Laparoscopic versus open distal gastrectomy for gastric cancer: a meta-analysis of randomized controlled trials and high-quality nonrandomized studies

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CRD summary
The authors concluded that laparoscopic versus open distal gastrectomy was safe for the treatment of gastric cancer on short-term outcomes but may result in clinically insignificant reductions in lymph node retrieval. There was some potential for review bias and the clinical significance of reduced lymph node retrieval remained unclear, but the authors’ conclusions seem generally reliable in Asian populations.

Authors’ objectives
To compare the effectiveness of laparoscopic distal gastrectomy versus open distal gastrectomy in patients with gastric cancer.

Searching
MEDLINE and EMBASE were searched between 1992 and March 2010 for articles published in English. The search strategy was reported. References from relevant articles and reviews were searched manually.

Study selection
Eligible studies were published randomised controlled trials (RCTs) and high quality non-randomised comparative studies (NRCTs). Eligible studies had to compare laparoscopic distal gastrectomy versus open distal gastrectomy with curative intent for early and advanced gastric cancer (adenocarcinoma). Primary outcomes of interest were operative mortality, complications (overall, medical and minor and major surgical complications) and number of harvested lymph nodes. Secondary outcomes were operative time, blood loss and hospital stay. Studies of patients with diseases other than gastric cancer and studies that included other types of resection or palliative resection were excluded unless data were presented separately.

Most of the included studies represented Eastern countries. Lymph node dissection was defined as D1 and D2. Most studies were in patients with stage I gastric cancer. Some studies included patients with advanced stage cancer. Most RCTs used totally laparoscopic distal gastrectomy. Most NRCTs used laparoscopic-assisted distal gastrectomy. Fourteen RCTs were adequately matched according to age, gender, American Society of Anaesthesiologists physical status classification/comorbidities, body mass index, lymphadenectomy, tumour size and tumour node metastasis/stage.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
The quality of RCTs was assessed using a modified version of the Cochrane risk of bias tool. NRCTs were assessed using a modified version of a validated tool (Methodological Index for Non-randomised Studies) for consecutive patients, prospective data, endpoints reported, unbiased outcome evaluation, appropriate controls, contemporary groups, equivalent groups and sample size. NRCTs could receive a maximum score of 16; studies that scored 12 or more were considered high quality and included in the meta-analysis.

Two reviewers extracted data necessary to assess study quality.

Data extraction
Continuous data were extracted to calculate mean differences and 95% confidence intervals. Dichotomous data were extracted to calculate odds ratios and 95% confidence intervals. Differences in lymph node retrieval between the two interventions were calculated based on the number of patients with fewer than 15 lymph nodes harvested, which was estimated from each study (assuming normal distribution) and reported as odds ratios. Primary authors were contacted where necessary.
Methods of synthesis
A random-effects model was used to combine odds ratios and 95% confidence intervals (CIs) and combine mean differences and 95% CIs to calculate weighted mean differences (WMDs). Data from RCTs and NRCTs were combined and also investigated separately.

Statistical heterogeneity was assessed using the Cochran Q statistic. Subgroup analyses were planned for studies with matched lymph node dissection, matched tumour node metastasis/stage, studies that selected only clinical stage I cancers for laparoscopy and the number of laparoscopies performed (50 cases cut-off value).

Results of the review
Six RCTs (666 patients) were included in the review. All trials addressed incomplete outcome data, five were free from selective reporting and four reported postoperative protocol. Three RCTs had unclear sequence generation and three had unclear allocation concealment. Thirty-two NRCTs were identified but only 19 (2,389 patients) were high quality and included in the review.

Primary outcomes: There were no statistically significant differences between the interventions in postoperative mortality (eight studies), major surgical complications (21 studies) and the odds of having fewer than 15 lymph nodes harvested (23 studies). Laparoscopic distal gastrectomy reduced overall complications (OR 0.59, 95% CI 0.47 to 0.74; 24 studies), medical complications (OR 0.49, 95% CI 0.31 to 0.77; 17 studies) and minor surgical complications (OR 0.62, 95% CI 0.46 to 0.83; 24 studies); these results were statistically significant. Open distal gastrectomy retrieved statistically significantly more lymph nodes compared to laparoscopic methods (WMD 3.9 nodes, 95% CI 2.4 to 5.4).

Secondary outcomes: Laparoscopic distal gastrectomy statistically significantly increased operation time compared to open techniques (WMD 48.3 minutes, 95% CI 34.2 to 62.4; 24 studies). Blood loss (WMD 118.9mL, 95% CI 91.1 to 146.6; 24 studies) and hospital stay (WMD 3.6 days, 95% CI 2.6 to 4.5; 24 studies) were significantly reduced. There was evidence of statistical heterogeneity for all secondary outcomes in RCTs and NRCTs.

Separate analyses for RCTs and NRCTs showed similar findings except that RCTs showed no statistically significant differences between interventions in medical and major surgical complications. NRCTs showed statistical heterogeneity for retrieval of lymph nodes (p<0.001).

Subgroup analyses did not significantly alter the findings (fully reported in the review).

Authors’ conclusions
Compared to open distal gastrectomy, laparoscopic distal gastrectomy is a safe option for the treatment of gastric cancer on short-term outcomes but may result in a clinically insignificant reduction in lymph node retrieval.

CRD commentary
The review question and supporting inclusion criteria were stated clearly. The literature search was restricted to published articles in English so potentially relevant data may have been missed. Study quality was assessed and only RCTs and high quality observational studies were included in the review. The quality of the RCTs was variable. It was unclear whether study selection was performed in duplicate so reviewer error and bias could not be ruled out.

The authors acknowledged the controversies surrounding pooling data from different study designs but they also reported results separately and performed subgroup analyses. There was some evidence of statistical heterogeneity and there was potential for clinical heterogeneity which made it unclear whether combining the studies was appropriate.

The authors’ conclusions reflected the overall evidence and results for RCTs and NRCTs were generally consistent.

Implications of the review for practice and research
There was potential for review bias and some evidence of heterogeneity but the evidence base was large and seemed generally reliable. Interpretation should take into account that data were from Asian countries and therefore generalisability to Western patients is unclear and that the clinical significance of reduced lymph node retrieval remains unclear.
Practice: The authors stated that the evidence comes from Asian countries but was highly likely to be replicable.

Research: The authors stated that prospective studies were needed to evaluate the use of laparoscopic distal gastrectomy in patients from Western countries, patients with higher body mass index and associated comorbidities. Further studies were needed to assess the impact on long-term survival of a reduction in retrieved lymph nodes. Studies were needed to assess the learning curve of laparoscopic D2 dissection and factors that may modify this.

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