NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of laparoscopic radical hysterectomy for early stage cervical cancer

Hysterectomy is the surgical removal of the uterus. When a hysterectomy is used to treat cervical cancer, many of the structures connected to the uterus also need to be removed. This is known as a radical hysterectomy. A laparoscopic radical hysterectomy is carried out through several small incisions in the abdomen ('keyhole' surgery), with the aid of an internal telescope and camera system (laparoscope).

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this 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 September 2009.

Procedure name

- Laparoscopic radical hysterectomy for early stage cervical cancer

Specialty societies

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

Description

Indications and current treatment

In 2006 there were 2873 new cases of cervical cancer diagnosed in the UK and the age-standardised (European) annual incidence was 8.5 per 100,000

women. Cervical cancer is the second most common cancer after breast cancer in women aged under 35 years, with 686 new cases diagnosed in the UK in 2006 (source: Cancer Research UK).

The most common symptoms of cervical cancer are abnormal vaginal bleeding or discharge, and discomfort during intercourse. Treatment largely depends on the type and stage of cancer at the time of diagnosis. The stage is defined by the International Federation of Gynecology and Obstetrics (FIGO) system: in stage IA, the cancer is identified only microscopically and invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm; stage IB are clinical lesions confined to the cervix or preclinical lesions greater than stage IA; stage IIA means the cancer involves up to the upper two-thirds of the vagina but there is no obvious parametrial involvement; stage IIB means there is obvious parametrial involvement but not into the pelvic sidewall; stage IIIA means the cancer has spread to the lower part of the vagina but not the pelvic sidewall; stage IIIB means there is extension into the pelvic sidewall or hydronephrosis or non-functioning kidney; in stage IVA, the cancer has spread into adjacent pelvic organs; in stage IVB the cancer has spread to distant organs. The cancer is graded according to how differentiated the cells are: grade 1 is low grade; grade 2 is intermediate; grade 3 is high grade. Surgery is usually the main treatment for early stage cervical cancer. Radiotherapy is also sometimes used, with or without surgery, and may be combined with chemotherapy. More advanced cervical cancer is generally treated with radiotherapy and chemotherapy, but not with surgery.

Radical hysterectomy (also known as Wertheim's hysterectomy) is the most common surgical treatment for cervical cancer and is conventionally carried out through an incision in the abdomen or through the vagina. It includes removal of the uterus and supporting ligaments, cervix and upper vagina, together with the pelvic lymph nodes and sometimes the para-aortic lymph nodes. Radical hysterectomy is further classified according to the extent of resection (type III is more extensive than type II).

What the procedure involves

Laparoscopic radical hysterectomy for early stage cervical cancer is performed with the patient under 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 conventional hysterectomy is performed 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 one of the abdominal incisions or through the vagina. The ureters are dissected to the point of their insertion into the

bladder. The specimen, including the upper vagina, cervix and uterus, is removed through the vagina.

The suggested benefits of the laparoscopic approach are shorter length of stay in hospital, shorter recovery period and minimal abdominal scarring.

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 performed.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to laparoscopic radical hysterectomy for cervical cancer. Searches were conducted of the following databases, covering the period from their commencement to 2 September 2009: 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 appendix C for details of 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 cervical cancer.
Intervention/test	Laparoscopic 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 overview

This overview is based on approximately 1176 patients from 4 non-randomised comparative studies, 4 case series and 2 case reports.

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

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

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Colombo PE (2009)[1] **Non-randomised comparative study** France Recruitment period: 2000–2008 Study population: women with locally advanced cervical cancer **n = 102 (46 LRH, 56 ARH)** Mean age (years) = 44 Patient selection criteria: patients with cervical cancer bulky stage IB, IIA and proximal IIB undergoing radical hysterectomy after concomitant chemoradiation therapy. Exclusion criteria not described. Technique: surgery was carried out 4–6 weeks after the end of chemoradiation therapy. Pelvic lymph nodes enclosed in a bag and removed through one of the abdominal ports. **Mean follow-up (months) = 31.2** Conflict of interest: none	Number of patients analysed: **102 (46 vs 56)** ***Mean operating time (min)*** • LRH = 157 (range 70–265) • ARH = 133 (range 60–220), p = NS ***Mean blood loss (ml)*** • LRH = 200 (range 30–1000) • ARH = 400 (range 80–2400), p < 0.01 ***Mean number of pelvic lymph nodes removed*** • LRH = 11 • ARH = 12, p = 0.8 ***Mean hospital stay (days)*** • LRH = 5 (range 3–13) • ARH = 8 (range 5–20), p < 0.01 ***Locoregional recurrence*** • LRH = 17.4% (8/46) • ARH = 17.9% (10/56), p = NS ***Distant recurrence*** • LRH = 13.0% (6/46) • ARH = 14.3% (8/56), p = NS ***3-year overall survival*** • LRH = 82% • ARH = 82%, p = NS ***3-year disease-free survival*** • LRH = 81% • ARH = 70%, p = NS	**Conversion to open surgery = 15% (7/46)** (1 to control bleeding, 2 to repair urinary wounds, 3 because of difficulties in dissecting fibrosis) ***Intraoperative complications*** • LRH = 10.9% (5/46) • ARH = 16.1% (9/56) *Haemorrhage* • LRH = 2.2% (1/46) • ARH = 8.9% (5/56) *Bladder injury* • LRH = 4.3% (2/46) • ARH = 1.8% (1/56) *Ureteral injury* • LRH = 2.2% (1/46) • ARH = 1.8% (1/56) *Digestive injury* • LRH = 2.2% (1/46) • ARH = 1.8% (1/56) ***Postoperative complications*** • LRH = 28.3% (13/46) • ARH = 46.4% (26/56), p = 0.04 *Pelvic infection* • LRH = 0% (0/46) • ARH = 3.6% (2/56) *Haemorrhage* • LRH = 2.2% (1/46) • ARH = 0% (0/56) *Urinary complications* • LRH = 23.9% (11/46) • ARH = 35.7% (20/56) *Pulmonary embolism* • LRH = 0% (0/46) • ARH = 1.8% (1/56) *Digestive fistulae* • LRH = 2.2% (1/46) • ARH = 1.8% (1/56) *Symptomatic lymphocysts* • LRH = 0% (0/46) ARH = 3.6% (2/56)	**Follow-up issues:** • Losses to follow-up were not described. **Study design issues:** • Prospective, consecutive patients. • LRH was progressively introduced during the study period. LRH was systematically used after January 2005. • Two obese patients were selected to undergo ARH rather than LRH but no other selection was made according to patients or tumour characteristics. **Study population issues:** • There were no differences in tumour characteristics between the two groups. **Other issues:** • Discrepancy over number of patients with distant recurrence in LRH group (5 cited in table and 6 in text).

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Malzoni M (2009)[2] **Non-randomised comparative study** Italy Recruitment period: 1995–2007 Study population: women with early-stage cervical cancer **n = 127 (65 LRH, 62 ARH)** Mean age (years): • LRH = 40.5 • ARH = 42.7 Patient selection criteria: patients with cervical cancer stage IA1 with lymphovascular space involvement, stage IA2 and IB1, tumour size < 4 cm, body mass index ≤ 35 kg/m^2, no evidence of node involvement on imaging studies. Laparoscopy was not considered when the uterus was ≥ 12-week size or where vaginal removal of the uterus may require morcellation. Technique: patients with stage IA2 and IB1 disease with primary lesion ≤ 2 cm underwent type II procedure and patients with stage IB1 disease with tumours > 2 cm underwent type III procedure. **Median follow-up (months):** • LRH = 52.5 (range 4–89) • ARH = 71.5 (range 5–151) Conflict of interest: not stated	Number of patients analysed: **127 (65 vs 62)** ***Mean number of pelvic lymph nodes removed*** • LRH = 23.5 • ARH = 25.2, p < 0.01 ***Median operating time (min)*** • LRH = 196 (182–240) • ARH = 152 (161–240), p < 0.01 ***Median blood loss (ml)*** • LRH = 55 (range 30–80) • ARH = 145 (range 60–225), p < 0.01 ***Median hospital stay (days)*** • LRH = 4 (range 3–7) • ARH = 7 (range 5–9), p < 0.01 ***Recurrence at follow-up*** • LRH = 7.7% (5/65) • ARH = 6.4% (4/62), p = NS ***Disease-free survival*** • LRH = 92.4% • ARH = 93.6%, p = 0.29	**Conversion to open surgery = 0% (0/65)** ***Blood transfusion*** • LRH = 0% (0/65) • ARH = 0% (0/62) ***Intraoperative bladder injury*** • LRH = 1.5% (1/65) (sutured laparoscopically) • ARH = 1.6% (1/62) ***Postoperative complications*** *Ureterovaginal fistula* • LRH = 1.5% (1/65) (diagnosed 1 month postoperatively. A ureteral stent was placed and removed after 3 months with no sequelae). • ARH = 0% (0/62) *Postoperative fever* • LRH = 9.2% (6/65) • ARH = 12.9% (8/62) *Lymphorrhoea* • LRH = 30.8% (20/65) • ARH = 27.4% (17/62) (In all cases, this condition resolved spontaneously.)	**Follow-up issues:** • Losses to follow-up not described. **Study design issues:** • Retrospective study. • Consecutive patients. • The decision to perform laparoscopic or open procedure was made according to surgeon's or patient's preference. **Study population issues:** • There were no significant differences between the groups with regard to histology type, grading, tumour stage or lymph node status.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Li G (2007)[3] **Non-randomised comparative study** China Recruitment period: 1998–2005 Study population: women with early-stage cervical cancer **n = 125 (90 LRH, 35 ARH)** Mean age (years): • LRH = 42 • ARH = 44 Patient selection criteria: patients with FIGO stage IB to IIA without preoperative brachytherapy or chemotherapy; tumour diameter ≤ 5 cm without significant pelvic adhesion discerned during surgery. Technique: type III radical hysterectomy. Both LRH and ARH included pelvic lymphadenectomy. Para-aortic node dissection was not routinely done. In LRH, the lymph nodes were put into a bag and taken out vaginally at the end of the procedure. **Median follow-up (months) = 26** Conflict of interest: not stated	Number of patients analysed: **125 (90 vs 35)** ***Operating time (min)*** • LRH = 263.0 • ARH = 217.2, p = 0.001 ***Blood loss (ml)*** • LRH = 369.8 • ARH = 455.1, p = NS ***Mean number of pelvic lymph nodes removed*** • LRH = 21.3 • ARH = 18.8, p = NS ***Recovery time of bowel (days)*** • LRH = 2.0 • ARH = 2.4, p = 0.025 ***Time to normal urine residual (days)*** • LRH = 10.7 • ARH = 8.6, p = NS ***Hospital stay (days)*** • LRH = 13.8 • ARH = 13.7, p = NS 20% of patients in LRH group and 11.4% of patients in ARH group received adjuvant radiotherapy or chemoradiation therapy for positive lymph nodes (p = NS). ***Recurrence at follow-up*** • LRH = 13.75% • ARH = 12%, p = NS ***Mortality rate*** • LRH = 10% • ARH = 8%, p = NS	**Conversion to open surgery = 2.2% (2/90)** (1 iliac vein injury and 1 cystotomy – all other injuries in the LRH group were repaired laparoscopically) ***Intraoperative complications*** • LRH = 8.9% (8/90) • ARH = 8.6% (3/35) *Iliac vein injury* • LRH = 4.4% (4/90) • ARH = 2.9% (1/35) *Bladder injury* • LRH = 4.4% (4/90) • ARH = 0% (0/35) *Ureteral injury* • LRH = 0% (0/90) • ARH = 5.7% (2/35) ***Postoperative complications*** • LRH = 40.0% (36/90) • ARH = 40.0% (14/35) *Urinary retention* • LRH = 32.2% (29/90) • ARH = 28.6% (10/35) *Ureteral fistula* • LRH = 1.1% (1/90) • ARH = 0% (0/35) *Vesicovaginal fistula* • LRH = 1.1% (1/90) • ARH = 0% (0/35) *Bowel obstruction* • LRH = 1.1% (1/90) • ARH = 2.9% (1/35) *Lymphocyst* • LRH = 4.4% (4/90) • ARH = 5.7% (2/35) *Wound dehiscence* • LRH = 0% (0/90) • ARH = 2.9% (1/35)	**Follow-up issues:** • Losses to follow-up = 11% (10/90) for LRH and 14% (5/35) for ARH. **Study design issues:** • Retrospective data collection • Consecutive cases **Study population issues:** • There was no difference between the two groups with regard to age, weight, tumour size, grade and pelvic lymph node metastases. • Proportion of early-stage cancer and proportion of squamous carcinoma was higher in laparoscopy group than laparotomy group (p = 0.046 and p = 0.009 respectively). • Proportion of tumours between 4 and 5 cm = 13% for LRH and 23% for ARH (p = NS). **Other issues:** • Where percentages only are given, actual numbers were not given in the paper.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Ghezzi F (2007)[4] **Non-randomised comparative study** Italy Recruitment period: 2004–2007 Study population: women with early-stage cervical cancer **n = 98 (50 LRH, 48 ARH)** Mean age (years): • LRH = 47 (range 24–78) • ARH = 53 (range 28–75) Patient selection criteria: patients with early-stage (stages IA2–IIA) cervical cancer. Exclusion criteria: neoadjuvant therapy or evidence of gross extrauterine disease on preoperative imaging modalities. Technique: patients with stage IA or IB disease and tumour size < 2 cm had a modified (type II) radical hysterectomy (only the medial half of the cardinal ligaments was removed). All others had a type III hysterectomy. Both LRH and ARH included pelvic lymphadenectomy. In LRH, a specimen bag was used to retrieve the lymph nodes, separately from each side wall. **Median follow-up (months):** • LRH = 10 (2–30) • ARH = 58 (32–96) Conflict of interest: not stated	Number of patients analysed: **98 (50 vs 48)** 16 patients in LRH group and 11 in ARH group had type II hysterectomy; all others had type III. ***Median operating time for type II RH (min)*** • LRH = 215 (150–400) • ARH = 205 (155–390), p = 0.47 ***Median operating time for type III RH (min)*** • LRH = 285 (170–375) • ARH = 260 (160–415), p = 0.80 ***Median blood loss for type II RH (ml)*** • LRH = 170 (100–220) • ARH = 400 (200–1500), p = 0.002 ***Median blood loss for type III RH (ml)*** • LRH = 200 (50–1000) • ARH = 500 (200–2500), p < 0.0001 ***Median hospital stay (days)*** • LRH = 6 (3–14) • ARH = 10 (4–32), p < 0.0001 ***Median number of pelvic lymph nodes removed (range)*** • LRH = 21 (8–49) • ARH = 23 (8–51), p = 0.07 ***Lymph node positivity*** • LRH = 14.0% (7/50) • ARH = 18.7% (9/48), p = 0.59 ***Positive parametrial margins*** • LRH = 6.0% (3/50) • ARH = 6.2% (3/48), p = 1.0 ***Positive vaginal margins*** • LRH = 0% (0/50) • ARH = 0% (0/48), p = 1.0 38% (19/50) of patients in LRH group and 29% (14/48) of patients in ARH group received adjuvant chemoradiotherapy for positive lymph nodes, close or positive margins, or a combination of risk factors. All patients in LRH group remained clinically disease free at the time of writing the report.	**Conversion to open surgery = 0% (0/50)** **B*lood transfusion*** • LRH = 0% (0/50) • ARH = 8.3% (4/48), p = 0.05 ***Intraoperative complications*** • LRH = 8.0% (4/50) • ARH = 10.4% (5/48) *Iliac vein injury* • LRH = 0% (0/50) • ARH = 2.1% (1/48) *Bladder injury* • LRH = 6.0% (3/50) • ARH = 4.2% (2/48) *Ureteral injury* • LRH = 2% (1/50) • ARH = 0% (0/48) *Left hypogastric vein injury* • LRH = 0% (0/50) • ARH = 2.1% (1/48) *Bowel injury during adhesiolysis* • LRH = 0% (0/50) • ARH = 2.1% (1/48) All the injuries in the LRH group were repaired laparoscopically with no long-term sequelae. ***Postoperative complications*** • LRH = 14% (7/50) • ARH = 22.9% (11/48), p = 0.30 Postoperative complications in LRH group included: ureterovaginal fistula (n = 1, managed conservatively), vesicovaginal fistula (n = 1, 'successfully repaired'), delayed ureteral fistula resulting from ischaemic necrosis (n = 1, required reoperation by open approach at day 14), bowel obstruction (n = 1, treated by laparotomy), pulmonary embolism (n = 1) and pelvic lymphocysts (n = 2, managed conservatively). Postoperative complications in ARH group included: intra-abdominal bleeding requiring reintervention (n = 1), pelvic haematoma (n = 1, managed conservatively), small bowel	**Follow-up issues:** • Losses to follow-up not described. **Study design issues:** • Prospective data collection for cases, historical controls. • Patients were included from three study centres. • Controls were selected from consecutive women having had ARH before the introduction of LRH who met the same criteria for eligibility as the cases. • The decision to plan a radical hysterectomy rather than treat with primary radiotherapy was at the discretion of the oncologist. **Study population issues:** • There were no significant differences between the groups with regard to age, body mass index, nulliparity, FIGO stage, histology, grade or size of tumour.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Ghezzi F (2007)[4] cont.		incarceration (n = 1, required open surgery), *E. coli* sepsis (n = 1), lymphoedema (n = 1), symptomatic pelvic lymphocysts (n = 2), fever (n = 2), wound infection with dehiscence (n = 1), wound hernia (n = 1).	

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Spirtos NM (2002)[5] **Case series** USA Recruitment period: 1994–1996 Study population: women with early-stage cervical cancer, with at least 3 years follow-up **n = 78** Median age (years) = 41.5 (range 26–62) Patient selection criteria: patients with Cervical cancer FIGO stage IA2 and IB, negative para-aortic lymph nodes, clinically normal pelvic lymph nodes at operation, no evidence of extracervical disease. Technique: type III radical hysterectomy, with or without bilateral salpingo-oophorectomy and pelvic and aortic lymph node dissection. **Mean follow-up (months)** = **66.8** Conflict of interest: not stated	Number of patients analysed: **78** Mean number of lymph nodes removed = 34 (range 19–68) Mean operating time (min) = 205 (range 150–430) Mean blood loss (ml) = 250 (range 50–700) Mean hospital stay (days) = 3 (range 1–7) ***Recurrences = 10.3% (8/78)*** 3 recurrences on the pelvic side wall, 1 isolated nodal recurrence on external iliac artery, 1 recurrence in the vaginal apex and base of the bladder, 1 liver metastasis, 1 lung metastasis and 1 patient had involvement of the suprarenal lymph nodes. Of the 8 patients with recurrences, 4 had undergone radiation therapy – 3 of whom had recurrence within the treatment field and died of the disease. ***Estimated 5-year disease-free interval after treatment = 89.7%*** ***Estimated 5-year survival = 93.6%***	**Conversion to open surgery = 6% (5/78)** (2 to control bleeding, 1 because of inability to maintain pneumoperitoneum after a retroperitoneal laparoscopic lymphadenectomy was performed, 1 to repair a cystotomy and 1 to place a ureteral stent). **Blood transfusion = 1.3% (1/78)** ***Intraoperative complications*** • Bladder injury (cystotomy) = 3.8% (3/78) (2 were repaired laparoscopically and 1 required laparotomy) ***Postoperative complications*** • Ureterovaginal fistula = 1.3% (1/78) • Deep venous thrombosis = 1.3% (1/78) • Urosepsis = 1.3% (1/78) • Vaginal cuff abscess = 1.3% (1/78) • Abdominal wall haematoma = 1.3% (1/78) • Pelvic lymphocysts = 2.6% (2/78)	**Follow-up issues:** • Losses to follow-up not described. **Study design issues:** • Prospective study. • Consecutive patients. **Study population issues:** • An additional 6 patients were excluded from the study because of macroscopically positive pelvic lymph nodes, positive aortic lymph nodes or intraperitoneal disease (these patients were treated by laparotomy). **Other issues:** • This study was included in the original overview for IPG 24 (published in November 2003).

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Chen Y (2008)[6] **Case series** China Recruitment period: 2001–2007 Study population: women with invasive cervical cancer **n = 295** Mean age (years) = 43 (range 25–77) Patient selection criteria: patients with invasive cervical cancer (FIGO stage IA2 to IIIB). Technique: type III or type IV radical hysterectomy, with or without bilateral salpingo-oophorectomy. Para-aortic lymph nodes were removed in 156 procedures. **Median follow-up (months) = 36.4 (range 8–76)** Conflict of interest: none stated	Number of patients analysed: **295** Mean number of lymph nodes removed = 22 (range 17–41) Mean operating time (min) = 162 (range 110–350) Mean blood loss (ml) = 230 (range 50–1200) Mean hospital stay (days) = 10 (range 6–14) ***Recurrences or metastasis = 16.3% (48/295)*** • Pelvic or vaginal stump = 16 • Abdominal cavity = 5 • Lymph nodes = 8 • Distant = 12 • Multiple sites = 6 • Port site = 1 ***Recurrence-free survival by stage:*** • Stage IA (n = 21) = 95.2% • Stage IB (n = 80) = 96.2% • Stage IIA (n = 71) = 84.5% • Stage IIB (n = 107) = 79.4% • Stage IIIA (n = 6) = 66.7% • Stage IIIB (n = 10) = 60.0% Statistically significant risk factors for recurrence: • Tumour FIGO stage > IB • Lymphovascular space and parametrial involvement • Lymph node metastasis	**Conversion to open surgery = 1.7% (5/295)** (2 to repair vascular injury, 1 to repair colon injury, 1 to repair ureter injury, 1 for hypercapnia). **Blood transfusion = 2.7% (8/295)** ***Intraoperative complications*** • Bladder injury (cystotomy) = 1.7% (5/295) (all repaired laparoscopically) • Vascular injuries = 2.4% (7/295) (5 repaired laparoscopically and 2 by open surgery) • Ureteral injury = 0.3% (1/295) (repaired laparoscopically) • Rectal injury = 0.7% (2/295) (sutured vaginally) • Colon injury = 0.3% (1/295) (conversion to open surgery) • Hypercapnia = 0.3% (1/295) (conversion to open surgery) ***Postoperative complications*** • Ureterovaginal fistula = 1.7% (5/295) (3 treated with ureteral stents, 2 ureteroneocystotomies) • Vesicovaginal fistula = 1.4% (4/295) (1 closed by conservative treatment, 3 repaired vaginally or abdominally) • Ureterostenosis = 1.0% (3/295) (treated with ureteral stents) • Deep venous thrombosis = 3.0% (9/295) (treated with drugs) • Lymphocyst = 1.4% (4/295) (managed conservatively) • Lymphoedema = 1.7% (5/295) (treated with Chinese medicine)	**Follow-up issues:** • No losses to follow-up were described. **Study design issues:** • Retrospective study. • Kaplan-Meier method was used to calculate survival. Prognostic factors were analysed in a univariate analysis using a log-rank test. **Study population issues:** • Neoadjuvant chemotherapy was given preoperatively to patients with stage III cancer for 2 or 3 courses and reduced the FIGO stage of cancer. **Other issues:** • The authors state that most of the major complications occurred in the first 100 procedures.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Puntambekar SP (2007)[7] **Case series** India Recruitment period: 2002–2006 Study population: women with early-stage cervical cancer **n = 248** Median age (years) = 61 (range 35–82) Patient selection criteria: patients with cervical cancer FIGO stage IA2 and IB1, good general condition, tumour < 4 cm, no evidence of nodal enlargement. Technique: type III radical hysterectomy. **Median follow-up (months): 36 (range 0–50)** Conflict of interest: none	Number of patients analysed: **248** Median number of lymph nodes removed = 18 (range 14–30) Median operating time (min) = 92 (range 65–120) Median blood loss (ml) = 165 (range 150–500) Median hospital stay (days) = 3 (range 3–6) 66.5% (165/248) patients underwent concomitant radiotherapy. ***Recurrences = 2.8% (7/248)*** • Port site = 1 • Vault = 4 • Para-aortic nodes = 2 At the last follow-up, 6 of the 7 patients who had recurrent disease were currently disease free. One patient was still alive with the disease. As of latest follow-up, all patients were described as doing well.	***Intraoperative complications (all recognised and managed laparoscopically)*** • Bladder injury (cystotomy) = 1.2% (3/248) • High ureteral injury = 0.4% (1/248) • Vascular injuries = 3.6% (9/248) • Bowel injury = 0.8% (2/248) ***Postoperative complications (arising within 2 months of surgery)*** • Urinary retention = 2.0% (5/248) (treated with intermittent catheterisation, resolved within 6 months) • Urinary tract infection = 0.8% (2/248) • Ureterovaginal fistula = 1.6% (4/248) (3 were repaired laparoscopically 1 with cystoscopic stenting) • Wound infection = 1.2% (3/248) • Ileus = 0.8% (2/248) (managed conservatively) • Secondary haemorrhage = 0.4% (1/248) (repeat laparoscopy and packing done)	**Follow-up issues:** • No losses to follow-up were described. **Study design issues:** • Retrospective study. • An additional 4 patients were excluded from the study after they were found to have bladder involvement.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details	Key efficacy findings	Key safety findings	Comments
Pellegrino A (2009)[8] **Case series** Italy Recruitment period: 2001–2007 Study population: women with stage IB1 cervical cancer **n = 101** Mean age: 44 years (range 28–76) Patient selection criteria: patients with cervical cancer stage IB1, good general condition, tumour size < 3 cm, no evidence of lymph node metastases in imaging study. Technique: sampling of para-aortic nodes was limited to patients with suspected nodal metastasis at surgical exploration. The lymph nodes were put into a bag and taken out vaginally at the end of the procedure. **Median follow-up (months) = 30** Conflict of interest: none	Number of patients analysed: **101** Median number of lymph nodes removed = 26 (range 11–48) Median duration of operation (min) = 305 (range 220–505) Median blood loss (ml) = 200 (range 50–550) Median length of hospital stay (days) = 4 (range 3–9) ***Recurrences = 10% (11/101)*** ***Survival rate = 95% (96/101)*** (5 patients died of the disease)	***Intraoperative complications*** • Bladder injury = 1.0% (1/101) (repaired laparoscopically) • Obturator nerve injury = 1.0% (1/101) ***Postoperative complications*** • Low/mild grade fever = 9.0% (9/101) • Bowel evisceration = 2.0% (2/101) (diagnosed after 20 and 35 days, both required vaginal cuff resuture) • Ureteral stenosis requiring ureteral reimplantation = 2.0% (2/101) • Subtotal ureteral stenosis = 3% (3/101) (treated with ureteral stent placement) • Ureteral fistula = 5% (5/101) (1 required ureteral reimplantation, 4 were treated with stents)	**Follow-up issues:** • Losses to follow-up were not described. **Study design issues:** • Prospective study. • An additional 6 patients were eligible for the study but conversion to laparotomy was necessary for metastatic disease in 3 patients and dense adhesions in 3 patients. They were excluded from further analysis.

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Kim MK (2009)[9] Case report South Korea Study population: woman with complete bladder gangrene after LRH for cervical cancer Age (years) = 70 Technique: LRH with salpingo-oophorectomy and bilateral hypogastric artery ligation Conflict of interest: none	**Complete bladder gangrene** Three weeks after LRH the patient had generalised weakness, inability to void and diffuse abdominal pain. At laparotomy, gangrenous bladder wall and rupture were visible. A total cystectomy and transureteroureterostomy with cutaneous ureterostomy was carried out. The patient was healthy without any further complications or cancer recurrence 33 months later.		
Iniesta MD (2007)[10] Case report Spain Study population: woman with splenic rupture after LRH for cervical cancer Age (years) = 56 Technique: LRH not otherwise described. Conflict of interest: none stated	**Splenic rupture** No complications were observed during surgery. No postoperative bleeding was observed. Five days later the patient became extremely pale, hypotensive and tachycardic. An emergency laparotomy revealed active bleeding from the spleen, which was decapsulated and injured. A splenectomy was carried out. The authors state that during laparoscopy, laceration or decapsulation of the spleen occurred followed by encapsulated haematoma, which acted as external compression and prevented haemorrhage.		

Abbreviations used: ARH, abdominal radical hysterectomy; FIGO, International Federation of Gynecology and Obstetrics; LRH, laparoscopic radical hysterectomy; NS, not significant; RH, radical hysterectomy

Study details

Chong G (2009)[11]

Case series

South Korea

Recruitment period: 1994–2004

Study population: patients with early and locally advanced cervical cancer (stage IA2–IIB)

n = 100

Mean age (years): first 50 cases = 48, second 50 cases = 51

Patient selection criteria: patients with stage IA2 to IIB cervical cancer. Protocol of cancer staging included a pelvic examination under general anaesthesia, conisation, computed tomography, and magnetic resonance imaging of the pelvis.

Technique: type 2 and 3 LRH according to stage, with pelvic and/or para-aortic lymphadenectomy.

Median follow-up (months) = 66.5

Conflict of interest: none reported

Key efficacy findings

Number of patients analysed**: 100**

Surgical data

	First 50 patients	Second 50 patients	p value
Mean operating time (min)	325	225	< 0.001
Mean blood loss (ml)	370	333	0.472
Mean pelvic node	15.8	26.9	< 0.001
Length of hospital stay (days)	10.9	7.3	< 0.001
Time to normal urine residual (days)	9.1	6.7	0.004
Transfusion	34% (17/50)	12% (6/50)	0.009
Haemorrhage > 500 ml	32% (16/50)	8% (4/50)	0.005

Recurrence = 10% (10/100) (9 of whom died)

5-year overall survival:

- First 50 cases = 96%
- Second 50 cases = 90%
- Overall = 93%

5-year disease-free survival:

- First 50 cases = 92%
- Second 50 cases = 90%
- Overall = 90%

Key safety findings

Complications

	First 50 patients	Second 50 patients	p value
Bladder injury	10% (5/50)	2% (1/50)	
Ureter injury	4% (2/50)	2% (1/50)	
Hydronephrosis	6% (3/50)	4% (2/50)	
Ileus	2% (1/50)	0	
Infected lymphocyst	2% (1/50)	0	
Voiding dysfunction	4% (2/50)	0	
Severe leg lymphoedema	2% (1/50)	0	
Vesicovaginal fistula	2% (1/50)	0	
Hypoxaemia	2% (1/50)	0	
Total	34% (17/50)	8% (4/50)	0.003

Comments

Follow-up issues:

- No losses to follow-up were reported.

Study design issues:

- Consecutive patients.
- One of the aims of the study was to assess the number of operations necessary to develop and standardise LRH.
- All operations were done by a single surgeon.

Population issues:

- Both groups were similar with respect to age, Quetelet index, FIGO stage and positive pelvic nodes.

Efficacy

Survival

One non-randomised comparative study of 102 patients with locally advanced cervical cancer reported 3-year overall survival of 82% for both abdominal and laparoscopic radical hysterectomy[1]. Disease-free survival was 81% for laparoscopic radical hysterectomy and 70% for abdominal radical hysterectomy ($p > 0.05$). A non-randomised comparative study of 127 patients with early stage cervical cancer reported a disease-free survival rate of 92% for laparoscopic radical hysterectomy and 94% for abdominal radical hysterectomy, with median follow-up periods of 53 and 72 months respectively ($p = 0.29$)[2]. A non-randomised comparative study of 125 patients with early stage cervical cancer reported a recurrence rate of 14% for laparoscopic radical hysterectomy and 12% for abdominal radical hysterectomy, with a median follow-up of 26 months ($p > 0.05$)[3]. A non-randomised comparative study of 98 patients stated that all patients were clinically disease free after laparoscopic radical hysterectomy at a median follow-up period of 10 months[4].

A case series of 78 patients reported an estimated 5-year overall survival rate of 94%[5]. A case series of 295 patients reported recurrence-free survival between 60% and 96, depending on the cancer stage at diagnosis, with a median follow-up of 36 months[6]. In another case series, 3% (7/248) of patients had disease recurrence after a median follow-up of 36 months[7]. In a case series of 101 patients, the recurrence rate was 10% (11/101) and the survival rate was 95% (96/101) after a median follow-up of 30 months[8]. In a case series of 100 patients the recurrence rate was 10% (10/100), the 5-year overall survival rate was 93% and the 5-year disease-free survival rate was 90%[11].

Number of lymph nodes removed

In 3 non-randomised comparative studies, the mean number of pelvic lymph nodes removed ranged from 11 to 24 for laparoscopic radical hysterectomy and from 12 to 25 for abdominal radical hysterectomy[1–3].

Hospital stay

The length of hospital stay was statistically significantly shorter in 3 of the 4 non-randomised comparative studies (5, 4 and 6 days for laparoscopic radical hysterectomy versus 8, 7 and 10 days respectively for abdominal radical hysterectomy)[1, 2, 4].

Operating time and estimated blood loss

Operating time was statistically significantly longer for laparoscopic radical hysterectomy in 2 of the 4 non-randomised comparative studies (196 and 263 minutes for laparoscopic radical hysterectomy versus 152 and 217 minutes for abdominal radical hysterectomy, $p < 0.01$ and $p = 0.001$ respectively)[2, 3].

In 3 of the 4 non-randomised comparative studies, estimated blood loss was significantly lower for laparoscopic radical hysterectomy compared with abdominal radical hysterectomy[1, 2, 4].

Safety

Intraoperative complications

Bladder injury

The rate of bladder injury for laparoscopic radical hysterectomy ranged from 1% (3/248 and 1/101) to 6% (3/50)[1–8]. In the case series of 100 patients the rate of bladder injury was 10% (5/50) in the first 50 patients treated and 2% (1/50) in the second group of 50 patients treated[11].The rate for abdominal radical hysterectomy ranged from 0% (0/35) to 4% (2/48)[1–4].

One case report described a case of complete bladder gangrene 3 weeks after laparoscopic radical hysterectomy[9].

Ureteric injury

The rate of ureteric injury for laparoscopic radical hysterectomy ranged from 0% (0/90) to 2% (1/46, 1/50)[1 3, 4, 6, 7]. In the case series of 100 patients the rate of ureter injury was 4% (2/50) in the first 50 patients and 2% (1/50) in the subsequent 50 patients[11].The rate for abdominal radical hysterectomy ranged from 0% (0/48) to 6% (2/35)[1, 3, 4].

Bowel injury

Three studies reported bowel injury in 1% (3/295 and 2/248) and 2% (1/46) of patients treated laparoscopically[1, 6, 7].

One case report described a case of splenic rupture that was identified 5 days after laparoscopic radical hysterectomy[10].

Conversion to open surgery

The rate of conversion to open surgery was reported in 6 studies and ranged from 0% (0/65, 0/50) to 15% (7/46)[1–6].

Postoperative complications

Fistulae

Five studies reported ureterovaginal fistula in 1% (1/78) and 2% (1/65, 1/50, 5/295 and 4/248) of patients undergoing laparoscopic radical hysterectomy[2, 4, 5, 6, 7]. Ureteric fistula was reported in 1% (1/90), 2% (1/50) and 5% (5/101) of patients[3, 4, 8]. Vesicovaginal fistula was reported in 1% (1/90, 4/295) and 2% (1/50, 1/50) of patients[3, 4, 6, 11].

Validity and generalisability of the studies

- There were no randomised controlled trials comparing laparoscopic radical hysterectomy with the open approach.
- Three studies specified that a type III radical hysterectomy was carried out, 2 described a combination of type II and type III, and 1 study included type III and type IV radical hysterectomies. Two studies did not state what kind of radical hysterectomy was used.
- In 4 studies, inclusion criteria included size of tumour; 1 stated a tumour size of more than 3 cm, 2 included tumour size of more than 4 cm and one stated 5 cm or more.
- The stage of cervical cancer included in the studies varied. Five studies included stage Ia (one IA1 and four IA2). Two studies included stage IIA cancers, 1 included stage IIB and 1 included stage IIIB cancers.
- One study excluded women with a body mass index greater than 35 kg/m^2. In another study, 2 obese women were selected to undergo laparotomy rather than laparoscopy.
- In 1 study, laparoscopy was only considered if the uterus was larger than 12-week size.

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. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Laparoscopic radical hysterectomy for early stage cervical cancer. NICE interventional procedures guidance 24 (2003). Currently under review (this overview). Available from www.nice.org.uk/IPG24
- Laparoscopic techniques for hysterectomy. NICE interventional procedures guidance 239 (2007). Available from www.nice.org.uk/IPG239
- High dose rate brachytherapy for carcinoma of the cervix. NICE interventional procedures guidance 160 (2006). Available from www.nice.org.uk/IPG160

Technology appraisals

- None

Clinical guidelines

- None

Public health guidance

- None

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 does not represent the view of the society.

Dr T Lopes, Professor D Luesley (Royal College of Obstetricians and Gynaecologists).

- One Adviser described the procedure as established practice and no longer new.
- The comparator would be open radical hysterectomy plus bilateral pelvic lymphadenectomy.
- Adverse events reported in the literature include conversion to open surgery because of bleeding. Theoretical adverse events include compromise in lymphadenectomy and margin of excision of primary tumour.
- Key efficacy outcomes are recurrence rates, pelvic recurrence rates, 5-year survival, number of lymph nodes removed, shorter recovery time and shorter length of hospital stay.
- There are no randomised studies reporting on survival data.
- The incidence of cervical cancer continues to fall.
- The procedure requires advanced laparoscopic skills.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

No additional issues were identified.

References

1. 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.
2. 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.
3. 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.
4. Ghezzi F, Cromi A, Ciravolo G et al. (2007) Surgicopathologic outcome of laparoscopic versus open radical hysterectomy. Gynecologic Oncology 106: 502–6.
5. Spirtos NM, Eisenkop SM, Schlaerth JB, Ballon SC. (2002) Laparoscopic radical hysterectomy (type III) with aortic and pelvic lymphadenectomy in patients with stage I cervical cancer: surgical morbidity and intermediate follow-up. American Journal of Obstetrics & Gynecology 187: 340–8.
6. 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.
7. 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.
8. 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 surgical and oncological outcome. European Journal of Surgical Oncology 35: 98–103.
9. 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.
10. Iniesta MD, de Santiago J, Ordas J. (2007) Splenic rupture following laparoscopic radical hysterectomy. International Journal of Gynecology & Obstetrics 99: 245–6.
11. 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.

Appendix A: Additional papers on laparoscopic radical hysterectomy for early stage cervical cancer

The following table outlines the studies that are considered potentially relevant to the 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.

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.
Belval CC, Barranger E, Dubernard G et al. (2006) Peritoneal carcinomatosis after laparoscopic radical hysterectomy for early-stage cervical adenocarcinoma. Gynecologic Oncology 102: 580–2.	Case report n = 1 Follow-up = 16 months	Peritoneal carcinomatosis diagnosed 16 months after LRH for FIGO stage IB1 cervical adenocarcinoma.	Case report of complication already described in table 2.
Diaz-Feijoo B, Gil-Moreno A, Perez-Benavente MA et al. (2008) Sentinel lymph node identification and radical hysterectomy with lymphadenectomy in early stage cervical cancer: laparoscopy versus laparotomy. Journal of Minimally Invasive Gynecology 15: 531–7.	Non-randomised comparative study n = 20 (LRH) n = 30 (ARH) Median follow-up = 35 months	No significant difference in overall survival and disease-free survival. Blood loss and length of stay were significantly lower in laparoscopic group but surgical time was significantly longer.	Larger comparative studies 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 comparative studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Frumovitz M, dos Reis R, Sun CC et al. (2007) Comparison of total laparoscopic and abdominal radical hysterectomy for patients with early-stage cervical cancer. Obstetrics & Gynecology 110: 96–102.	Non-randomised comparative study n = 89	LRH associated with reduced blood loss, postoperative infectious morbidity and postoperative length of stay but with increased operative time.	Larger comparative studies are included.
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 comparative studies with longer follow-up are included.
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.
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 significantly reduced as compared to 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) Laparoscopic radical hysterectomy with lymphadenectomy in patients with early cervical cancer: our instruments and technique. Surgical Oncology 18: 289–97.	Case series. n = 77 Median follow-up = 64 months	Recurrence rate = 6.4% Disease-free survival: •Stage IA1 = 100% •Stage IA2 and IB1 = 93.5% One patient had ureterovaginal fistula	Larger case series are included
Malzoni M, Tinelli R, Cosentino F et al. (2007) Feasibility, morbidity, and safety of total laparoscopic radical hysterectomy with lymphadenectomy: our experience. Journal of Minimally Invasive Gynecology 14: 584–90.	Case series n = 65 Median follow-up = 46.5 months	1 postoperative ureterovaginal fistula Recurrence = 7.7% (5/65) (all on vaginal cuff) Disease-free survival = 100% for stage IA1 and 91% for stage IA2 and IB1.	Larger case series are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Obermair A, Ginbey P, McCartney AJ. (2003) Feasibility and safety of total laparoscopic radical hysterectomy. Journal of the American Association of Gynecologic Laparoscopists 10: 345–9.	Case series n = 55 Median follow-up = 36.5 months	Intraoperative complications: 3 vascular injuries, 1 obturator nerve palsy. Postoperative complications: deep vein thrombosis, pulmonary embolism, bladder infection and dysfunction, vaginal fistula, lymphoedema, pelvic abscess, lymphocysts, pelvic cellulitis, hyperaesthesia of the leg, small bowel obstruction. 87% (34/39) of women with cervical cancer were alive and disease free at follow-up.	Multiple indications.
Pellegrino A, Villa A, Fruscio R et al. (2008) Total laparoscopic radical hysterectomy and pelvic lymphadenectomy in early stage cervical cancer. Surgical Laparoscopy, Endoscopy & Percutaneous Techniques 18: 474–8.	Case series n = 57 Median follow-up = 13 months	Relapse = 7% (4/56) Intraoperative complication = 1 cystotomy Postoperative complications = 2 ureteral stenosis, 2 vaginal cuff diastasis	Larger case series with longer follow-up are included.
Persson J, Reynisson P, Borgfeldt C et al. (2009) Robot assisted laparoscopic radical hysterectomy and pelvic lymphadenectomy with short and long term morbidity data. Gynecologic Oncology 113: 185–90.	Case series n = 80 Follow-up = '≥ 12 months'	Dehiscence of the vaginal cuff = 6.2% (5/80) Trocar site hernia requiring reoperation = 2.5% (2/80) Ureter stricture = 1.2% (1/80) Death due to pulmonary embolism = 1.2% (1/80)	Larger case series with longer follow-up are included.
Pomel C, Atallah D, Le Bouedec G et al. (2003) Laparoscopic radical hysterectomy for invasive cervical cancer: 8-year experience of a pilot study. Gynecologic Oncology 91: 534–9.	Case series n = 50 Median follow-up = 44 months	Overall survival rate of FIGO stage IA2 and IB1 patients = 96% 1 bladder fistula, 1 ureteral stenosis	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 adeno-carcinoma, the other was for menorrhagia and cancer risk reduction)	Vaginal cuff dehiscence and small bowel evisceration.	Case report of complication already mentioned in table 2.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
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. n = 38 (20 LRH, 18 ARH) plus 35 healthy women as controls.	Laparoscopic approach was not associated with a reduction in the adverse impact on sexual function.	Larger studies are included.
Sobiczewski P, Bidzinski M, Derlatka P et al. (2009) Early cervical cancer managed by laparoscopy and conventional surgery: comparison of treatment results. International Journal of Gynecological Cancer 19: 1390–5.	Non-randomised comparative study n = 80 (22 LRH, 58 ARH) Median follow-up = 26 months (after LRH)	Recurrence rate: • LRH = 14% • ARH = 12% Predicted 3-year survival: • LRH = 82% • ARH = 86% In 2 patients, intraperitoneal spread occurred after laparoscopy.	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., which is 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)	A study from the same centre with longer follow-up is included (Chen et al, 2008).

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
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 Follow-up not described	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 case series with longer follow-up 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	No conversions to open surgery. LRH had statistically significant lower mean blood loss, shorter hospital stay but longer operating time than ARH.	Larger comparative studies with longer follow-up are included.

Appendix B: Related NICE guidance for laparoscopic radical hysterectomy for early stage cervical cancer

Guidance	Recommendations
Interventional procedures	***Original guidance:*** **Laparoscopic radical hysterectomy for early stage cervical cancer. NICE interventional procedures guidance 24 (2003)** 1.1 Current evidence on the safety and efficacy of laparoscopic radical hysterectomy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Clinicians wishing to undertake laparoscopic radical hysterectomy should inform the clinical governance leads in their Trusts. They should ensure that patients offered it understand the uncertainty about the procedure's safety and efficacy and should provide them with clear written information. Use of the Institute's *Information for the Public* is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and longer-term efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking any further investigation at present. 1.2 Clinicians undertaking this procedure should undergo training as recommended by the Royal College of Obstetricians and Gynaecologists Working Party on Training in Endoscopic Surgery (www.rcog.org.uk). **Laparoscopic techniques for hysterectomy. NICE interventional procedures guidance 239 (2007).** 1.1 Current evidence on the safety and efficacy of laparoscopic techniques for hysterectomy (including laparoscopically-assisted vaginal hysterectomy [LAVH], laparoscopic hysterectomy [LH], laparoscopic supracervical hysterectomy [LSH] and total laparoscopic hysterectomy [TLH]) appears adequate to support their use, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should advise women that there is a higher risk of urinary tract injury and of severe bleeding associated with these procedures, in comparison with open surgery. 1.3 Advanced laparoscopic skills are required for these procedures, and clinicians should undergo special training and mentorship. The Royal College of Obstetricians and Gynaecologists has developed an Advanced Training Skills Module, 'Benign Gynaecological Surgery: Laparoscopy' (www.rcog.org.uk/index.asp?PageID=1951). This would need to be supplemented by further training in order to achieve the skills required for total laparoscopic hysterectomy.

	High dose rate brachytherapy for carcinoma of the cervix. NICE interventional procedures guidance 160 (2006). 1.1 Current evidence on the safety and efficacy of high dose rate brachytherapy for carcinoma of the cervix appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should ensure that patients have appropriate counselling and pain management. In addition, use of the Institute's *Information for the public* is recommended (available from www.nice.org.uk/IPG160publicinfo).

Appendix C: Literature search for laparoscopic radical hysterectomy for early stage cervical cancer

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	02/09/2009	Issue 3, 2009
Database of Abstracts of Reviews of Effects – DARE (CRD website)	03/09/2009	-
HTA database (CRD website)	03/09/2009	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	02/09/2009/	Issue 3, 2009
MEDLINE (Ovid)	02/09/2009	1950 to August Week 3 2009
MEDLINE In-Process (Ovid)	02/09/2009	September 01, 2009
EMBASE (Ovid)	02/09/2009	1980 to 2009 Week 35
CINAHL (NLH Search 2.0/EBSCOhost)	02/09/2009	1981-Present
BLIC (Dialog DataStar)	03/09/2009	-

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/
2	Uterine Cervical Dysplasia/
3	Cervical Intraepithelial Neoplasia/
4	exp Uterine Cervical Diseases/
5	CIN.tw.
6	(Cervic* adj3 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or dysplasis* or disease*)).tw.
7	or/1-6
8	exp laparoscopy/
9	exp laparoscopes/
10	exp surgical procedures, Minimally Invasive/
11	laparoscop$.tw.
12	or/8-11
13	exp Hysterectomy/
14	(Hysterectom* or Hysterctom*).tw.
15	or/13-14
16	12 and 15
17	(lsh or lavh or larvh or tlh).tw.
18	16 or 17
19	18 and 7

20	limit 19 to yr="2001 - 2009
21	Animals/
22	Humans/
23	21 not (21 and 22)
24	20 not 23
25	from 24 keep 1-279
26	limit 25 to ed=20090115-20090930
27	from 26 keep 1-28