A comparison of pancreaticoduodenectomy with extended pancreaticoduodenectomy: a meta-analysis of 1909 patients

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CRD summary
This review showed no difference in survival and little difference in adverse events between patients who underwent standard and extended pancreaticoduodenectomy. The possibility of missing studies, unclear validity of the included studies and limitations in the analysis mean that these findings should be interpreted with caution.

Authors' objectives
To compare pancreaticoduodenectomy and extended pancreaticoduodenectomy.

Searching
MEDLINE, EMBASE and The Cochrane Library were searched for peer-reviewed full-text studies published up to July 2006 (exact search dates not reported). Search terms were reported. No language restrictions were applied. References of retrieved studies were screened.

Study selection
Studies that compared pancreaticoduodenectomy and extended pancreaticoduodenectomy and reported at least one of the following outcomes were eligible for inclusion: survival (primary outcome); operative time (minutes); blood loss (mL); blood transfusion requirement (units of blood); duration of nasogastric tube drainage; length of hospital stay (days); administration of chemotherapy or radiotherapy; and short-term adverse events (wound infection, postoperative mortality, delayed gastric emptying, biliary leak and fistula, pancreatic leak and fistula, intra-abdominal abscess, cholangitis, postoperative haemorrhage and need for relaparotomy). The proportion of men in the included studies was 45% (where reported). Age at surgery ranged from 57 to 66 years.

Two reviewers independently selected studies for inclusion; discrepancies were resolved by a third reviewer.

Assessment of study quality
The Newcastle-Ottawa Scale was used to assess non-randomised study quality; the authors stated that they modified the scale to fit the review, but exact details on items assessed was unclear. It was unclear whether this scale was also used to assess the quality of the randomised controlled trials (RCTs). All studies were assessed for patient selection, comparability of the two study groups and assessment of outcome. Studies that scored 8 or more stars were considered to be of high quality, but it was unclear how the quality score was estimated or what the maximum score was. Two reviewers independently assessed study quality. Disagreements were resolved by a third reviewer.

Data extraction
Survival from the time of resection following pancreaticoduodenectomy and extended pancreaticoduodenectomy was extracted as hazard ratios (HR) and standard errors from Kaplan-Meier plots. Odds ratios (OR) were calculated for dichotomous outcomes. Mean differences (MD) were calculated for continuous measures. To allow calculation of ORs for studies that contained 0 in one cell of the 2x2 table, 0.5 was added to all cells. Two reviewers independently extracted data.

Methods of synthesis
Pooled hazard ratios, odds ratios and weighted mean differences (WMD) were estimated, together with 95% confidence intervals, using random-effects models. Heterogeneity was assessed using Cochran’s Q test. Heterogeneity was investigated by restricting the analysis to randomised controlled trials (RCTs), high-quality studies and studies published from 2000 onwards. Publication bias was assessed using funnel plots based on the hazard ratios.

Results of the review
Fifteen studies were included (n=1,909): three RCTs (n=454); three prospective non-randomised studies; and nine
retrospective studies. Study quality scores ranged from 5 to 12. The maximum quality score was unclear and results for individual items were not presented.

Survival was improved in extended pancreaticoduodenectomy compared with pancreaticoduodenectomy, but this result was not statistically significant and there was substantial heterogeneity between studies (p=0.006). Restriction of the analysis to RCTs showed no differences in survival between the two techniques, although heterogeneity was reduced (p=0.20).

Significantly more lymph nodes were harvested from patients who underwent extended pancreaticoduodenectomy (WMD 14 nodes, 95% CI 11 to 17; seven studies) and operative time was longer (WMD 48.9 minutes, 95% CI 28.0 to 69.9; eight studies). Restriction of the analysis to RCTs supported these findings, although effects were smaller (WMD 7 nodes, 95% CI 1 to 13; three RCTs and WMD 37 minutes, 95% CI -56.8 to -17.1; three RCTs).

There was some evidence of increased delayed gastric emptying with extended pancreaticoduodenectomy (OR 0.59, 95% CI 0.36 to 0.96; six studies), but this was not found in the analysis restricted to RCTs. Perioperative adverse events and mortality were similar between the groups.

**Authors’ conclusions**

Extended pancreaticoduodenectomy was associated with greater nodal harvest and fewer positive resection margins than pancreaticoduodenectomy. However, the risk of delayed gastric emptying was increased and no significant survival benefit was shown.

**CRD commentary**

The review addressed a clear question. Inclusion criteria were defined in terms of intervention and outcomes; broad criteria were applied to study design. The literature search was adequate for published studies, but the review was restricted to full-text peer-reviewed published articles and so there was a possibility of publication bias (assessed in the review). Appropriate steps were taken to minimise bias and errors in the selection of studies and extraction of data, but it was unclear whether such steps were also taken for the assessment of study quality. Study quality was assessed, but the criteria on which this was based were not clearly reported and results were presented as summary quality scores with the maximum possible score unclear. The validity of the included studies was, therefore, unclear. Very limited details were provided on the included studies, especially in relation to participants, so the generalisability of the review findings was unclear. Individual study results were not reported, which made it difficult to interpret most meta-analyses. Methods of analysis were appropriate and some attempts were made to investigate heterogeneity. A sensitivity analysis restricted to RCTs was conducted; this was not given appropriate emphasis in the results, which focused on the pooled measures derived from all studies. The authors’ conclusions should be interpreted with caution due to the possibility of publication bias, limitations in the quality assessment and failure to place appropriate emphasis on the sensitivity analysis based on the RCTs.

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

**Practice**: The authors stated that standard standard pancreaticoduodenectomy was the procedure of choice for pancreatic head adenocarcinoma and peri-ampullary neoplasm.

**Research**: The authors stated that better designed, adequately powered studies that compared pancreaticoduodenectomy with extended pancreaticoduodenectomy were required, especially in subgroups with peri-ampullary neoplasm.

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