Meta-analysis of short-term outcomes after laparoscopy-assisted distal gastrectomy

Hosono S, Arimoto Y, Ohtani H, Kanamiya Y

CRD summary
This review reported that laparoscopy-assisted distal gastrectomy used to treat early gastric cancer is associated with lower morbidity, less pain, faster bowel function recovery and a shorter hospital stay in comparison with conventional open distal gastrectomy. The review data support these conclusions, but their reliability is unclear given the lack of a validity assessment and the potential for publication bias.

Authors' objectives
To compare the short-term outcomes of laparoscopy-assisted distal gastrectomy (LADG) with conventional open distal gastrectomy (CODG) for patients with gastric cancer.

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from January 1991 to August 2006; the search terms were reported. Reference lists were also checked for additional studies. Only studies written in English were eligible for inclusion in the review. The most recent publication was included if studies had multiple publications, unless the older study reported data from an RCT.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and prospective or retrospective non-randomised studies were eligible for inclusion in the review.

Specific interventions included in the review
Studies comparing LADG and CODG were eligible for inclusion. Lymph node dissections levels D1 and/or D2 with or without alpha or beta were reported in the included studies; the majority of studies reported D1 dissections.

Participants included in the review
Patients with gastric cancer were eligible for inclusion. The majority of included patients were assumed to have early gastric cancer (EGC) infiltrating the mucosa and/or submucosa.

Outcomes assessed in the review
Studies had to report short-term outcomes to be eligible for inclusion. The primary outcome measures evaluated in the review were operative findings, post-operative complications and operation-related mortality, and post-operative clinical course. Operative findings included operating time, blood loss and total number of dissected lymph nodes. Post-operative complications included overall complications, anastomotic leakage and stenosis, post-operative ileus, pulmonary complications and wound infection. Post-operative clinical course included bowel function recovery, frequency of additional analgesic requirements, number of days with body temperatures of more than 37 degrees C, duration of post-operative hospital stay, and white blood cell counts and C-reactive protein levels on days 1, 3 and 7.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

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

Data extraction
Two authors independently extracted the study data; any discrepancies were resolved through consensus. Raw data were extracted where possible and, if not, data were estimated from graphs where available and used to calculate a mean difference with standard deviation. If necessary, mean differences and standard deviations were estimated from medians and ranges; in the absence of a range or measure of dispersion, the standard deviation was estimated by halving
the mean or median. For dichotomous data, odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects meta-analysis to give a pooled weighted mean difference (WMD) or OR with 95% CIs.

How were differences between studies investigated?
Statistical heterogeneity was evaluated using the chi-squared test (significance threshold, p<0.1) and the results of the I-squared test were reported. Some subgroup analyses of study design (i.e. RCT versus non-randomised studies) were reported.

Results of the review
Sixteen studies (n=1,611) were included in the review: 4 RCTs and 12 non-randomised retrospective studies. All but one of the included studies was conducted in either Japan or Korea; most were published in 2005 or 2006.

The results presented are for RCTs only, unless otherwise stated.

Operative outcomes.

Compared with LADG, CODG was associated with statistically significantly shorter operating times (WMD 83.1 minutes, 95% CI: 40.5, 125.6, p<0.001; there was evidence of statistical heterogeneity) and a statistically significantly greater number of dissected lymph nodes (WMD -4.34, 95% CI: -6.66, -2.02, p<0.001; there was no evidence of statistical heterogeneity). LADG was also associated with significantly less blood loss than CODG (WMD -104.3, 95% CI: -189.0, -19.5, p=0.02; there was evidence of statistical heterogeneity).

Morbidity and mortality.

Compared with CODG, LADG was associated with statistically significantly fewer overall complications (OR 0.41, 95% CI: 0.20, 0.85, p=0.02). The likelihood of post-operative ileus was significantly lower after LADG than CODG (OR 0.27, 95% CI: 0.09, 0.84, p=0.92 for 6 studies; OR 0.31, 95% CI: 0.01, 7.91 for 1 RCT only). No statistically significant differences were reported between LADG and CODG in anastomotic stenosis (5 studies including 2 RCTs), anastomotic leakage (7 studies including 2 RCTs), wound infection (9 studies including 2 RCTs) or mortality (2 retrospective non-randomised studies).

Post-operative clinical course.

Compared with CODG, LADG was associated with a significantly shorter bowel function recovery period, as measured by the number of days to first flatus (WMD -0.68 days, 95% CI: -1.26, -0.09, p=0.02; based on 3 RCTs; there was evidence of statistical heterogeneity), and required less post-operative analgesics (WMD -1.69, 95% CI: -2.18, -1.21, p<0.001; based on 3 RCTs). No statistically significant difference was shown in the length of hospital stay (WMD -3.32 days, 95% CI: -7.69, 1.05, p=0.14; there was evidence of statistical heterogeneity); however, the results of all 15 studies showed that LADG was associated with shorter length of stay than CODG. LADG was also associated with significantly fewer numbers of days with a body temperature greater than 37 degrees C (WMD -1.25, 95% CI: -1.69, -0.82, p<0.001; based on 5 retrospective non-randomised studies). White blood cell counts and C-reactive protein levels were significantly lower in patients given LADG than in patients given CODG on post-operative days 1 and 3, but there were no significant differences between the two groups on day 7 (refer to publication for results).

Authors’ conclusions
Compared with CODG, LADG is associated with lower morbidity, less pain, faster bowel function recovery and a shorter hospital stay when used to treat early gastric cancer.

CRD commentary
This review answered a clear research question and searched for a wide range of study designs in three main electronic databases.
databases. Some relevant studies might have been missed because of language restrictions (particularly as the included studies were mostly conducted in Japan or Korea) and the apparent lack of specific attempts to locate unpublished studies. The generalisability of the findings may also be limited given that the majority of the included studies were from either Japan or Korea. It is difficult to assess the risk of error and bias in the review methods since the authors did not report how the studies were selected for inclusion. However, both non-randomised and more robust RCTs were included in the review.

The authors carried out subgroup analyses according to study design but, nevertheless, the lack of a validity assessment makes it difficult to assess the reliability of the findings, even from the RCTs. Randomised studies have a more robust overall design in comparison with non-randomised studies, but may still suffer from significant methodological weaknesses which can affect their reliability. The inclusion of a wide range of study designs also appears to contribute to the high level of statistical heterogeneity observed in the overall effect sizes; statistical heterogeneity is usually reduced, however, by including only RCTs. Other factors contributing to the observed heterogeneity were not explored. This suggests that the overall effect sizes are likely to be unreliable.

Overall, the review’s general conclusions appear to be supported by the data presented, but the reliability of the effect sizes is unclear given the lack of a validity assessment and the potential for language and publication bias.

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

Research: The authors stated that further studies are required to investigate ‘the prevalence of standard techniques and the development of an education and training system’. In addition, large well-designed RCTs are required to follow ‘the learning curve of LADG in order to increase the statistical power and to elucidate oncological clearance, including the quality of lymphadenectomy and long-term outcomes’.

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