Systematic lymphadenectomy for survival in epithelial ovarian cancer: a meta-analysis

Kim HS, Ju W, Jee BC, Kim YB, Park NH, Song YS, Kim SC, Kang SB, Kim JW

CRD summary
This review concluded that systematic lymphadenectomy could improve overall survival in patients with advanced epithelial ovarian cancer, but further research was needed and the results should be interpreted with caution. There were some data limitations and problems with the review methods, but the authors' recommendations for further research and caution in interpreting the findings appear to be reasonable.

Authors' objectives
To evaluate the impact of systematic lymphadenectomy compared with unsystematic lymphadenectomy on overall survival in patients with epithelial ovarian cancer.

Searching
PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and EMBASE were searched for articles published in English from January 1995 to December 2008. Search terms were reported. The reference lists of relevant articles were also searched.

Study selection
Studies of systematic compared with unsystematic lymphadenectomy, in patients with epithelial ovarian cancer, were eligible for inclusion. Studies had to report the overall survival difference between systematic and unsystematic lymphadenectomy.

The included studies compared systematic with unsystematic lymphadenectomy in patients with epithelial ovarian cancer at International Federation of Gynecology and Obstetrics (FIGO) stages I to IV. Studies were undertaken between 1995 and 2008. Various lymphadenectomy surgeries were undertaken and the details were provided. Four studies reported that an unsystematic lymphadenectomy was one that was not performed. Debulking surgery, where reported, was generally optimal, but in some studies it was reported as suboptimal.

Two reviewers independently selected the studies.

Assessment of study quality
The reviewers did not state that they assessed validity.

Data extraction
Two reviewers independently extracted data for the overall survival, from Kaplan Meier curves, and used these data to calculate hazard ratios and 95% confidence intervals. Disagreements were resolved by consultation with a third reviewer.

Methods of synthesis
A fixed-effect meta-analysis was undertaken to calculate the pooled hazard ratios for overall survival. Statistical heterogeneity was assessed using the I^2 and χ^2 tests. Subgroup analyses were presented for study design, debulking surgery, and stage of disease. Publication bias was assessed in a funnel plot. Sensitivity analysis was performed by removing the studies that added the greatest weight to the findings.

Results of the review
Nine studies were included (n=21,919 patients, with 5,014 receiving systematic and 16,905 receiving unsystematic lymphadenectomy); two were RCTs and seven were observational studies.

There was a statistically significant greater overall survival with systematic compared with unsystematic lymphadenectomy (HR 0.72, 95% CI 0.68 to 0.76; nine studies). Sensitivity analysis did not significantly alter the results, but the subgroup analysis including randomised controlled trials (RCTs) only showed no statistically significant
difference between the two treatment groups.

There was a statistically significant difference in overall survival between systematic and unsystematic lymphadenectomy in patients with FIGO stages I-II (HR 0.80, 95% CI 0.70 to 0.92; three studies). The findings remained significant for the two observational studies only, but the other RCT showed no difference and after removal of the study with the largest weight there was no significant difference. For FIGO stages III-IV patients, the findings were statistically significant for all six studies in favour of systematic lymphadenectomy, and were significant for sensitivity and subgroup analyses, except for the RCT, which showed no significant difference. Other results were presented.

There was no evidence of significant statistical heterogeneity in any of the analyses and publication bias was not detected.

**Authors’ conclusions**
The findings suggested that systematic lymphadenectomy could improve overall survival for patients with advanced epithelial ovarian cancer, but further data was needed and the results should be interpreted with caution.

**CRD commentary**
The inclusion criteria were clearly defined and three relevant databases were searched. There was the potential for language bias as only English-language articles were included. Publication bias was assessed and was not detected. Attempts were made to reduce reviewer error and bias during data extraction and study selection. A quality assessment was not reported, but most of the included studies were observational and their quality was likely to be variable. The two RCTs that were included showed no significant differences between systematic and unsystematic lymphadenectomy, for any comparisons, which indicates potential bias in the observational studies. The definitions of systematic and unsystematic lymphadenectomy varied across studies, which the authors acknowledged, and there were large differences in the numbers of patients who received unsystematic versus systematic lymphadenectomy. The studies were pooled using meta-analysis and the statistical heterogeneity was assessed. Given the differences in definitions, the differences in results between observational studies and RCTs, and the lack of detail on the patient characteristics, this pooling of data might not have been appropriate.

The authors noted some of these concerns, and their recommendations for further research and to interpret the findings with caution seem to be appropriate.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research was needed, but a large trial was underway and this might address some of the issues.

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