Guidewire versus conventional contrast cannulation of the common bile duct for the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis
Cheung J, Tsoi KK, Quan WL, Lau JY, Sung JJ

CRD summary
The review concluded that endoscopic retrograde cholangiopancreatography guide-wire cannulation in reduced the occurrence of post-endoscopic retrograde cholangiopancreatography pancreatitis compared with conventional contrast cannulation; it was associated with greater cannulation success, less risk after pancreatic duct manipulation, and no increase in adverse events. The authors acknowledged some limitations with the review and urged some caution when interpreting results, which appears warranted.

Authors’ objectives
To compare guide-wire guided cannulation with conventional contrast guided bile duct cannulation for the prevention of post-endoscopic retrograde cholangio-pancreatography pancreatitis.

Searching
PubMed, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), DARE, Scopus, Web of Science, ClinicalTrials.gov, CenterWatch, and OCLC PaperFirst were searched to November 2008 for articles published in any language. Search terms were reported. Four relevant conference proceedings were searched. Google Scholar was searched for the top 30 citations. Reference lists of relevant trials and review articles were scanned. Trial authors were contacted to identify additional relevant trials.

Study selection
Randomised controlled trials (RCTs) that compared guide-wire guided cannulation with conventional contrast cannulation for endoscopic retrograde cholangiopancreatography were eligible for inclusion. Trials had to report data on pancreatitis and had to report data suitable for calculating relative risks. Both cross-over and non cross-over trials were included. Trials were excluded if they were preliminary reports when final reports were available.

The included RCTs studied sphincterotome and standard catheter cannular types, with Teflon or hydrophilic soft tip guide-wires (size of 0.035 inches), where reported. The mean age of included patients ranged from 53 to 70 years; the proportion of females ranged from 27 to 62%, where reported. The percentage of common bile duct stones varied from 51 to 89%, where reported. Some trials used pancreatic duct stents and some trials used pre-cut sphincterotomy. The reported outcomes were pancreatitis, primary cannulation success, cannulation success after cross-over and adverse events.

Two reviewers independently performed study selection; disagreements were resolved by consensus or discussion with a third reviewer.

Assessment of study quality
Quality assessment was undertaken independently by two reviewers using the Jadad scale, which assessed randomisation, blinding, allocation concealment, intention-to-treat, and withdrawals/drop-outs. Trials were scored out of a maximum of 5 points. Disagreements between reviewers were resolved by consensus or discussion with a third reviewer.

Data extraction
Data were extracted on pancreatitis, primary cannulation success, cannulation success after cross-over and adverse events, and used to calculate relative risks (RR) and 95% confidence intervals (CIs).

The authors did not state how many reviewers extracted data.
Methods of synthesis
Random-effects meta-analysis, using the Mantel-Haenszel model, was utilised to generate pooled relative risks and 95% confidence intervals. Cross-over trials were pooled separately to non cross-over trials for pancreatitis. Statistical heterogeneity was calculated using the $I^2$ statistic. The number needed to treat (NNT) was calculated for all significant outcomes.

Sensitivity analyses were performed to assess the effects of meta-analysis model, publication type, and losses to follow-up. Subgroup analyses were undertaken for pre-cut sphincterotomy, and inadvertent pancreatic duct insertion/injection.

Results of the review
Seven RCTs were included in the review (n=2,128 participants), including two cross-over trials (n=745 patients) and five non cross-over trials (n=1,383 patients). Trial quality was variable, with scores ranging from 1 to 3 points. The main quality issues were unclear allocation concealment and lack of reporting of blinding of assessors.

Post-post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP): In non-crossover trials, there was a statistically significantly greater risk of PEP with conventional contrast compared with guide-wire cannulation (RR 0.38, 95% CI 0.19 to 0.76; $I^2=33%$; five trials; NNT=18). The result was not statistically significant in cross-over trials (RR 0.97, 95% CI 0.53 to 1.80). Sensitivity analysis revealed differences between full-text (RR 0.27, 95% CI 0.09 to 0.82; $I^2=56%$; three trials) and abstract only publications (RR 0.59, 95% CI 0.21 to 1.66; $I^2=0%$; two trials). There was a statistically significantly lower occurrence of PEP in the pancreatic duct manipulation guide-wire group compared with pancreatic duct manipulation CC group in the pancreatic duct manipulation subgroup (RR 0.19, 95% CI 0.06 to 0.58; $I^2=0%$; four trials; NNT =12). There was no statistical difference between treatments in the pre-cut sphincterotomy subgroups.

Bile duct cannulation success: There was a statistically significantly greater primary bile duct cannulation success rate with guide-wire compared with conventional contrast (RR 1.19, 95% CI 1.05 to 1.35; $I^2=81%$, four trials; NNT=9). There was no significant difference between groups in cannulation success after cross-over.

Adverse events: There was no statistically significant difference in the overall adverse event rate (RR 1.05, 95% CI 0.39 to 2.83; $I^2=4%$).

Sensitivity analysis that assessed the effect of losses to follow-up did not significantly alter overall effect for PEP. The use of fixed-effect modelling had no impact on results apart from in the pre-cut sphincterotomy subgroup.

Authors' conclusions
Endoscopic retrograde cholangiopancreatography guide-wire cannulation reduced the occurrence of post-endoscopic retrograde cholangiopancreatography pancreatitis compared with conventional contrast cannulation, and was associated with greater cannulation success, less risk after pancreatic duct manipulation, with no increase in adverse events.

CRD commentary
Inclusion criteria for the review were clearly defined. Several relevant databases were searched with no language restrictions. Publication bias was not assessed, although the authors searched several grey literature sources. Attempts were made to reduce reviewer error and bias in study selection and quality assessment, but it was unclear if such attempts were made for data extraction.

Quality assessment was based on a standard tool, which indicated the variable quality of the included trials. Trials were pooled using meta-analysis. Statistical heterogeneity was assessed.

The authors acknowledged that the included trials may not be representative of clinical practice for the interventions (cannulation with guide-wire or conventional contrast alone). They also cautioned that the results may not apply to less experienced endoscopists performing endoscopic retrograde cholangio-pancreatography or to patients at a higher risk of post-endoscopic retrograde cholangiopancreatography pancreatitis. Given the poor quality of some of the included trials, this caution seems warranted.
Implications of the review for practice and research

**Practice:** The authors stated that experienced endoscopists should consider the use of guide-wire as the initial endoscopic retrograde cholangio-pancreatography cannulation method, especially when a guide-wire is likely to be required subsequently.

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

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