Systematic review and meta-analysis of prophylactic gastroenterostomy for unresectable advanced pancreatic cancer

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CRD summary
The review evaluated safety and effectiveness of prophylactic gastroenterostomy for unresectable advanced pancreatic cancer and found a significantly lower level of long-term gastric outlet obstruction with no significant difference in morbidity and mortality. The limitations of the review make the extent to which the authors’ conclusions are reliable unclear.

Authors' objectives
To evaluate the safety and effectiveness of prophylactic gastroenterostomy for unresectable advanced pancreatic cancer.

Searching
National Centre for Biotechnology Information, NLM Gateway and Cochrane Central Register of Controlled Trials (CENTRAL) databases were searched to August 2008 for publications in any language. The Internet and authors’ libraries were searched. The bibliography of each retrieved article was handsearched. Search terms were reported.

Study selection
Retrospective and prospective studies that compared a prophylactic gastroenterostomy, biliary bypass or both against no gastroenterostomy for unresectable pancreatic cancer were eligible for inclusion. Studies from before 1990 were excluded. The intervention in all included prospective studies was gastrojejunostomy. Controls in two prospective studies received no prophylactic bypass. In the third prospective study the intervention was gastrojejunostomy plus biliary bypass versus biliary bypass alone. Patients in two prospective studies had unresectable periampullary cancer. No details of patients’ age or sex was provided. Range of mean survival was 7.6 to 8.3 months. Eligible outcomes were overall morbidity and mortality, number of clinically relevant gastric outlet obstructions, delayed gastric emptying and duration of hospital stay.

Two independent researchers were involved in the literature search and study selection. The authors did not state how disagreements were resolved.

Assessment of study quality
Methodological quality was assessed separately for the prospective studies using the following criteria: definition of outcome variables and complications; completeness of follow-up; and statistical analyses. Further details of the methods of assessment of methodological quality were published in Michalski et al. 2007 (see Other Publications of Related Interest).

The authors reported neither how many reviewers performed the validity assessment nor how the quality assessment was performed for the retrospective studies.

Data extraction
The number of events for each outcome was extracted in order to calculate summary odds ratio (OR) and 95% confidence intervals (95%CI).

The authors did not report how many reviewers performed the extraction.

Methods of synthesis
Odds ratios for the three included prospective trials were pooled using a random-effects model (DerSimonian and
Effects on duration of hospital stay were analysed using weighted mean differences (WMD). Between-study heterogeneity was determined using I² tests and visually using forest plots; p<0.05 was considered to be significant. A sensitivity analysis was carried out to assess effects of study size, grade or stage of disease and type of surgery performed. A narrative synthesis was provided for the retrospective studies, but it was not comprehensive for the eight included retrospective studies and included non-eligible studies.

**Results of the review**

Three prospective studies were included in the meta-analysis (n=218 patients): two randomised controlled trials (n=152); and one non-randomised study with a control group (n=66 patients). In the nonrandomised study, double bypass was performed only in patients with signs and intraoperative findings of gastric outlet obstruction. Eight retrospective studies and three reviews were also reported in the text of the review.

Meta-analysis of prospective studies found a significantly lower number of long-term gastric outlet obstructions with prophylactic gastroenterostomy versus controls (OR 0.06, 95% CI 0.02 to 0.21, p<0.001; I²=0%, p=0.7), but no significant differences for rates of delayed gastric emptying, postoperative morbidity or postoperative mortality. There was no significant heterogeneity for long-term gastric outlet obstruction, delayed gastric emptying and postoperative morbidity or mortality.

Meta-analysis was possible for two trials for mortality. Following prophylactic gastroenterostomy, duration of hospital stay was significantly longer than controls (WMD 3.1 days, 95% CI 0.7 to 5.5, p=0.01; I²=99.1%, p<0.001). A meta-analysis for the two trials that compared prophylactic gastroenterostomy versus no bypass (excluding a trial that combined gastrojejunostomy plus biliary bypass versus biliary bypass alone) found no significant difference in duration of hospital stay with significant heterogeneity (I²=97.9%, p<0.001).

The single trial of gastrojejunostomy plus biliary bypass versus biliary bypass alone showed a significantly higher duration of hospital stay for the double bypass group (WMD 6.9 days, 95% CI 6.01 to 7.79).

The authors reported that analysis of retrospective studies did not reveal any advantage or disadvantage for prophylactic gastroenterostomy.

**Authors' conclusions**

Prophylactic gastroenterostomy should be performed during surgical exploration of patients with unresectable pancreatic head tumours because it reduced incidence of long-term gastroduodenal obstruction without impairment of short-term outcome.

**CRD commentary**

The review question was defined. Inclusion criteria for prospective studies were defined in terms of study design, participants, intervention and control outcomes and participants. Inclusion criteria for retrospective studies were not clearly defined and the review included results from some ineligible studies (such as reviews). Some relevant databases were searched in any language. No adequate attempts were made to identify unpublished studies. Publication bias was not assessed. Quality of prospective studies was apparently assessed, but no details of criteria or results were reported, which meant that results from these studies and hence the review may not be reliable. Methods were used to minimise error and bias during the selection of studies; it was not reported whether similar methods were used for data extraction and validity. Some relevant study details were reported, but many were not. A narrative synthesis was provided for the retrospective studies; unfortunately this included both included and excluded studies and it was difficult to differentiate between the two. Reporting results from prospective and retrospective studies separately was appropriate, but pooling data from studies of different designs (RCTs and nonrandomised studies) may not have been appropriate. RCTs were analysed separately only for the duration of hospital stay. Groups in the non-randomised study appeared dissimilar at baseline (only patients with gastric outlet obstruction underwent the double bypass) and this may have influenced results. A sensitivity analysis was carried out for the prospective studies, but limited details were reported. In view of the potential limitations arising from the review process, uncertainties about the quality of included studies and the fact that the conclusions were based on evidence from relatively small studies, the reliability of the authors’ conclusions is unclear.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

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

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