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Impact of guidewire caliber on ERCP outcomes: Systematic review and meta-analysis comparing 0.025- and 0.035-inch guidewires

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ABSTRACT

Background and study aims The impact of guidewire caliber on endoscopic retrograde pancreatography (ERCP) outcomes are not clear. Recent studies have compared two guidewires, 0.035- and 0.025-inch, in randomized controlled trials (RCTs). We performed a systematic review and meta-analysis of available RCTs to assess if different caliber would change the outcomes in ERCP.

Patients and methods A systematic search of PubMed/Medline, Embase, Cochrane, SciELO, Global Index Medicus and Web of Science was undertaken through November 23, 2021 to identify relevant RCTs comparing the two guidewires. Binary variables were compared using random effects model and DerSimonian-Laird approach. For each outcome, risk-ratio (RR), 95 % confidence interval (CI), and *P* values were generated. $P<0.05$ was considered significant.

Results Three RCTs with 1079 patients (556 in the 0.035-inch group and 523 in the 0.025-inch group) were included. The primary biliary cannulation was similar in both groups (RR: 1.02, CI: 0.96–1.08, $P=0.60$). The overall rates of PEP were also similar between the two groups (RR: 1.15, CI: 0.73–1.81, $P=0.56$). Other outcomes (overall cannulation rate, cholangitis, perforation, bleeding, use of adjunct techniques) were also comparable.

Conclusions The results of our analysis did not demonstrate a clear benefit of using one guidewire over other. The endoscopist should consider using the guidewire based on his technical skills and convenience.

* These authors contributed equally.

Introduction

Since its first use, endoscopic retrograde cholangiopancreatography (ERCP) has advanced tremendously and has become the standard of care for the endoscopic evaluation and treatment of pancreaticobiliary diseases [1]. Nonetheless, even in 2022, biliary cannulation can present challenges and the risk of post-ERCP pancreatitis (PEP) looms over every procedure [2]. Failure of biliary tree cannulation has been noted to be as high as 20 % when attempts are made in non-specialized centers [3]. In addition, the rate of PEP following procedure varies between 1 % to 15 % [4, 5]. A recent systematic review of 13,296 patients noted an overall incidence of PEP in 9.7 %, of which 0.7% cases were severe [6].

Two most common methods of achieving biliary cannulation include contrast-assisted and guidewire-assisted biliary cannulation. The European Society of Gastrointestinal Endoscopy (ESGE) favors the use of guidewire-assisted biliary cannulation over the contrast-assisted method due to higher successful rates of biliary cannulation [7]. In addition, use of guidewire-assisted cannulation also reduces the rate of PEP [8]. Still, data on impact of guidewire caliber during ERCP are limited and need further exploration.

Recent randomized controlled trials (RCTs) have compared and evaluated the efficacy and safety of 0.025– and 0.035-inch guidewire during ERCP. Due to the small sample size of each study, we performed a systematic review and meta-analysis of available literature to perform a definitive analysis of this subject.

Methods

Search strategy

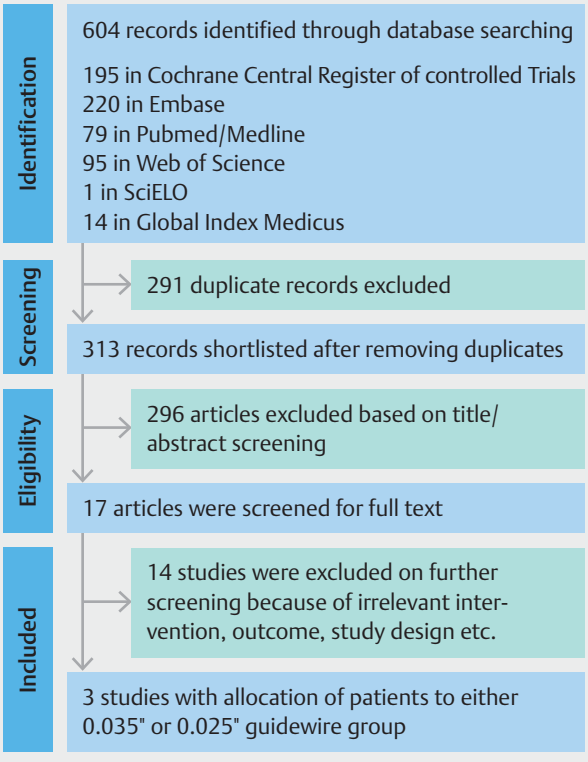
For this meta-analysis, we searched the following databases: PubMed/Medline (PubMed platform, National Center for Biotechnology Information), Embase (Embase.com platform, Elsevier), Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley), Web of Science Core Collection and SciELO (Web of Science Platform, Clarivate), and Global Index Medicus (World Health Organization) from inception through November 23, 2021, to identify all the relevant articles. Controlled subject terms and truncated keywords synonyms used for this study included terms related to ERCP, and guidewire. The search strategy was formulated for Embase and translated to vocabularies and syntax of the other databases. The search strategy was created by an experienced librarian (W.L-S) and cross-checked by another reviewer (A.I). Results were exported to EndNote (Clarivate, Philadelphia, Pennsylvania, United States) and duplicates were identified and removed using successive software algorithms with visual inspection. Relevant articles for final data extraction were shortlisted by two reviewers (A.I. and M.A.). The example search strategy using PubMed is highlighted in **Supplementary Table 1**.

Inclusion and exclusion criteria

The following parameters were considered during study screening: (1) patients undergoing ERCP for any indication; (2) utilization and comparison of 0.025- and 0.035-inch caliber guidewire for biliary cannulation; and (3) successful biliary cannulation and PEP as outcomes. We limited our screening to only include RCTs. We excluded all other studies, including editorials, case reports, case series, and case-control and cohort studies. Our search was not restricted to language or date. We further excluded abstracts as quality/bias assessment is difficult due to limited data.

Data collection

Baseline demographic data (age, sex) and outcomes (rate of successful biliary cannulation and PEP) were extracted where applicable. Two independent reviewers performed the data collection (A.I. and M.A.), and any discrepancy was discussed and resolved. In case of a crossover study, we limited our data collection up until the point of crossover. Data collection was performed in Microsoft Excel (Microsoft, Redmond, Washington, United States).



▶ **Fig.1** PRISMA diagram. From: *Page MJ, McKenzie JE, Bossuyt PM* et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: 71

▶ **Table 1** Baseline study characteristics and demographics.

	Bassan et al., 2018	Halttunen et al., 2012	Kitamura et al., 2015
Study period	June 2010 – August 2012	June 2011 – February 2012	April 2011 – March 2013
Single/multicenter	Multicenter	Single center	Single center
Total participants, n			
▪ 0.035-inch group	346	50	160
▪ 0.025-inch group	364	50	109
Study completion			
▪ 0.035-inch group	335	50	160
▪ 0.025-inch group	357	50	109
Mean age, years (SD)			
▪ 0.035-inch group	60	67.5 (17.3)	65.3 (22.2)
▪ 0.025-inch group	58	63.8 (19.1)	66.8 (17.0)
Females, n (%)			
▪ 0.035-inch group	168 (50.1 %)	33 (66.0 %)	83 (51.9 %)
▪ 0.025-inch group	186 (51.9 %)	27 (54.0 %)	68 (62.4 %)
ERCP indication, n (%)			
▪ Choledocholithiasis (suspected/established)	318	66	155
▪ Cholangitis	105	NR	8
▪ Benign stricture	8	33	12
▪ Other	261	1	94
Equipment used			
▪ 0.035-inch group	straight 5-cm hydrophilic tip (Boston Scientific)	260-cm long wire (Hydrosteer; St. Jude Medical)	450-cm long wire with outer diameter 0.91 mm, straight tip (Jagwire, Boston Scientific)
▪ 0.025-inch group	straight 7-cm hydrophilic tip (Visiglide, Olympus Corporation)	270-cm long wire (VisiGlide; Olympus Corporation)	450-cm long wire with outer diameter 0.65 mm (Boston Scientific)

NR, not reported; SD, standard deviation.

Outcomes

The primary outcomes of our analysis were the rate of successful primary biliary cannulation and incidence of PEP using either caliber of guidewire. Secondary outcomes included overall cannulation rate, use of double guidewire technique, precut sphincterotomy, pancreatic stent placement, cholangitis, bleeding, and perforation.

Study definitions

Primary biliary cannulation is defined as successful cannulation without using additional techniques (double guidewire, precut sphincterotomy). Overall cannulation is defined as the final cannulation rate after using adjunct techniques as mentioned above.

Data synthesis and statistical analysis

The DerSimonian-Laird approach with a random effects model was primarily used for pooling and comparing outcomes due to presumed heterogeneity across studies [9]. The random effects model using Empirical Bayes and Restricted Maximum Likelihood approach as well as Daimonian fixed effects model using Mantel-Haenszel approach was used as a sensitivity tool. The per-protocol method was used for assessing outcomes and the intention to treat (ITT) method was used as a sensitivity analysis. For binary outcomes, risk ratios (RR) with 95 % confidence intervals (CI) and *P* values were determined. If significant heterogeneity was encountered, a 95 % prediction interval (PI) was also calculated using the effect size, 95 % CI and tau square (T^2) heterogeneity. Forest plots were generated for each outcome. The I^2 statistic, as defined by the Cochrane handbook for systematic reviews, was used to measure heterogeneity

▶ **Table 2** Outcomes for individual studies.

	Bassan et al., 2018	Halttunen et al., 2012	Kitamura et al., 2015
Primary biliary cannulation, n (%)			
▪ 0.035-inch group	269 (80.3 %)	40 (80.0 %)	138 (86.3 %)
▪ 0.025-inch group	288 (80.7 %)	40 (80.0 %)	88 (80.7 %)
Overall cannulation, n (%)			
▪ 0.035-inch group	306 (91.3 %)	50 (100.0 %)	156 (97.5 %)
▪ 0.025-inch group	326 (91.3 %)	49 (98.0 %)	101 (92.7 %)
Post-ERCP pancreatitis, n (%)			
▪ 0.035-inch group	31 (9.3 %)	1 (2.0 %)	4 (2.5 %)
▪ 0.025-inch group	28 (7.8 %)	1 (2.0 %)	3 (2.8 %)
Double guidewire cannulation, n (%)			
▪ 0.035-inch group	19 (5.7 %)	1 (2.0 %)	21 (13.1 %)
▪ 0.025-inch group	24 (6.7 %)	5 (10.0 %)	15 (13.8 %)
PD stent placement, n (%)			
▪ 0.035-inch group	16 (4.8 %)	NR	25 (15.6 %)
▪ 0.025-inch group	24 (6.7 %)	NR	16 (14.7 %)
Precut sphincterotomy, n (%)			
▪ 0.035-inch group	31 (9.3 %)	NR	11 (6.9 %)
▪ 0.025-inch group	32 (9.0 %)	NR	9 (8.3 %)
Cholangitis, n (%)			
▪ 0.035-inch group	5 (1.5 %)	0 (0 %)	2 (1.3 %)
▪ 0.025-inch group	7 (2.0 %)	0 (0 %)	0 (0 %)
Bleeding, n (%)			
▪ 0.035-inch group	6 (1.8 %)	NR	1 (0.6 %)
▪ 0.025-inch group	10 (2.8 %)	NR	2 (1.8 %)
Perforation, n (%)			
▪ 0.035-inch group	3 (0.9 %)	0 (0 %)	0 (0 %)
▪ 0.025-inch group	5 (1.4 %)	0 (0 %)	0 (0 %)

PD, pancreatic duct.

across trials [10]. Significant heterogeneity was described as a percentage of I^2 greater than 50 %. $P<0.05$ was considered statistically significant for all of the outcomes studied. Open Meta Analyst was used to compute the results (CEBM, University of Oxford, Oxford, United Kingdom). Our manuscript conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

GRADE assessment

The authors used Grading of Recommendations, Assessment, Development and Evaluations (GRADE) to assess the quality of evidence. A subjective assessment was made and translated as very low, low, moderate, and high quality based on quality of evidence [11].

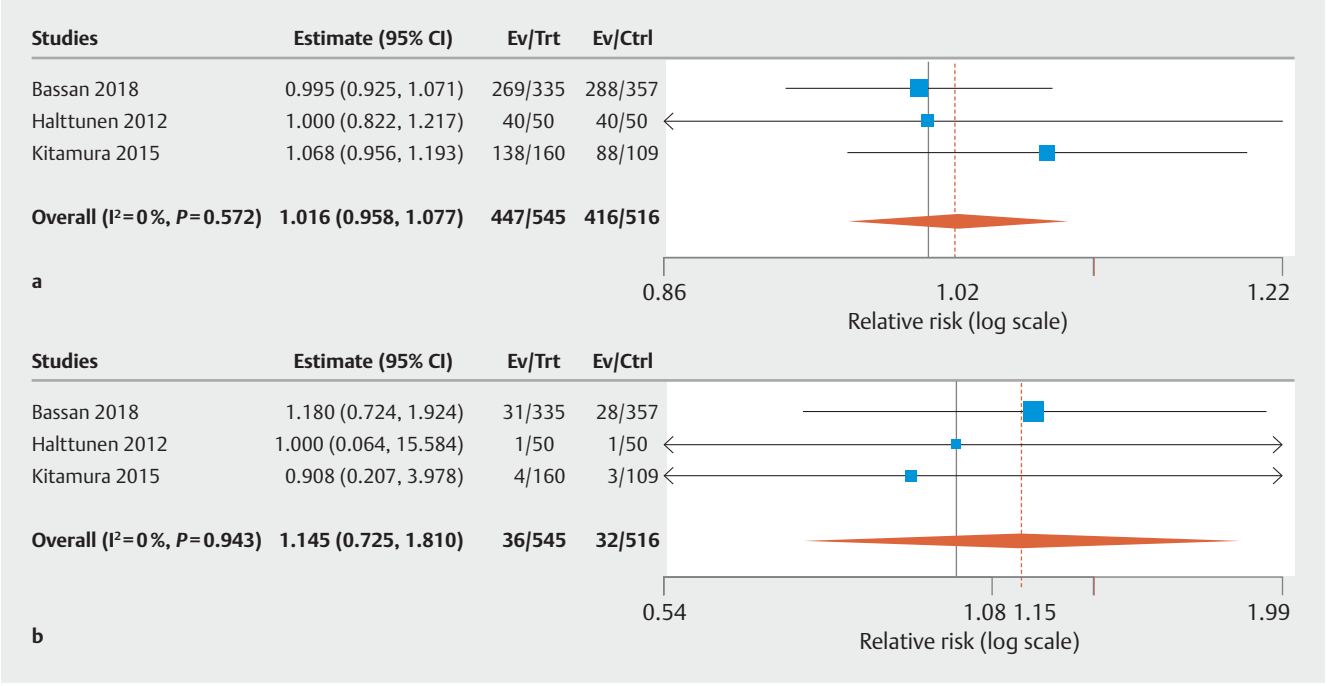
Bias assessment

The Cochrane Risk of Bias Tool was used to assess bias in included RCTs subjectively [12]. Publication bias was measured qualitatively and quantitatively using funnel plot and Egger's regression analysis, respectively. $P<0.05$ was considered significant for publication bias.

Results

Study details and demographics

After using machine deduplication and applying the selection criteria, a total of 3 RCTs with 1079 patients (556 in the 0.035-inch group and 523 in the 0.025-inch group) were included



▶ **Fig. 2** Forest plot comparing the 0.035– and 0.025-inch guidewire for rates of **a** primary biliary cannulation; and **b** post-ERCP pancreatitis.

[13–15]. Details of study selection are summarized in PRISMA diagram (▶ **Fig. 1**). The study completion rate was 98.0% and 98.7% for each group, respectively. The weighted average age was 62.2 years vs 60.4 years and female proportion was 52.1% vs. 54.5%, respectively, for the 0.035– and 0.025-inch groups. The studies were published between 2012 and 2018. The details of the study are highlighted in ▶ **Table 1**. Only one study included cases of acute gallstone pancreatitis and chronic pancreatitis [13] and only one study included cases of pancreatic cancer [15]. All studies excluded patients with altered anatomy such as (Billroth-II and Roux-En-Y) and previous sphincterotomy for any reason.

Primary outcomes

Outcomes for individual studies are summarized in ▶ **Table 2**. The primary biliary cannulation was achieved in 82.0% vs. 80.6% in 0.035– and 0.025-inch groups, respectively. This was not statistically significant (RR: 1.02, CI: 0.96–1.08, $P=0.60$, $I^2=0\%$) (▶ **Fig. 2a**). The overall rates of PEP were also similar across the group, 6.6% vs. 6.2% respectively (RR: 1.15, CI: 0.73–1.81, $P=0.56$, $I^2=0\%$) (▶ **Fig. 2b**). One study used prophylactic gabexate mesylate for prevention of PEP in all patients [15]. The results did not differ when this study was eliminated (8.3% vs. 7.1%, RR: 1.17, CI: 0.73–1.90, $P=0.51$, $I^2=0\%$). The T^2 heterogeneity was 0.0 for all outcomes and hence the PI was the same as the CI.

Secondary outcomes

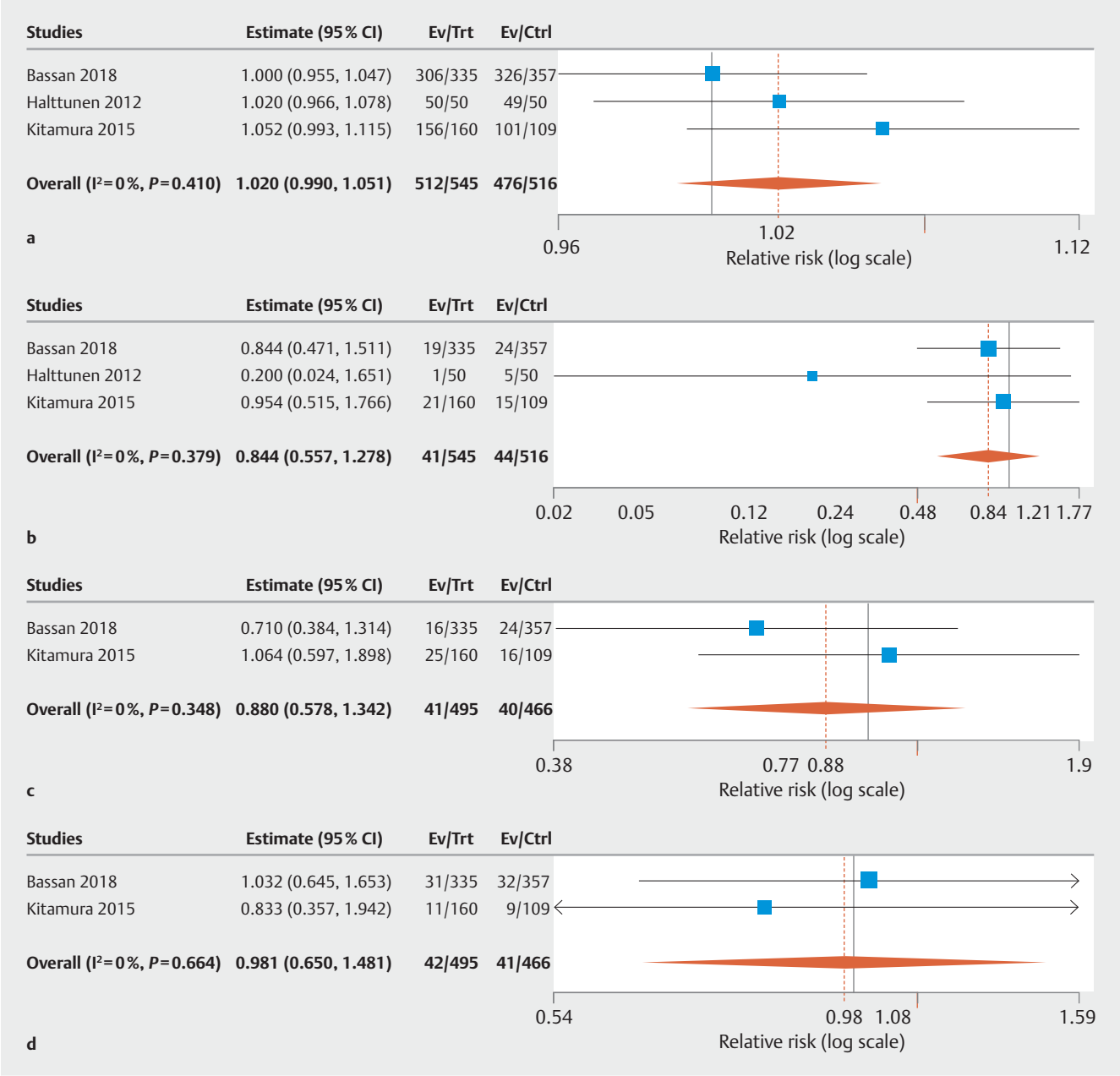
The overall cannulation rate for either group was also similar, 93.9% vs. 92.2% for 0.035-inch and 0.025-inch group respectively (RR: 1.02, CI: 0.99–1.05, $P=0.20$, $I^2=0\%$) (▶ **Fig. 3a**). Double guidewire technique was utilized in 7.5% and 8.5% of the patients in 0.035-inch and 0.025-inch group respectively (RR: 0.84, CI: 0.56–1.28, $P=0.42$, $I^2=0\%$) (▶ **Fig. 3b**). Pancreatic duct (PD) stent placement was reported by two studies and was similar between the two groups (8.3% vs. 8.6%, RR: 0.88, CI: 0.58–1.34, $P=0.55$, $I^2=0\%$) (▶ **Fig. 3c**). Similarly, the use of precut sphincterotomy was not significantly different between the two groups (8.5% vs. 8.8%, RR: 0.98, CI: 0.65–1.48, $P=0.93$, $I^2=0\%$) (▶ **Fig. 3d**). The PI was noted to be the same as CI for all outcome due to minimal T^2 heterogeneity.

Adverse events

The two groups were similar in terms of cholangitis (1.3% vs. 1.4%, RR: 0.92, CI: 0.33–2.6, $p=0.88$, $I^2=0\%$), bleeding (1.4% vs. 2.6%, RR: 0.58, CI: 0.23–1.47, $p=0.25$, $I^2=0\%$), and perforation (0.6% vs. 1.0%, RR: 0.68, CI: 0.19–2.39, $P=0.54$, $I^2=0\%$) for 0.035-inch and 0.025-inch group respectively (▶ **Fig. 4a**, ▶ **Fig. 4b**, ▶ **Fig. 4c**). The T^2 heterogeneity was none and hence the PI was same as CI for all outcomes.

Sensitivity analysis/bias assessment

The outcomes did not change when sensitivity analysis was performed using the alternate approach (random model with Restricted Maximum Likelihood and Empirical Bayes approach), fixed effects model as well as the ITT method. The publication bias was difficult to assess both qualitatively and quantitatively due to lack of adequate number of studies. The endoscopists were not blinded due to practical reasons and hence all studies were at high risk of bias.



▶ **Fig. 3** Forest plot comparing the 0.035– and 0.025-inch guidewire for rates of: **a** overall cannulation; **b** double guidewire cannulation; **c** pancreatic duct stent placement; and **d** precut sphincterotomy.

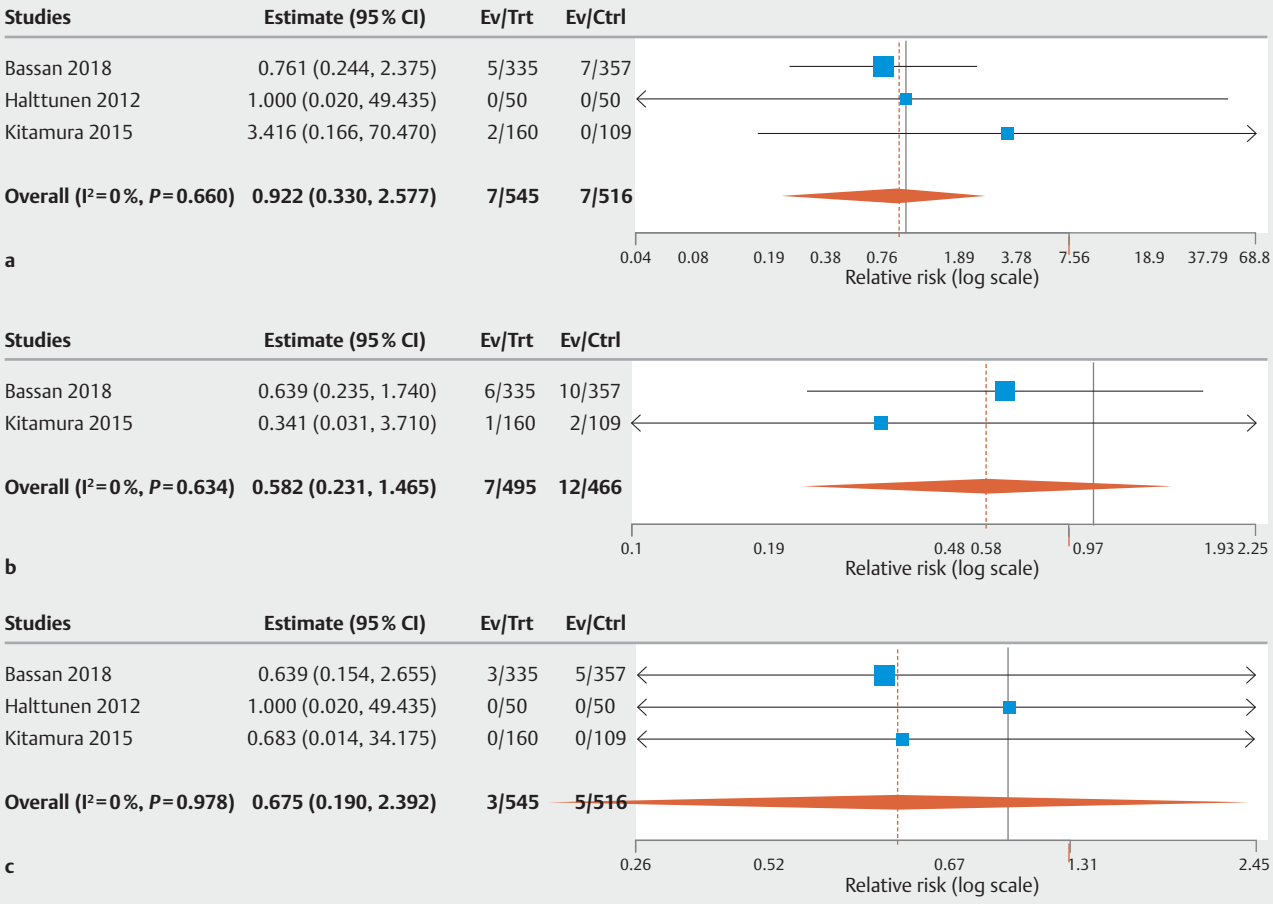
Certainty of evidence

Based on the GRADE assessment, all outcomes were rated as low quality. The rating was downgraded for inherent high risk of bias noted in **Supplementary Table 2** and different guidewire and technique used for each study.

Discussion

This meta-analysis did not reveal clear a benefit with regards to using 0.025– versus 0.035-inch guidewires with regards to ERCP outcomes, specifically primary biliary cannulation and PEP rates. In addition, no difference was noted for other outcomes i. e. use of other techniques (precut sphincterotomy, double guidewire technique, and PD stent placement) as well as adverse outcomes (cholangitis, perforation, and bleeding).

For successful therapeutic ERCP, successful cannulation of the desired duct is essential, however, cannulation (most commonly of the bile duct) can be technically challenging even in experienced hands, with success rates of 50 % to 90 % reported in literature [7]. Guidewire cannulation has been reported to increase the effective cannulation rate as well as reduce the incidence of PEP compared to contrast-assisted method [7]. In a meta-analysis of RCTs, guidewire-assisted cannulation significantly increased the rates of biliary cannulation (OR: 2.05, CI:



▶ **Fig. 4** Forest plot comparing the 0.035– and 0.025-inch guidewire for rates of: **a** cholangitis; **b** bleeding; and **c** perforation.

1.27–3.31) and decreased the incidence of PEP (OR = 0.23, CI: 0.13–0.41) [16]. Recently, studies have compared normal (0.035-inch) and thin (0.025-inch) guidewires to assess outcomes in ERCP and found no differences in outcomes.

There are a multitude of guidewire available in the market that differ based on a variety of physical parameters: shape of tip (straight, angled, curved), tip coating (ethylene tetrafluoroethylene, hydrophilic polyurethane, hydrophilic polytetrafluoroethylene), presence of spiral coiled spring, tip core material (platinum, stainless steel, nitinol, tungsten), length (205 cm, 450 cm, 480 cm) and diameter/caliber (0.018-inch, 0.025-inch vs. 0.035 inch) [17]. Endoscopists select and use guidewires based on their personal preference, technical skills, expertise and comfort level. Many endoscopists have strong preferences for one wire over another based on personal experience. The current meta-analysis is the first one to compare two different types of guidewires based on diameter/caliber. We encourage endoscopists and investigators to compare other features of guidewire in RCTs to determine the best possible wire for achieving optimal outcomes in ERCP.

Most patients included in the study were average risk for PEP. The most common indication for performing ERCP was choledocholithiasis (50.8 %), either established or suspected. The study also did not differ on the demographics of the included patients. Unfortunately, we were unable to determine predictors of PEP due to limitations of data.

The major limitation of our analysis was the low number of included studies (n = 3). Another limitation was that the studies used guidewires of different manufacturers with different features i. e., length, tip etc. We were also not able to account for endoscopists experience level, indication for ERCP, and high risk ERCP. The studies also did not comment on ability to maneuver through strictures and pushability of tools. Strengths of our study include a large number of patients (which have historically been difficult to recruit into ERCP studies). In addition, our meta-analysis only included RCTs to generate the best possible evidence. The heterogeneity in our study was almost nil further strengthening our study results. Our results were consistent across all sensitivity analyses.

Conclusions

Overall, technical outcomes and adverse events are similar between 0.025- and 0.035-inch guidewires for ERCP. Based on our findings, we recommend the endoscopists to choose a guidewire based on their comfort, preference, and skill level. We fur-

ther encourage investigators to compare other features of guidewire to assess outcomes in ERCP.

Competing interests

The authors declare that they have no conflict of interest.

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