An evidence-based medicine review of lymphadenectomy extent for gastric cancer

CRD summary
This review concluded that D2 and D3 lymphadenectomy, compared with D1 surgery, may not offer specific advantages for gastric cancer and may yield poorer patient outcomes. The authors conclusions were appropriately cautious, but are unlikely to be definitive in light of a number of shortcomings in the review process.

Authors’ objectives
To assess the safety and effectiveness of lymphadenectomy with gastrectomy for the treatment of gastric cancer.

Searching
EMBASE, MEDLINE, Cochrane Central Register of Controlled Trials and the Chinese Biomedical Database were searched without language restrictions from 1966 to May 2007; search terms were reported. Colleagues were contacted regarding clinical trials or unpublished material to identify additional studies.

Study selection
Randomised controlled trials (RCTs) that compared lymphadenectomies for the treatment of gastric cancer in patients with clearly defined types of nodal dissection were eligible for inclusion. Included interventions compared D1, D2, and D3 (D2+ or D4) lymphadenectomy. Eligible patients had histologically proven adenocarcinoma of the stomach by preoperative endoscopic biopsy without clinical evidence of the metastasis; inspected para-aortic metastases were considered distant metastases. Patients with gastric cancer with a distant organ metastasis, oesophageal involvement, peritoneal dissemination or a Borrmann-type cancer classification were excluded, as were those with concurrent liver cirrhosis, serious circulatory or respiratory disorders or renal dysfunction. Included outcomes comprised 3- or 5-year survival, postoperative morbidity, 30-day postoperative mortality, hospital stay and operative time.

The authors stated neither how the papers were selected for review nor how many reviewers performed the selection.

Assessment of study quality
Methodological quality was assessed by three reviewers who used previously published criteria: randomisation; concealment of allocation; blinding; comparability of groups; and adherence to the intention-to-treat principle. Disagreements were resolved by discussion.

Data extraction
Data for dichotomous outcomes were extracted to calculate odds ratios (OR). Means and standard deviations were extracted for continuous outcomes to calculate the mean difference and 95% CI.

Three reviewers extracted data. Disagreements were resolved by discussion.

Methods of synthesis
Pooled odds ratios and weighted mean differences (WMD), and their 95% CI, were calculated using a fixed-effect model. A random-effects model was used if significant heterogeneity was present. Heterogeneity was assessed using the X² test.

Results of the review
Fourteen RCTs (n=3,432, range 43 to 711) were included in the review. Studies were moderate or poor quality: blinding was not reported for any studies, five studies reported use of allocation concealment and one reported intention-to-treat analysis.

Compared with D1 surgery, D2 surgery produced significantly higher operative mortality (OR 0.50, 95% CI: 0.32 to 0.76; eight studies) and postoperative morbidity (OR 0.40, 95% CI: 0.32 to 0.49; eight studies). Operative time was
shorter in D1 (WMD \(-44.51\), 95% CI: \(-58.38\) to \(-30.64\); two studies). Outcomes for three- and five-year survival were not significant. Comparisons for the D2 versus the D3 surgical groups were not significant. There was no statistically significant heterogeneity for these analyses.

**Authors' conclusions**

Compared with D1 surgery, D2 and D3 surgery may not offer specific advantages for gastric cancer and may yield poorer patient outcomes.

**CRD commentary**

The review question and inclusion criteria were clear. A number of relevant databases were searched for studies in all languages and an effort was made to locate unpublished studies by contacting experts in the clinical field. It was unclear how many reviewers were involved in study selection, so the selection process may have been subject to bias; data extraction was undertaken in duplicate. Appropriate criteria were used to assess the quality of the included studies, which was undertaken in duplicate. Most of the included studies were of moderate to poor quality. Suitable methods were used for the meta-analysis. Heterogeneity was reportedly assessed and found to be absent, but results were not reported. The findings of this review were limited by uncertainty over parts of the review process, a lack of good-quality data and uncertainty over generalisability given that the groups of patients for some included studies were not well matched for clinical features, medical risk factors and tumour stage. The authors conclusions were appropriately cautious, but are unlikely to be definitive in light of the shortcomings in the review process.

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

**Practice:** The authors stated that the prevalence of standard techniques and development of an education and training system would be important in the future.

**Research:** The authors stated that the medical community needed to rethink lymphadenectomy extent and perform a well-designed trial for gastric cancer surgery.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.