Pancreatic stents for prophylaxis against post-ERCP pancreatitis: a meta-analysis and systematic review

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CRD summary
This review of pancreatic stent placement after ERCP concluded that they significantly decreased the odds of post-ERCP pancreatitis and lowered both mild and moderate post-ERCP pancreatitis. Despite the lack of detail on study selection, this was a well-conducted review and its conclusions and recommendation for further research seem appropriate.

Authors' objectives
To review the role of prophylactic pancreatic stents for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis (ERCP).

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to January 2010 without language restrictions; search terms were reported. Reference lists were searched and a manual search of abstracts submitted between 2000 and 2009 to Digestive Disease Week, American College of Gastroenterology and United European Gastroenterology Week was also performed.

Study selection
Studies that compared pancreatic stents with placebo or no treatment in adults were eligible. All study designs, apart from case series, were included. Studies that didn't report post-ERCP pancreatitis as a study endpoint, or studies that compared stents with other drugs or other stents or drains were excluded.

All trials were published between 1993 to 2009, six studies were conducted in the United States and two in Japan. The proportion of female patients ranged from 36% to 84.2% in the studies and mean/median ages ranged from 44 to 69 years. All trials used stents sizes of size 5F, or 5F to 7F. Four trials used stents of 2 to 2.5cm in length and three trials used stents 3cm or longer. One trial did not report the stent length. Flanged stents were used in four trials and one trial used un-flanged stents. Five trials used polyethylene stents. The indications for ERCP varied. Outcomes were post-ERCP pancreatitis, hyperamylasaemia, severity of pancreatitis and complications.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
The quality of randomised controlled trials (RCTs) was assessed using the Jadad scale which scores from zero to five (high quality) and covered randomisation, blinding and reporting of drop-outs.

Two reviewers independently performed the assessment, and disagreements were resolved by consensus.

Data extraction
Information on the sizes and diameter of stents and outcomes of post-ERCP pancreatitis, hyperamylasaemia and adverse events were extracted by two independent reviewers, and disagreements were resolved with the involvement of a third reviewer. For binary outcomes odds ratios (OR) were calculated, and mean differences (MD) for continuous outcomes, both with 95% confidence intervals.

Methods of synthesis
Results from RCTs were combined using fixed-effect or random-effects meta-analysis depending on the level of heterogeneity. Absolute risk reduction and number-needed-to-treat were also calculated. Heterogeneity was assessed with I² and publication bias with funnel plots. As all trials reported results on a per-protocol basis, the main meta-analysis was also performed this way. An additional intention-to-treat analysis was performed assuming that patients with a failed stent placement developed pancreatitis. Subgroup analysis was performed to assess the effect of stent size...
Results of the review
Eight RCTs (656 patients) and 10 non-randomised studies (4,904 patients) were included. Five trials had a Jadad score of three and one scored two (two trials were abstracts only and did not provide enough information for assessment).

Post-ERCP pancreatitis: Stent placement significantly reduced the odds of pancreatitis (OR 0.22, 95% CI 0.12 to 0.38; eight trials with minimal heterogeneity $I^2=0.3\%$). There was no evidence of publication bias.

Severity of pancreatitis: All studies used the Cotton et al. criteria for assessing the severity of pancreatitis. Stent placement significantly reduced the odds of mild (OR 0.39, 95% CI 0.20 to 0.76; seven trials with $I^2=0\%$) as well as moderate pancreatitis (OR 0.19, 95% CI 0.07 to 0.51; seven trials with $I^2=0\%$). However, although a trend was noted stent placement did not significantly affect severe pancreatitis.

Hyperamylasaemia: Pancreatic stent placement significantly reduced the mean levels of amylase compared with control (weighted mean difference -309.22, 95% CI -350.95 to -267.49; four trials with no significant heterogeneity).

Adverse events: Two trials reported on complications with pancreatic stents. One reported one patient with cholangitis, two with pancreatitis after stent removal and one with guidewire perforation (graded as severe). The other trial did not report any complications.

No significant differences between groups were seen in any subgroup analyses and sensitivity analyses showed similar results to the main analysis. The cumulative meta-analysis showed the efficacy of pancreatic stent placement was established by the publication of the second trial and remained constant with later trials.

Non-randomised studies: All studies except one included high-risk patients and sample sizes varied from 28 to 2,861 patients (further details of the 10 studies were tabulated in the paper). A statistically significant reduction in the incidence of post-ERCP pancreatitis was reported in five studies.

Authors' conclusions
Pancreatic stent placement after ERCP significantly decreased the odds of post-ERCP pancreatitis and lowered both mild and moderate post-ERCP pancreatitis in high risk patients.

CRD commentary
This review had clearly stated inclusion criteria. The search included efforts to locate unpublished studies and was not restricted by language so the risk of publication and language bias was low. Studies were quality assessed and data extracted by more than one person which reduced the chance of errors, but it was unclear if studies were selected in this way. Only the results from randomised trials were combined using meta-analysis; the methods seemed appropriate and additional subgroup and sensitivity analyses were performed. The results of the non-randomised studies were presented in a table.

Despite the lack of information on study selection most of this review was well-conducted and the conclusions and recommendation for further research seem appropriate.

Implications of the review for practice and research
Practise: The authors stated that pancreatic stent placement was beneficial in high-risk individuals for the prevention of post-ERCP pancreatitis.

Research: The authors suggested that future research should focus on identifying patients who would most benefit from a stent, the best timing for placement and the optimal stent duration. More research was also needed into the role of pharmacological agents in combination with stents, and the short and long-term consequences and complications of stent placement.
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