Meta-analysis of effectiveness and safety of D2 plus para-aortic lymphadenectomy for resectable gastric cancer

CRD summary
The authors concluded that there was no definite indication that D2 plus para-aortic lymphadenectomy should be used to treat resectable gastric cancer. The authors’ conclusions reflected the limited evidence presented, but the reliability of the review is hindered by potential biases in the search and study selection stages.

Authors’ objectives
To evaluate the effectiveness and safety of D2 plus para-aortic lymphadenectomy (PALD) compared with the conventional D2 technique in patients with resectable gastric cancer.

Searching
PubMed, EMBASE and The Cochrane Library were searched for published English-language articles up to May 2009. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared D2 plus para-aortic lymphadenectomy (including dissection of middle para-aortic lymph nodes, 16a2, 16b1) with standard D2 lymphadenectomy in patients with resectable, biopsy-diagnosed, gastric adenocarcinoma were eligible for inclusion in the review. Studies had to report more than one of the specified outcome measures. The primary outcome of interest was five-year overall survival. Secondary outcomes were in-hospital or postoperative 30-day mortality and postoperative morbidity (including anastomotic leakage, pancreatic fistula, abdominal abscess, postoperative bleeding, obstruction or ileus, wound infection and cardiocirculatory and pulmonary complications associated with the procedure).

The included trials were carried out in Poland, Japan, Korea and Chinese Taiwan areas. Most participants had T1 to T4 stage cancer. One trial accepted use of adjuvant chemotherapy.

The authors did not state how many reviewers selected the studies.

Assessment of study quality
Trial quality assessment was carried out using the Jadad scale to award a score between zero (lowest quality) and 5 (highest quality) based on randomisation, blinding, withdrawals and dropouts.

Two reviewers independently assessed trial quality. Disagreements were resolved by discussion or reference to a third reviewer.

Data extraction
Data were extracted by two independent reviewers on the number of events (derived from percentages, where possible) for primary and secondary outcomes. These data were used to calculate relative risks (RR) and 95% confidence intervals (CI). Disagreements were resolved by discussion or reference to a third reviewer.

Methods of synthesis
Relative risks and 95% CIs were pooled in a fixed-effect meta-analysis (Mantel-Haenszel method). Where statistically significant heterogeneity was present (measured by $X^2$ and $I^2$ statistics), a random-effects model was used. Sensitivity analysis was carried out by excluding one trial with spurious results.

Results of the review
Three RCTs (n=1,067) were included in the review. Two trials scored 2 and one trial scored 3 in the quality assessment.
There was no statistically significant survival benefit for D2 plus para-aortic lymphadenectomy compared with the conventional D2 technique (two trials, n=792, $I^2=0\%$) or increased probability of postoperative mortality (three trials, n=1,067, $I^2 = 45\%$). Postoperative morbidity was not significantly different between the two interventions. However, the relative risk for the latter became statistically significant when one trial was removed from the analysis, which suggested an overall higher postoperative morbidity rate for D2 plus para-aortic lymphadenectomy (RR 1.41, 95% CI 1.12 to 1.78; two trials, n=792).

**Authors' conclusions**
There was no definite indication that D2 plus para-aortic lymphadenectomy should be used to treat resectable gastric cancer.

**CRD commentary**
The review question was clear and supported by detailed inclusion criteria. Relevant data sources were searched, but language bias could not be ruled out. There were no reported attempts to locate unpublished material, which meant that publication bias was also a possibility. Attempts were made to minimise error and bias in the processes of validity assessment and data extraction; the process of study selection was less clear. An appropriate validity assessment tool was used to evaluate trial quality, although only summary scores were presented and demonstrated limited reliability. Study details were presented clearly, heterogeneity was assessed and the chosen methods of synthesis appeared appropriate. The authors' conclusions reflected the limited evidence presented. The reliability of the review is hindered by potential biases in the search and study selection stages.

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

**Practice:** The authors stated that D2 plus para-aortic lymphadenectomy was not recommended as routine surgical treatment for gastric cancer.

**Research:** The authors did not state any implications for research.

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