Meta-analysis of D1 versus D2 gastrectomy for gastric adenocarcinoma
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CRD summary
This review concluded that limited D1 gastrectomy was associated with significantly fewer anastomotic leaks, lower postoperative complications, lower re-operations, decreased hospital stay and lower 30-day mortality than extended D2 gastrectomy, with comparable five-year survival, in patients with stomach cancer. The poor quality of the evidence base and potential variables mean that caution is warranted when interpreting the authors’ conclusions.

Authors' objectives
To assess the efficacy and drawbacks of limited D1 (including dissection of the lymph nodes around the stomach) versus extended D2 (including dissection of the lymph nodes around the coeliac axis) gastrectomy for proven gastric adenocarcinoma (malignant stomach cancer).

Searching
PubMed, EMBASE, Science Citation Index and Current Contents were searched from 1980 up to December 2008 for articles published in English peer-reviewed journals. Search terms were reported. Reference lists of relevant articles were handsearched.

Study selection
Randomised controlled trials (RCTs) that compared limited D1 versus extended D2 gastrectomy for the treatment of histologically proven gastric adenocarcinoma in adult patients were eligible for inclusion. Trials had to report at least one of six outcomes: overall complication rate, anastomotic leak rate, re-operation rate, 30-day mortality rate, five-year survival rate, or length of hospital stay. Abstracts were excluded.

All the included trials compared limited D1 versus extended D2 gastrectomy. The trials were conducted in Europe, Asia, and Africa. The mean age of patients in the D1 group ranged from 45 to 68 years; the mean age in the D2 group was from 56 to 67 years. A surgical resection margin of at least 5cm, both proximally and distally, was considered minimum in all the RCTs (except for one trial where the minimum margin was 2.5cm). The surgeons involved had varying degrees of experience in performing gastrectomies. The rates of splenectomy and pancreatectomy differed between treatment groups.

Three reviewers appeared to be involved in study selection; disagreements were resolved by discussion.

Assessment of study quality
Trial quality was assessed using the Jadad scale, which appraised randomisation, blinding, and withdrawals to give a maximum score of 5 points.

Three reviewers were involved in quality assessment; disagreements were resolved by discussion.

Data extraction
Data were extracted on the six clinical outcomes (overall complication rate, anastomotic leak rate, re-operation rate, 30-day mortality rate, five-year survival rate, and length of hospital stay). These were used to calculate odds ratios (ORs) or mean differences, with 95% confidence intervals (CIs).

Three reviewers were involved in data extraction, and disagreements were resolved by discussion.

Methods of synthesis
Random-effects meta-analysis was undertaken to calculate pooled odds ratios and weighted mean differences (WMDs), with 95% confidence intervals. Statistical heterogeneity was assessed using the Cochran Q and I². Publication bias was assessed using funnel plots.

Results of the review
Six RCTs were included in the review (1,876 patients). The trial sample sizes ranged from 43 to 711 patients. All of the trials scored 2 out of 5 points on the Jadad scale, indicating poor quality. None of the trials adequately performed blinding or reported withdrawals.

Compared with extended D2 gastrectomy, limited D1 gastrectomy was associated with statistically significantly shorter hospital stay (WMD -6.37 days, 95% CI -10.66 to -2.08; I²=86%; six RCTs), a 58% reduction in the risk of developing postoperative complications (OR 0.42, 95% CI 0.27 to 0.66; I²=58%; six RCTs), a 60% reduction in anastomotic breakdown (OR 0.40, 95% CI 0.25 to 0.63; I²=0%; six RCTs), a 67% reduction in reoperation rate (OR 0.33, 95% CI 0.15 to 0.72; I²=0%; four RCTs), and a 41% reduction in 30-day mortality (OR 0.59, 95% CI 0.40 to 0.85; I²=0%; six RCTs). There was no significant difference in five-year mortality (five RCTs). Three of the outcomes had high levels of statistical heterogeneity.

There was evidence of publication bias for length of hospital stay and post-operative complications.

Authors' conclusions
Limited D1 gastrectomy was associated with significantly fewer anastomotic leaks, lower postoperative complication rate, lower reoperation rate, decreased length of hospital stay and lower 30-day mortality than extended D2 gastrectomy, with comparable five-year survival rates.

CRD commentary
Inclusion criteria for the review were clearly defined and several relevant data sources were searched.There was the potential for language bias, as only English language studies were included. Publication bias was assessed and was detected in some analyses, although the meaningfulness of funnel plots with less than ten trials may be limited. It appeared that attempts were made to reduce reviewer error and bias throughout the review.

Quality assessment indicated that the quality of the evidence was poor. Some of the trials also had small sample sizes. The authors noted that there were confounding factors in the trials such as surgical technique learning curve effect, trial population selection, and pancreatic or splenic resection. Trials were combined using standard statistical techniques and statistical heterogeneity was assessed, which was appropriate.

The poor quality of the evidence base and potential confounding factors means that a degree of caution is warranted when interpreting the authors' conclusions.

Implications of the review for practice and research
Practice: The authors stated that available best clinical evidence comparing limited D1 gastrectomy with extended D2 gastrectomy did not favour the D2 resection.

Research: The authors stated that further well-designed, high-quality RCTs of D1 versus D2 need to be considered, along with other treatment modalities such as chemotherapy. Further research should consider: the surgical experience in performing D2 resections to prevent breaches and contaminations; number of gastrectomies needed to be performed yearly to participate in such trials; standardization of D2 dissection; training requirement and standards; accurate pathological staging; and the costs and benefits of treatments.

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