
Systematic lymphadenectomy for survival in patients with endometrial cancer: a meta-analysis

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CRD summary

The review concluded that systematic lymph node removal increased overall survival in patients with intermediate-risk or high-risk uterine endometrial cancer, but had limited effects in low-risk patients. Given the uncertain quality of the evidence base, lack of effects in included trials and potential problems with the meta-analysis, caution is warranted when interpreting the authors' results and conclusions.

Authors' objectives

To determine the efficacy of systematic lymphadenectomy for overall survival in endometrial cancer patients.

Searching

PubMed, EMBASE, and Cochrane Central Register of Controlled Trials were searched from January 2000 up to August 2010 for articles in English. Search terms were reported.

Study selection

Studies of systematic lymphadenectomy (defined as the removal of more than 10 lymph nodes) versus unsystematic lymphadenectomy in patients with uterine endometrial cancer were eligible for inclusion. Eligible studies had to report overall survival.

The included studies considered systematic lymphadenectomy versus unsystematic lymphadenectomy in patients with low-risk, intermediate-risk and high-risk endometrial cancer. The definition of systematic and unsystematic lymphadenectomy varied across studies. The International Federation of Gynaecology and Obstetrics criteria ranged from stage I to IV. Histology varied across studies. Other details were not reported.

Two reviewers undertook study selection.

Assessment of study quality

The authors did not state whether they assessed study quality.

Data extraction

Data were extracted on overall survival and used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs).

Two reviewers independently extracted the data and disagreements were resolved by consensus.

Methods of synthesis

A Mantel-Haenszel fixed-effect meta-analysis was used to calculate pooled hazard ratios and 95% confidence intervals. Statistical heterogeneity was assessed using I^2 .

Subgroup analyses were undertaken on the basis of study type, definition of lymphadenectomy and type of cancer risk (low to high risk).

Publication bias was estimated using funnel plots.

Results of the review

Nine studies were included in the review (16,995 patients) comprising two randomised controlled trials (RCTs) and seven observational studies. Study sample size ranged from 211 to 12,333 patients.

Systematic lymphadenectomy was associated with a statistically significantly reduced risk of death (HR 0.89, 95% CI 0.82 to 0.97; nine studies; $I^2=46%$) compared with unsystematic lymphadenectomy.

Subgroup analysis on the basis of study type showed that the results were not significant for RCTs (HR 1.05, 95% CI 0.84 to 1.31; two RCTs; $I^2=0\%$), but were statistically significant in observation studies (HR 0.87, 95% CI 0.80 to 0.95; seven studies; $I^2=36\%$).

Subgroup analysis for high-risk versus intermediate-risk endometrial cancer indicated a statistically significant reduced risk of death with in patients with systematic lymphadenectomy (HR 0.77, 95% CI 0.70 to 0.86; four studies; $I^2=47\%$). Low-risk endometrial cancer did not show a significant difference (three studies).

Subgroup analysis on the basis of definition of lymphadenectomy indicated statistically significant differences in overall survival in favour of systematic lymphadenectomy defined as removal of more than 10 lymph nodes (HR 0.88, 95% CI 0.81 to 0.97; five studies; $I^2=41\%$) compared with systematic lymphadenectomy defined as removal of less than 10 to 11 lymph nodes. Results in studies with other definitions were not significant (results reported in review).

There was no evidence of publication bias.

Authors' conclusions

Systematic lymphadenectomy (defined as removal of more than 10 lymph nodes) increased overall survival in patients with intermediate-risk or high-risk endometrial cancer, but had limited effects in low-risk patients.

CRD commentary

Inclusion criteria for the review were appropriately defined. Several relevant databases were searched. There may have been the potential for language bias, as only English language studies were included. Publication bias was assessed and was not detected, although an analysis with less than 10 studies would be unlikely to be informative. Attempts appear to have been made to minimise reviewer error and bias throughout the review.

Quality assessment did not appear to have been undertaken, which made it difficult to assess the quality of the evidence base; most studies were observation. Fixed-effect meta-analysis was undertaken and statistical heterogeneity was assessed. However, data from RCTs and observation studies were pooled in some analyses, which may not be appropriate. The authors' conclusions were mainly based on individual subgroup analyses which had small numbers of studies and may not be reliable; the RCT data did not show an effect.

Given the concerns with the meta-analysis together with the uncertain quality of the evidence base, caution is warranted when interpreting the authors' results and conclusions.

Implications of the review for practice and research

Practice: The authors stated that the detection of lymph node metastasis should be considered important as it could lead to preoperative low-risk endometrial disease patients being re-graded to a higher classification.

Research: The authors stated that the fact that the review found that systematic lymphadenectomy (defined as removal of more than 10 lymph nodes) increased overall survival in patients with intermediate-risk or high-risk endometrial cancer was something that could help plan further RCTs.

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