Laparoscopic treatment for endometrial cancer: a meta-analysis of randomized controlled trials (RCTs)

Palomba S, Falbo A, Mocciaro R, Russo T, Zullo F

CRD summary
The authors concluded that laparoscopic procedure was a safe and effective treatment for early stage endometrial cancer, with advantages over laparotomy (less blood loss and post-operative complications), despite longer operative time. These conclusions reflected the results of this generally well-conducted review, but some caution may be required given the small size and limited quality of the included trials.

Authors' objectives
To evaluate the effectiveness of laparoscopic treatment of endometrial cancer.

Searching
MEDLINE, ISI Web of Science, National Health Institute Registry, Australian New Zealand Clinical Trials registry and the websites for the registration of controlled trials were searched with no language restrictions from 1966 to June 2008. Search terms were reported. The bibliographies of retrieved articles, books, expert opinion review articles and bibliographies from subject experts were handsearched.

Study selection
Randomised controlled trials (RCT) of laparoscopic or laparotomic treatment in women with histologically confirmed endometrial cancer were eligible for inclusion. The primary outcome was overall survival at six, 12, 24 and 36 months follow-up. Secondary outcomes included disease free survival, cancer-related survival, quality of life, operative time, blood loss, nodes yield, complication rates and costs.

Included trials were of laparoscopic assisted vaginal hysterectomy with bilateral salpingo-oophorectomy combined in some instances with laparoscopic pelvic lymphadenectomy and laparoscopic para-aortic lymphadenectomy compared to standard laparotomic surgery. Women with a variety of histologically confirmed endometrial cancers were included in the review, including endometroid, serous, adenosquamous and mucinous histotypes. The majority of the participants in the included trials had stage I cancer.

Two reviewers independently selected the studies for review with disagreements resolved by consensus or arbitration.

Assessment of study quality
The methodological quality of included studies was assessed using the Cochrane Guidelines according to the following criteria: allocation concealment, blinding, intention-to-treat analysis and follow-up.

The authors did not state how many reviewers performed the validity assessment.

Data extraction
For dichotomous data, the number of events in each group were extracted and used to calculate odds ratios with 95% confidence intervals. For continuous outcomes, the mean difference between laparoscopic and laparotomic surgery conditions was calculated. Where necessary, the data were recalculated on an intention-to-treat basis. Authors were contacted for additional data.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled odds ratios with 95% confidence intervals were calculated for dichotomous outcomes and weighted mean...
difference with 95% confidence intervals were calculated for continuous outcomes. Random-effects models were used where statistically significant heterogeneity was found. Mantel-Haenszel fixed-effect models were used in the absence of any statistically significant heterogeneity. Both intention-to-treat and per protocol analyses were conducted. Statistical heterogeneity was assessed using the Cochran Q-test using a significance level of p value lower than 0.05.

**Results of the review**

Four randomised controlled trials (RCTs) were included for the review (n=313 patients). Allocation concealment was adequate in one trial and unclear in the other three. Blinding was not reported in three trials and the fourth trial was single blind. Intention-to-treat analyses were used in two trials. The follow-up period of two trials was the short-term post-operative period; for the remaining two trials, follow-up was 44 months and 79 months.

There were no statistically significant differences between laparoscopic and laparotomic surgery for endometrial cancer in terms of overall survival (odds ratio 0.80, 95% confidence interval (CI):0.37 to 1.70; two RCTs, n=200 patients). There was no statistically significant difference between groups for other survival outcomes. There was no evidence of statistically significant heterogeneity for these outcomes.

Laparoscopic surgery was associated with significantly longer operative times (weighted mean difference 53.48 95% CI: 37.28 to 69.68; p=0.0002, two RCTs, n=139 patients), but significantly less blood loss (weighted mean difference -266.86, 95% CI:-454.82 to -78.90; p=0.005, three RCTs, n=261 patients) and post-operative complications (odds ratio 0.40, 95% CI: 0.23 to 0.70; p=0.007, four RCTs, n=313 patients) compared to laparotomic surgery. The units for operative times and blood loss were not reported. There was evidence of significant heterogeneity for blood loss (p<0.0001) but not for operative time or post-operative complications. There were no significant differences between laparoscopic and laparotomic surgery in the pelvic or para-aortic nodes yield, or in intra-operative complications.

**Authors' conclusions**

The laparoscopic procedure was a safe and effective treatment for early stage endometrial cancer, with some advantages over laparotomy in terms of less blood loss and post-operative complications, despite longer operative time.

**CRD commentary**

The review addressed a clear question with well-defined inclusion criteria. Several relevant databases were searched and appropriate steps were taken to minimise language and publication bias. The study selection was conducted independently by two reviewers, but it was unclear whether similar steps were taken in the validity assessment and data extraction stages, so reviewer error and bias could not be ruled out. A recognised tool was used to assess the methodological quality of the included trials, but the available trials were of only moderate quality. It should be noted that there were discrepancies between the table of population characteristics and the forest plots for numbers of patients included in the trials; the patient numbers cited in this abstract are taken from the forest plots. Appropriate methods were used to combine the trials and statistical heterogeneity was assessed, but only two trials were available for the primary outcomes. The authors’ conclusions reflected the results of this generally well-conducted review, but some caution may be required given the small size and limited quality of the included trials.

**Implications of the review for practice and research**

**Practice:** The authors did not state any recommendations for practice.

**Research:** The authors stated that further well-designed multi-centre RCTs are needed, with adequate power to assess overall, disease-free and cancer-related survival, evaluating short term outcomes and with long-term follow up.

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