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Laparoscopically assisted radical vaginal hysterectomy versus radical abdominal hysterectomy for the treatment of early cervical cancer (Review)

Kucukmetin A, Biliatis I, Naik R, Bryant A

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[Intervention Review]

Laparoscopically assisted radical vaginal hysterectomy versus radical abdominal hysterectomy for the treatment of early cervical cancer

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ABSTRACT

Background

Cervical cancer is the second most common cancer among women and is the most frequent cause of death from gynaecological cancers worldwide. Standard surgical management for selected early-stage cervical cancer is radical hysterectomy. Traditionally, radical hysterectomy has been carried out via the abdominal route and this remains the gold standard surgical management of early cervical cancer. In recent years, advances in minimal access surgery have made it possible to perform radical hysterectomy with the use of laparoscopy with the aim of reducing the surgical morbidity and promoting a faster recovery.

Objectives

To compare the effectiveness and safety of laparoscopically assisted radical vaginal hysterectomy (LARVH) and radical abdominal hysterectomy (RAH) in women with early-stage (1 to 2A) cervical cancer.

Search methods

We searched the Cochrane Gynaecological Cancer Group Trials Register, and Cochrane Register of Controlled Trials (CENTRAL) Issue 7, 2013, MEDLINE, and EMBASE up to July 2013. We also searched registers of clinical trials, abstracts of scientific meetings, reference lists of included studies and contacted experts in the field.

Selection criteria

Randomised controlled trials (RCTs) that compared laparoscopically assisted radical hysterectomy and radical abdominal hysterectomy, in adult women diagnosed with early (stage 1 to 2A) cervical cancer.

Data collection and analysis

Two review authors independently abstracted data and assessed risk of bias.

Main results

We found one RCT, which included 13 women, that met our inclusion criteria and this trial reported data on LARVH versus RAH.

Women who underwent LARVH for treatment of early-stage cervical cancer appeared to have less blood loss compared with those who underwent RAH. The trial reported a borderline significant difference between the two types of surgery (median blood loss 400 mL (interquartile range (IQR): 325 to 1050) and 1000 mL (IQR: 800 to 1025) for LARVH and RAH, respectively, P value = 0.05). RAH was associated

with significantly shorter operation time compared with LARVH (median: 180 minutes with LARVH versus 138 minutes with RAH, P value = 0.05).

There was no statistically significant difference in the risk of perioperative complications in women who underwent LARVH and RAH. The trial reported two (29%) and four (57%) cases of intraoperative and postoperative complications, respectively, in the LARVH group and no (0%) reported cases of intraoperative complications and five (83%) cases of postoperative complications in the RAH group. There were no reported cases of severe perioperative complications.

Bladder and bowel dysfunction of either a transient or chronic nature remain major morbidities after radical hysterectomy, and the one included study showed that there may be significantly less after LARVH.

Authors' conclusions

The included trial lacked statistical power due to the small number of women in each group and the low number of observed events. Therefore, the absence of reliable evidence, regarding the effectiveness and safety of the two surgical techniques for the management of early-stage cervical cancer, precludes any definitive guidance or recommendations for clinical practice. The trial did not report data on long-term outcomes, but was at moderate risk of bias due to very low numbers of included women.

PLAIN LANGUAGE SUMMARY

Key hole-assisted vaginal extended (radical) hysterectomy versus open radical hysterectomy for the treatment of early cervical cancer

Background

Cervical cancer is the second most common cancer among women. A woman's risk of developing cervical cancer by 65 years of age ranges from 0.69% in developed countries to 1.38% in developing countries. In Europe, about 60% of women with cervical cancer are alive five years after diagnosis. Standard treatment for selected early cervical cancer is radical hysterectomy, involving removal of the cervix, uterus (womb) and supporting tissues (parametrium), together with the pelvic lymph glands (nodes) and a top part of the vagina (cuff). Traditionally, radical hysterectomy has been performed as open surgery for more than a century. In recent years this operation has also been performed laparoscopically (key hole surgery) to reduce the size of the abdominal incision.

Study characteristics

We carried out a systematic review and searched for published and unpublished randomised controlled trials (RCTs) that compared open and laparoscopically assisted vaginal methods of performing radical hysterectomy in women with early cervical cancer. The evidence is current to July 2013.

We found only one relevant trial. It included only 13 women; seven had a laparoscopically assisted radical vaginal hysterectomy (LARVH) and six had radical abdominal hysterectomy (RAH).

Key results

Women who underwent LARVH appeared to have less blood loss, shorter hospital stay and less requirement for pain medication compared with those who underwent RAH. There was no statistically significant difference in the risk of complications related to the operation in women who underwent LARVH and RAH. However, RAH had a significantly shorter operation time compared with LARVH.

The trial did not assess overall survival and progression-free survival (PFS; the time that a woman lives with the cancer but does not get worse) or quality of life (QoL) as the main focus of the trial was to examine short-term complications.

Quality of the evidence

Due to the small number of cases and the short-term scope of the trial, we were unable to reach any definite conclusions about the relative benefits and harms of the two forms of treatment and we were unable to identify subgroups of women who are likely to benefit from one treatment or the other.

BACKGROUND

Description of the condition

Cervical cancer is the second most common cancer among women up to 65 years of age and is the most frequent cause of death from gynaecological cancers worldwide. A woman's risk of developing cervical cancer by 65 years of age ranges from 0.69% in developed countries to 1.38% in developing countries (GLOBOCAN 2008). In Europe, about 60% of women with cervical cancer are alive five years after diagnosis (EUROCARE 2003).

Early-stage cervical cancer includes a broad range of disease, from clinically undetectable or microinvasive tumours to large bulky lesions replacing the entire cervix. The International Federation of Gynaecology and Obstetrics (FIGO) system divides Stage 1 tumours into four categories: 1A1 (microinvasive tumour, less than 3 mm depth), 1A2 (microinvasive tumour, less than 5 mm depth and no wider than 7 mm), 1B1 (clinical lesions no greater than 4 cm or preclinical lesions greater than Stage 1A) and 1B2 (clinical lesions greater than 4 cm) (Pecorelli 2009).

Description of the intervention

Women with Stage 1A tumours may be treated with a loop cone or simple hysterectomy (although some centres will perform radical surgery on Stage 1A2 disease), while women with Stage 1B disease traditionally require a so-called radical abdominal hysterectomy (RAH) and pelvic lymph node dissection due to the increased risk of extension beyond the primary lesion, which is greater than 5%.

RAH involves removal of the cervix, uterus (womb) and supporting tissues (parametrium), together with the pelvic lymph nodes and a cuff of vagina. The ovaries may also be removed depending on the age and wishes of the woman. The operation is traditionally performed via an open or abdominal approach, utilising either a midline subumbilical or a transverse suprapubic incision. It is a highly successful operation in terms of oncological outcome, resulting in cure rates in excess of 90% for node negative disease (Comerci 1998). However, it carries significant morbidity, particularly in terms of large volume blood loss, bladder and bowel dysfunction because the surgery is in close proximity to the major organs and vessels within the pelvis (Di Saia 2002). Around 20% of women will experience long-term postoperative pelvic floor symptoms that interfere with their lives (Bergmark 2002), and, as the disease affects mainly younger women, potential solutions for reducing these side effects and improving quality of life (QoL) are of particular importance.

Minimal access surgery (keyhole surgery) has largely replaced the open approach for many common surgical procedures, such as removal of the appendix and gall bladder. The consequent reduction in trauma to the abdominal wall and pelvic organs confers a number of potential advantages, including a shorter hospital stay, faster recovery time and more rapid return to normal function (Cuschieri 1999). Thus, it is an attractive prospect for surgeons seeking to reduce the morbidity of open RAH. As the trend towards minimal access surgery increases, it is essential that these techniques be evaluated further in order to confirm that the new technique reduces risks without jeopardising the likelihood of cure. A systematic review examining all the relevant outcomes is needed in order to enable women to make informed choices about their preferred route of surgery.

The main area of concern with laparoscopically assisted radical vaginal hysterectomy (LARVH) is the suggestion that the radicality of the vaginal part of the procedure (i.e. the extent of the dissection and amount of tissue removed) is, at best, variable, and probably reduced, even in the hands of an experienced surgeon (Hagen 2000), although there are few objective data to support this. As a consequence, there are concerns that survival may be compromised. In addition, there is little doubt that technical factors, such as nulliparity, poor vaginal access and the bony structure of the pelvis, may contribute to problems with the vaginal access (Eltabbakh 2000), and specific complications, such as lower urinary tract injury, may ensue. Injury to the bowel or great vessels while siting the surgical instruments is also a risk and conversion from the laparoscopic to an open approach may be required due to such difficulties during the operation.

Laparoscopic hysterectomy is performed using a viewing instrument (laparoscope) and other surgical instruments inserted through a number of small abdominal incisions. Once the cervix, uterus and surrounding tissues are detached, they are removed from the body through the vagina. There are three laparoscopic procedures comparable to open RAH (Canis 1992; Childers 1995; Spirtos 1996). Laparoscopic vaginal radical hysterectomy was the first technique to be reported (Dargent 1987). With this technique, the pelvic node dissection is performed laparoscopically followed by the radical dissection and excision of the uterus, which is performed through a small vaginal incision, rather than an abdominal incision.

The second technique, combined or LARVH (Dargent 2003), and its adaptations (Kadar 1993; Querleu 1993), involves dissecting the tissues through a combination of laparoscopic and vaginal surgery, followed by a laparoscopic node dissection. The third technique, total laparoscopic radical hysterectomy (TLRH), involves a total laparoscopic procedure whereby all the surgery is performed laparoscopically before the tissues are removed through the vagina (Canis 1992; Spirtos 1996).

Why it is important to do this review

Studies comparing laparoscopic versus open surgery for early-stage cervical cancer are only available after 1991, when the technique was first applied in its current form. We considered that it was important to conduct this review as, to our knowledge, there have been no systematic reviews comparing the two surgical techniques. It is also important to review the current evidence to be able to make recommendations for the design of future randomised trials in this subject.

OBJECTIVES

To compare the effectiveness and safety of laparoscopically assisted radical vaginal hysterectomy (LARVH) and radical abdominal hysterectomy (RAH) in women with early-stage (1 to 2A) cervical cancer.

METHODS

Criteria for considering studies for this review

Types of studies

- Randomised controlled trials (RCTs).

Types of participants

Adult women requiring radical surgery for histologically confirmed early-stage (stage 1 to 2A) cervical cancer.

Types of interventions

Interventions:

- Laparoscopically assisted radical vaginal hysterectomy (LARVH).
- Radical abdominal hysterectomy (RAH).

Types of outcome measures

We considered the following outcome measures.

Primary outcomes

- Overall survival (OS): survival until death from all causes.
- Progression- or disease-free survival (PFS or DFS).

Secondary outcomes

- Blood loss.
- Hospital stay.
- QoL, measured using a scale that has been validated through reporting of norms in a peer-reviewed publication.
- Adverse events classified according to Common Terminology Criteria for Adverse Events (CTCAE 2006):
  - direct surgical morbidity (e.g. death within 30 days; vascular injury; injury to bladder, ureter, small bowel or colon; presence and complications of adhesions; febrile morbidity; intestinal obstruction; anastomotic leak; haematoma; collection, local infection);
  - surgically related systemic morbidity (e.g. chest/wound/urine infection, thromboembolic events (deep vein thrombosis and pulmonary embolism), cardiac events (cardiac ischaemia, myocardial infarction and cardiac failure), cerebrovascular accident, transfusion reaction, pulmonary oedema);
  - recovery: delayed discharge, unscheduled re-admission;
  - longer-term problems, such as bladder dysfunction and lymphoedema;
  - other adverse event not categorised above.

Search methods for identification of studies

We sought papers in all languages and carried out translations when necessary.

Electronic searches

See: Cochrane Gynaecological Cancer Group methods used in reviews (www.cochrane-gyncan.org/).

We searched the following electronic databases:

- the Cochrane Gynaecological Cancer Collaborative Review Group's Trial Register to July 2013;
- Cochrane Central Register of Controlled Trials (CENTRAL), Issue 7, 2013;
- MEDLINE to July 2013;
- EMBASE to July 2013.

The CENTRAL, MEDLINE, EMBASE and search strategies based on terms related to the review topic are presented in Appendix 1, Appendix 2 and Appendix 3, respectively.

We searched databases from January 1991 to July 2013.

We identified all relevant articles found on PubMed and using the 'related articles' feature, and carried out a further search for newly published articles.

Searching other resources

Unpublished and grey literature

We searched *meta*Register, Physicians Data Query, www.controlled-trials.com/rct, www.clinicaltrials.gov and www.cancer.gov/clinicaltrials for ongoing trials. We contacted the main investigators of any relevant ongoing trials for further information and any major co-operative trials groups active in this area.

Handsearching

We handsearched reports of conferences in the following sources:

- British Journal of Cancer;
- British Cancer Research Meeting;
- Annual Meeting of the International Gynecologic Cancer Society;
- Annual Meeting of the British Gynaecological Cancer Society (BGCS);
- Annual Meeting of the American Society of Gynecologic Oncologist (SGO);
- Annual Meeting of European Society of Medical Oncology (ESMO);
- Annual Meeting of the American Society of Clinical Oncology (ASCO).

Reference lists and correspondence

We checked the citation lists of included studies and contacted experts in the field to identify further reports of trials.

Data collection and analysis

Selection of studies

We downloaded all titles and abstracts retrieved by electronic searching to the reference management database Endnote, removed duplicates and two review authors (AB, AK) independently examined the remaining references. We excluded those studies that clearly did not meet the inclusion criteria and obtained copies of the full text of potentially relevant references. Two review authors (AB, AK) independently assessed the eligibility of retrieved papers. The two review authors resolved any disagreements by discussion. We documented reasons for exclusion.

Data extraction and management

For included studies, we abstracted data as follows:

- author, year of publication and journal citation (including language);
- country;
- setting;
- inclusion and exclusion criteria;

- study design, methodology;
- study population; the following were abstracted by treatment arm when possible:
  - total number enrolled;
  - patient characteristics;
  - age;
  - ethnicity;
  - co-morbidities;
- cervical cancer details at diagnosis:
  - FIGO stage;
  - histological cell type;
  - differentiation;
  - performance status;
- surgical details:
  - type of surgeon (gynae-oncologist, gynaecologist, general surgeon);
  - type of surgery (LARVH versus RAH);
  - duration of operation;
- risk of bias in study (see below);
- duration of follow-up;
- outcomes (see above) - OS, PFS or DFS, QoL, operative time, blood loss, conversion rate and adverse events:
  - for each outcome: outcome definition (with diagnostic criteria if relevant);
  - unit of measurement (if relevant);
  - for scales: upper and lower limits, and whether high or low score is good;
  - results: number of participants allocated to each intervention group;
  - for each outcome of interest: sample size; missing participants.

We extracted data on outcomes as below:

- for dichotomous outcomes (e.g. adverse events), we extracted the number of women in each treatment arm who experienced the outcome of interest and the number of women assessed at endpoint, in order to estimate a risk ratio (RR).

Where possible, all data extracted were those relevant to an intention-to-treat analysis, in which participants were analysed in groups to which they were assigned.

We noted the time points at which outcomes were collected and reported.

Two review authors (AK, AB) independently abstracted data onto a data abstraction form specially designed for the review. We resolved any disagreements by discussion.

Assessment of risk of bias in included studies

We used The Cochrane Collaboration's 'risk of bias' tool to assess included RCTs and the criteria specified in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). This included assessment of:

- selection bias:
  - random sequence generation;
  - allocation concealment;
- performance bias:
  - blinding of participants and personnel (participants and treatment providers): assessment of blinding was restricted to blinding of outcome assessors, since it is generally not possible to blind participants and treatment providers to surgical interventions;
- detection bias:
  - blinding of outcome assessment;
- attrition bias:
  - incomplete outcome data: we recorded the proportion of participants whose outcomes were not reported at the end of the study; we coded a satisfactory level of loss to follow-up for each outcome as:
    - low risk of bias, if fewer than 20% of participants were lost to follow-up and reasons for loss to follow-up were similar in both treatment arms;
    - high risk of bias, if more than 20% of participants were lost to follow-up or reasons for loss to follow-up differed between treatment arms;
    - unclear risk of bias if loss to follow-up was not reported;
- reporting bias:
  - selective reporting of outcomes;
- other possible sources of bias.

Two review authors (AB, AK) independently applied the 'Risk of bias' tool and resolved differences by discussion. Results are presented in a 'Risk of bias' summary plot.

Measures of treatment effect

We used the following measures of the effect of treatment:

- for dichotomous outcomes, we used the RR.

Dealing with missing data

We did not impute missing outcome data for any outcomes.

Data synthesis

We only identified one trial so it was not possible to perform meta-analyses. Therefore, it was not relevant to assess heterogeneity between results of trials and we were unable to assess reporting biases using funnel plots or conduct any subgroup analyses or sensitivity analyses.

RESULTS

Description of studies

Results of the search

The search strategy identified 88 unique references, 87 of which obviously did not meet our inclusion criteria and were excluded. We retrieved only one article in full and this reported on one relevant completed RCT that met our inclusion criteria (see the Characteristics of included studies table).

Searches of the grey literature did not identify any additional trials.

Included studies

We included one single-centre trial, which recruited women with early-stage 1B cervical cancer requiring radical surgical treatment

over a 20-month period (Naik 2010). The trial randomised 15 women, of whom 13 were assessed at the end of the trial.

The objective of the trial was to compare short-term surgical data, such as blood loss and perioperative complications, in women with early-stage 1B cervical cancer randomised to either LARVH or RAH. All women had histologically confirmed carcinoma of the cervix, FIGO Stage 1B1, less than 2 cm in size, requiring radical hysterectomy and potentially suitable for surgery via a laparoscopic vaginal route. Unusual high-risk histological subtypes (e.g. glassy cell, clear cell, etc. were excluded), pregnant women and those with concomitant or previous malignancy likely to interfere with treatment or comparison were excluded. Adenocarcinoma and adenosquamous histology were included. Participants completed a visual analogue scale to measure their level of pain and were evaluated at two to four weeks to assess scarring, wound healing and adverse effects. Participants returned every three months for one year for pelvic examination and cytology to assess recurrence, but recurrence was not one of the study outcomes. Follow-up colposcopy and biopsy were used at the discretion of the treating physician.

At enrolment, age, body mass index (BMI), parity, smoking status, whether diagnostic large loop excision of the transformation zone (LLETZ) was performed, histology, whether there was lympho-vascular space involvement, lateral tumour size and depth of invasion were recorded. Eight of the 15 women were randomised to LARVH and seven women to RAH. Median age for the LARVH group was 38.5 years (interquartile range (IQR): 33.5 to 53.5) and 37 years for the RAH group (IQR: 29.5 to 46). Mean BMI was 24.8 (standard deviation (SD) 1.3) and 25 (SD 1.8) in the LARVH and RAH groups, respectively. Median parity was two in both groups (IQR: 1 to 3 and 1 to 2 in the LARVH and RAH groups, respectively). Twelve (92%) women had diagnostic LLETZ and two (15%) had lympho-vascular space involvement. There were more non-smokers than smokers in the trial (8 (62%) smokers versus 5 (38%) non-smokers) and the tumour histological type was adenocarcinoma in two (15%) women and squamous cell carcinoma in 11 (85%) women. The mean lateral tumour size in the LARVH group was 1.2 cm (SD 0.3 cm) and 1.4 cm in the RAH group (SD 0.2 cm). The mean depth of invasion was 5.6 mm (SD 1.2 mm) and 5.8 mm (SD 1.1 mm) in the LARVH and RAH groups, respectively. There was no statistically significant difference between the two groups with respect to any of the reported baseline characteristics.

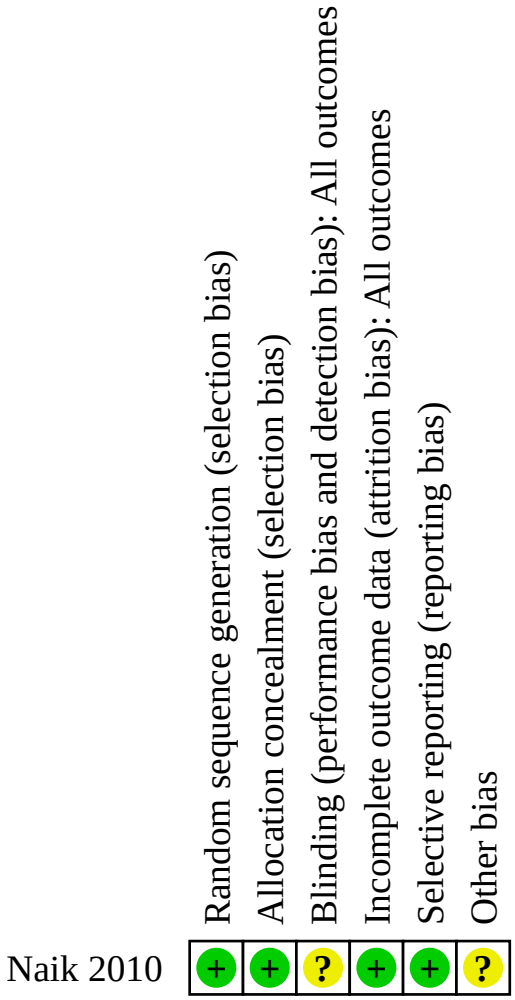
All women received intraoperative broad-spectrum antibiotics for the duration of their surgery. Deep vein thrombosis prophylaxis was via perioperative subcutaneous low-molecular-weight heparin and intraoperative pneumatic calf compression devices. All women received morphine (1 mg/mL) via a patient-controlled analgesia system for the first 24 hours postoperatively and oral analgesia thereafter.

The outcomes reported were: need for urinary catheterisation (continuous or intermittent) in days; operating time in minutes (measured from the time of skin incision to the closure of the skin or vagina); estimated blood loss (measured as the sum of suctioned fluids and weighed sponges and drapes at completion of surgery); duration of hospital stay; opiate pain relief requirements in first 36 hours after surgery; intraoperative complications (defined as cardiopulmonary events, cystotomy, enterotomy, ureteric injury and injury of a great vessel or nerve); nodal yield; resection size and postoperative complications (defined as cardiac events (cardiac failure, cardiac arrest), deep vein thrombosis, pulmonary embolism, haematoma (radiologically confirmed), urinary tract infection, chest infection and wound infection (microbiologically confirmed)). Additional bladder and bowel function outcomes were also assessed. These were not discussed in the paper but were obtained by correspondence from the trialists. All women completed a Bowel and Urinary Symptoms Questionnaire (BBUSQ-22) two weeks post operatively. The questionnaire comprised of a self completed 22-item inventory, separating into four domains covering constipation, evacuation, incontinence and urinary symptoms. Each domain was scored separately according to a scoring algorithm but did not assess QoL. All participants completed the BBUSQ-22 questionnaire, including the one RAH participant who declined postoperative urodynamic tests. The 'Urinary symptoms' domain is scored out of 100 and scores of greater than 20% are considered clinically abnormal by the questionnaire's authors.

Risk of bias in included studies

The one included trial was at moderate risk of bias as it satisfied four criteria used to assess risk of bias (see Figure 1) (Naik 2010).

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



The trial reported the method of generation of the sequence of random numbers used to allocate women to treatment arms and made an effort to conceal this allocation sequence from participants and healthcare professionals involved in the trial. However, it was not reported whether the outcome assessors were blinded to all outcomes but they were blinded to the randomisation allocation of the participants who completed the BBUSQ-22. Loss to follow-up was deemed satisfactory, as 87% of women randomised were analysed at endpoint. It seemed unlikely that outcomes had been selectively reported as we obtained results from additional outcomes from correspondence with the trialists (some longer-term outcomes were being prepared to be reported in a second paper, which may be published in the future), but it was unclear if any other bias may have been present. If the surgeons were the ones making the assessment, they were unblinded (clearly) and there may be moderate to high risk of bias, since it would be the surgeons who decided when women were fit for discharge, when a trial without catheter (TWOC) could be performed, etc.

Effects of interventions

We found only one trial that assessed 13 women that met our inclusion criteria and reported data on LARVH versus RAH (Naik 2010). For dichotomous outcomes, we were unable to estimate finite confidence intervals (CI) for the RR for the perioperative complications outcome, as women in the RAH group did not experience any events. For continuous outcomes, we were unable to use the mean difference method as the median and IQR were reported, rather than the mean and SD.

Blood loss

Women who underwent LARVH for treatment of early-stage cervical cancer appeared to have less blood loss compared with those

who underwent RAH. The trial reported a borderline significant difference between the two types of surgery (median 400 mL (IQR: 325 to 1050) and 1000 mL (IQR: 800 to 1025) for LARVH and RAH, respectively, P value = 0.05).

Hospital stay

Women who underwent LARVH for treatment of early-stage cervical cancer had a significantly shorter hospital stay compared to those who underwent RAH (median 5 days (range: 4 to 7) and 7 days (range: 6 to 7) for LARVH and RAH, respectively, P value = 0.04).

Intraoperative complications

There was no statistically significant difference in the risk of perioperative complications in women who underwent LARVH or RAH. The trial reported two (29%) cases (enterotomy, cystotomy) of intraoperative complications in the LARVH group and no (0%) cases in the RAH group. Neither woman suffered any long-term sequelae.

Postoperative complications

There was no significant difference in the risk of postoperative complications between women who underwent LARVH or RAH (RR 0.08, 95% CI 0.01 to 1.19). The trial reported two (29%) cases (wound infection, transient leg paraesthesia) of postoperative complications in the LARVH group and five (83%) cases (three urinary tract infection, wound infection, re-admission within 60 days) in the RAH group. No severe postoperative complications were reported.

Bladder function

One woman in the LARVH group experienced an intraoperative bladder injury, but this was repaired vaginally and there were no long-term sequelae. No other lower urinary tract injuries were noted in either group at the time of surgery and no fistulae were reported during follow-up.

Baseline scores for both groups were similar. However, at two weeks post surgery there was a significant difference between the groups (median domain score 14% for LARVH versus 24% for RAH, P value = 0.03). There were no statistically significant differences between the two study arms at six weeks or four months, although the authors reported that the scores in the RAH group may be considered as clinically abnormal at six weeks.

Bowel function

There were no statistically significant differences for mean resting anal pressure, cough pressure, squeeze pressure or rectal sensation between the two groups as measured by ano-manometry.

The BBUSQ-22 questionnaire identified statistically significant differences in participant-rated bowel function at two weeks (median score 8% for LARVH versus 29% for RAH, P value = 0.04) in the evacuatory domain and at the four-month assessment (median score 53% for LARVH versus 72% for RAH, P value = 0.05) in the constipation domain. There were no statistically significant differences in the faecal incontinence domain at any time point. There was no significant difference between preoperative and postoperative median scores in the evacuatory and constipation domains within the LARVH group. However, scores in the RAH group increased significantly after surgery in the RAH group (P value < 0.05).

Two women in the LARVH group required laxatives at two and six weeks after surgery versus six women in the RAH group. No women in the LARVH required laxatives at four months versus four women in the RAH group. One woman in the RAH group had been admitted to hospital with severe constipation during this time period. Senna and lactulose were the common laxatives used.

Operative time

The median operating time was significantly longer for women undergoing LARVH compared with RAH (180 minutes versus 138 minutes, P value = 0.05).

DISCUSSION

Summary of main results

We found only one RCT, which included only 13 women, that met our inclusion criteria and this trial reported data on LARVH versus RAH. However, our primary outcomes were not reported and most of the secondary outcomes were incompletely documented because the trial focused on short-term outcomes or longer-term outcomes, such as bladder and bowel function, with relatively short follow-up.

There was no statistically significant difference in the risk of intra- and postoperative complications between women who received LARVH and those who received RAH, although women appeared to have lost more blood if they underwent RAH (median 400 mL (IQR 325 to 1050) and 1000 mL (IQR 800 to 1025) for LARVH and RAH, respectively (P value = 0.05). There is no evidence as to whether LARVH or RAH is the more effective and safe surgical method for the treatment of early-stage cervical cancer.

We did not expect to identify a large number of RCTs, but the review was restricted to high-quality evidence as various retrospective case series are of inadequate quality and in many instances do not allow for comparison. The main limitation of this review was the fact that the one included trial had a different scope our outcomes and chose to focus on short-term outcomes. We could not examine the effectiveness of the surgical techniques in terms of OS and PFS and many of the important secondary outcomes that we specified in the review. For dichotomous adverse event outcomes such as perioperative complications, the trial lacked the statistical power to detect any difference in risk that might have been present, due to sparse data.

Overall completeness and applicability of evidence

Overall, the quality of the evidence was low (GRADE Working Group), as it only included a small number of women with early-stage cervical cancer (n = 13), primary survival outcomes were not reported and secondary outcomes were incompletely reported. We did not identify any prospective randomised trials with long-term follow-up that compared LARVH and RAH so no definitive conclusions can be drawn with respect to an optimal surgical technique for the surgical management of early-stage cervical cancer in women needing radical hysterectomy. However, the trial suggests short-term surgical benefits of LARVH, although the size of data is inadequate to support this. In addition, LARVH may be a less radical procedure than RAH, supporting the need for strict participant selection and to restrict the procedure to small tumours.

The single identified RCT does not address OS or PFS, QoL or examine longer-term adverse events. The absence of such outcome data do not allow for any firm conclusions to be made.

Quality of the evidence

The one trial that met the inclusion criteria included a small number of women (n = 13), was at moderate risk of bias, and pertinent long-term outcomes were not reported. All participants received the treatment to which they were allocated with no blinding, and a low level of loss to follow-up was reported. The only obvious risk of bias was from the uncertainty as to whether any additional risk of bias may have been present. The trial was not adequately powered to detect differences in dichotomous adverse events. Therefore, from the included RCT, we cannot reach any definitive conclusions about the benefit or harms of either type of surgery.

No woman experienced a severe perioperative complication, but other important outcomes were incompletely reported and the trial focused on short-term outcomes, so there is a great need for data on long-term outcomes, such as OS and QoL, to ensure higher-quality evidence.

Potential biases in the review process

We performed a comprehensive search, including a thorough search of the grey literature, and two review authors independently sifted all references and extracted data. We restricted the included studies to RCTs as they provide the strongest level of evidence available. Hence, we have attempted to reduce bias in the review process.

The greatest threat to the validity of the review is likely to be the possibility of publication bias (i.e. studies that found the treatment to have been ineffective may not have been published). We were unable to assess this possibility as the analyses were restricted to the results of a single trial.

Unfortunately, we were unable to find any trials that reported data on long-term outcomes, but have adequately documented the limitations of reporting only incomplete short-term outcomes or outcomes such as bladder and bowel dysfunction with relatively short follow-up.

One of the review authors was also the first author on the included study and this is a potential source of bias.

Agreements and disagreements with other studies or reviews

Although we included only one RCT in our systematic review, other comparative retrospective studies have suggested LARVH as an alternative surgical option to RAH in selected cases with small tumour size (Jackson 2004; Malur 2001; Pahisa 2010; Sharma 2006).

The matched controlled single-centre study compared LARVH and RAH for cervical cancer (Jackson 2004). Women undergoing LARVH between 1996 and 2003 were identified and matched for age, FIGO stage, histological subtype and nodal metastases using a control group of women who underwent RAH during the same time period. Fifty-seven women were listed for LARVH and 50 cases were matched successfully using the criteria above. The majority of cases were FIGO stage 1B1. The study found no significant difference between recurrence rates or OS in the two arms after a median follow-up of 52 months for LARVH and 49 months for RAH (94% for LARVH versus 96% for RAH). The duration of surgery was significantly greater for the LARVH procedure than the RAH procedure (median 180 minutes versus 120 minutes). Similarly blood loss (median 350 mL versus 875 mL), hospital stay (median five days versus eight days) and duration of continuous bladder catheterisation (median three days versus seven days) were significantly less for LARVH compared with RAH. There were no statistically significant differences with regards to nodal yield, completeness of surgical margins or perioperative complication rate. There were few major complications in the study and there was no statistically significant difference between the two arms (four (8%) in the LARVH group and three (6%) in the RAH group). Postoperative bladder dysfunction and constipation requiring regular laxatives was less common in the LARVH group compared with the RAH group, but these differences approached borderline significance (3 women versus 12 women had seen a specialist regarding postoperative bladder dysfunction (P value = 0.04) and no women versus six women reported constipation requiring regular laxatives (P value = 0.03) in the LARVH and RAH groups, respectively). This rate appears low for LARVH suggesting QoL may be improved without compromising survival.

Similarly, the Sharma 2006 single-centre study compared the safety, efficacy and short-term benefits of LARVH (the Coelio-Schauta procedure) with RAH. After excluding ineligible women, 27 women with stage 1B disease who had LARVH and 28 women with stage 1B disease who had RAH were included. The cohorts were similar in age, bodyweight, previous abdominal surgery, histological subtype, FIGO stage, resection margins, node count and node status, length of follow-up and recurrence. There were statistically significant differences between LARVH and RAH for duration of surgery (mean 160 minutes versus 132 minutes), intraoperative blood loss (479 mL versus 715 mL), hospital stay (mean 5 days versus 9.3 days), postoperative complications (6 women versus 20 women) and duration of bladder catheterisation (mean 4.4 days versus 8.8 days). Four women in the LARVH group and no women in the RAH group had urinary tract injury that was repaired. None had long-term sequelae. The data suggested that LARVH is a suitable alternative to RAH for small-volume stage 1B1 cervical cancer with similar clinical efficacy and a superior postoperative recovery and postoperative morbidity profile.

The Pahisa 2010 study suggested similar intraoperative complication rates with marginally less blood loss and transfusion rates in 67 LARVH cases with similar long-term bladder and bowel functions. Recurrence rates and mortality were similar in both groups. Malur 2001 compared short-term outcome in 70 cases of LARVH with 70 cases of RAH. The control group was not matched with the study group. This study also showed less blood loss and transfusion rates with shorter hospital stay in the LARVH group. However, intraoperative complication rates were significantly higher in the LARVH group.

Hertel 2003 analysed 200 LARVH cases and compared the survival rates in different risk groups. Overall, five-year survival was 83%. In the absence of risk factors such as tumour size less than 4 cm, no lympho-vascular space involvement and negative lymph nodes, five-year survival was 98%. Unfortunately, this study did not compare the survival rates with RAH.

More recently, TLRH and robotic-assisted TLRH have been more commonly used surgical methods than LARVH as the radicality of surgery may be more similar to RAH than LARVH. LARVH has been mostly indicated for tumours smaller than 2 cm (Naik 2010). As reviewed by Roy 2011, there are no published studies to date comparing LARVH versus TLRH or robotic-assisted TLRH. To design a trial to compare the two procedures seems to be an unrealistic target now since the popularities of TLRH and robotic-assisted TLRH have been consistently increasing. Robot is an advanced laparoscopic tool and the perioperative and short-term survival outcomes of women treated with robotic-assisted TLRH have been promising (Cantrell 2010; Geisler 2010). The advantages of the robotic surgery include shorter learning curves, three-dimensional magnification, tremor reduction and motion downscaling with improved ergonomics (Yim 2011). An international multicentre RCT, Laparoscopic Approach to Cervical Cancer (LACC), has been recruiting participants since 2008 to compare RAH with TLRH or robotic-assisted TLRH. This trial is estimated to be completed in July 2017 (Obermair 2008).

AUTHORS' CONCLUSIONS

Implications for practice

We found only low-quality evidence comparing laparoscopically assisted radical hysterectomy (LARVH) and radical abdominal hysterectomy (RAH) for the treatment of early-stage cervical cancer. The included trial lacked statistical power due to the small number of women in each group and the low number of observed events. The trial objectives focused on short-term outcomes and, therefore, did not report overall and progression-free survival or pertinent long-term adverse events or quality of life (QoL) measures. Therefore, the absence of reliable evidence regarding the effectiveness and safety of the two surgical techniques precludes any definitive conclusions to be made. However, the trial suggests possible short-term surgical benefits of LARVH. LARVH has been shown to be a less radical procedure in the one included trial and a number of retrospective studies, supporting the need for strict participant selection and to restrict the procedure to small tumours.

Implications for research

A sufficiently powered randomised controlled trial (RCT) comparing LARVH and RAH for the treatment of early-stage cervical cancer that examines long-term outcomes is required. Non-randomised studies assessing the relative benefits and potential harms of the two forms of surgery have been conducted and further studies would offer relatively little benefit due to the obvious problems regarding selection biases. Even studies that use multivariable analysis to adjust for differences in prognostic factors between the treatment groups are potentially liable to problems of bias. An RCT in this area has been performed on short-term outcomes, so this needs to be extended to important longer-term outcomes such as overall and progression-free survival and QoL and needs to recruit an adequate number of women in multicentre trials. These trials should also consider the inclusion of total laparoscopic radical hysterectomy (TLRH) (NICE 2010) and robotic-assisted TLRH arms.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Naik 2010

Study characteristics	
Methods	Comparative phase II randomised controlled trial
Participants	15 women with histologically confirmed early-stage 1B cervical cancer requiring radical surgical treatment

Naik 2010 *(Continued)*

	8 of the 15 women with early-stage cervical cancer were randomised to LARVH and 7 women to RAH Median age for LARVH group was 38.5 years (IQR: 33.5 to 53.5) and 37 years for the RAH group (IQR: 29.5 to 46) Mean BMI in the LARVH group was 24.8 (SD 1.3) and 25 in the RAH group (SD 1.8) Median parity in the LARVH group was 2 (IQR: 1 to 3) and 2 in the RAH group (IQR: 1 to 2) 12 (92%) women had diagnostic LLETZ 2 (15%) women had lympho-vascular space involvement Smoking status was 5 (38%) women were smokers and 8 (62%) women were non-smokers The tumour histological type was adenocarcinoma in 2 (15%) women and squamous cell carcinoma in 11 (85%) women The mean lateral tumour size was 1.2 cm (SD 0.3 cm) in the LARVH group and 1.4 cm (SD 0.2 cm) in the RAH group The mean depth of invasion was 5.6 mm (SD 1.2 mm) in the LARVH group and 5.8 mm (SD 1.1 mm) in the RAH group There was no statistically significant difference between the 2 groups with respect to any of the reported baseline characteristics
Interventions	**Intervention:** **LARVH:** LARVH is performed using a viewing instrument (laparoscope) and other surgical instruments inserted through a number of small abdominal incisions. Laparoscopic lymph node dissection is followed by dissection of the uterus and surrounding tissues. Rest of the operation is carried out vaginally and the specimens are removed from the body through the vagina (Dargent 2000) **Comparison:** **RAH:** RAH involves removal of the cervix, uterus (womb) and supporting tissues (parametrium), together with the pelvic lymph nodes and a cuff of vagina. The operation is performed via an open or abdominal approach, utilising either a midline subumbilical or a transverse suprapubic incision (Lopes 1995) All women received intraoperative broad-spectrum antibiotics for the duration of their surgery. Deep vein thrombosis prophylaxis was via perioperative subcutaneous low-molecular-weight heparin and intraoperative pneumatic calf compression garments. All women received morphine (1 mg/mL) via a patient-controlled analgesia system for the first 24 hours postoperatively and oral analgesia thereafter
Outcomes	• Requirement in days for bladder catheterisation after surgery • Operating time • Blood loss • Hospital stay • Opiate pain relief • Complication rate • Time to normal activities • Resection size of major ligaments and vaginal cuff
Notes	15 women were recruited to the study over a 20-month period. The trial was stopped at the end of the funding period because extension would not increase the precision of the estimated differences There were 2 exclusions after randomisation. 1 woman in the LARVH arm declined her allocation, exited the trial and defaulted to standard treatment. 1 woman in the RAH arm had her surgery abandoned

Naik 2010 *(Continued)*

	before hysterectomy could be performed because a synchronous bowel tumour with multiple liver metastases was discovered intraoperatively In the group assigned to laparoscopic surgery, there was 1 intraoperative conversion to the open procedure (14%) because of an enterotomy. After examination under anaesthetic, another woman was found to have a cervical defect (because of previous conisation) potentially compromising the vaginal part of the procedure and the decision for open surgery was made Statistically significant differences (P value < 0.05) were found for the following when LARVH was compared with RAH: the median duration of catheterisation, median operating time, median blood loss, median hospital stay and median opiate requirement in the first 36 hours postoperatively There were 2 intraoperative complications in the LARVH group - 1 enterotomy requiring conversion to the open procedure and 1 cystotomy, which was repaired vaginally. Neither woman suffered any long-term sequelae Postoperative complications encountered were minor. 1 woman was readmitted to hospital after 32 days with severe constipation after RAH

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The participants underwent a 1:1 randomisation to either laparoscopic or standard open surgery using computer-generated block randomisation"
Allocation concealment (selection bias)	Low risk	"The block size was four and this information was not known to the researchers until the trial had closed"
Blinding (performance bias and detection bias) All outcomes	Unclear risk	It was not reported whether the outcome assessors were blinded to all outcomes but they were blinded to the randomisation allocation of the women who completed the BBUSQ-22
Incomplete outcome data (attrition bias) All outcomes	Low risk	% analysed: 13/15 (87%)
Selective reporting (reporting bias)	Low risk	Scope of trial was short-term effects so it is unlikely any outcomes were selectively reported. Survival outcomes were not reported as these are long-term outcomes
Other bias	Unclear risk	Insufficient information to assess whether an additional risk of bias exists

BBUSQ-22: Bowel and Urinary Symptoms Questionnaire 22-item inventory; BMI: body mass index; IQR: interquartile range; LARVH: laparoscopic assisted radical vaginal hysterectomy; LLETZ: large loop excision of the transformation zone; RAH: radical abdominal hysterectomy; SD: standard deviation.

APPENDICES

Appendix 1. CENTRAL search strategy

CENTRAL

1. MeSH descriptor Uterine Cervical Neoplasms explode all trees
2. cervi* near/5 (cancer* or tumor* or tumour* or malignan* or carcinoma* or neoplas*)
3. (#1 OR #2)
4. MeSH descriptor Hysterectomy explode all trees
5. hysterectom*

6. (#4 OR #5)
7. MeSH descriptor Laparoscopy explode all trees
8. laparoscop* or keyhole or minimal*
9. abdominal* or open
10. (#7 OR #8 OR #9)
11. (#6 AND #10)
12. Coelio-Schauta
13. (#11 OR #12)
14. (#3 AND #13)

Appendix 2. MEDLINE search strategy

MEDLINE

1. exp Uterine Cervical Neoplasms/
2. (cervi* adj5 (cancer* or tumor* or tumour* or malignan* or carcinoma* or neoplas*)).mp.
3. 1 or 2
4. exp Hysterectomy/
5. hysterectom*.mp.
6. 4 or 5
7. Laparoscopy/
8. (laparoscop* or keyhole or minimal*).mp.
9. (abdomin* or open).mp.
10. 7 or 8 or 9
11. 6 and 10
12. Coelio-Schauta.mp.
13. 11 or 12
14. 3 and 13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. randomized.ab.
18. placebo.ab.
19. clinical trials as topic.sh.
20. randomly.ab.
21. trial.ti.
22. 15 or 16 or 17 or 18 or 19 or 20 or 21
23. 14 and 22

key:

mp=title, original title, abstract, name of substance word, subject heading word, unique identifier

pt=publication type

ab=abstract

sh=subject heading

Appendix 3. EMBASE search strategy

EMBASE

1. exp uterine cervix cancer/
2. (cervi* adj5 (cancer* or tumor* or tumour* or malignan* or carcinoma* or neoplas*)).mp.
3. 1 or 2
4. exp hysterectomy/
5. hysterectom*.mp.
6. 4 or 5

7. laparoscopy/
8. (laparoscop* or keyhole or minimal*).mp.
9. (abdomin* or open).mp.
10. 7 or 8 or 9
11. 6 and 10
12. Coelio-Schauta.mp.
13. 11 or 12
14. 3 and 13
15. crossover procedure/
16. double blind procedure/
17. randomized controlled trial/
18. single blind procedure/
19. random*.mp.
20. factorial*.mp.
21. crossover*.mp.
22. cross over*.mp.
23. cross-over*.mp.
24. placebo*.mp.
25. (doubl* adj blind*).mp.
26. (singl* adj blind*).mp.
27. assign*.mp.
28. allocat*.mp.
29. volunteer*.mp.
30. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 14 and 30

key:

mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name

WHAT'S NEW

Date	Event	Description
5 January 2022	Amended	No longer for update as any future update will require the development of a new protocol reflecting current Cochrane methodological criteria.

HISTORY

Protocol first published: Issue 3, 2007
Review first published: Issue 10, 2013

CONTRIBUTIONS OF AUTHORS

R Naik and A Kucukmetin provided clinical expertise and designed the protocol. K Deane provided systematic review methodological expertise and advice in the protocol.

A Kucukmetin and R Naik provided clinical expertise and wrote the clinical sections of the review. A Bryant and A Kucukmetin sifted references and extracted data. A Bryant wrote the methodological and statistical sections of the review. All authors agreed to the final version of the review.

DECLARATIONS OF INTEREST

Raj Naik is an author of the included randomised controlled trial and was involved in the conduct of the trial.

SOURCES OF SUPPORT

Internal sources

- Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead, UK

External sources

- Department of Health, UK

  NHS Cochrane Collaboration Programme Grant Scheme CPG-506

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Restriction to RCTs

The search strategy identified one RCT that met our inclusion criteria, so we restricted the review to RCTs as they provide the best level of evidence. We were also concerned about the threat of selection bias in non-randomised studies. In the protocol, we had stated the following:

"As we expect to find few, if any, RCTs of surgical interventions (Johnson 2008), non-randomised studies with concurrent comparison groups will be included:

- Quasi-randomised trials, non-randomised trials, prospective and retrospective cohort studies, and case series of 30 or more patients.

Case-control studies, uncontrolled observational studies and case series of fewer than 30 patients will be excluded.

In order to minimise selection bias, we will include only studies that use statistical adjustment for baseline case mix using multivariable analyses (e.g. age, performance status, grade, etc) if any constraints are placed on treatment allocation (e.g. women with poor performance status would not be given radical abdominal hysterectomy) or it is based on clinician preference."

Searches

In the protocol, we stated:

"The main investigators of any relevant ongoing trials will be contacted for further information, as will any major co-operative trials groups active in this area."

However, we did not find any relevant ongoing trials or active trials groups, so we did not make these contacts.

Risk of bias

Risk of bias was not examined in non-randomised studies as the review was restricted to RCTs. In the protocol, we stated the following:

"The risk of bias in non-randomised controlled trials will be assessed in accordance with four additional criteria:

Cohort selection

1. Were relevant details of criteria for assignment of patients to treatments provided?

- Yes
- No
- Unclear

2. Was the group of women who received the experimental intervention (LARVH surgery) representative?

- Yes, if they were representative of women with early-stage cervical cancer.
- No, if group of patients was selected.
- Unclear, if selection of group was not described.

3. Was the group of women who received the comparison intervention (RAH surgery) representative?

- Yes, if drawn from the same population as the exposed cohort.
- No, if drawn from a different source.
- Unclear, if selection of group not described.

Comparability of treatment groups

1. Were there no differences between the two groups or were differences controlled for, in particular with reference to age, FIGO stage, histological cell type, differentiation and type of surgeon (Gynaeoncologist, Gynaecologist, General surgeon)?

- Yes, if at least three of these characteristics were reported and any reported differences were controlled for.
- No, if the two groups differed and differences were not controlled for.
- Unclear, if fewer than three of these characteristics were reported even if there were no other differences between the groups, and other characteristics were controlled for."

Time-to-event and continuous outcome data

Time-to-event outcome data were not reported in the trial of Naik 2010 as the trial focused on short-term outcomes and continuous outcomes were reported in terms of median and IQR, so the following sections in the protocol, which discussed the handling of data for survival and continuous outcomes, were removed as they were unnecessary:

"Data extraction and management

Data on outcomes will be extracted as below:

- For time to event (overall and progression-free or disease-free survival) data, we will extract the log of the hazard ratio [log(HR)] and its standard error from trial reports; if these are not reported, we will attempt to estimate them from other reported statistics using the methods of Parmar 1998.
- For continuous outcomes (e.g. QoL measures), we will extract the final value and standard deviation of the outcome of interest and the number of patients assessed at endpoint in each treatment arm at the end of follow-up, in order to estimate the mean difference (if trials measured outcomes on the same scale) or standardised mean differences (if trials measured outcomes on different scales) between treatment arms and its standard error.

Measures of treatment effect

- For time to event data, we will use the HR, if possible. The HR summarises the chances of survival in women who received one type of treatment compared to the chances of survival in women who received another type of treatment. However, the logarithm of the HR, rather than the HR itself, is generally used in meta-analyses.
- For continuous outcomes, we will use the mean difference between treatment arms".

Data synthesis

We only identified one included trial so it was not possible to perform meta-analyses. Therefore, it was not relevant to assess heterogeneity between results of trials and we were unable to assess reporting biases using funnel plots or conduct any subgroup analyses or sensitivity analyses. The following sections of the protocol were, therefore, removed:

"Assessment of heterogeneity

Heterogeneity between studies will be assessed by visual inspection of forest plots, by estimation of the percentage heterogeneity between trials which cannot be ascribed to sampling variation (Higgins 2003), by a formal statistical test of the significance of the heterogeneity (Deeks 2001) and, where possible, by subgroup analyses (see below). If there was evidence of substantial heterogeneity, the possible reasons for this were investigated and reported.

Assessment of reporting biases

Funnel plots corresponding to meta-analysis of the primary outcome will be examined to assess the potential for small study effects such as publication bias. If these plots suggest that treatment effects may not be sampled from a symmetric distribution, as assumed by the random effects model, further meta-analyses will be performed using fixed effects models.

Data synthesis

If sufficient, clinically similar studies are available, their results will be pooled in meta-analyses. Adjusted summary statistics will be used if available; otherwise unadjusted results will be used.

- For time-to-event data, HRs will be pooled using the generic inverse variance facility of RevMan 5.
- For any dichotomous outcomes, the RR will be calculated for each study and these will then be pooled.
- For continuous outcomes, the mean differences between the treatment arms at the end of follow-up will be pooled if all trials measured the outcome on the same scale, otherwise standardised mean differences will be pooled.

Random effects models with inverse variance weighting will be used for all meta-analyses (DerSimonian 1986).

Subgroup analysis and investigation of heterogeneity

We do not plan to carry out any subgroup analyses.

Factors such as age, stage, grade, performance status, type of surgeon, will be considered in interpretation of any heterogeneity.

Sensitivity analysis

Sensitivity analyses will be performed excluding studies at high risk of bias".

INDEX TERMS

Medical Subject Headings (MeSH)

Hysterectomy [*methods]; Hysterectomy, Vaginal [methods]; Laparoscopy [*methods]; Neoplasm Staging; Randomized Controlled Trials as Topic; Uterine Cervical Neoplasms [pathology] [*surgery]

MeSH check words

Adult; Female; Humans