficient clinical or pathological data. Patients who had robotic radical hysterectomy were excluded. Patients who had LRH within the first 2 years of the procedure being introduced in the 2 centres were excluded. Only patients who had preoperative MRI were included.
Technique	LRH or ORH
Follow-up	• **LRH=median 34.5 months** • **ORH=median 112.5 months, p<0.001**
Conflict of interest/source of funding	None

Analysis

Follow up issues: During follow-up, patients had CT scans every 3 to 4 months for the first 2 years, every 6 months for the next 2 years and thereafter, every year or when symptoms or examination findings were suspicious for recurrence.

Study design issues: Retrospective matched multicentre cohort study. The study was conducted in 2 high-volume tertiary institutional hospitals. Sample matching was done by Mahalanobis distance-based sample matching, using the following variables: stage, histology, cervical mass size on preoperative MRI, and pathologically confirmed parametrial invasion and lymph node metastasis. Three individual sampling process were done: all patients (matching 1), stage 1B1 patients (matching 2) and stage 1B1 patients with cervical mass size 2 cm or smaller on preoperative MRI (matching 3). The main aim of the study was to compare survival outcomes of LRH and ORH. From the date of initial diagnosis, overall survival and progression-free survival were defined as the period to the date of cancer-related death or the end of the study and the date of progression, respectively. Disease progression was assessed according to the Response Evaluation Criteria in Solid Tumours version 1.1.

Study population issues: After matching, the 2 groups had similar age, histological type, FIGO stage, proportions of preoperative conisation, and cervical mass size measured by MRI. The para-aortic lymph nodes were more frequently removed in the ORH group compared with the LRH group (24.8% versus 13.5%, p=0.003). The LRH group had a statistically significant shorter follow-up period than the ORH group (34.5 months compared with 112.5 months, p<0.001). There were no statistically significant differences in the 3 high-risk factors (parametrial involvement, resection margin involvement, and lymph node metastasis) or 2 intermediate risk factors (lymphovascular space invasion and invasion depth).

Other issues: Of the 565 patients, 343 were also included in Kim SI et al., 2019a (study 3 in overview).

Key efficacy and safety findings

Efficacy

Number of patients analysed: 565 (222 LRH, 343 ORH)

Matched patients with stage 1B1-1B2 cervical cancer (median follow-up=59.1 months; 34.5 for LRH and 112.5 for ORH, p<0.001)

- Mortality=5.4% (24/444)
- Recurrence=11.5% (51/444)

Matched patients with stage 1B1 cervical cancer (median follow-up=61.6 months; 37.1 for LRH and 121.6 for ORH, p<0.001)

- Mortality=5.6% (22/392)
- Recurrence=10.5% (41/392)

Matched patients with stage 1B1 cervical cancer and mass size ≤2 cm on preoperative MRI (median follow-up=66.2 months; 46.8 for LRH and 133.4 for ORH, p<0.001)

- Mortality=4.5% (11/244)
- Recurrence=8.6% (21/244)

5-year overall survival

	Patients with stage 1B1-1B2 cervical cancer	**Patients with stage 1B1 cervical cancer**	**Patients with stage 1B1 and mass size ≤2 cm on preoperative MRI**
LRH	96.9%	97.2%	98.6%
ORH	94.6%	94.4%	96.4%
p	0.4	0.3	0.6

3-year progression-free survival

	Patients with stage 1B1-1B2 cervical cancer	**Patients with stage 1B1 cervical cancer**	**Patients with stage 1B1 and mass size ≤2 cm on preoperative MRI**
LRH	85.4%	87.6%	90.0%
ORH	91.8%	92.3%	93.1%
p	0.036	0.1	0.8

There were no statistically significant differences in recurrence patterns between the 2 treatment groups.

Abbreviations used: CI, confidence interval; HR, hazard ratio; LRH, laparoscopic radical hysterectomy; ORH, open radical hysterectomy

Study 17 Martin-Hirsch P (2019)

Details

Study type	**Cohort study**
Country	UK (8 centres)
Recruitment period	Not reported
Study population and number	**n=779 (463 laparoscopic or robotic radical hysterectomy)** Patients with stage 1B1 cervical cancer
Age	Median 40 years (range 23 to 88)
Patient selection criteria	Women who had surgical treatment for stage 1B1 cervical cancer in 8 major tertiary referral centres.
Technique	Of the 779 patients, 597 (77%) had radical hysterectomy and of these, 463 (78%) had a laparoscopic or robotic approach. Of the remainder, 7% had a simple hysterectomy, 6% had a radical trachelectomy and 8% had a conisation procedure.
Follow-up	**Median 23 months**
Conflict of interest/source of funding	There was no external funding for the study. Of the 24 authors, 3 are preceptors for Intuitive Robotic Surgery. The remaining authors have no relevant interests.

Analysis

Study design issues: Retrospective multicentre cohort study. Baseline characteristics of the UK cohort were compared with those of the patients who had open surgery in the Laparoscopic Approach to Cervical Cancer (LACC) study (Ramirez et al., 2018).

Study population issues: The baseline characteristics of the UK cohort were not described separately for different types of surgery. Comparison between the UK cohort and the open surgery arm of the LACC study are shown below.

	UK series	%	LACC study	%	p
Median age (years)	40		46		
Histological type					
Squamous	416	56	210	67	<0.01
Adeno	252	35	80	27	
Mixed	28	4	6	2	
Other	27	4			
Not recorded	56		16		
Grade					
1	129	22	29	10	<0.05
2	278	47	111	39	
3	185	31	61	22	
Not recorded	187		81	29	
Lymphovascular space invasion					
Present	289	37	81	29	<0.01
Absent	406	52	185	66	
Not recorded	84	11	16	6	
Size of tumour					
<2 cm	452	58	147	52	<0.01
≥2 cm	256	33	121	43	
Not recorded	71	9	14	5	

Key efficacy and safety findings

Efficacy

Number of patients analysed: 779

Recurrence=4.6% (36/779) (most occurred early in the follow-up period)

Death

- Whole cohort=1.4% (11/779)
- LRH=1.6% (6/366)
- Robotic radical hysterectomy=2.1% (2/97)
- ORH=2.3% (3/130)

Prognostic factors in the UK cohort

	Number	Deaths	Rate (%)	p
Histological type				
Squamous	338	3	0.89	Not significant
Adeno	200	5	2.5	
Mixed	34	2	5.9	
Grade				
1	134	2	1.5	Not significant
2	262	2	0.76	
3	175	6	3.4	
Lymphovascular space invasion				
Present	296	7	2.4	<0.01
Absent	407	1	0.2	
Size				
<2 cm	452	3	0.6	<0.01
≥2 cm	256	8	3.1	

Abbreviations used: CI, confidence interval; HR, hazard ratio; MIS, minimally invasive surgery; ORH, open radical hysterectomy

Study 18 National Cancer Registration and Analysis Service (NCRAS)

Details

Study type	**Non-randomised comparative study**
Country	UK
Recruitment period	2013 to 2016
Study population and number	**n=929 (564 minimal access [MIS], 365 open)** Patients with FIGO stage 1A2, 1B or 1B1 cervical carcinoma
Age	Mean 42 years (minimal access) and 43 years (open)
Patient selection criteria	Women resident in England with early stage diagnosis (1A2, 1B, 1B1) of cervical cancer treated surgically by either minimal access or open approach and diagnosed during 2013-2016 formed the analysis cohort. Patients with neoadjuvant treatment were excluded.
Technique	Minimal access surgery included laparoscopic and robotic approaches.
Follow up	**Range 129-1824 days, median 1116 days, mean 1109 days**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: Definition of treatment groups was principally based on linked cancer registration and Hospital Episodes Statistics data, using OPCS-IV procedure classification codes to define whether the surgical approach was by minimal access or open. The Systemic Anti-Cancer Therapy and Radiotherapy Dataset data was used to define whether patients who had surgical treatment also had adjuvant therapy (chemotherapy or radiotherapy) during the first 9 months from diagnosis. The main outcomes were overall survival and time to death.

Study population issues: The baseline patient and tumour characteristics were similar between the groups. There was a small, though not statistically significant difference in use of adjuvant therapy (14.4% in the minimal access group and 18.1% in the open surgery group).

Other issues: The use of minimal access surgery increased from 48% in 2013 to 74% in 2016 (with a reciprocal decrease in open surgery). There was no adjustment for surgical experience and possible impact of learning curve for surgeons adopting minimal access surgery; laparoscopic and robotic surgery approaches within the minimal access group; and other surgical outcomes including surgical complication rates, and short- and long-term surgical morbidity.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **929 (564 MIS, 365 open)**

Overall survival

	3 months	6 months	1 year	2 years	3 years	4 years	4.5 years
MIS	100%	99.8% (98.8 to 100)	99.1% (97.9 to 99.6)	96.6% (94.6 to 97.9)	94.7% (92.0 to 96.5)	93.9% (90.6 to 96.1)	93.1% (89.2 to 95.6)
Open	100%	100%	99.7% (98.1 to 100)	99.4% (97.7 to 99.9)	98.3% (95.9 to 99.3)	98.3% (95.9 to 99.3)	97.2% (93.0 to 98.9)
p value	-	-	0.583	0.081	0.111	0.028	0.007

Differences by surgical approach were similar when stratifying the analysis by early stage category. When stratifying the analysis by adjuvant treatment status, differences between the 2 groups were more pronounced among women who had adjuvant management.

Unadjusted Cox regression analysis indicated evidence for variation in outcomes by surgical approach, with the minimal access group having a hazard ratio value of 3.3 (p=0.009).

In multivariate Cox regression analysis adjusting for diagnosis year, age, socio-economic status, Charlson comorbidity score, stage at diagnosis, English region, route to diagnosis, and adjuvant treatment status the difference in outcomes between the 2 surgical approach groups remained, becoming slightly larger (hazard ratio 4.0, p=0.007).

Abbreviations used: FIGO, International Federation of Gynecology and Obstetrics; MIS, minimally invasive surgery

Validity and generalisability of the studies

- One large, recent RCT was identified. This included data from the US, Asia and Europe but no patients were from the UK. The RCT did not reach its final intended enrolment because of safety concerns.
- There are different types of hysterectomy and techniques varied between and within studies. Some studies included robot-assisted procedures, but some specifically excluded them.
- Some comparative studies used historical controls and patients in the open surgery groups were treated earlier than those in the minimally invasive groups.
- Some studies included their early experience with laparoscopic or robot-assisted radical hysterectomies.
- Patient populations are heterogenous with regard to tumour stage, grade and size.
- In some studies, the follow-up periods were different for the different treatment groups.
- There are some long-term follow-up data.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer. NICE interventional procedures guidance 356 (2010). Available from http://www.nice.org.uk/guidance/IPG356

- Laparoscopic techniques for hysterectomy. NICE interventional procedures guidance 239 (2007). Available from http://www.nice.org.uk/guidance/IPG239

Additional information considered by IPAC

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Five Specialist Adviser Questionnaires for minimally invasive radical hysterectomy for early stage cervical cancer were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

NICE received 1 submission from a patient organisation.

Issues for consideration by IPAC

- The British Gynaecological Cancer Society (BGCS) posted a position statement on laparoscopic radical hysterectomy for cervical cancer on their website in May 2019. The statement finishes with the following paragraph:

  'In light of this analysis, the BGCS recommends that clinicians and patients exercise caution when considering undergoing minimal access radical hysterectomy for the management of early-stage cervical cancer. We recommend gynaecological oncologists and nurse specialists counsel patients regarding the potential risks and benefits of short-term morbidity

versus long term survival in surgery for early-stage cervical cancer, to enable women and their families to make a fully informed choice regarding the surgical options.'

- Ongoing trials:
  - SUCCOR-Surgery in Cervical Cancer Comparing Different Surgical Approaches in Stage IB1 Cervical Cancer (SUCCOR) (NCT03958305); Observational cohort study; Spain; estimated enrolment 1,000; study start date: May 2019; estimated study completion date: December 2019
  - Laparoscopic Approach to Cervical Cancer (LACC) (NCT00614211); RCT; US, Argentina, Australia, Brazil, Bulgaria, Canada, China, Colombia, Italy, Republic of Korea, Mexico, Peru, Puerto Rico; actual enrolment 636; study start date: January 2008; estimated study completion date: July 2022
  - Robot-assisted Approach to Cervical Cancer (RACC) (NCT03719547); RCT; Sweden; estimated enrolment 800; study start date: May 2019; estimated study completion date: February 2027
  - Different Surgical Approaches in Patients of Early-stage Cervical Cancer (NCT03739944); RCT; China; estimated enrolment 700; study start date: November 2018; estimated study completion date: November 2023
  - Longitudinal Study of Different Surgical Approaches in Chinese Patients of Cervical Cancer (NCT03738969); retrospective observational cohort study; China; estimated enrolment 3,000; study start date: November 2018; estimated study completion date: December 2023

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8. Zhang SS, Ding T, Cui ZH et al. (2019) Efficacy of robotic radical hysterectomy for cervical cancer compared with that of open and laparoscopic surgery: A separate meta-analysis of high-quality studies. Medicine 98: e14171

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13. Orfanelli T, Chung S, Kohut A et al. (2018) Ogilvie's syndrome after robotic-assisted radical hysterectomy for cervical cancer. Journal of Minimally Invasive Gynecology 25: 175-9
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16. Kim SI, Lee M, Lee S et al. (2019) Impact of laparoscopic radical hysterectomy on survival outcome in patients with FIGO stage IB cervical cancer: A matching study of two institutional hospitals in Korea. Gynecologic Oncology 155: 75-82
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18. National Cancer Registration and Analysis Service (NCRAS) (2019) Comparisons of overall survival in women diagnosed with early stage cervical cancer during 2013-2016, treated by radical hysterectomy using minimal access or open approach. Available from https://www.bgcs.org.uk/wp-content/uploads/2019/07/NCRAS-cervical-cancer-surgery-analysis-May-2019-final.pdf

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	24/10/2019	Issue 10 of 12, October 2019
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	24/10/2019	Issue 10 of 12, October 2019
HTA database (CRD website)	24/10/2019	n/a
MEDLINE (Ovid)	24/10/2019	1946 to October 21, 2019
MEDLINE In-Process (Ovid)	24/10/2019	1946 to October 22, 2019
Medline ePub ahead (Ovid)	24/10/2019	October 22, 2019
EMBASE (Ovid)	24/10/2019	1974 to 2019 October 23

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Uterine Cervical Neoplasms/ (71679)
2 Uterine Cervical Dysplasia/ (3710)
3 Cervical Intraepithelial Neoplasia/ (9497)
4 exp Uterine Cervical Diseases/ (78835)
5 CIN.tw. (8587)
6 (Cervic* adj4 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or dysplasis* or disease*)).tw. (57380)

7	or/1-6 (101033)
8	exp Laparoscopy/ (92203)
9	exp Laparoscopes/ (3682)
10	exp Minimally Invasive Surgical Procedures/ (485816)
11	(laparoscop* or celioscop* or peritoneoscop*).tw. (102275)
12	(minimal* adj4 invasiv* adj4 surg*).tw. (15480)
13	LRH.tw. (928)
14	("robot assist*" or "robot-assist*" or keyhole* or key-hole* or "key hole*").tw. (9775)
15	or/8-14 (516279)
16	exp Hysterectomy/ (29560)
17	(Hysterectom* or Hysterctom*).tw. (30490)
18	or/16-17 (42227)
19	15 and 18 (6929)
20	(lsh or lavh or larvh or tlh).tw. (1122)
21	19 or 20 (7434)
22	7 and 21 (1196)
23	animals/ not humans/ (4552498)
24	22 not 23 (1196)
25	limit 24 to ed=20100101-20190630 (539)
26	limit 25 to english language (475)

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Case series with fewer than 100 patients have been excluded. Case reports have been excluded unless they describe a safety event.

Article	Number of patients/ Follow up	Direction of conclusions	Reasons for non-inclusion in table 2
Abu-Rustum NR, Gemignani ML, Moore K et al. (2003) Total laparoscopic radical hysterectomy with pelvic lymphadenectomy using the argon-beam coagulator: Pilot data and comparison to laparotomy. Gynecologic Oncology 91: 402–9	Non-randomised comparative study n = 19 (LRH) n = 195 (ARH)	Conversion to open surgery=10.5% (2/19) No ureteral injuries or fistula formation. Laparoscopic approach had longer operating time, but less blood loss and shorter postoperative hospital stay.	Small patient numbers in laparoscopic group and no long-term follow up.
Anagnostopoulos A, Mitra S, Decruze B et al. (2017) Safety and cost considerations during the introduction period of laparoscopic radical hysterectomy. Obstetrics & Gynecology International 2103763	Non-randomised comparative study (laparoscopic versus open) n=72	Although no statistically significant difference in the intraoperative or postoperative complications was found more urinary tract injuries were recorded in the laparoscopic cohort. Laparoscopic surgery had statistically significantly longer duration (206 versus 159 minutes), lower lymph node harvest (12.6 versus 16.9), and slower bladder function recovery.	Larger studies are included.
Arispe C, Pomares AI, De Santiago J et al. (2016) Evolution of radical hysterectomy for cervical cancer along the last two decades: Single institution experience. Chinese Journal of Cancer Research 28: 215-20	Non-randomised comparative study (laparoscopic versus open) n=102	Regarding the disease-free interval, there were statistically significantly better outcomes in the group of laparotomy compared with laparoscopy (p=0.015). Laparoscopic RH is an acceptable surgery with advantages such as magnified vision of the operation's field, lower surgical complications, shorter hospital stay and earlier resumption to daily activities.	Larger studies are included.
Asciutto KC, Kalapotharakos G, Lofgren M et al. (2015) Robot-assisted surgery in cervical cancer patients reduces the time to normal activities of daily living. Acta Obstetricia et Gynecologica Scandinavica 94: 260-5	Non-randomised comparative study (robotic versus open) n=249	Laparoscopic robotic-assisted surgery is preferable to laparotomy for cervical cancer patients because it entails a statistically significantly shorter hospital stay, less blood loss, fewer intraoperative complications and shorter time to normal daily activities.	Only reports short-term outcomes.
Baffert S, Alran S, Fourchotte V et al. (2016)	Non-randomised comparative	There was no difference in operative time, or intraoperative	Larger studies are included.

Laparoscopic hysterectomy after concurrent radiochemotherapy in locally advanced cervical cancer compared to laparotomy: A multi institutional prospective pilot study of cost, surgical outcome and quality of life. European Journal of Surgical Oncology 42: 391-9	study (laparoscopic versus open) n=62 FU=6 months	and post-operative complication rates between the 2 groups. Intraoperative transfusion and abdominal drain were statistically significantly lower in the laparoscopy group (respectively, p=0.04 and p<0.01), as well as the duration of hospital stay (7 days vs 6 days, p<0.001). All patients who had laparoscopic hysterectomy were discharged to home, whereas 4 laparotomy patients used convalescence homes (p=0.01). Sexual activity is better for the laparoscopy group at 6 months (p=0.01).	
Balaya V, Mathevet P, Magaud L et al. (2019) Predictive factors of severe perioperative morbidity of radical hysterectomy with lymphadenectomy in early-stage cervical cancer: A French prospective multicentric cohort of 248 patients. European Journal of Surgical Oncology 45: 650-8	Non-randomised comparative study (laparoscopic assisted vaginal, total laparoscopic, robotic, and open) n=248 FU=49 months	This study based on prospective data showed that radical hysterectomy has low severe postoperative complications. The main complications were urinary infections and lower limb lymphedema. Patients with early-stage cervical cancer should be referred to expert centres to ensure best surgical outcomes.	Studies with more patients or longer follow up are included.
Bogani, Giorgio; Rossetti, Diego; Ditto, Antonino; et al. (2019) Minimally invasive surgery improves short-term outcomes of nerve-sparing radical hysterectomy in patients with cervical cancer: a propensity-matched analysis with open abdominal surgery. Journal of Gynecologic Oncology 30: e27	Non-randomised comparative study (nerve-sparing laparoscopic versus open) n=70	Laparoscopic approach resulted in a faster recovery of bladder function in comparison to open surgery for patients having nerve-sparing radical hysterectomy.	Only reports short-term outcomes.
Bogani, G.; Rossetti, D. O.; Ditto, A.; et al. (2018) Nerve-sparing approach improves outcomes of patients undergoing minimally invasive radical hysterectomy: a systematic review and meta-analysis. Journal of Minimally Invasive Gynecology 25: 402-10	Systematic review (nerve sparing versus conventional minimally invasive) n=675	Survival outcomes are not influenced by the type of surgical approach (recurrence [OR=1.27; 95% CI 0.49 to 3.28] and death [OR=1.01; 95% CI 0.36 to 2.83]) rates. The pooled data suggested that NS-MRH is equivalent to MRH for the treatment of cervical cancer and may be superior in reducing pelvic floor dysfunction rates.	Review focuses on nerve-sparing approach.
Bogani G, Cromi A, Uccella S et al. (2014) Laparoscopic versus open abdominal management of cervical cancer: long-term results from a propensity-matched analysis. Journal of	Non-randomised comparative study (laparoscopic versus open) n=130	Laparoscopy ensures the same results as open surgery insofar as radicality and long-term survival. Use of the laparoscopic approach is associated with improved short-term results, minimising the	Larger studies are included.

Minimally Invasive Gynecology 21: 857-62		occurrence of severe postoperative complications.	
Bogani G, Cromi A, Serati M et al. (2014) Predictors of postoperative morbidity after laparoscopic versus open radical hysterectomy plus external beam radiotherapy: a propensity-matched comparison. Journal of Surgical Oncology 110: 893-8	Non-randomised comparative study (laparoscopic versus open) n=90	Open approach is the main predictor for developing morbidity among cervical cancer patients having radical hysterectomy followed by adjuvant radiotherapy. Laparoscopic surgery enhances peri-operative surgical results and minimises the occurrence of late complications.	Larger studies are included.
Bogani G, Cromi A, Uccella S et al. (2014) Nerve-sparing versus conventional laparoscopic radical hysterectomy: a minimum 12 months' follow-up study. International Journal of Gynecological Cancer 24: 787-93	Non-randomised comparative study (nerve sparing versus conventional) n=106	No differences in 3-year disease-free survival (p=0.72) and overall survival (p=0.71) were recorded. The beneficial effects (in terms of operative time and number of nodes harvested) of NS-LRH are likely determined by the expertise of the surgeon because NS approach was introduced after having acquired adequate background in conventional LRH. Our data show that in experienced hands NS-LRH is safe and feasible. Moreover, NS technique reduces catheterisation time and the rate of postoperative urinary dysfunction.	Larger studies are included.
Bolles O, Borowsky M (2011) Port-site metastasis following robotic-assisted radical hysterectomy for squamous cell cervical cancer. Gynecologic Oncology Case Reports 2: 32-4	Case report n=1	**Port-site metastasis**. Large port-site metastasis following a robotic-assisted laparoscopic radical hysterectomy and postoperative adjuvant chemoradiation therapy for early stage squamous cell cervical carcinoma.	Case report of safety event already described.
Cai J, Yang L, Dong W et al. (2016) Retrospective comparison of laparoscopic versus open radical hysterectomy after neoadjuvant chemotherapy for locally advanced cervical cancer. International Journal of Gynaecology & Obstetrics 132: 29-33	Non-randomised comparative study (laparoscopic versus open) n=129 FU=26 months	LRH was similar to ARH in terms of safety, feasibility, and morbidity, with less blood loss among women with locally advanced cervical cancer who had neoadjuvant chemotherapy. Long-term outcomes need to be documented.	Larger studies are included.
Campos L, Limberger L, Stein A et al. (2013) Postoperative pain and perioperative outcomes after laparoscopic radical hysterectomy and abdominal radical hysterectomy in patients with early cervical cancer: a randomised	RCT n=30 (laparoscopic versus open)	Four patients (25%) in the LRH group and 5 patients (36%) in the ARH group had transoperative or serious postoperative complications. All of the transoperative complications occurred in the LRH group. The relative risk of presenting with complications was 0.70; CI 95% (0.23 to 2.11); p=0.694. LRH group mean pain score was	The primary outcome was postoperative pain.

controlled trial. Trials 14: 293		statistically significantly lower than ARH after 36 hours. (p=0.044; mean difference score: 1.42; 95% CI: 0.04 to 2.80).	
Canturk M, Ozben V, Kose MF et al. (2017) Robotic repair of vaginal evisceration after hysterectomy and the role of intraoperative near-infrared fluorescence imaging. Journal of Robotic Surgery 11: 383-6	Case report n=1	**Vaginal evisceration** evisceration of small bowel outside the vulvar introitus after robotic hysterectomy for cervical cancer. It was repaired using a robotic approach.	Case report of safety event already described (wound dehiscence)
Chen CH, Chiu LH, Chang CW et al. (2014) Comparing robotic surgery with conventional laparoscopy and laparotomy for cervical cancer management. International Journal of Gynecological Cancer 24: 1105-11	Non-randomised comparative study (robotic versus laparoscopic versus open) n=100 FU=14 to 37 months	The robotic group showed a shorter operation time, less blood loss, lower transfusion rate, and lower laparotomy conversion rate than the laparoscopic or laparotomy group. As for the postoperative parameters, the robotic group showed reduced postoperative and 24-hour pain scores, shortened length of hospital stay, and decreased time to full diet resumption compared with the other 2 surgical groups. No statistically significant differences were found between the groups in perioperative complication rate or disease-free survival.	Larger studies are included.
Chen CH, Wang PH, Chiu LH et al. (2013) Comparing thermal welding instrument-assisted laparoscopic radical hysterectomy versus conventional radical hysterectomy in the management of FIGO IB1 squamous cell cervical carcinoma. European Journal of Gynaecological Oncology 34: 442-5	Non-randomised comparative study n=53 FU=median 4 years	Thermal welding instrument-assisted laparoscopic radical hysterectomy is a safe and efficient method for laparoscopic radical hysterectomy with reduction of morbidity for early-stage cervical cancer. The recurrence rate between the 2 groups was similar (9% compared with 13%).	Larger studies are included.
Chen L, Zhang W, Zhang S et al. (2014) Effect of laparoscopic nerve-sparing radical hysterectomy on bladder function, intestinal function recovery and quality of sexual life in patients with cervical carcinoma. Asian Pacific Journal of Cancer Prevention 15: 10971-5	RCT (nerve-sparing versus conventional laparoscopic radical hysterectomy) n=65	The mean duration of the postoperative catheterisation in the nerve-sparing group (LNRH) was shorter than that in the conventional group (LRH), p<0.001. The maximum flow rate, maximum cystometric capacity, maximum detrusor pressure and urinary complications in group LNRH were better than those in group LRH. The quality of sexual life evaluated according to the female sexual function index was better in group LNRH than in those who had LRH. The intestinal function of patients in group LNRH also recovered	Small study, comparing nerve-sparing laparoscopic radical hysterectomy with conventional laparoscopic radical hysterectomy.

		better compared with patients in group LRH.	
Chen SQ, Kong LZ, Jiang HY et al. (2015) Early cervical cancer impact of peritoneal vaginoplasty combined with laparoscopic radical hysterectomy improved sexual function. International Journal of Gynecological Cancer 25: 526-32	Non-randomised comparative study n=79 FU=1 year	Peritoneal vaginoplasty to lengthen the vagina improves sexual function of patients with early cervical cancer having LRH in sexual satisfaction, lubrication, and pain.	Study focuses on impact of peritoneal vaginoplasty.
Chen Y, Xu H, Li Y et al. (2008) The outcome of laparoscopic radical hysterectomy and lymphadenectomy for cervical cancer: a prospective analysis of 295 patients. Annals of Surgical Oncology 15: 2847–55	Case series n=295 FU=median 36 months	Conversion to open surgery=2% (5/295): bleeding (n=3), bowel injury (n=1), and hypercapnia (n=1). Other major intraoperative injuries=4% (n=12). Positive lymph nodes were detected in 80 patients (27%), lymphovascular space invasion in 54 (18%), and surgical margins were negative for tumour in all patients. Postoperative complications=11%: ureterovaginal fistula (n=5), vesicovaginal fistula (n=4), ureterostenosis (n=3), deep venous thrombosis (n=9), lymphocyst (n=4), lymphedema (n=5), and 1 patient with trocar insertion site metastasis. Other medical problems included 47 cases (16%) of bladder dysfunction and 62 cases (21%) of rectum dysfunction or constipation. Recurrences or metastasis=16%. The overall disease-free survival was 95% for 1A, 96% for 1B, 84% for 2A, 79% for 2B, 67% for 3A, and 60% for 3B.	More recent studies are included.
Choi CH, Lee JW, Lee YY et al. (2012) Comparison of laparoscopic-assisted radical vaginal hysterectomy and laparoscopic radical hysterectomy in the treatment of cervical cancer. Annals of Surgical Oncology 19: 3839-48	Non-randomised comparative study n=293 FU=2 to 79 months	Lower rate of blood loss, early return of bowel activity, and possible less frequent intraoperative complication are in favour of LRH and learning skills for doing radical vaginal trachelectomy is in favour of LARVH. However, the choice between vaginal and total laparoscopic approach should depend on the experience of the surgeon and the wishes of the patient.	More recent studies are included.
Chong GO, Lee YH, Lee HJ et al. (2018) comparison of the long-term oncological outcomes between the initial learning period of robotic	Non-randomised comparative study (robotic	Postoperative complication rates were statistically significantly higher in the RRH group than in the LRH group (48% vs 27%; p=0.0188). No difference in the	Larger studies are included.

and the experienced period of laparoscopic radical hysterectomy for early-stage cervical cancer. International Journal of Gynecological Cancer 28: 226-32	versus laparoscopic) n=125 FU=63 months	estimated disease-free survival rates was observed between the 2 groups (p=0.3152); however, the estimated overall survival of RRH was lower than that of LRH with marginal significance (p=0.0762). There was no statistically significant difference in terms of recurrence pattern between the 2 groups (p=0.7041). However, peritoneal recurrences occurred only in the RRH group.	
Chong GO, Lee YH, Hong DG et al. (2013) Robot versus laparoscopic nerve-sparing radical hysterectomy for cervical cancer: a comparison of the intraoperative and perioperative results of a single surgeon's initial experience. International Journal of Gynecological Cancer 23: 1145-9	Non-randomised comparative study (nerve-sparing robotic versus laparoscopic) n=100	During the first 50 cases, surgical outcomes and complication rates of nerve-sparing RRH were found to be comparable to those of nerve-sparing TLRH. Moreover, the mean blood loss and intraoperative complication rate in the robotic group were statistically significantly lower than those in the laparoscopic group.	Larger studies are included.
Chong GO, Hong DG, Cho YL et al. (2010) Vaginal evisceration after total laparoscopic radical hysterectomy in cervical cancer. American Journal of Obstetrics & Gynecology 202: e7-8	Case report n=1	**Vaginal evisceration** Vaginal evisceration happened 7 months after a total laparoscopic radical hysterectomy. It was repaired by a laparoscopic-vaginal approach without a laparotomy. This is the first report of vaginal evisceration after a total laparoscopic radical hysterectomy.	Case report of safety event already described in table 2.
Chong GO, Park NY, Hong DG et al. (2009) Learning curve of laparoscopic radical hysterectomy with pelvic and/or para-aortic lymphadenectomy in the early and locally advanced cervical cancer. International Journal of Gynecological Cancer 19: 1459–64	Case series n=100 FU=median 66.5 months	The intraoperative and postoperative complication rates profoundly decreased in group 2 (second 50 cases) as compared with group 1 (first 50 cases). After a median follow up of 66.5 months, 10 patients had a recurrence, 9 of whom died. The 5-year overall survival rates were 96% in group 1 and 90% in group 2, and 5-year disease-free survival rates were 92% in group 1 and 90% in group 2.	Larger studies are included.
Clark LH, Barber EL, Gehrig PA et al. (2016) Does the robotic platform reduce morbidity associated with combined radical surgery and adjuvant radiation for early cervical cancers? International Journal of Gynecological Cancer 26: 1485-9	Non-randomised comparative study (robotic versus open) n=243 FU=23 months	We found no difference in long-term complications between patients who had robotic surgery compared with open radical hysterectomy with adjuvant radiation. There may be fewer adhesion-related complications with robotic surgery. However, as many radiation-related complications occur at later time points, continued follow up to	Studies with longer follow up are included.

		evaluate for potential differences between the 2 groups is necessary.	
Colombo PE, Bertrand MM, Gutowski M et al. (2009) Total laparoscopic radical hysterectomy for locally advanced cervical carcinoma (stages IIB, IIA and bulky stages IB) after concurrent chemoradiation therapy: surgical morbidity and oncological results. Gynecologic Oncology 114: 404–9	Non-randomised comparative study (laparoscopic versus open) n=102 FU=mean 31 months	There were no statistically significant differences in locoregional recurrence, distant recurrence, 3-year overall survival or 3-year disease-free survival. Postoperative complications: • LRH=28% (13/46) • Open=46% (26/56), p=0.04	Larger studies are included.
Corrado G, Vizza E, Legge F et al. (2018) Comparison of different surgical approaches for stage IB1 cervical cancer patients: a multi-institution study and a review of the literature. International Journal of Gynecological Cancer 28: 1020-8	Non-randomised comparative study (open versus laparoscopic versus robotic) n=341 FU=median 82, 42 and 47 months.	Compared with ORH, the minimally invasive surgery group was safer in terms of estimated blood loss, transfusion rates, and hospital stay. Robotic surgery was equivalent to laparoscopy in terms of intraoperative and postoperative complications, hospital stay, conversions, and reintervention. Robotic surgery had better outcomes compared with laparoscopy in terms of transfusion rates and was equivalent to abdominal surgery and laparoscopy in regard to oncological outcomes.	Studies with more patients or longer follow up are included.
Corrado G, Cutillo G, Saltari M et al. (2016) Surgical and oncological outcome of robotic surgery compared with laparoscopic and abdominal surgery in the management of locally advanced cervical cancer after neoadjuvant chemotherapy. International Journal of Gynecological Cancer 26: 539-46	Non-randomised comparative study (robotic versus laparoscopic versus open) n=125 FU=60 months	The median estimated blood loss, operative time, and length of hospital stay were statistically significant and in favour of the robotic group. No conversion to laparotomy in the robotic group was necessary. There were no statistically significant differences between the 3-year overall survival and disease-free survival rates in the minimally invasive groups.	Larger studies are included.
Deshmukh U, McAdow M, Black J et al. (2017) Isolated port site recurrence of node-negative clinical stage IB1 cervical adenocarcinoma. Gynecologic Oncology Reports 20: 54-7	Case report n=1	**Port-site metastasis** Isolated port-site recurrence in a patient who had robotic-assisted laparoscopic surgery for early-stage cervical adenocarcinoma with negative margins and negative lymph nodes. The mechanism underlying this isolated recurrence remains unknown.	Case report of safety event already described.
Diaz-Feijoo B, Gil-Moreno A, Perez-Benavente MA et al. (2008) Sentinel lymph node identification and radical hysterectomy with	Non-randomised comparative study n=20 (LRH)	No statistically significant difference in overall survival and disease-free survival.	Larger studies are included.

lymphadenectomy in early stage cervical cancer: laparoscopy versus laparotomy. Journal of Minimally Invasive Gynecology 15: 531–7	n=30 (ARH) Median follow up = 35 months	Blood loss and length of stay were statistically significantly lower in laparoscopic group, but surgical time was statistically significantly longer.	
Ditto A, Martinelli F, Bogani G et al. (2015) Implementation of laparoscopic approach for type B radical hysterectomy: a comparison with open surgical operations. European Journal of Surgical Oncology 41: 34-9	Non-randomised comparative study (laparoscopic versus open) n=120	Patients having laparoscopic radical hysterectomy (LRH) had longer operative time than patients having randomised abdominal hysterectomy (RAH); while LRH correlated with shorter length of hospitalisation and lower blood loss compared with RAH. Intra- and post-operative complication rate was similar between groups (p=1.00). The execution of LRH or RAH did not influence site of recurrence (p>0.2) as well as survival outcomes, in term of 5-year disease-free (p=0.29, log-rank test) and overall survivals (p=0.50, log-rank test).	Larger studies are included.
Diver E, Hinchcliff E, Gockley A et al. (2017) Minimally invasive radical hysterectomy for cervical cancer is associated with reduced morbidity and similar survival outcomes compared with laparotomy. Journal of Minimally Invasive Gynecology 24: 402-6	Non-randomised comparative study (minimally invasive versus open) n=383	Minimally invasive surgery (MIS) does not compromise patient outcomes, including overall survival, rate of recurrence, and the frequency of pelvic lymph node dissection or positivity. Morbidity was decreased in the MIS group, including decreased estimated blood loss, fewer blood transfusions, and shorter hospital stay.	Larger studies are included.
Dos Reis R, Andrade CEMC, Frumovitz M et al. (2018) Radical hysterectomy and age: outcomes comparison based on a minimally invasive vs an open approach. Journal of Minimally Invasive Gynecology 25: 1224-30	Non-randomised comparative study (minimally invasive versus open) n=548	The between-group difference in postoperative non-infectious complication rate in the oldest age group was twice that in either of the other 2 age groups (p=0.0324), even though the MIS patients were older, heavier, and had a longer operative time compared with the laparotomy patients.	Studies with longer follow up are included.
Estape R, Lambrou N, Diaz R et al. (2009) A case matched analysis of robotic radical hysterectomy with lymphadenectomy compared with laparoscopy and laparotomy. Gynecologic Oncology 113: 357–61	Non-randomised comparative study n=17 (LRH) n=14 (ARH) n=32 (robotic) Mean follow up=31 months (LRH)	Robotic group had higher mean number of nodes retrieved than LRH or ARH. Postoperative complications: • Robotic = 19% • LRH = 24% • ARH = 29%	Larger studies are included.
Frumovitz M, dos Reis R, Sun CC et al. (2007) Comparison of total	Non-randomised comparative study	LRH associated with reduced blood loss, postoperative infectious morbidity and	Larger studies are included.

laparoscopic and abdominal radical hysterectomy for patients with early-stage cervical cancer. Obstetrics & Gynecology 110: 96–102	n=89	postoperative length of stay but with increased operative time.	
Gallotta V, Conte C, Federico A et al. (2018) Robotic versus laparoscopic radical hysterectomy in early cervical cancer: A case matched control study. European Journal of Surgical Oncology 44: 754-9	Non-randomised comparative study (robotic versus laparoscopic) n=210 FU=36 months	Conversion to laparotomy was necessary in 4 patients (2%) in the whole series. No difference was found in terms of intraoperative and postoperative complications between the 2 groups. During the observation period, 34 (16%) patients had any grade postoperative complications, and 21 (10%) had >G2 complications. The 3-yr DFS was 88% versus 84% in robotic and laparoscopic group, respectively (p value=0.866). Central and/or lateral pelvic disease represented the most common site of relapse. The 3-yr OS was 91% in patients who had robotic RH versus 94% in patients who had laparoscopic RH (p value=0.924).	Larger studies are included.
Garabedian C, Merlot B, Bresson L et al. (2015) Minimally invasive surgical management of early-stage cervical cancer. International Journal of Gynecological Cancer 25: 714-21	Case series n=170 FU=median 48 months	14 severe perioperative complications (8%); 5 patients (3%) needed conversion to an open procedure: 3 bowel injuries, 3 haemorrhages, 2 ureteral injuries, 3 bladder injuries, 2 severe adhesions, and 1 intolerance to the Trendelenburg position. The 5-year overall survival was 94% (range 88% to 97%), and the 5-year disease-free survival was 89% (range 81% to 93%).	Larger studies are included.
Geetha P, Nair M (2012) Laparoscopic, robotic and open method of radical hysterectomy for cervical cancer: A systematic review. Journal of Minimal Access Surgery; 2012; vol. 8 (no. 3); 67-73	Systematic review 47 studies	The current evidence shows that minimally invasive surgery is associated with less morbidity compared with open surgery and can be considered as an alternate option for surgical management of cervical cancer without compromising the oncologic outcome.	More recent studies are included.
Geisler JP, Orr CJ, Khurshid N et al. (2010) Robotically assisted laparoscopic radical hysterectomy compared with open radical hysterectomy. International Journal of Gynecological Cancer 20: 438-42	Non-randomised comparative study (robotic versus open) n=60	Radical surgery for cervical cancer can be accomplished using the da Vinci surgical system with acceptable blood loss, operating time, parametrial margins, and nodal yield. Future studies need to address long-term outcomes.	Larger studies are included.

Ghezzi F, Cromi A, Ditto A et al. (2013) Laparoscopic versus open radical hysterectomy for stage IB2-IIB cervical cancer in the setting of neoadjuvant chemotherapy: a multi-institutional cohort study. Annals of surgical oncology 20: 2007-15	Non-randomised comparative study (laparoscopic versus open) n=341 FU=35 months	In the propensity score-matched cohort, Cox proportional hazards model including tumour stage, grade, histotype, nodal status, institution, and time period of surgery showed that laparoscopic approach was not associated with impaired survival.	Includes some patients with stage IIb disease.
Ghezzi F, Fanfani F, Malzoni M et al. (2013) Minilaparoscopic radical hysterectomy for cervical cancer: multi-institutional experience in comparison with conventional laparoscopy. European Journal of Surgical Oncology 39: 1094-100	Non-randomised comparative study (mini-laparoscopic versus laparoscopic) n=257	No statistically significant differences were observed between groups in terms of operative time, blood loss, lymph node yield, amount of parametrial or vaginal cuff tissue removed, and percentage of intra- or postoperative complications, both in the entire cohort and in the propensity score matched group. No conversions were needed from minilaparoscopy to standard laparoscopy or to open surgery. Conversion from standard laparoscopy to open surgery was necessary in 2 patients. A shorter hospital stay was observed among women who had mLRH than in those having LRH [2 (1-10) vs 4 (1-14) days, p=0.005]. This difference remained statistically significant after propensity score matching.	Study focuses on minilaparoscopic technique.
Ghezzi F, Cromi A, Ciravolo G et al. (2007) Surgicopathologic outcome of laparoscopic versus open radical hysterectomy. Gynecologic Oncology 106: 502–6	Non-randomised comparative study (laparoscopic versus open) n=98	The results suggest that patients with laparoscopically managed cervical cancer have a similar extent of surgery as those with cancer treated with the traditional ARH, as judged by objective pathologic criteria.	Larger studies are included.
Gilabert-Estelles J, Favero R, Paya V et al. (2010) Small bowel incarceration in the umbilical artery following total laparoscopic radical hysterectomy. Gynecological Surgery 7: 185-8	Case report n=1	**Small bowel obstruction caused by a loop incarceration in the umbilical artery** Treated using a wide segmental bowel resection with end to end anastomosis.	Case report of safety event already described (organ injury)
Gortchev G, Tomov S, Tantchev L et al. (2011) Robot-assisted radical hysterectomy-perioperative and survival outcomes in patients with cervical cancer compared to laparoscopic and open radical surgery. Gynecological Surgery: 1-8	Non-randomised comparative study (robotic versus laparoscopic versus open) n=294 FU=1,531 days	Type of surgical procedure did not influence disease-free survival, as well as overall survival. Robot-assisted radical hysterectomy has been established to be a safe procedure with proven advantages in regard to operative time and hospital stay. The absence of statistically significant differences in survival is a substantial reason to continue,	More recent studies are included.

		from an oncologic point of view, the application of this method.	
Guo J, Yang L, Cai J et al. (2018) Laparoscopic procedure compared with open radical hysterectomy with pelvic lymphadenectomy in early cervical cancer: a retrospective study. OncoTargets and therapy 11: 5903-8	Non-randomised comparative study (laparoscopic versus open) n=551 FU=39 months	Estimated blood loss and transfusion needs were statistically significantly lower in the LRH group. Postoperative hospital stay was also statistically significantly shorter in the LRH group. A statistically significant difference was found in the number of pelvic lymph nodes retrieved between the LRH and open radical hysterectomy with pelvic lymphadenectomy (ORH) groups. There were no differences in operating time, perioperative complications, progression-free survival, and overall survival between the LRH and ORH groups.	Studies with more patients or longer follow up are included.
Han L, Yan P, Yao L et al. (2019) Safety and effectiveness of robotic hysterectomy versus conventional laparoscopic hysterectomy in patients with cervical cancer in China. Archives of Gynecology & Obstetrics 21: 21	Non-randomised comparative study (robotic versus laparoscopic) n=152	The RH group showed shorter operative time (p=0.008) and more lymph nodes (p=0.001) than the LH group. As for the postoperative parameters, the RH group showed shorter time to remove drainage tube (p=0.019) and length of hospital stay (p=0.001). No statistically significant difference was found between the groups in estimated blood loss, time to first flatus, time to a full diet, and postoperative complication.	Studies with more patients or longer follow up are included.
Han L, Cao R, Jiang JY et al. (2014) Preset ureter catheter in laparoscopic radical hysterectomy of cervical cancer. Genetics & Molecular Research 13: 3638-45	Non-randomised comparative study (with or without ureteral catheter) n=176	A ureteral catheter that is placed preoperatively can help to identify the ureter in laparoscopic radical hysterectomy but does not decrease the incidence of ureteral injury.	Study focuses on the use of preoperative ureteral catheters.
Hao X, Han S, Wang Y (2015) Comparison of conventional laparoscopy and robotic radical hysterectomy for early-stage cervical cancer: A meta-analysis. Journal of Cancer Research & Therapeutics 11: C258-64	Systematic review n=12 studies	Meta-analysis showed that although LRH and RRH were similar in terms of operating time, the length of hospital stay, and number of pelvic lymph nodes resected, RRH presented less blood loss and overwhelming advantage against LRH with the respect of complications.	A more recent review is included.
Hong JH, Choi JS, Lee JH et al. (2012) Can laparoscopic radical hysterectomy be a standard surgical modality in stage IA2-IIA cervical cancer? Gynecologic Oncology 127: 102-6	Case series n=118 FU=median 31 months	There was no unplanned conversion to laparotomy. Intra- and postoperative complications occurred in 16 (14%) and 8 (7%) patients, respectively. In a median follow up of 31 months (range, 1-89), 5-year recurrence-free and overall survival rates were 90%	Larger studies are included.

		and 89%, respectively. Univariate analysis showed that cervical stromal invasion (p=0.023) and lymph node metastasis (p=0.018) affected survival rate. Cox-proportional hazards regression analysis showed that lymph node metastasis was the only independent factor for poor prognosis (hazard ratio=7.0, p=0.022).	
Hwang JH, Lim MC, Joung JY et al. (2012) Urologic complications of laparoscopic radical hysterectomy and lymphadenectomy. International Urogynecology Journal 23: 1605-11	Case series n=146	Double ureteral stents were inserted prophylactically in 13 patients (9%), 2 of whom had postoperative urologic complications. Nine patients (6%) had postoperative urologic complications. Of 4 patients with ureterovaginal fistulas, 2 had conservative treatment with cystoscopic placement of ureteral stents and 2 had ureteroneocystostomies. Vesicovaginal fistulas occurred in 2 patients, both of whom had vesicovaginal fistula repairs. One patient noted to have a bladder injury intraoperatively had a laparoscopic repair, and 1 patient noted to have a ureteral injury postoperatively had conservative treatment with cystoscopic placement of ureteral stents.	Includes patients with cervical or endometrial cancer.
Iniesta MD, de Santiago J, Ordas J. (2007) Splenic rupture following laparoscopic radical hysterectomy. International Journal of Gynecology & Obstetrics 99: 245–6	Case report n=1	**Splenic rupture** Splenic rupture was recognised 5 days after LRH for cervical cancer, treated with splenectomy.	Case report of safety event already described (organ injury).
Jiang H, Zhu J, Guo SW et al. (2016) Vaginal extension improves sexual function in patients receiving laparoscopic radical hysterectomy. Gynecologic Oncology 141: 550-8	Non-randomised comparative study n=216	While the sexual function in patients having vaginal extension (VX) procedure does not fully achieve the preoperational level, the improvement is global and statistically significant. Ovarian preservation procedure during LRH may also help improve the sexual function. Therefore, VX and ovarian preservation may be desirable for patients with early-stage cervical cancer who have RH.	Study focuses on effect of vaginal extension.
Jiang W, Liang M, Han D et al. (2019) A modification of laparoscopic type C1 hysterectomy to reduce postoperative bladder dysfunction: a retrospective	Non-randomised comparative study (type C1 versus type C2) n=152	There was no statistically significant difference in bladder storage dysfunction, such as urinary incontinence and frequent urination, between two groups. The 3-year disease-free survival	Study focuses on technique.

study. Journal of Investigative Surgery 32: 272-80		rates and 3-year overall survival rates in the two groups were both similar.	
Jin YM, Liu SS, Chen J et al. (2018) Robotic radical hysterectomy is superior to laparoscopic radical hysterectomy and open radical hysterectomy in the treatment of cervical cancer. PLoS ONE [Electronic Resource] 13: e0193033	Network meta-analysis n=17 studies	The network meta-analysis showed that patients had RRH and LRH had lower estimated blood loss compared with patients had ORH (WMD=-399.52, 95% CI=-600.64 to -204.78; WMD=-277.86, 95%CI=-430.84 to -126.07, respectively). Patients had RRH and LRH had less hospital stay (days) than those by ORH (WMD=-3.49, 95% CI=-5.79 to -1.24; WMD=-3.26, 95% CI=-5.04 to -1.44, respectively). Compared with ORH, patients had RRH had lower postoperative complications (OR=0.21, 95% CI=0.08 to 0.65).	A review with a more recent search date is included.
Kahramanoglu I, Sal V, Bese T (2016) Post-coital vaginal cuff dehiscence with small bowel evisceration after laparoscopic type II radical hysterectomy: A case report. International Journal of Surgery Case Reports 26: 81-3	Case report n=1	**Vaginal cuff dehiscence** Vaginal cuff dehiscence with small bowel evisceration in a woman who had laparoscopic type II hysterectomy for stage IA2 cervical cancer. Patients who have had hysterectomy should be advised about when to restart coitus. Vaginal repair of vaginal cuff dehiscence is recommended if intestinal ischemia is excluded.	Case report of safety event already described.
Kanao H, Matsuo K, Aoki Y et al. (2019) Feasibility and outcome of total laparoscopic radical hysterectomy with no-look no-touch technique for FIGO IB1 cervical cancer. Journal of Gynecologic Oncology 30: e71	Non-randomised comparative study (laparoscopic versus open) n=163 FU=30 months	Surgical outcomes of TLRH were superior to ARH for operative time (294 vs 376 minutes), estimated blood loss (185 vs 500 mL), and length of hospital stay (14 vs 18 days) (all p<0.001). Oncologic outcomes were similar between the 2 groups, including disease-free survival (DFS) (p=0.591) and overall survival (p=0.188). When stratified by tumour size (<2 vs ≥2 cm), DFS was similar between the 2 groups (p=0.897 and p=0.602, respectively). The loco-regional recurrence rate following TLRH was similar to the rate after ARH (6% vs 10%, p=0.566). Multiple-pelvic recurrence was observed in only 1 patient in the TLRH group.	Larger studies are included.
Kim JY, Lee YH, Chong GO et al. (2015) Comparative study between total laparoscopic and total robotic radical hysterectomy for cervical carcinoma:	Non-randomised comparative study (robotic versus laparoscopic) n=63	Total robotic radical hysterectomy surgical outcomes were associated with less blood loss and more harvested pelvic lymph nodes but longer operative times with statistical significance. The short-term postoperative HRQOL	Larger studies are included.

clinical study. Anticancer Research 35: 5015-21	FU=3 months	outcomes did not show any statistically significant inter-group differences.	
Kim MK, Oh BC, Kim HJ et al. (2009) Complete bladder gangrene caused by bilateral hypogastric artery ligation during laparoscopic radical hysterectomy. Journal of Minimally Invasive Gynecology 16: 76–7	Case report n=1	**Bladder gangrene** Gangrenous bladder wall and rupture were visible 3 weeks after LRH. A total cystectomy and transureteroureterostomy with cutaneous ureterostomy were done.	Case report of safety event already described (organ injury).
Kim TH, Choi CH, Choi JK et al. (2014) Robotic versus laparoscopic radical hysterectomy in cervical cancer patients: a matched-case comparative study. International Journal of Gynecological Cancer 24: 1466-73	Non-randomised comparative study (robotic versus laparoscopic) n=92 FU=58 months	Intraoperative and postoperative complications were not statistically significantly different between the 2 groups (4% for RRH vs 2% for LRH; p=0.439). Recurrences were 2 (9%) in the RRH and 7 (10%) in the LRH group. The overall 3-year recurrence-free survival was 91% in RRH group and 90% in the LRH group (p=0.778).	Larger studies are included.
Kim B, Huh SJ, Kim BG (2013) Port site metastasis after robotic-assisted laparoscopic hysterectomy for uterine cervical cancer: a case report and literature review. Taiwanese Journal of Obstetrics & Gynecology 52: 558-63	Case report n=1	**Port-site metastasis** Port-site metastasis after robotic-assisted laparoscopic hysterectomy for stage IB1 uterine cervical cancer. The patient had concurrent chemoradiotherapy, which resulted in a rapid decrease in tumour size and relief of abdominal pain.	Case report of safety event already described.
Kiran A, Hilton P, Cromwell DA (2016) The risk of ureteric injury associated with hysterectomy: a 10-year retrospective cohort study. BJOG: An International Journal of Obstetrics & Gynaecology 123: 1184-91	Non-randomised comparative study (laparoscopic versus open) n=1,792	In 2001-2010, 377,073 women had a hysterectomy and 1,792 (0.5%) experienced a ureteric injury. The rate of injury was higher in 2006-2010 than 2001-2005. After 2006, ureteric injuries were most common for abdominal radical hysterectomy for uterine cancer (11%; 95% CI 7 to 15%). The proportion of women having a ureteric injury was similar for ovarian and cervical cancer (2 to 4% depending on type of procedure).	Study focuses on the rate of ureteric injury after any kind of hysterectomy and includes benign and malignant indications.
Ko EM, Muto MG, Berkowitz RS et al. (2008) Robotic versus open radical hysterectomy: a comparative study at a single institution. Gynecologic Oncology 111: 425-30	Non-randomised comparative study n=48 Short-term follow up	Robotic radical hysterectomy results in lower blood loss and shorter hospital stay than open radical hysterectomy. Intraoperative and postoperative complication rates are comparable.	Larger studies are included.
Kobayashi E, Nagase T, Fujiwara K et al. (2012) Total laparoscopic hysterectomy in 1253 patients using an	Case series n=1,253	24 patients had major complications (2%). Complications included 10 intraoperative urologic injuries, 5	More recent studies are included.

early ureteral identification technique. Journal of Obstetrics and Gynaecology Research 38: 1194-200		cases of postoperative hydronephrosis, 5 cases of vaginal dehiscence, 1 bowel injury, 1 postoperative haemorrhage, 1 bowel obstruction, and 1 ureterovaginal fistula. All 11 cases of intraoperative visceral injury were recognised during the surgery and repaired during the same laparoscopic surgical procedure. Of the risk factors analysed, a history of abdominal surgery was the only one associated with the occurrence of major complications, with an odds ratio of 2.48 (95% confidence interval 1.23 to 6.49).	
Kong TW, Chang SJ, Piao X et al. (2016) Patterns of recurrence and survival after abdominal versus laparoscopic/robotic radical hysterectomy in patients with early cervical cancer. Journal of Obstetrics & Gynaecology Research 42: 77-86	Non-randomised comparative study n=128 FU=20.5 months	Total laparoscopic/robotic intracorporeal colpotomy under CO_2 pneumoperitoneum may carry a risk of positive vaginal cuff margin, as well as intraperitoneal tumour spreads in patients with early-stage cervical cancer treated with LRH/RRH.	Larger studies are included.
Kong TW, Chang SJ, Lee J et al. (2014) Comparison of laparoscopic versus abdominal radical hysterectomy for FIGO stage IB and IIA cervical cancer with tumor diameter of 3 cm or greater. International Journal of Gynecological Cancer 24: 280-8	Non-randomised comparative study (laparoscopic versus open) n=88	Disease-free survival rates were 98% in both groups. Laparoscopic radical hysterectomy might be a feasible therapeutic procedure for the management of FIGO stage 1B and 2A cervical cancer with tumour diameter of 3 cm or greater.	Larger studies are included.
Lambaudie E et al (2010) Role of robot-assisted laparoscopy in adjuvant surgery for locally advanced cervical cancer. European Journal of Surgical Oncology, 36: 409 - 13	Non-randomised comparative study (laparoscopic versus robotic open) n=58	Robot-assisted laparoscopy is feasible after concurrent chemoradiation and brachytherapy in cases of locally advanced cervical cancer. This new surgical approach reduces hospital stay, and seems to result in less severe complications than conventional laparotomy without modifying the oncological outcome.	Larger studies are included.
Laterza RM, Uccella S, Casarin J et al. (2016) Recurrence of early stage cervical cancer after laparoscopic versus open radical surgery. International Journal of Gynecological Cancer 26: 547-52	Non-randomised comparative study (laparoscopic versus open) n=150 FU=44 months	Patients who had LRH had less blood loss (100 vs 400 mL, $p<0.0001$), fewer lymph nodes removed (20 vs 31, $p=0.001$), and shorter recovery (4 vs 8 days, $p=0.0005$) in comparison with the ARH group. No statistically significant differences were found regarding recurrence rate (9 vs 13, $p=0.17$) and time to	Larger studies are included.

		recurrence (8 vs 17 months, p=0.066) between LRH and ARH group. Sites of recurrence were also comparable between the 2 groups: 2/9 versus 2/13 local recurrence, 4/9 versus 8/13 pelvic recurrence, 4/9 versus 7/13 distant recurrence in LRH and ARH groups, respectively. The most frequent sites of recurrence were pelvic and distant (44%) in LRH group and pelvic (62%) in ARH group.	
Laterza RM, Salvatore S, Ghezzi F et al. (2015) Urinary and anal dysfunction after laparoscopic versus laparotomic radical hysterectomy. European Journal of Obstetrics, Gynecology, & Reproductive Biology 194: 11-6	Non-randomised comparative study (laparoscopic versus open) n=54 FU=6 months	Laparoscopic approach for radical hysterectomy seems to reduce the postoperative occurrence of urge incontinence, increased bladder sensation and constipation by obstructed defecation, in comparison with abdominal radical surgery.	Studies with longer follow up are included.
Lee B, Kim K, Park Y et al. (2018) Impact of hospital care volume on clinical outcomes of laparoscopic radical hysterectomy for cervical cancer: A systematic review and meta-analysis. Medicine 97: e13445	Systematic review n=59 studies	In high-volume hospitals (HVH), a higher number of lymph nodes (24.5 vs 21.1; p=0.037) were retrieved by LRH in older women (48.4 vs 44.5 years; p=0.010) with tendencies of shorter operation time (224 vs 256 minutes; p=.096) and less blood loss (253 vs 322 mL; p=0.080). Compared with low-volume hospitals, HVH had fewer patients with stage 1A disease (14 vs 24%; p=0.003) and more patients with stage 2A disease (15 vs 7%; p=0.052) with comparable 5-year overall survival (93 vs 89%; p=0.112).	Review focuses on impact of hospital care volume.
Lee EJ, Kang H, Kim DH (2011) A comparative study of laparoscopic radical hysterectomy with radical abdominal hysterectomy for early-stage cervical cancer: a long-term follow-up study. European Journal of Obstetrics, Gynecology, & Reproductive Biology 156: 83-6	Non-randomised comparative study (laparoscopic versus open) n=72 FU=median 78 months	No statistically significant difference existed between the 2 groups with respect to operative time, pelvic lymph node count, frequency of lymph node involvement, extent of parametrial or vaginal resection margins, adjuvant treatment and intra-operative complications. There was no statistically significant difference in the 5-year disease-free survival rate between the groups (91% and 93% for LRH and RAH, respectively; p=0.918).	Larger studies are included.
Lee CL, Wu KY, Huang KG et al. (2010) Long-term survival outcomes of laparoscopically assisted radical hysterectomy in treating early-stage cervical cancer. American Journal of	Case series n=139 FU=median 92 months	Major intraoperative complications included 1 great vessel injury, 1 ureteral injury, 1 colon injury, and 6 cystotomies. In a median follow up of 92 months, the mean +/- SEM cumulative disease-free and overall survival rates were 91%	Larger studies are included.

Obstetrics & Gynecology 203: 165.e1-7		+/- 2.8% and 93% +/- 3.1%, respectively.	
Lee CL, Huang KG, Wang CJ et al. (2007) Laparoscopic radical hysterectomy using pulsed bipolar system: Comparison with conventional bipolar electrosurgery. Gynecologic Oncology 105: 620–4	Non-randomised comparative study n=76	Pulsed bipolar system has less blood loss, shorter operative time and fewer postoperative complications than conventional bipolar electrosurgery.	Comparison of pulsed bipolar system and conventional bipolar electrosurgery.
Lei H, Gui D, He Y (2017) Short- and long-term outcomes of laparoscopic radical hysterectomy for obese patients with cervical cancer. Journal of Balkan Union of Oncology 22: 958-65	Non-randomised comparative study (obese versus non-obese) n=243 FU=41 months	Compared with the non-obese group, the obese patients had longer operative time (p=0.039), more intraoperative blood loss (p=0.025), and a higher rate of conversion (p=0.025). There was no statistically significant difference between the 2 groups in terms of intraoperative and postoperative 30-day complications. Both groups had similar tumour recurrence rates, 5-year overall survival rates, and 5-year disease-free survival rates.	Non-randomised study, comparing outcomes in obese patients compared with non-obese patients.
Li L, Ma S, Tan X et al. (2019) The urodynamics and survival outcomes of different methods of dissecting the inferior hypogastric plexus in laparoscopic nerve-sparing radical hysterectomy of type C: a randomized controlled study. Annals of Surgical Oncology 26: 1560-8	RCT (waterjet versus blunt dissection) n=180 FU=median 33 months	Waterjet dissection of the inferior hypogastric plexus in laparoscopic nerve-sparing radical hysterectomy resulted in a more rapid return of normal urodynamics without compromising survival outcome.	Study focuses on effect of waterjet dissection.
Li G, Yan X, Shang H et al. (2007) A comparison of laparoscopic radical hysterectomy and pelvic lymphadenectomy and laparotomy in the treatment of Ib-IIa cervical cancer. Gynecologic Oncology 105: 176–80	Non-randomised comparative study (laparoscopic versus open) n=125 FU=median 26 months	Excluding the lost cases, the recurrence rate (14% vs 12%) and the mortality rate (10% vs 8%) between groups was similar.	Larger studies are included.
Liang Z, Chen Y, Xu H. et al. (2010) Laparoscopic nerve-sparing radical hysterectomy with fascia space dissection technique for cervical cancer: description of technique and outcomes. Gynecologic Oncology 119: 202-7	Non-randomised comparative study (nerve sparing versus conventional) n=163 FU=mean 22 months	No patient had a recurrence or metastasis. The technique described in this preliminary study appears to be safe, feasible, and easy in our population, with satisfactory recovery of voiding function.	Study focuses on specific technique.
Lim TYK, Lin KKM, Wong WL et al. (2019) Surgical and oncological outcome of total laparoscopic radical	Non-randomised comparative study	Postoperative complications occurred in 3 (6%) TLRH patients and 8 (9%) RAH patients. With a median follow up of 117 (range	Larger studies are included.

hysterectomy versus radical abdominal hysterectomy in early cervical cancer in Singapore. Gynecology & Minimally Invasive Therapy 8: 53-8	(laparoscopic versus open) n=136 FU=median 117 weeks	1.6 to 314.6) weeks in the TLRH group and 143.3 (range 0.4 to 304.7) weeks in the RAH group, 9 (18%) TLRH patients and 7 (8%) RAH patients had recurrence. There was no statistically significant difference in the overall 3-year survival between the TLRH group and the RAH group for tumour size ≤2 cm (100% vs 97%, p=0.37). However, there was a trend toward lower survival for the TLRH group for tumour size >2 cm (62% vs 85%; p=0.06).	
Lim YK, Chia YN, Yam KL. (2013) Total laparoscopic Wertheim's radical hysterectomy versus Wertheim's radical abdominal hysterectomy in the management of stage I cervical cancer in Singapore: a pilot study. Singapore Medical Journal 54: 683-8	Non-randomised comparative study (laparoscopic versus open) n=48 FU=median 37 weeks	No intraoperative bladder, ureteric or bowel complications were observed in the 2 groups. Postoperative complications occurred in 2 (11%) TLRH patients and 4 (13%) RAH patients. With a median follow up of 37 (range 10 to 68) weeks, the rate of recurrence was 6% for the TLRH group and 10% for the RAH group.	Larger studies are included.
Liu Z, Li X, Tao Y et al. (2016) Clinical efficacy and safety of laparoscopic nerve-sparing radical hysterectomy for locally advanced cervical cancer. International Journal of Surgery 25: 54-8	Non-randomised comparative study (nerve sparing versus conventional) n=120	Laparoscopic nerve-sparing radical hysterectomy is a feasible and safe procedure for locally advanced cervical cancer after neoadjuvant chemotherapy and reduces surgical complications.	Larger studies are included.
Long Y, Yao DS, Pan XW et al. (2014) Clinical efficacy and safety of nerve-sparing radical hysterectomy for cervical cancer: a systematic review and meta-analysis. PLoS ONE [Electronic Resource] 9: e94116	Systematic review n=17 studies	NSRH may be a reliable technique for treating early cervical cancer. Available evidence suggests that it is better than RH for postoperative recovery of pelvic organ function and postoperative morbidity, while the 2 techniques involve similar clinical safety and extent of resection. These results should be considered preliminary since they are based on a relatively small number of controlled trials, most of which were non-randomised. The findings should be verified in larger, well-designed studies.	Review focuses on nerve-sparing approach.
Luo C, Liu M, Li X. (2018) Efficacy and safety outcomes of robotic radical hysterectomy in Chinese older women with cervical cancer compared with laparoscopic radical hysterectomy. BMC Women's Health 18: 61	RCT (robotic versus laparoscopic) n=60 FU=24 months	There were less postoperative complications in the RRH group than in the LRH group ($p<0.05$). Shorter indwelling time of bladder and drain catheters was observed in the RRH group than in the LRH group ($p<0.05$). Length of hospital stay in the RRH group was shorter compared with the LRH group ($p<0.05$). Patients in the 2	Larger studies are included.

		groups had similar rates of recurrence and death.	
Magrina JF, Kho RM, Weaver AL et al. (2008) Robotic radical hysterectomy: comparison with laparoscopy and laparotomy. Gynecologic Oncology 109: 86-91	Non-randomised comparative study n=93 Mean follow up=31 months	Blood loss, rate of blood loss and length of hospital stay were similar for laparoscopy and robotics and statistically significantly reduced as compared with laparotomy. Operating times were similar for robotics and laparotomy and longer for laparoscopy.	Results also include patients with endometrial cancer.
Malzoni M, Tinelli R, Cosentino F et al. (2009) Total laparoscopic radical hysterectomy versus abdominal radical hysterectomy with lymphadenectomy in patients with early cervical cancer: our experience. Annals of Surgical Oncology 16: 1316–23	Non-randomised comparative study (laparoscopic versus open) n=127 FU=median 52 weeks (LRH)	The median blood loss in the ARH group was greater than TLRH group (p<0.01). The median length of hospital stay was statistically significantly greater in the ARH group than TLRH group (p<0.01). No statistically significant difference was found between the two groups when the recurrence rate was compared.	Larger studies are included.
Marra AR, Puig-Asensio M, Edmond MB et al. (2019) Infectious complications of laparoscopic and robotic hysterectomy: a systematic literature review and meta-analysis. International Journal of Gynecological Cancer 29: 518-30	Systematic review n=176,016 (50 studies)	There was no statistically significant difference in the number of infectious complication events between robotic-assisted hysterectomy and laparoscopic-assisted hysterectomy (pooled OR 0.97; 95 % CI 0.74 to 1.28). In a stratified analysis, similar results were found with no statistically significant difference in infectious complications comparing robotic-assisted hysterectomy with laparoscopic-assisted hysterectomy among patients with benign uterine disease (pooled OR 1.10; 95 % CI 0.70 to 1.73), endometrial cancer (pooled OR 0.97; 95 % CI 0.55 to 1.73), or cervical cancer (pooled OR 1.09; 95 % CI 0.60 to 1.97).	Review focuses on infectious complications and includes mixed indications.
McDonnell RM, Hollingworth JL, Chivers P et al. (2018) Advanced training of gynecologic surgeons and incidence of intraoperative complications after total laparoscopic hysterectomy: a retrospective study of more than 2000 cases at a single institution. Journal of Minimally Invasive Gynecology 25: 810-5	Case series n=2,013	The incidence of any major intraoperative complication was 2% (36/2013). Forty-five patients (2%) had a postoperative complication, and 74 (4%) patients were readmitted to the hospital after discharge. The incidence of any major intraoperative complication was statistically significantly higher among general gynaecologists compared with subspecialists (3% vs 1%, p=0.002). No association was found between time in specialist practice and the incidence of major intraoperative complications (p=0.629). A	Study includes patients with benign or malignant conditions.

		statistically significant association for major intraoperative complications was observed for surgeons who had done <100 laparoscopic hysterectomies during the study period (p=0.032).	
Medical Advisory Secretariat (2010) Robotic-assisted minimally invasive surgery for gynecologic and urologic oncology. an evidence-based analysis. Ontario Health Technology Assessment Series 10: 1-118	Review	The results of this evidence-based analysis show that robotic surgery has a more favourable profile with respect to a reduced length of hospitalisation and less blood loss compared with laparotomy for women having any hysterectomy surgery for the surgical treatment and management of endometrial and cervical cancers. For robotic surgery compared with laparoscopy, the greatest benefit of robotic surgery was shown for the reduced number of conversions owing to the established technical difficulties of laparoscopy.	More recent reviews are included.
Mendivil AA, Rettenmaier MA, Abaid LN et al. (2016) Survival rate comparisons amongst cervical cancer patients treated with an open, robotic-assisted or laparoscopic radical hysterectomy: A five year experience. Surgical Oncology 25: 66-71	Non-randomised comparative study (robotic versus laparoscopic versus open) n=146 FU=60 months	The results from this study suggest that, irrespective of operative approach, patients who had a radical hysterectomy for early stage cervical cancer attained similar 5-year disease free and overall survival outcomes.	Larger studies are included.
Nam JH, Park JY, Kim DY et al. (2012) Laparoscopic versus open radical hysterectomy in early-stage cervical cancer: long-term survival outcomes in a matched cohort study. Annals of Oncology 23: 903-11	Non-randomised comparative study (laparoscopic versus open) n=526 FU=91 months	Compared with ORH (n=263), LRH (n=263) did not have higher risks of recurrence [hazard ratio (HR)=1.28; 95% confidence interval (CI) 0.62 to 2.64] or death (HR=1.46; 95% CI 0.62 to 3.43). Even in patients with tumours >2 cm in diameter, the risks of recurrence (HR=0.82; 95% CI 0.31 to 2.16) or death (HR=1.01; 95% CI 0.35 to 2.95) were not higher for LRH than for ORH. The LRH and ORH group had 5-year recurrence-free survival rates of 93% and 94%, respectively (p=0.499). LRH resulted in lower estimated blood loss (p<0.001) and shorter postoperative hospital stay (p<0.001). Intraoperative complication rates were similar in the two groups (7% versus 6%, p=0.711), but postoperative complication rate was lower in the LRH than in the ORH group (9% versus 21%, p<0.001).	More recent studies are included.

Nevis IF, Vali B, Higgins C et al. (2017) Robot-assisted hysterectomy for endometrial and cervical cancers: a systematic review. Journal of Robotic Surgery 11: 1-16	Systematic review n=35 studies	The quality of evidence for all reported outcomes was very low. For women with cervical cancer, there were no differences in estimated blood loss or removal of lymph nodes between robot-assisted and laparoscopic procedure. Compared with laparotomy, robot-assisted hysterectomy for cervical cancer showed an overall reduction in estimated blood loss. Although robot-assisted hysterectomy is clinically effective for the treatment of both endometrial and cervical cancers, methodologically rigorous studies are lacking to draw definitive conclusions.	A more recent systematic review is included.
Nie JC, Yan AQ, Liu XS (2017) Robotic-assisted radical hysterectomy results in better surgical outcomes compared with the traditional laparoscopic radical hysterectomy for the treatment of cervical cancer. International Journal of Gynecological Cancer 27: 1990-9	Non-randomised comparative study (robotic versus laparoscopic) n=933	The treatment with robotic radical hysterectomy (RRH) was generally superior to traditional laparoscopic radical hysterectomy (TLRH) with respect to operating time, blood loss, length of hospitalisation, duration of bowel function recovery, and postoperative complications. On follow up of patients, there were no relapses reported in the RRH group compared with 4% of relapse cases and 3% of deaths because of metastasis in the TLRH group. No conversion of laparotomy occurred in the RRH group. No statistically significant difference was found with respect to intraoperative complications and blood transfusion between both groups.	Follow up period is not reported.
Odetto D, Puga MC, Saadi J et al. (2019) Minimally invasive radical hysterectomy: an analysis of oncologic outcomes from Hospital Italiano (Argentina). International Journal of Gynecological Cancer 29: 863-8	Case series n=108 FU=median 39 months	The recurrence rate after laparoscopic radical hysterectomy was 15%, and in tumours ≤2 cm it was 12%. The 3-year disease-free survival was 81%. Given these results our hospital has changed the approach to open radical hysterectomy.	Larger studies are included.
Oman SA, Schwarz D, Muntz HG (2016) Lower limb compartment syndrome as a complication of radical hysterectomy. Gynecologic Oncology Reports 16: 39-41	Case report n=1	**Lower limb compartment syndrome** The patient had multiple risk factors for the development of well-leg compartment syndrome. She had a robotically assisted LRH, bilateral salpingo-oopherectomy and pelvic and para-aortic lymph node dissection for adenocarcinoma of the cervix and a concurrent malignant left	Case report of safety event already described.

		ovarian mass. Total time in lithotomy with Trendelenburg positioning was about 6 hours. Immediately afterwards, she was diagnosed with compartment syndrome of her left leg and needed emergency lower extremity decompression fasciotomy to avoid amputation of her left leg.	
Oyama K, Kanno K, Kojima R et al. (2019) Short-term outcomes of robotic-assisted versus conventional laparoscopic radical hysterectomy for early-stage cervical cancer: A single-center study. Journal of Obstetrics & Gynaecology Research 45: 405-11	Non-randomised comparative study (laparoscopic versus robotic) n=121	The operative time was statistically significantly longer and blood loss greater in the RARH than LRH group. A greater number of lymph nodes were removed in the RARH group. However, these differences seem to be within a clinically acceptable range, showing that RARH is as feasible and safe as LRH in terms of short-term outcomes.	Study does not report longer term outcomes.
Park DA, Yun JE, Kim SW et al. (2017) Surgical and clinical safety and effectiveness of robot-assisted laparoscopic hysterectomy compared to conventional laparoscopy and laparotomy for cervical cancer: A systematic review and meta-analysis. European Journal of Surgical Oncology 43: 994-1002	Systematic review and meta-analysis n=22 studies	RRH appears to have a positive effect in reducing overall complications, individual adverse events including wound infection, fever, urinary tract infection, transfusion, length of stay, blood loss, and time to diet than ORH for cervical cancer patients. Compared with LRH, the current evidence is not enough to clearly determine its clinical safety and effectiveness.	A more recent review with most of the same studies is included.
Park JY, Kim D, Suh DS et al. (2016) The role of laparoscopic radical hysterectomy in early-stage adenocarcinoma of the uterine cervix. Annals of Surgical Oncology 23: 825-33	Non-randomised comparative study (laparoscopic versus open) n=293 FU=59 months	There were no differences in disease-free survival (DFS) and overall survival (OS) between the LRH and ORH groups (89% vs 84%, p=0.725; and 93% vs 87%, p=0.735) for univariate analysis and multivariate analysis after adjusting for other significant prognostic factors. There was no difference in the patterns of recurrence between the two surgery groups (p=0.220). The median time interval between surgery and the first recurrence were 25 months (range, 3 to 100 months) for LRH group and 14 months (range, 3 to 128 months) for ORH group (p=0.230). The LRH group had fewer postoperative complications (p<0.001), less estimated blood loss (p<0.001), faster bowel movement recovery (p<0.001), shorter postoperative hospital stay (p< 0.001), and a lower rate	Studies with more patients or longer follow up are included.

		of wound dehiscence, ileus, lymphedema, infected lymphocele, and pelvic abscess (p=0.004, 0.011, 0.017, and 0.040, respectively).	
Park JY, Nam JH (2014) Laparotomy conversion rate of laparoscopic radical hysterectomy for early-stage cervical cancer in a consecutive series without case selection. Annals of Surgical Oncology 21: 3030-5	Case series n=260	The conversion rate to laparotomy among patients who had LRH for early-stage cervical cancer was 1.5% when done exclusively in consecutive patients. LRH showed comparable feasibility and effectiveness to open radical hysterectomy in the treatment of early-stage cervical cancer.	Studies with more patients or longer follow up are included.
Park JY, Kim DY, Kim JH et al. (2013) Laparoscopic versus open radical hysterectomy in patients with stage IB2 and IIA2 cervical cancer. Journal of Surgical Oncology 108: 63-9	Non-randomised comparative study (laparoscopic versus open) n=303 FU=30 months	Two patients (2%) in the LRH group needed conversion to laparotomy. There was no difference with respect to operating time, perioperative change in haemoglobin level, and need for transfusion. However, in the LRH group, estimated blood loss (p=0.003) was lower, time to recovery of bowel movement (p<0.001) and length of postoperative hospital stay (p<0.001) were shorter, and postoperative complications were less frequent (p=0.036). The 5-year disease-free survival was 78% in the LRH group and 77% in the ORH group (p=0.718), and 5-year overall survival was 83% in both groups (p=0.746). There were no differences in pattern of recurrence (p=0.225) and median time to recurrence (12 vs 13 months; p=0.240).	Studies with more patients or longer follow up are included.
Park JY, Kim DY, Kim JH et al. (2012) Laparoscopic versus open radical hysterectomy for elderly patients with early-stage cervical cancer. American Journal of Obstetrics & Gynecology 207: 195.e1-8	Non-randomised comparative study (laparoscopic versus open) n=258 FU=median 45 months	One patient (1%) in LRH group needed conversion to laparotomy. Operating time (p=0.035), estimated blood loss (p=0.002), recovery of bowel movement (p<0.001), and postoperative hospital stay (p<0.001) were statistically significantly shorter or lower in LRH group. Postoperative complications were statistically significantly less frequent in LRH group (p=0.026). The 5-year disease-free survival (95% vs 93%, p=0.350) and overall survival (96% vs 95%, p=0.361) did not differ between the groups.	Study focuses on elderly patients. Studies with more patients or longer follow up are included.
Park JY, Kim DY, Kim JH et al. (2012) Laparoscopic compared with open radical hysterectomy in obese	Non-randomised comparative study	Compared with open radical hysterectomy, laparoscopic radical hysterectomy was associated with a statistically	Study focuses on obese patients.

women with early-stage cervical cancer. Obstetrics & Gynecology 119: 1201-9	(laparoscopic versus open) n=166 FU=median 44 months	significant reduction in the following: interval to return of bowel movements (p<0.001); duration of postoperative hospital stay (p<0.001), postoperative complications (6% compared with 18%, p=0.032), and estimated blood loss (p=0.009). The 5-year disease-free survival rate was 88% for the laparoscopic radical hysterectomy group and 85% for the open radical hysterectomy group (p=0.682). The 5-year overall survival rate was 97% for the laparoscopic radical hysterectomy group and 90% for the open radical hysterectomy group (p=0.220).	Studies with more patients or longer follow up are included.
Park NY, Chong GO, Hong DG et al. (2011) Oncologic results and surgical morbidity of laparoscopic nerve-sparing radical hysterectomy in the treatment of FIGO stage IB cervical cancer: long-term follow-up. International Journal of Gynecological Cancer 21: 355-62	Case series (nerve-sparing) n=125 FU=53 months	There were high urological complications (13/125, 10%) related to radical surgery. Forty-one patients (33%) needed transfusions. Positive surgical margins did not exist. The return rates to normal voiding function at postoperative 14 and 21 days were 92% and 95%, respectively. Thirteen patients (1B1 n=9, IB2 n=4) had a recurrence postoperatively. Six patients (1B1 n=3, 1B2 n=3) died of recurrent disease. Five-year disease-free survival rates of cervical cancer 1B1 and 1B2 were 92% and 78%, respectively (p=0.1772). Five-year overall survival rates of cervical cancer 1B1 and 1B2 were 96% and 83%, respectively (p=0.0437).	Larger studies are included.
Pellegrino A, Damiani GR, Loverro M et al. (2017) Comparison of robotic and laparoscopic radical type-B and C hysterectomy for cervical cancer: Long-term-outcomes. Acta Bio-Medica de l Ateneo Parmense 88: 289-96	Non-randomised comparative study (laparoscopic versus robotic) n=52 FU=median 30 months	Median number of pelvic lymph nodes was similar, but a major number of nodes was observed in RRH group (36 vs 24; p=0.05). The overall median length of follow up was 59 months (range: 9-92) and 30 months (range: 90-6) for RRH and LRH group respectively. Overall survival rate (OSR) was 100% for RRH group and 83% for LTRH group. The DFS (disease-free survival rate) was 97% and 89% in RRH and LRH group respectively.	Larger studies are included.
Pellegrino A, Vizza E, Fruscio R et al. (2009) Total laparoscopic radical hysterectomy and pelvic lymphadenectomy in patients with Ib1 stage cervical cancer: analysis of	Case series n=107 FU=median 30 months	After a median follow up of 30 months 11 patients had a recurrence; survival rate was 95%.	Larger studies are included.

surgical and oncological outcome. European Journal of Surgical Oncology 35: 98–103			
Philp L, Covens A, Vicus D et al. (2017) Feasibility and safety of same-day discharge after laparoscopic radical hysterectomy for cervix cancer. Gynecologic Oncology 147: 572-6	Case series n=119	Same-day discharge after laparoscopic radical hysterectomy for cervix cancer is safe, with a low risk of post-operative morbidity and hospital readmission.	Study focuses on same-day discharge.
Piedimonte S, Czuzoj-Shulman N, Gotlieb W et al. (2019) Robotic radical hysterectomy for cervical cancer: a population-based study of adoption and immediate postoperative outcomes in the United States. Journal of Minimally Invasive Gynecology 26: 551-7	Non-randomised comparative study (laparoscopic versus robotic versus open) n=3,563	Robotic radical hysterectomy is being increasingly done in the US and is associated with shorter length of stay and less postoperative morbidity; however, long-term oncologic outcomes need additional attention.	Study does not report longer term outcomes.
Puljiz M, Marcelic L, Alvir I et al. (2018) Rare case of early-onset drain-site hernia after laparoscopic surgery. Libri Oncologici 46: 20-3	Case report n=1	**Small bowel herniation and incarceration in a 12 mm port site** The patient had LRH with pelvic lymph node dissection for cervical cancer.	Case report of safety event already described.
Puntambekar SP, Palep RJ, Puntambekar SS et al. (2007) Laparoscopic total radical hysterectomy by the Pune technique: our experience of 248 cases. Journal of Minimally Invasive Gynecology 14: 682–9	Case series n=248 FU=median 36 months	All 15 intraoperative complications were tackled laparoscopically. No patients were converted to the open technique. There were no deaths. Seventeen patients had complications within 2 months of surgery. Seven patients had recurrences after a median follow up of 36 months.	More recent studies are included.
Raspagliesi F, Bogani G, Martinelli F et al. (2016) Incorporating 3D laparoscopy for the management of locally advanced cervical cancer: a comparison with open surgery. Tumori 102: 393-7	Non-randomised comparative study (laparoscopic versus open) n=30	Patients having 3D-LNSRH had longer operative time (p=0.005), lower blood loss (p<0.001), and shorter length of hospital stay (p=0.03) compared with patients having open abdominal procedures. No intraoperative complication occurred. One patient had conversion to open surgery because of technical difficulties and the inability to insert the uterine manipulator. A trend towards higher complication (grade 2 or worse) rate was observed for patients having NSRH compared with 3D-LNSRH (p=0.06). Considering only severe complications (grade 3 or worse), no difference was observed (0/10 vs 2/20; p=0.54).	Larger studies are included.

Ratiu D, Luncescu C, Morgenstern B et al. (2019) Comparison of minimally invasive surgery and abdominal surgery among patients with cervical cancer. Anticancer Research 39: 2661-4	Non-randomised comparative study (minimally invasive versus open) n=75 FU=39 months	Statistically, no significant difference in overall survival (OS) was observed in both groups. Disease-free survival showed a statistically significant difference in favour of the minimally invasive group.	Larger studies are included.
Robinson BL, Liao JB, Adams SF et al. (2009) Vaginal cuff dehiscence after robotic total laparoscopic hysterectomy. Obstetrics & Gynecology 114 (2 Pt 1): 369–72	Case reports. n=2 (1 robotic LRH was for endocervical adenocarcinoma, the other was for menorrhagia and cancer risk reduction)	**Vaginal cuff dehiscence and small bowel evisceration.**	Case report of safety event already described.
Schreuder HWR, Zweemer RP, van Baal WM et al. (2010) From open radical hysterectomy to robot-assisted laparoscopic radical hysterectomy for early stage cervical cancer: aspects of a single institution learning curve. Gynecological Surgery 7: 253-8	Non-randomised comparative study (robotic versus open) n=28	Introduction of this new technique needs a learning curve of less than 15 cases that will reduce the operating time to a level comparable to open surgery.	Larger studies are included.
Segaert A, Traen K, Van Trappen P et al. (2015) Robot-assisted radical hysterectomy in cervical carcinoma: the Belgian experience. International Journal of Gynecological Cancer 25: 1690-6	Case series n=109 FU=median 27.5 months	Eighteen patients relapsed, and 5 died of disease. The 2- and 5-year overall survival was 96% and 89%, respectively. The 2- and 5-year disease-free survival (DFS) was 88% and 72%, respectively. The 2-year DFS per stage was 100% for 1A, 88% for 1B1, 100% for 1B2, and 83% for 2. The 5-year DFS per stage was 100% for stage 1A and 75% for 1B1. The complications were as expected for radical hysterectomy.	Larger studies are included.
Serati M, Salvatore S, Uccella S et al. (2009) Sexual function after radical hysterectomy for early-stage cervical cancer: is there a difference between laparoscopy and laparotomy? Journal of Sexual Medicine 6: 2516-22	Non-randomised comparative study (laparoscopic versus open) n=73	Radical hysterectomy worsens sexual function, regardless of the type of surgical approach. In this study, laparoscopy did not show any benefit on women's sexuality over the abdominal surgery for cervical cancer.	Larger studies are included.
Sert BM, Boggess JF, Ahmad S et al. (2016) Robot-assisted versus open radical hysterectomy: A multi-institutional experience for early-stage cervical cancer. European Journal of Surgical Oncology 42: 513-22	Non-randomised comparative study (robotic versus open) n=491 FU=mean 39 months	RRH had improved clinical outcomes compared with ORH in the treatment of early-stage cervical cancer in terms of estimated blood loss, intra-operative complications, transfusion rates, length of stay, and preoperative cone. Disease	Studies with more patients or longer follow up are included.

		recurrence and survival were comparable for the 2 procedures.	
Sert MB, Abeler, V (2011) Robot-assisted laparoscopic radical hysterectomy: comparison with total laparoscopic hysterectomy and abdominal radical hysterectomy; one surgeon's experience at the Norwegian Radium Hospital. Gynecologic Oncology 121: 600-4	Non-randomised comparative study (robotic versus laparoscopic versus open) n=68 FU=mean 36 to 70 months	The mean follow up times were 36, 56 and 70 months in patients who had RALRH, TLRH and ARH respectively. Until now there have been 5 recurrences and 1 cervical cancer related death in the robot-assisted group and no recurrences in both the laparoscopy and the laparotomy group.	Larger studies are included.
Shah CA, Beck T, Liao JB et al. (2017) Surgical and oncologic outcomes after robotic radical hysterectomy as compared to open radical hysterectomy in the treatment of early cervical cancer. Journal of Gynecologic Oncology 28: e82	Non-randomised comparative study (robotic versus open) n=311 FU=3 years	Length of stay (LOS) was considerably shorter in the robotic group (p<0.001) as was estimated blood loss (p<0.001). There were more complications in the open radical hysterectomy group, 23% vs 9% in the robotic group (p=0.002). The recurrence rate was 10% in both groups. In multivariate adjusted analysis, robotic surgery was not a statistically significant predictor of PFS (p=0.230) or OS (0.85).	Studies with more patients or longer follow up are included.
Shazly SA, Murad MH, Dowdy SC et al. (2015) Robotic radical hysterectomy in early stage cervical cancer: A systematic review and meta-analysis. Gynecologic Oncology 138: 457-71	Systematic review 26 studies	Current evidence suggests that RRH may be superior to ARH with lower EBL, shorter hospital stay, less febrile morbidity and wound-related complications. RRH and LRH appear equivalent in intraoperative and short-term postoperative outcomes and thus the choice of approach can be tailored to the choice of patient and surgeon.	Another systematic review with most of the same studies is included.
Shi R, Wei W, Jiang P (2016) Laparoscopic nerve-sparing radical hysterectomy for cervical carcinoma: emphasis on nerve content in removed cardinal ligaments. International Journal of Gynecological Cancer 26: 192-8	Non-randomised comparative study (nerve sparing versus conventional) n=106	Disease-free survival rate did not differ between the LNSRH (91%) and LRH (88%) groups (p=0.643). The LNSRH is a safe, feasible, and easy procedure for trained laparoscopic surgeons. Patients who had LNSRH had a more satisfactory quality of life than patients who had LRH.	Larger studies are included.
Simsek T, Ozekinci M, Saruhan Z et al. (2012) Laparoscopic surgery compared to traditional abdominal surgery in the management of early stage cervical cancer. European Journal of Gynaecological Oncology 33: 395-8	Non-randomised comparative study (laparoscopic versus open) n=88	There is no difference in anatomical considerations between laparoscopic and laparotomic radical surgery in the surgical management of cervical cancer.	Larger studies are included.
Sobiczewski P, Bidzinski M, Derlatka P et al. (2009) Early cervical cancer managed by	Non-randomised comparative study	Predicted 3-year disease-free survival rates in the "open surgery" and "laparoscopy"	Larger studies are included.

laparoscopy and conventional surgery: comparison of treatment results. International Journal of Gynecological Cancer 19: 1390-5	(laparoscopic versus open) n=80 FU=median 26 months	groups were 0.86 (standard deviation [SD], 0.049) and 0.82 (SD, 0.098), respectively (p=0.53). Recurrence rate was 14% after laparoscopy and 12% in open surgery. In 2 patients, intraperitoneal spread occurred after laparoscopy. The operation time was longer and hospitalisation shorter after laparoscopy.	
Soliman PT, Frumovitz M, Sun CC et al. (2011) Radical hysterectomy: a comparison of surgical approaches after adoption of robotic surgery in gynecologic oncology. Gynecologic Oncology 123: 333-6	Non-randomised comparative study (laparoscopic versus robotic versus open) n=95	Minimally invasive surgery has made a significant impact on patients having radical hysterectomy including decrease in blood loss and transfusion rates however; operative times were statistically significantly longer compared with open radical hysterectomy. The findings suggest that the robotic approach may have the added benefit of even shorter length of stay compared with traditional laparoscopy.	Larger studies are included.
Stanciu P, Anastasiu DM, Ionescu M et al. (2013) Laparoscopic radical hysterectomy vs. classical radical hysterectomy. comparative study of complications and quality of life in patients with early stage cervical cancer. Obstetrica si Ginecologie 61: 221-5	Non-randomised comparative study (laparoscopic versus open) n=76 FU=6 months	In the laparoscopy group, the pain score was statistically significantly lower, and the quality of life index was higher than in the abdominal route group. Peri and postoperative complications were similar in both study groups.	Larger studies are included.
Suh DH, Cho HY, Kim K et al. (2015) Matched-Case Comparisons in a Single Institution to Determine Critical Points for Inexperienced Surgeons' Successful Performances of Laparoscopic Radical Hysterectomy versus Abdominal Radical Hysterectomy in Stage IA2-IIA Cervical Cancer. PLoS ONE [Electronic Resource] 10: e0131170	Non-randomised comparative study (laparoscopic versus open) n=161 FU=44 months	After matching for age and risk factors, the vaginal tumour-free margin of LRH was shorter than that of ARH in experienced surgeon group (1.3 versus 1.7 cm, p=0.007); however, the vaginal tumour-free margin was longer than that of ARH in the inexperienced surgeon group (1.8 versus 1.3 cm, p=0.035). The postoperative hospital stay of LRH was shorter than that of ARH in experienced surgeon group (p<0.001), but not different from that of ARH in the inexperienced surgeon group. Vaginal tumour-free margin >1.8 cm (OR 7.33, 95% CI 1.22 to 40.42), stage >1B1 (OR 8.83, 95% CI 1.51 to 51.73), and estimated blood loss >575 mL (OR 33.95, 95% CI 4.87 to 236.79) were independent risk factors for longer postoperative	Larger studies are included.

		hospital stay in the inexperienced surgeon group. There was no difference of 5-year-progression-free survival of LRH patients between experienced surgeon and inexperienced surgeon groups after matching (55 versus 33%, p=0.391).	
Sullivan SA, Clark LH, Staley AS et al. (2017) Association between timing of cervical excision procedure to minimally invasive hysterectomy and surgical complications. Gynecologic Oncology 144: 294-8	Case series n=138	Definitive MIS for cervical cancer within 6 weeks after cervical excision is associated with increased risk for 30-day complications. Providers should consider delaying definitive surgical procedures for at least 6 weeks following excision to reduce surgical complications.	Study focuses on timing of hysterectomy after cervical excision procedure.
Sun H, Cao D, Shen K et al. (2018) Piver type II vs. Type III hysterectomy in the treatment of early-stage cervical cancer: Midterm follow-up results of a randomized controlled trial. Frontiers in Oncology 8: 568	RCT (type II versus type III) n=93 FU=28 months	The 2-year DFS rate in the type 2 group was 100% compared with 98% in the type 3 group. Compared with the type 3 group, the patients who had type 2 hysterectomy had a shorter surgical time (p=0.014), less intraoperative blood loss (p=0.047), less postoperative urinary retention (5/46 vs 11/47, p=0.109), and milder bladder injuries. The postoperative symptom experience scores of the type 2 group were statistically significantly lower than those of the type 3 group.	Study focuses on comparison of type II with type III laparoscopic hysterectomy.
Taylor SE, McBee Jr WC, Richard SD et al. (2011) Radical hysterectomy for early stage cervical cancer: Laparoscopy versus laparotomy. Journal of the Society of Laparoendoscopic Surgeons 15: 213-7	Non-randomised comparative study (laparoscopic versus open) n=27	Laparoscopic radical hysterectomy is a feasible alternative to laparotomy for early stage cervical cancer. Similar surgical outcomes are achieved with statistically significantly less morbidity.	Larger studies are included.
Tinelli R, Malzoni M, Cosentino F et al. (2011) Robotics versus laparoscopic radical hysterectomy with lymphadenectomy in patients with early cervical cancer: a multicenter study. Annals of Surgical Oncology 18: 2622-8	Non-randomised comparative study (laparoscopic versus robotic) n=99 FU=46 months	Robotic radical hysterectomy can be considered a safe and effective therapeutic procedure for managing early-stage cervical cancer without statistically significant differences, if compared with laparoscopic radical hysterectomy, in terms of the recurrence rate and intraoperative and postoperative complications, although multicentre randomised clinical trials with longer follow up are necessary to evaluate the overall oncologic outcomes of this procedure.	More recent studies are included.

Toptas T, Simsek T (2014) Total laparoscopic versus open radical hysterectomy in stage IA2-IB1 cervical cancer: disease recurrence and survival comparison. Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A 24: 373-8	Non-randomised comparative study (laparoscopic versus open) n=68 FU=median 42.5 months	The estimated 3-year PFS (86% versus 91%, respectively; p=0.32) and overall survival (100% vs 95%, respectively; p=0.82) were comparable in the TLRH and ORH groups.	Larger studies are included.
Uccella S, Laterza R, Ciravolo G et al. (2007) A comparison of urinary complications following total laparoscopic radical hysterectomy and laparoscopic pelvic lymphadenectomy to open abdominal surgery. Gynecologic Oncology 107: S147–9	Non-randomised comparative study n=98	Laparoscopic approach is comparable to laparotomy in terms of urinary lesions and postoperative retention.	Same study as Ghezzi et al.
Uppal S, Liu R et al. (2019) Trends and comparative effectiveness of inpatient radical hysterectomy for cervical cancer in the United States (2012-2015). Gynecologic Oncology 152: 133-8	Non-randomised comparative study (minimally invasive versus open) n=7,180 FU=30 days	By intention-to-treat analysis, the rate of at least 1 complication for abdominal cases was 25% compared with 10% for MIS (p<0.001). On multivariate analysis, abdominal cases had higher odds of any 1 complication (OR 2.9, 95% CI 2.12 to 4.00), medical complication (OR 3.25, 95% CI 2.15 to 4.19), infectious complication (OR 3.76,95% CI 2.1 to 6.1) but not for surgical complications (OR 1.7, 95% CI 0.5 to 5.6). AH resulted in longer hospital stay compared with MIS (4.3 vs 1.9 days, p<0.001).	Studies with longer follow up are included.
Uzan C, Merlot B, Gouy S et al. (2013) Laparoscopic radical hysterectomy after preoperative brachytherapy for stage IB1 cervical cancer: feasibility, results, and surgical implications in a large bicentric study of 162 consecutive cases. Annals of Surgical Oncology 20: 872-80	Case series n=162 FU=median 39 months	The procedure was feasible in 160 patients (99%) (2 conversions to laparotomy). Eight perioperative complications occurred. Nineteen patients had nodal involvement. Peri- or postoperative ureteral morbidity occurred in 10 patients (6%). Twenty-four patients (15%) had postoperative dysuria. Histologically, 9 patients had residual cervical disease ≥5 mm, and 1 patient had parametrial lymphovascular space involvement (associated with nodal spread). No patient had vaginal disease or involved surgical margins. After a median follow-up of 39 (range 3-118) months, 9 patients had relapse.	Studies with more patients or longer follow up are included.

		Five-year overall survival was 95% (range 88 to 98%).	
Vizza E, Corrado G, Mancini E et al. (2015) Laparoscopic versus robotic radical hysterectomy after neoadjuvant chemotherapy in locally advanced cervical cancer: a case control study. European Journal of Surgical Oncology 41: 142-7	Non-randomised comparative study (laparoscopic versus robotic) n=25	The median estimated blood loss was statistically significant in favour of RRH group. There was no statistically significant difference in terms of intraoperative and postoperative complications between groups but in the RRH group we observed a greater number of total complications compared with the control group.	Larger studies are included.
Wallin E, Floter Radestad A, Falconer H (2017) Introduction of robot-assisted radical hysterectomy for early stage cervical cancer: impact on complications, costs and oncologic outcome. Acta Obstetricia et Gynecologica Scandinavica 96: 536-42	Non-randomised comparative study (robotic versus open) n=304 FU=62 months	Blood loss, length of stay and intraoperative complications were statistically significantly lower as well as lymph node yield after RRH. No differences in postoperative complications were observed between the 2 groups. Recurrence of disease was detected in 13% and 10% after RRH and ORH, respectively. Regression analysis demonstrated that histology, tumour size, positive lymph nodes and type of operation (RRH) were statistically significantly associated with recurrence.	Larger studies are included.
Wang W, Chu HJ, Shang CL et al. (2016) Long-term oncological outcomes after laparoscopic versus abdominal radical hysterectomy in Stage IA2 to IIA2 cervical cancer. International Journal of Gynecological Cancer 26: 1264-73	Non-randomised comparative study n=406 FU=mean 68 months	5-year recurrence-free survival (Kaplan-Meier) • LRH=91.3% • ORH=90.4%, p=0.83 5-year overall survival (Kaplan-Meier) • LRH=93.2% • ORH=92.1%, p=0.94 In multivariate analysis, pelvic lymph node metastasis and tumour size were independent prognostic factors. Patients with pelvic lymph node metastasis or tumour size >4 cm were statistically significantly associated with poor prognosis.	A similar, more recent study is included (Hu TWY et al., 2019)
Wang YZ, Deng L, Xu HC et al. (2015) Laparoscopy versus laparotomy for the management of early stage cervical cancer. BMC Cancer 15: 928	Systematic review n=12 studies	LRH compared with RH was associated with a statistically significant reduction of intraoperative blood loss (weighted mean difference = -268.4 mL (95% CI -361.6 to -175.1; p<0.01), a reduced risk of postoperative complications (OR=0.46; 95% CI 0.34 to 0.63) and shorter hospital stay (weighted mean difference = -3.22 days; 95% CI -4.21 to -2.23 days;	A review with a later search date is included.

		p<0.01). These benefits were at the cost of longer operative time (weighted mean difference = 26.9 min (95% CI 8.08-45.82). The rate of intraoperative complications was similar in the two groups. Lymph nodes yield and positive resection margins were similar between the two groups. There were no statistically significant differences in 5-year overall survival (HR 0.91, 95% CI 0.48 to 1.71; p=0.76) and 5-year disease-free survival (hazard ratio [HR] 0.97, 95% CI 0.56 to 1.68; p=0.91).	
Wright JD, Herzog TJ, Neugut AI et al. (2012) Comparative effectiveness of minimally invasive and abdominal radical hysterectomy for cervical cancer. Gynecologic Oncology 127: 11-7	Non-randomised comparative study (laparoscopic versus robotic versus open) n=1,894	Perioperative complications were noted in 16% of patients who had abdominal surgery, 9% who had laparoscopy, and 13% who had a robotic procedure (p=0.04). Both laparoscopic and robotic radical hysterectomies were associated with lower transfusion needs and shorter hospital stays than abdominal hysterectomy (p<0.05).	Only short-term outcomes are reported.
Wu J, Ye T, Lv J et al. (2019) Laparoscopic nerve-sparing radical hysterectomy vs laparoscopic radical hysterectomy in cervical cancer: a systematic review and meta-analysis of clinical efficacy and bladder dysfunction. Journal of Minimally Invasive Gynecology 26: 417-426.e6	Systematic review n=2,743 (30 articles)	LNSRH was associated with lower rates of impaired bladder function and a shorter extent of resection compared with LRH. Clinical applications involving LNSRH should be explored with caution.	Review focuses on nerve-sparing technique.
Xiao M, Gao H, Bai H et al. (2016) Quality of life and sexuality in disease-free survivors of cervical cancer after radical hysterectomy alone A comparison between total laparoscopy and laparotomy. Medicine 95 (no. 36)	Non-randomised comparative study (laparoscopic versus open) n=58 FU=46 months	To the date of submission, 21% (9/42) of patients in the laparoscopy group and 31% (5/16) of patients in the laparotomy group had not resumed sexual behaviour. The scores on the FSFI items were comparable between the 2 groups; however, the total FSFI scores were 19.7 and 17.4 for total laparoscopy and laparotomy survivors, respectively, both of which were less than the validated cut-off value of 26.6 for diagnosing female sexual dysfunction. Disease-free cervical cancer survivors after RH and/or lymphadenectomy were able to cope well, although RH could greatly impair sexual function regardless of surgical approach. The long-term quality of life and	Larger studies are included.

		sexual function of survivors seemed to be independent of the surgical approach chosen.	
Xiao M, Zhang Z (2015) Total Laparoscopic versus laparotomic radical hysterectomy and lymphadenectomy in cervical cancer: an observational study of 13-year experience. Medicine 94: e1264	Non-randomised comparative study (laparoscopic versus open) n=154 FU=48 months	Patients in laparoscopy group had superior surgical outcomes, such as statistically significantly lower blood transfusion compared with those in laparotomy group. Furthermore, patients had statistically significantly lower postoperative complication rate in laparoscopy group compared with that in laparotomy group (25% vs 52%) (p=0.001). Three patients (3%) in laparoscopy group had unplanned conversion to laparotomy. Disease-free survival rates were 90% and 89% in laparoscopy and laparotomy groups (p=0.39), respectively, and overall survival rates were 90% in laparoscopy group and 91% in laparotomy group (p=0.40).	Larger studies are included.
Xu H, Chen Y, Li Y et al. (2007) Complications of laparoscopic radical hysterectomy and lymphadenectomy for invasive cervical cancer: experience based on 317 procedures. Surgical Endoscopy 21: 960–4	Case series n=317 Follow up=6 months	Overall conversion rate=1.3% Intraoperative complications=4.4% (7 vessel injuries, 5 cystotomies,1 hypercapnia, 1 bowel injury) Postoperative complications=5.1% (5 ureterovaginal fistula, 4 vesicovaginal fistula, 1 ureterostenosis, 6 urinary retention)	Studies with longer follow up are included.
Yan X, Li G, Shang H et al. (2012) Outcome and prognostic factors of laparoscopic radical hysterectomy and pelvic lymphadenectomy in 148 patients with stage IB1 cervical cancer. International Journal of Gynecological Cancer 22: 286-90	Case series n=148 FU=median 28 months	21 patients had a recurrence. The overall 5-year survival rate was 82%. Univariate analysis showed the factors affecting the survival rate were non-squamous histologic type, high grade, deep cervical stromal invasion, lymphovascular space invasion, and lymph node metastasis (p=0.016, p=0.045, p=0.021, p=0.038, and p<0.001). The Cox proportional hazards regression analysis indicated only lymph node metastasis (odds ratio =6.293, p<0.001) was an independent poor prognostic factor.	Larger studies are included.
Yan X, Li G, Shang H et al. (2011) Twelve-year experience with laparoscopic radical hysterectomy and pelvic lymphadenectomy in cervical	Case series n=240 FU=median 35 months	5-year survival rate for 1A2, 1B1, 1B2, 2A was 100%, 82%, 66%, 60%, respectively. Univariate analysis showed factors impacting the survival rate were FIGO stage>1B1, non-squamous histologic type, deep cervical	Larger studies are included.

cancer. Gynecologic Oncology 120: 362-7		stromal invasion, and lymph node metastasis (p=0.027, 0.023, 0.007, 0.000). The Cox-proportional hazards regression analysis indicated that only lymph node metastasis (OR=3.827, p=0.000) was independent of poor prognostic factor. The 5-year survival rates in 1B1 were 88% with negative lymph nodes and 59% with positive lymph nodes (p=0.000).	
Yan X, Li G, Shang H et al. (2009) Complications of laparoscopic radical hysterectomy and pelvic lymphadenectomy--experience of 117 patients. International Journal of Gynecological Cancer 19: 963–7	Case series n=117	Overall conversion rate=1.7% (2/117) 4 vessel injuries 5 cystotomies Postoperative complications=38.5% (45/117) (38 urinary retention, 4 lymphocyst, 1 ureteral fistula, I mild adynamic bowel obstruction, 1 vesicovaginal fistula)	Larger studies are included.
Yang L, Cai J, Dong W et al. (2015) Laparoscopic radical hysterectomy and pelvic lymphadenectomy can be routinely used for treatment of early-stage cervical cancer: a single-institute experience with 404 patients. Journal of Minimally Invasive Gynecology 22: 199-204	Case series n=403 FU=median 31 months	Two patients had positive surgical margins. Intraoperative complications occurred in 7 patients, and 2 patients had conversion to open surgery (0.5%). Postoperative urinary tract fistula developed in 3 patients. Sixty-nine patients had adjuvant therapy. Thirty patients developed recurrent disease with a median disease-free interval of 12 months (range, 6 to 23 months), and 24 died of disease. The estimated 3-year overall survival rate was 95% in the women with a tumour ≤ 1B1 and 81% in those with a tumour >1B1, and the 3-year progression-free survival rates were 94% and 80%, respectively.	Studies with longer follow up are included.
Yeon J, Jung YW, Yang SS et al. (2017) Lower limb compartment syndrome by reperfusion injury after treatment of arterial thrombosis post-laparoscopic radical hysterectomy and pelvic lymph node dissection for cervical cancer. Obstetrics & Gynecology Science 60: 223-6	Case report n=1	**Lower limb compartment syndrome** The patient was diagnosed as compartment syndrome caused by reperfusion injury after treatment of arterial thrombosis, which occurred after laparoscopic radical hysterectomy and pelvic lymph node dissection for cervical cancer.	Case report of safety event already described.
Yim GW, Kim SW, Nam EJ et al. (2014) Surgical outcomes of robotic radical hysterectomy using three robotic arms versus	Non-randomised comparative study (robotic	RRH showed favourable outcomes over LRH in terms of estimated blood loss (p=0.037), early postoperative complication rates (17% vs 31%, p=0.028), and	Larger studies are included.

conventional multiport laparoscopy in patients with cervical cancer. Yonsei Medical Journal 55: 1222-30	versus laparoscopic) n=102 FU=median 44 months	postoperative complications necessitating intervention by Clavien-Dindo classification. Total operative time mean number of lymph node yield and median length of postoperative hospital stay were comparable between robotic and laparoscopic group, respectively. The median follow-up time was 44 months with 2 recurrences in the robotic and 3 in the laparoscopic cohort.	
Yin XH, Wang ZQ, Yang SZ et al. (2014) Clinical observation of laparoscopic radical hysterectomy for cervical cancer. International Journal of Clinical and Experimental Medicine 7: 1373-7	Non-randomised comparative study (laparoscopic versus open) n=45	Blood loss, postoperative hospital stay, complication rate, postoperative recovery of gastrointestinal tract and bladder function of the laparoscopy group of the laparoscopic group were all better than those of the laparotomy group (all $p<0.05$). The operative time was longer in the laparoscopy group than the laparotomy group ($p<0.05$). There was no statistically significant difference in the number of excised lymph nodes and the duration time of postoperative urinary catheterisation between the two groups.	Larger studies are included.
Zakashansky K, Chuang L, Gretz H et al. (2007) A case-controlled study of total laparoscopic radical hysterectomy with pelvic lymphadenectomy versus radical abdominal hysterectomy in a fellowship training program. International Journal of Gynecological Cancer 17: 1075–82	Non-randomised comparative study n=30 (LRH) n=30 (ARH) Median follow up=20 months	There were no conversions to open surgery. LRH had statistically significant lower mean blood loss, shorter hospital stay but longer operating time than ARH.	Larger studies are included.
Zanagnolo V, Minig L, Rollo D, et al. (2016) Clinical and oncologic outcomes of robotic versus abdominal radical hysterectomy for women with cervical cancer: experience at a referral cancer center. International Journal of Gynecologic Cancer 26:568-74	Non-randomised comparative study (robotic versus open) n=307 FU=median 42 months	Robotic radical hysterectomy is safe and feasible and is associated with improved clinical outcomes. Although longer follow up is needed, early data show equivalent oncologic outcomes compared with other surgical modalities.	Studies with more patients or longer follow up are included.
Zhao D, Li B; Wang Yet al. (2019) Clinical outcomes in early cervical cancer patients treated with nerve plane-sparing laparoscopic radical hysterectomy.	Non-randomised comparative study (nerve plane-sparing versus conventional) n=615	Compared with the LRH group, the nerve plane sparing-LRH group had a shorter length of operation (239 minutes vs 260 minutes $p<0.01$), less intraoperative bleeding ($p<0.01$), more resected lymph nodes ($p=0.028$), shorter duration of	Studies with longer follow up are included.

Journal of Minimally Invasive Gynecology 07	FU=28 months	urinary catheterisation (p<0.01), lower incidences of postoperative hydronephrosis (p=0.04), less long-term frequent urination (p<0.01), less acute urinary incontinence (p<0.01), poor bladder sensation (p=0.028), and constipation (p=0.029). There were no statistically significant differences in the disease-free survival and overall survival between the 2 groups (p=0.769 and 0.973, respectively).	
Zhao Y, Hang B, Xiong GW et al. (2017) Laparoscopic radical hysterectomy in early stage cervical cancer: a systematic review and meta-analysis. Journal or Laparoendoscopic & Advanced Surgical Techniques 27: 1132–44	Systematic review and meta-analysis n=4,205 (23 studies)	LRH was associated with lower estimated blood loss (p<0.00001), longer operation time, p<0.00001), fewer retrieved lymph nodes (p=0.007), shorter hospital stay, quicker return to normal bowel activity (p<0.00001), and shorter duration of bladder catheterisation (p<0.004) than ORH. LRH also demonstrated lower odds of transfusion (OR=0.47, 95% CI=0.30 to 0.73, p=0.0007), and ileus (OR=0.34, 95% CI=0.12 to 0.91, p=0.03) than ORH.	Another systematic review with similar outcomes, which also reports survival, is included.
Zhong XZ, Wang ZQ, Tang J et al. (2018) Port site metastasis after minimally invasive surgery of cervical carcinoma: Case report and review of the literature. European Journal of Gynaecological Oncology 39: 671-5	Case report n=1	**Port-site metastasis** Port-site metastasis in a 45-year-old woman with Stage IB2 squamous caner of the cervix. It occurred at the port site 18 months after laparoscopic surgery and completion of radiation and chemotherapy. Local excision of the mass was done, and histopathologic examination revealed metastasis of the squamous cell carcinoma of the cervix. The patient was still alive without recurrence and still participating in the follow up.	Case report of safety event already described.
Zhou J, Xiong BH, Ma L et al. (2016), Robotic vs laparoscopic radical hysterectomy for cervical cancer: a meta-analysis. The International Journal of Medical Robotics + Computer Assisted Surgery: MRCAS 12: 145-54	Systematic review and meta-analysis n=1,161 (15 studies)	Compared with LRH, RRH was associated with less blood loss and shorter hospital stay. There were no statistically significant differences in operative time, complications, mortality, transfusion, conversions, number of retrieved lymph nodes, recurrence or disease-free survival between the 2 groups.	A more recent systematic review is included.
Zhu T, Chen X, Zhu J et al. (2017) Surgical and pathological outcomes of laparoscopic versus abdominal radical	Non-randomised comparative study (laparoscopic versus open)	Laparoscopic radical hysterectomy (LRH) exhibited favourable results compared with abdominal radical hysterectomy (ARH) in terms of operating time,	Larger studies are included.

hysterectomy with pelvic lymphadenectomy and/or para-aortic lymph node sampling for bulky early-stage cervical cancer. International Journal of Gynecological Cancer 27: 1222-7	n=112 FU=46 months	blood loss, intestinal exhaust time, and length of hospital stay. Recurrence was observed in 5 LRH patients (17%) and 9 ARH patients (12%).	