Can wire-guided cannulation reduce the risk of post-endoscopic retrograde cholangiopancreatography pancreatitis: a meta-analysis of randomized controlled trials

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CRD summary
The authors concluded that wire-guided cannulation did not significantly reduce the incidence of pancreatitis compared with contrast-assisted cannulation; further research is needed. This was a generally well-conducted review and the findings reflected the data presented, but given the small number of available trials, and the presence of statistical and clinical heterogeneity, the authors' conclusions should be treated with caution.

Authors' objectives
To compare the impact of wire-guided cannulation with conventional contrast-assisted cannulation on the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis.

Searching
PubMed, EMBASE, the Cochrane Library and the Science Citation Index were searched up to May 2009. Search terms were reported. Reference lists of retrieved articles were handsearched. The proceedings of the American Gastroenterological Digestive Disease Week and the United European Gastroenterology Week were searched from 2006 to 2008.

Study selection
Randomised controlled trials (RCTs) comparing wire-guided cannulation with conventional contrast-assisted cannulation using sphincterotomes, in patients undergoing endoscopic retrograde cholangiopancreatography, were eligible for inclusion. The outcome of interest was incidence of pancreatitis.

Included trials evaluation wire-guided cannulation compared with contrast assisted cannulation in therapeutic or diagnostic endoscopic retrograde cholangiopancreatography in patients with biliary or biliopancreatic diseases. Trials varied as to whether they used pre-cut or pancreatic stent if necessary. In all but one trial, the procedure was carried out by a single experienced endoscopist; in the remaining trial it was carried out by multiple endoscopists. The mean age of included patients ranged from 53.4 to 63.2 years and the proportion of women ranged from 33.3 to 60.8%. The percentage with sphincter of Oddi dysfunction ranged from 1.3 to 6.7%. Pancreatitis was diagnosed according to consensus guideline definitions, or pancreatic-like pain persisting for 24 hours with serum amylase increase to more than five times the upper normal limit. The severity of pancreatitis was graded according to number of days hospitalisation or Ranson's criteria. All trials were single centre and conducted in a variety of different countries.

Two reviewers independently selected the studies for review, with disagreements resolved by consensus.

Assessment of study quality
The validity of the included trials was assessed using the Jadad scale, using a three item checklist assessing randomisation, blinding and withdrawals/drop-outs. The scale gave a maximum score of 5 points; trials scoring 3 or more points were deemed high quality. The authors also assessed the adequacy of allocation concealment.

Two reviewers independently performed validity assessment, with disagreements resolved by consensus.

Data extraction
The number of patients with pancreatitis was extracted for each group and stratified according to severity. Relative risks (RR) with 95% confidence intervals (CI) were calculated for each trial. For the main analysis, data from the crossover trial were only extracted from the first stage. Intention-to-treat analyses were carried out treating patients according to their status at randomisation. The authors of the primary trials were contacted for raw data where necessary.
Two reviewers independently extracted the data, with disagreements resolved by discussion.

Methods of synthesis
Pooled relative risks with 95% confidence intervals were calculated using a fixed-effect model in the absence of statistical heterogeneity. Where statistical heterogeneity was detected at p<0.05, a random-effects model was used. Statistical heterogeneity was assessed using the $\chi^2$ test. Analyses were carried out using an intention-to-treat method.

Subgroup analyses were carried out according to the cannulation protocol (crossover versus non-crossover) and use of pre-cut technique (yes or no). It was unclear whether subgroup analyses were determined a priori.

Results of the review
Four RCTs were included for review (n=1,413); three parallel RCTs (n=1,000) and one crossover RCT (n=413). All studies scored three on the Jadad scale. One had adequate allocation concealment. None of the studies were double-blinded due to the nature of the intervention.

Incidence of pancreatitis: When all trials were combined, wire-guided cannulation did not significantly reduce the risk of pancreatitis (RR 0.34, 95% CI 0.10 to 1.17) compared with conventional contrast-assisted cannulation. There was evidence of significant statistical heterogeneity (p<0.008).

Subgroup analyses: When only parallel RCTs were included in the analysis, wire-guided cannulation was associated with a significant reduction in pancreatitis (RR 0.20, 95% CI 0.09 to 0.40). There were no significant differences between the groups in the crossover study. Wire-guided cannulation significantly reduced the risk of pancreatitis when pre-cut was used (RR 0.23 95% CI 0.11 to 0.48; two RCTs, n=600), but not when pre-cut was not used. There was no evidence of significant statistical heterogeneity for these outcomes.

Adverse Events: The incidence of bleeding was similar in the wire-guided cannulation (4.7%) and the contrast-assisted cannulation (4.0%) groups. The incidence of perforation was less in the wire-guided cannulation (0.7%) than the contrast-assisted cannulation (2.0%) groups. There were no cases of mortality in either group.

Authors' conclusions
Wire-guided cannulation did not significantly reduce the incidence of pancreatitis compared with contrast-assisted cannulation. Further research is needed.

CRD commentary
The review addressed a clear question with well-defined inclusion criteria. Several relevant databases were searched. However, only limited attempts were made to identify unpublished data and publication bias was not assessed, so bias could not be ruled out. It was unclear whether language restrictions were applied during the search, so language bias was possible. Appropriate steps were taken at all stages of the review process to minimise reviewer error or bias.

A suitable validity assessment was carried out and the included trials were of high quality. Suitable methods were used to combine the trials, but evidence of significant statistical heterogeneity was found. Some subgroup analyses were carried out. However, as the authors noted, the small number of available trials and the clinical heterogeneity between studies may have affected the reliability of the findings.

This was a generally well-conducted review and the findings reflected the data presented but, given the small number of available trials and the presence of statistical and clinical heterogeneity, the authors' conclusions should be treated with caution.

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

Research: The authors stated that further well-designed RCTs are needed, particularly in patients who are easy to
cannulate.

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