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SYSTEMATIC REVIEWS AND META-ANALYSES

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Early Precut Sphincterotomy Does Not Increase Risk During Endoscopic Retrograde Cholangiopancreatography in Patients With Difficult Biliary Access: A Meta-analysis of Randomized Controlled Trials

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BACKGROUND & AIMS: **Use of precut sphincterotomy during endoscopic retrograde cholangiopancreatography (ERCP) can increase the odds for cannulation success but is associated with increased risk of post-ERCP pancreatitis. Earlier, rather than delayed, use of precut sphincterotomy for cases with difficult biliary access might reduce this risk. We performed a meta-analysis of randomized controlled trials to determine how early use of precut sphincterotomy affects the risk of pancreatitis and rate of cannulation success compared with persistent standard cannulation.**

METHODS: **We searched MEDLINE, EMBASE, and the Cochrane central register of controlled trials, along with meeting abstracts, through August 2014 for randomized controlled trials in which early precut sphincterotomy was compared with persistent standard cannulation in adults with difficult biliary access. Outcomes considered included primary cannulation success, overall cannulation success, incidence of post-ERCP pancreatitis, and overall adverse event rate. Findings from a random-effects model were expressed as pooled risk ratios (RRs) with 95% confidence intervals (CIs).**

RESULTS: **We analyzed data from 5 studies (523 participants). The incidence of post-ERCP pancreatitis and success of overall cannulation did not differ significantly between the early precut and persistent standard therapy groups. Early use of precut sphincterotomy was associated with increased odds for primary cannulation success (RR, 1.32; 95% CI, 1.04–1.68). In subgroup analysis of studies that involved only fully qualified biliary endoscopists (not fellows), we found a significant reduction in risk of pancreatitis among patients receiving early precut vs the standard technique (RR, 0.29; 95% CI, 0.10–0.86).**

CONCLUSION: **Compared with standard therapy, early use of precut sphincterotomy did not increase the risk of post-ERCP pancreatitis in a meta-analysis. When the procedure is performed by qualified biliary endoscopists, early precut can reduce the risk of post-ERCP pancreatitis. Rates of primary cannulation increase with early precut. Further studies are needed to confirm these findings.**

Keywords: Post ERCP Pancreatitis; Literature Review; Risk Factor; Surgery; Liver.

Successful biliary cannulation is a key step in endoscopic retrograde cholangiopancreatography (ERCP). However, biliary cannulation can fail in up to 5%–20% of cases using standard cannulation techniques. The use of precut sphincterotomy in cases of difficult biliary access has been associated with success rates approaching 100%.[1] A precut sphincterotomy is most commonly performed by using a needle knife by either the freehand papillotomy technique, where the cut is made starting at the papillary orifice and extended incrementally upwards, or the fistulotomy technique, where the cut starts above the orifice and is extended downwards.

Despite its potential for success, the current practice is to use precut sphincterotomy only as a last resort salvage measure after multiple failed attempts at biliary cannulation by using standard techniques.[2] Reluctance for using

Abbreviations used in this paper: CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; RCT, randomized controlled trial; RR, risk ratio.

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precut sphincterotomy stems from observational reports suggesting that it is an independent risk factor for the development of post-ERCP pancreatitis.[3] Whether this observed relationship between precut and post-ERCP pancreatitis is truly causal or whether it is confounded as a result of multiple cannulation attempts that cause papillary trauma before precutting is unknown.[4]

Early, rather than delayed, institution of precut sphincterotomy during difficult biliary access may reduce the risk of post-ERCP pancreatitis by avoiding repeated papillary trauma.[5] A previous meta-analysis of randomized controlled trials (RCTs) compared post-ERCP pancreatitis incidence in early implementation of precut sphincterotomy with the standard approach and concluded that early implementation of precut sphincterotomy reduced incidence of post-ERCP pancreatitis.[6] However, this meta-analysis included 2 RCTs in which the study population was not patients with difficult biliary access.[7,8] The relationship between precut sphincterotomy and post-ERCP pancreatitis in people with difficult biliary access therefore remains unclear.

We performed a meta-analysis of RCTs to determine how use of early precut sphincterotomy affects the risk of pancreatitis and cannulation success rate when compared with persistent standard cannulation in patients with difficult biliary access.

Methods

Eligibility Criteria

We included RCTs where early precut sphincterotomy was compared with persistent standard cannulation in adults with difficult biliary access. The term *difficult biliary access* is poorly defined, so we included all RCTs where patients were randomized after a period of initial failed cannulation. Both papillotomy and fistulotomy techniques of precut were allowed in the intervention arm. No language restrictions were placed.

For meta-analysis we included studies that considered the outcomes of (1) post-ERCP pancreatitis and (2) overall cannulation success. In defining overall cannulation success in the standard therapy arm, we included studies that considered cannulation to be successful even if the use of salvage precut was required to complete the ERCP; this is in concordance with standard clinical practice. For analysis of secondary outcomes we included studies that considered (1) successful primary cannulation, which is defined as success with randomized technique alone (ie, without need for salvage therapy), and (2) overall adverse event rate.

Information Sources

Trials were identified by using electronic searching of MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) (inception to August 2014) by using a comprehensive search strategy (Supplementary Table 1). The bibliographies of each potential RCT and review articles identified were searched for additional articles. Hand searching of abstracts submitted for American Gastroenterology Association Digestive Disease Week 2014 was also performed.

Data Collection and Data Items

All potential RCTs were assessed independently by 2 reviewers for relevance. If any issues regarding inclusion or exclusion were identified, they were resolved through discussion.

Two reviewers extracted data from eligible studies through the use of a standardized template. The following details were recorded:

- Methods: study design, number of study centers and location, definition of difficult biliary access, and date of study;
- Participants: number screened and randomized, mean age, gender, indication for ERCP, inclusion criteria, and exclusion criteria;
- Interventions: study treatment, comparison, number of patients crossed over, use of post-ERCP pancreatitis prophylaxis (if yes, then what type), fellow involvement;
- Primary outcomes: (1) post-ERCP pancreatitis, (2) overall cannulation success;
- Secondary outcomes: (1) primary cannulation success, which was defined as success with randomized technique alone (ie, success without need for any salvage procedure), (2) overall adverse event rate (combined incidence of (a) pancreatitis, (b) cholangitis, (c) bleeding, (d) perforation).

Risk of Bias in Individual Studies

Risk of bias was assessed independently by 2 reviewers who used criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions.*[9] Risk of bias was assessed according to the following domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective outcome reporting, and (7) other bias.

Statistical Analysis

Data from individual studies were pooled by using Review Manager (RevMan) Version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). A random-effects model was decided on

a priori, because significant heterogeneity in study design between individual trials was evident.

Heterogeneity was assessed with inspection of the forest plots and by using χ^2 tests with n-1 degrees of freedom, where n = number of studies involved. A *P* value $\leq$.10 was defined as significant. The I^2 statistic was also inspected, with values greater than 50% consistent with significant heterogeneity. All outcomes were dichotomous variables. We expressed the summary estimate of the effect of the intervention on outcome measures as a risk ratio (RR) with 95% confidence interval (CI).

We stated a priori that endoscopist experience may affect the likelihood of pancreatitis and so planned subgroup analyses to explore whether results varied for studies performed solely by experienced endoscopists.

Results

Study Selection

Figure 1 summarizes the literature search. Six hundred fifty-seven references were identified by electronic searching of MEDLINE (N = 183), Chochrane Central Register of Controlled Trials (N = 269), and EMBASE (N = 205). One additional reference was found in the bibliographies of potential RCTs and review articles. Hand searching of abstracts submitted for American Gastroenterology Association Digestive Disease Week 2014 did not reveal any references. Three hundred two duplicate records were discarded. The remaining 356 records were screened by title and abstract. Three hundred forty-eight of these were excluded because they studied the wrong intervention (ie, not precut), had a non-randomized study design, or both.

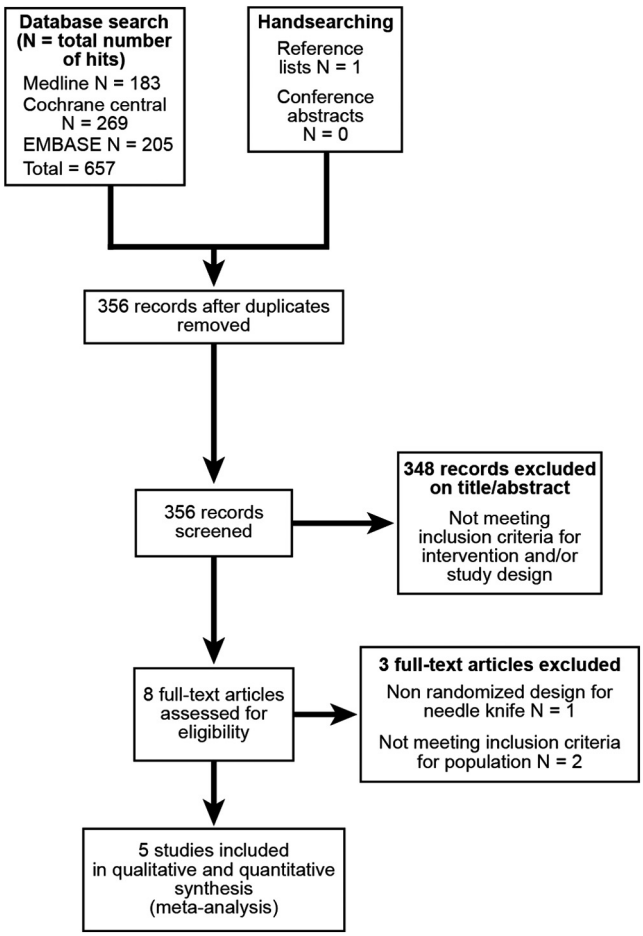

Figure 1. Search results.

Eight full-text records were reviewed for inclusion. Two studies were excluded because patients were randomized immediately to receive standard therapy or precut without any prior attempt at initial cannulation[7,8]; therefore, the population of these 2 studies could not be considered to be patients with difficult biliary access. One further study was excluded because it was a retrospective analysis of previously collected RCT data.[5] The initial RCT that this retrospective analysis was based on was not designed to study precut sphincterotomy as an intervention.

Characteristics of Included Studies

Five studies (530 participants) were included in our systematic review and meta-analysis. Study characteristics are summarized in Table 1. All studies had a randomized parallel design. One study did not describe how pancreatitis was defined.[10] All remaining studies used published consensus criteria,[11] which define post-ERCP pancreatitis as a 3-fold increase in amylase with abdominal pain <24 hours after ERCP. However, 1 study only included moderate or severe cases of pancreatitis in the final analysis.[12]

One study used prophylactic techniques to try to prevent post-ERCP pancreatitis, but this was not part of the randomized treatment, so it should not affect the comparison between the study arms.[13] The endoscopic fellow was involved in the study before randomization in 2 studies.[13,14] Only one of these studies allowed fellow participation after randomization.[13]

Several methodological differences were noted between studies. First, indication for ERCP varied. The chief indication for ERCP in most trials was for therapy of established or suspected common bile duct stones. Second, the definition of difficult biliary cannulation varied widely, ranging anywhere between failed initial cannulation after 5–12 minutes or >2–4 inadvertent pancreatic duct cannulations. Third, the time allowed for persistent attempts after randomization varied widely. Studies allowed between 10 and 20 minutes in the standard cannulation arm after randomization before deeming primary cannulation a failure. Finally, precut sphincterotomy technique varied among studies. Two studies used the freehand papillotomy technique, whereas 2 other studies used the fistulotomy technique. One study allowed both techniques.

All studies excluded patients who had previous sphincterotomy, a recent episode of acute pancreatitis, and patients with altered biliary anatomy. Sphincter of

Table 1. Characteristics of Included Trials

	Tang, 2005	Zhou, 2006	Manes, 2009	Cennamo, 2009	Swan, 2013
Methodology					
Design	Parallel[a]	Parallel	Parallel[a]	Parallel[a]	Parallel[b]
Intervention (precut technique)	Fistulotomy	Papillotomy or fistulotomy	Fistulotomy	Papillotomy	Papillotomy
Control (cannulation technique)	Non-wire guided	Both wire and non-wire guided	Both wire and non-wire guided	Wire guided	Wire guided
Location	Canada; single center	China; single center	Italy; multicenter	Italy; single center	Australia; single center
Definition of difficult biliary cannulation	Time >12 min	Time >10 min OR >2 pancreatic duct cannulations	Time >10 min OR >4 pancreatic duct cannulations	Time >5 min OR >2 pancreatic duct cannulations	Time >10 min OR >3 pancreatic duct cannulations
Endoscopic fellow involved in procedures	Yes	No	No	No	Yes
PostERCP pancreatitis prophylaxis used? (type)	No	No	No	No	Yes (pancreatic stent, wire-guided cannulation)
Randomization					
Total patients enrolled	642	948	1654	1078	690
Total randomized (ie, number with difficult cannulation)	62	91	158	146	73
• Early precut arm	32	43	80	36	39
• Standard therapy arm	30	48	78	110	34
Number of patients in control arm requiring salvage precut	3/30	N/A	50/74	32/110	22/34
Baseline demographics					
Mean age (*y*)					
• Early precut	64	63	66	68	57
• Standard therapy	67	64	65	71	59
% Female					
• Early precut	53	40	34	56	72
• Standard therapy	53	40	33	54	66
Most common indication for ERCP	Abdominal pain (54%)	Dilated CBD (30%)	Choledocholithiasis[b] (49%)	Choledocholithiasis[b] (73%)	Suspected CBD stone(s) (49%)

CBD, common bile duct.
[a]Salvage allowed after primary cannulation failure.
[b]Includes established and suspected.

Oddi dysfunction was not an exclusion criterion in any study, although only 3 trials eventually enrolled patients with sphincter of Oddi dysfunction.[13–15] One trial excluded patients with pancreatic malignancy.[13] Two trials excluded ampullary malignancy.[12,13]

Risk of Bias in Studies

Quality assessment is summarized in Table 2. All studies were conducted with a randomized controlled design, but none were blinded. However, 1 study did have blinding of outcome assessors.[15] All studies described adequate methods for sequence allocation (computer-generated list), and only 1 study failed to describe adequate concealment of allocation.[15] All but 1 study had 100% follow-up of outcome data and intention-to-treat analysis.[15] One study did not mention inclusion or exclusion criteria.[10] Two studies reported subgroup analyses that were not pre-specified a priori[13,15]; however, this was not for outcomes considered in this meta-analysis.

One study did not report calculations of statistical power.[10] All remaining studies were underpowered to detect clinically significant differences for both overall cannulation rates and post-ERCP pancreatitis incidence between the treatment arms. One study was terminated by the researchers after interim analysis found it to be significantly underpowered.[13]

Synthesis of Results

Table 3 provides a summary of results; outcome data from individual studies are provided in Supplementary Tables 2 and 3.

Comparing early precut sphincterotomy with persistent standard cannulation (with salvage precut if required), we found that there was no difference in the overall rates of successful biliary cannulation (5 studies,

Table 2. Study Quality Characteristics

	Sequence generation	Allocation concealment	Blinding: Personnel/ participants	Blinding: Outcome assessment	Outcome data	Selective reporting	Other sources of bias
Tang, 2005	✓	✓	✗	✗	✓	✓	✓
Zhou, 2006	✓	✓	✗	✗	✓	✗ - (1) Inclusion criteria not mentioned	✓
Manes, 2009	✓	?- Method of concealment not described	✗	✓	✗ - Analysis not by intention to treat.	? - (1) Primary outcomes measures not clearly stated; (2) Subgroup analysis not planned a priori[a]	✓
Cennamo, 2009	✓	✓	✗	✗	✓	✗ - Only moderate–severe cases of pancreatitis reported	✓
Swan, 2013	✓	✓	✗	✗	✗ - Trial stopped early after interim analysis showing underpowered study	✓- Subgroup analysis not planned a priori[a]	?- Pancreatitis prophylaxis used

✓Low risk of bias.
✗High risk of bias.
?Unclear risk of bias.
[a]Subgroup analysis did not affect outcomes examined in meta-analysis.

523 participants; RR, 1.01; 95% CI, 0.93–1.09), indicating no difference in success rates with either strategy.

There was no difference in overall rates of post-ERCP pancreatitis between early precut and standard cannulation (5 studies, 523 participants; RR, 0.62; 95% CI, 0.28–1.36), indicating similar risk with both strategies.

Comparison of early precut with persistent standard cannulation for primary cannulation rates found improved primary cannulation success with early precut sphincterotomy (4 studies, 372 participants; RR, 1.32; 95% CI, 1.04–1.68), although there was statistically significant heterogeneity in this analysis (Figure 2).

There was no difference in overall adverse event rates when comparing early precut with persistent standard cannulation (5 studies, 523 patients; RR, 0.85; 95% CI, 0.52–1.38), indicating equivalent risk of overall adverse events with each strategy.

Analysis of funnel plots did not reveal any evidence of publication bias for the primary outcomes (Supplementary Figures 1 and 2).

Additional Analyses

In comparing primary cannulation rates between early precut and persistent standard therapy, there was significant heterogeneity between studies ($I^2 = 74\%$). Visual inspection of the forest plot suggested that the results from Swan et al[13] were significantly discrepant from the remaining studies, although the direction of benefit was the same. The exact cause of this heterogeneity is unclear but probably relates to elements in the study design. This study varied in several ways to other studies. First, the study population had a high percentage of women and no patients with ampullary or pancreatic

Table 3. Summary of Results

	Studies (participants)	RR (95% CI)	Tests for heterogeneity: *P* value[a]	Tests for heterogeneity: I^2[b]
Primary outcomes				
Overall cannulation success rate %	5 (523)	1.01 (0.93–1.09)	.18	36%
Overall post-ERCP pancreatitis rate %	5 (523)	0.62 (0.28–1.36)	.3	19%
Secondary outcomes				
Primary cannulation success rate %	4 (372)	1.32 (1.04–1.68)	.01	74%
Overall adverse events	5 (523)	0.85 (0.52–1.38)	.52	0%

[a]*P* value of χ^2 test for heterogeneity.
[b]I^2 test for heterogeneity.

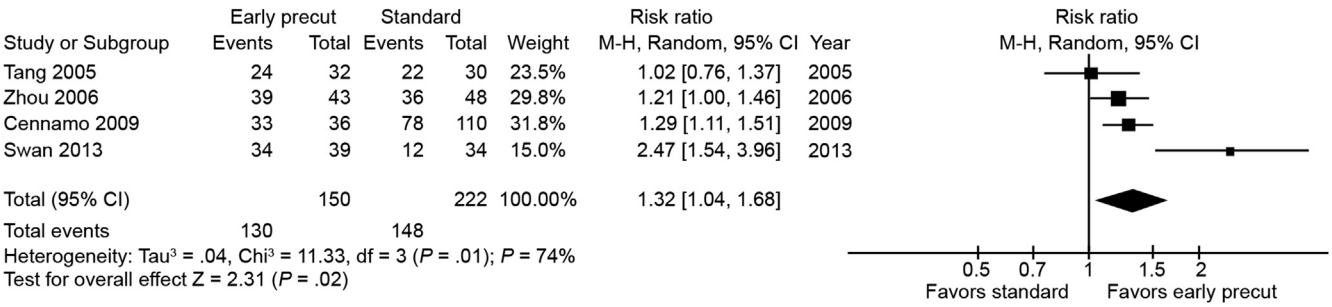

Figure 2. Primary cannulation. Early precut vs persistent standard therapy. M-H, Mantel Haenszel.

malignancy. Second, it was the only study in which a fellow participated in ERCP both before and after randomization.

We compared studies where only experienced endoscopists performed ERCP with studies where fellows were involved in ERCP. Studies involving fellows showed no difference in pancreatitis rates when comparing early precut with standard therapy (RR, 1.11; 95% CI, 0.47–2.61). However, studies involving only experienced endoscopists found a significant reduction in pancreatitis rate with early precut compared with standard technique (RR, 0.29; 95% CI, 0.10–0.86) (Figure 3).

Discussion

This meta-analysis examines how early precut sphincterotomy affects post-ERCP pancreatitis risk and cannulation success compared with persistent standard therapy in patients with difficult biliary access. We included studies that allowed the use of salvage precut sphincterotomy. The hypothesis was that the early precut strategy should result in less papillary trauma, thereby improving cannulation and reducing post-ERCP pancreatitis rates. We found no difference between the 2 strategies in either overall cannulation rate or overall post-ERCP pancreatitis rate. Overall adverse event rates were also the same.

Several aspects of this study require further analysis. First, although overall cannulation rates were similar between the 2 study arms, a large proportion of the total patients (43%) randomized to the persistent standard therapy arm eventually required salvage precut sphincterotomy to achieve successful cannulation. This meant that primary cannulation was 32% more likely to be successful with early precut sphincterotomy compared with persistent standard technique. This would suggest that once biliary access is identified as difficult, an early precut sphincterotomy strategy is more likely to be successful than persisting with standard cannulation techniques. This strategy could avoid prolonged attempts at cannulation and the need for a delayed salvage procedure, thereby reducing time under anesthesia and unnecessary papillary trauma.

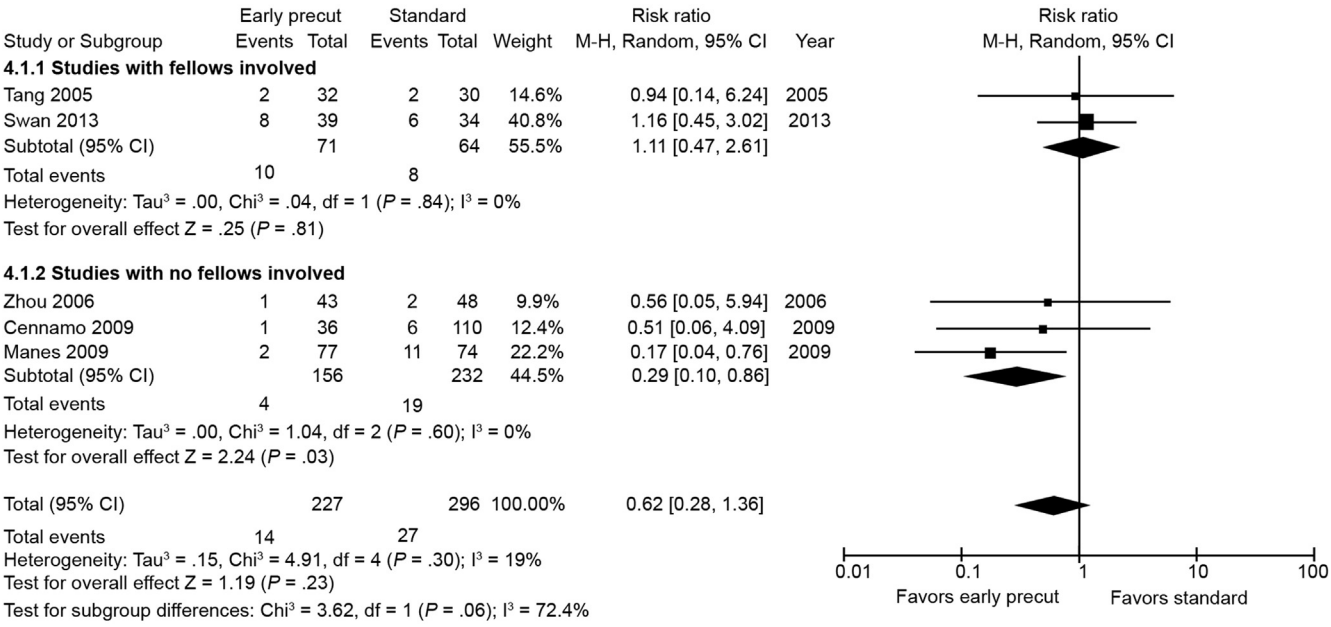

Figure 3. Subgroup analysis. Comparison of post-ERCP pancreatitis rates between early precut sphincterotomy and persistent standard therapy by fellow involvement.

Second, endoscopist inexperience and the involvement of an endoscopic trainee or fellow have been shown to be an independent risk factor for post-ERCP pancreatitis.[16,17] On subgroup analysis, studies involving only experienced endoscopists showed 3.4-fold reduction in post-ERCP pancreatitis rates with the early precut sphincterotomy strategy compared with persistent standard therapy. This would suggest that in experienced hands, early precut sphincterotomy does reduce the incidence of post-ERCP pancreatitis when compared with persistent standard therapy.

The strength of this meta-analysis is in its inclusion of only RCTs. All included trials were generally well-conducted. Furthermore, this meta-analysis had a predefined population group, patients with difficult biliary access. This population reflects those who are most likely to be subject to precut sphincterotomy in the routine clinical setting.

The main limitations of this meta-analysis relate to the small number of trials available for analysis and the heterogeneity between the designs of the included trials. The definition of difficult cannulation varied between included trials. This reflects the current absence of a consensus regarding the definition of difficult biliary access.[4] Therefore, cannulation time varied between studies before randomization into treatment groups. It is difficult to assess the impact this had on overall results because the optimal time to transition to second tier cannulation techniques like precut sphincterotomy is unknown.[18] The included trials also varied in precut sphincterotomy technique. Several precut sphincterotomy techniques are described, but the needle knife papillotomy and fistulotomy techniques are the most commonly used. Success rates have not been shown to vary between the 2 techniques.[19,20] However, there is some evidence that the fistulotomy technique may reduce the risk of post-ERCP pancreatitis compared with needle knife papillotomy.[19,20] A subgroup analysis to further investigate this was not planned because of the low number of trials that would be available in each subgroup.

Most studies included in this meta-analysis did not use post-ERCP pancreatitis prophylaxis techniques. Only the study by Swan et al[13] incorporated the use of pancreatic stents for post-ERCP pancreatitis prophylaxis. Several RCTs have proven a role for prophylactic pancreatic stenting in reducing post-ERCP pancreatitis in patients with difficult biliary cannulation.[21,22] No trials used rectal nonsteroidal anti-inflammatory drugs, which have also been shown to reduce the incidence of post-ERCP pancreatitis in high-risk patients.[23] Thus, the methods used in some of these studies do not entirely mirror current clinical practice for prophylaxis of pancreatitis. Absolute incidence of post-ERCP pancreatitis may have been lower if prophylactic measures had been used. This is unlikely to have affected the comparison of early precut with continued standard therapy because the outcomes measured in this meta-analysis were relative (ie, relative risk) rather than absolute.

All trials included in this meta-analysis were conducted in high-volume tertiary centers with involvement of highly experienced endoscopists. Correspondingly, cannulation success rates were high, and adverse event rates were low. The generalizability of these results outside of this setting is therefore questionable.

There are a number of issues highlighted by this study. First, our study suggests that the early precut strategy is at least as safe as the current standard of therapy. Therefore, endoscopists experienced in this technique should not be hesitant to use it. Second, there is a need for consensus criteria to be developed for defining difficult cannulation. Such criteria would be necessary to correctly identify the critical period beyond which the patient is at significantly increased risk of developing ERCP-related adverse events. This period would be the optimal time for institution of second tier interventions such as precut. This definition would also be important in designing future studies assessing the safety and efficacy of precut sphincterotomy. Finally, the results of this meta-analysis are based on a small number of heterogeneous studies and thus require confirmation through further randomized trials.

In conclusion, our study shows that although there is no difference in overall cannulation rate, the institution of early precut sphincterotomy significantly improves primary cannulation rates compared with persistent standard therapy in patients with difficult biliary access. The early use of precut sphincterotomy does not increase the risk of post-ERCP pancreatitis and in experienced hands may actually reduce this risk. Further studies that use consensus criteria for defining difficult biliary access are required to confirm the safety of precut and to determine the optimal time to institute it.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at http://dx.doi.org/10.1016/j.cgh.2015.06.035.

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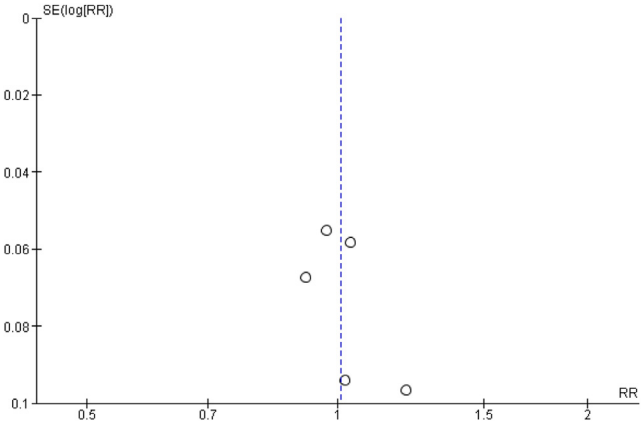
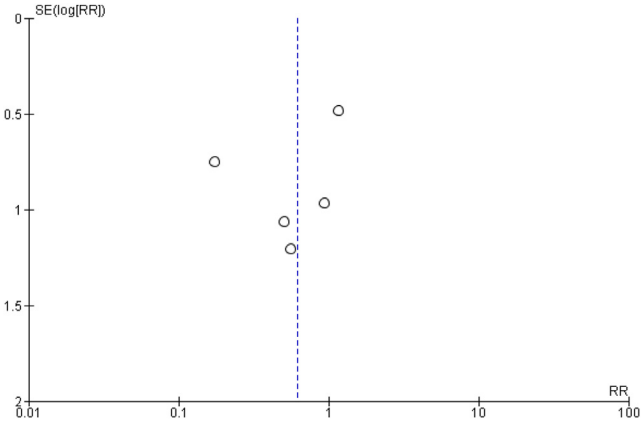
Conflicts of interest
The authors disclose no conflicts.



Supplementary Figure 1. Funnel plot of overall cannulation success rates.

Supplementary Table 1. Medline Search

	Search term	Hits
1	expCholangiopancreatography, Endoscopic Retrograde/	13,265
2	ERCP.tw,ab,ti.	6686
3	difficultcannulation.tw,ab,ti.	90
4	1 or 2 or 3	15,154
5	expSphincterotomy, Endoscopic/	2826
6	precutsphincterotomy.tw,ab,ti.	71
7	precutpapillotomy.tw,ab,ti.	50
8	needle-knife.tw,ab,ti.	436
9	5 or 6 or 7 or 8	3171
10	4 and 9	1817
11	randomized controlled trial.pt.	387,973
12	controlled clinical trial.pt.	89,778
13	randomized.ab.	283,989
14	clinical trials as topic.sh.	173,007
15	randomly.ab.	200,735
16	trial.ti.	123,439
17	11 or 12 or 13 or 14 or 15 or 16	856,240
18	10 and 17	183



Supplementary Figure 2. Funnel plot of overall post-ERCP pancreatitis rate.

Supplementary Table 2. Summary of Outcomes

	Tang, 2005	Zhou, 2006	Manes, 2009	Cennamo, 2009	Swan, 2013
Overall cannulation success rate					
Early precut	31/32	39/43	63/77	33/36	34/39
Standard	28/30	36/48	66/74	104/110	29/34
Overall pancreatitis rate					
Early precut	2/32	1/43	2/77	1/36	8/39
Standard	2/30	2/48	11/74	6/110	6/34
Primary cannulation success rate					
Early precut	24/32	39/43	NC	33/36	34/39
Standard	22/30	36/48	NC	78/110	12/34
Overall complication rate					
Early precut	4/32	2/43	7/77	3/38	9/30
Standard	2/30	2/48	14/74	7/110	8/34

NC, not calculable from given data.

Supplementary Table 3. Breakdown of Overall Complications

	Tang, 2005	Zhou, 2006	Manes, 2009	Cennamo, 2009	Swan, 2013
Cholangitis					
Early precut	1/32	0/43	0/77	0/36	0/39
Standard	0/30	0/48	0/74	0/110	0/34
Pancreatitis					
Early precut	2/32	1/43	2/77	1/36	8/39
Standard	2/30	2/48	11/74	6/110	6/34
Bleeding					
Early precut	1/32	1/43	5/77	1/36	1/39
Standard	0/30	0/48	2/74	1/110	2/34
Perforation					
Early precut	0/32	0/43	0/77	1/36	0/39
Standard	0/30	0/48	0/74	0/110	0/34
Perforation					
Early precut	0/32	0/43	0/77	1/36	0/39
Standard	0/30	0/48	0/74	0/110	0/34