

The ballooning time in endoscopic papillary balloon dilation for removal of bile duct stones A systematic review and meta-analysis

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Abstract

Background: So far, there was no consensus regarding balloon dilation time in endoscopic papillary balloon dilation (EPBD). Thus, we conducted a systematic review and meta-analysis to compare the stone removal and overall complication rates of dilation of short and long duration with EPBD.

Methods: The Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane Library), Web of Science, EMBASE Databases, and PubMed were searched from their inception to December 1, 2019 for all articles regarding balloon dilation time in EPBD for removal of bile duct stones. The data were extracted and the methodology quality was assessed. Meta-analysis was performed using RevMan5.3 software.

Results: Four studies involving a total of 1553 patients were included, 918 in the short dilation group and 635 in the long dilation group. The results of meta-analysis showed that there was no significant difference between the 2 different dilation groups in the complete stone removal in randomized controlled trails (RCTs) group(P=.10) and non-RCTs group (P=0.45), mechanical lithotripsy requirement (RCTs: P=.92; non-RCTs: P=.47), pancreatitis (RCTs: P=.48; non-RCTs: P=.45), bleeding (RCTs: P=.95; non-RCTs: P=.60), infection of biliary (RCTs: P=.58; non-RCTs: P=.29), perforation (RCTs: P=.32; non-RCTs: P=.37).

Conclusion: This systematic review suggests that there no significant difference in the efficacy and safety of dilation of short and long duration for removal of bile duct stones with EPBD.

Abbreviations: CBDS = common bile duct stones, EPBD = endoscopic papillary balloon dilation, ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, OR = odds ratio, RCT = randomized controlled trails.

Keywords: common bile duct stones, endoscopic papillary balloon dilation, meta-analysis, systematic review

1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) as an alternative treatment for common bile duct stones (CBDS) prior to surgical or percutaneous approaches has become a widely available and routine procedure.^[1] Endoscopic sphincterotomy

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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(EST) is indicated as standard treatment for bile duct stones during ERCP, as well as for various endoscopic diagnoses and other treatments involving the bile duct^[2]; however, EST is associated with adverse events, such as perforation, cholangitis, and bleeding.^[3] Because of the serious complications of EST, endoscopic papillary balloon dilation (EPBD) as an alternative for removal of bile duct stones was first reported by Staritz et al^[4] in 1982. Two meta-analyses^[5,6] found that EPBD results in similar outcomes with respect to overall successful stone removal compared with EST. In addition, EPBD preserves sphincter of Oddi function and decreases hemorrhage and perforation rates.^[7,8] Two recent studies^[9,10] reported that EPBD reduces the incidence of cholecystitis, cholangitis, and bile duct stone recurrence compared with EST; however, a high risk of pancreatitis following EPBD has been shown in numerous RCT studies.^[11–13]

The pancreatitis rate after EPBD ranges from 0% to 15.4% in different studies.^[5,6,14] The study reported by Tsujino et al^[15] illustrated that dilation of short duration (15 seconds) decreases the tendency for post-procedural pancreatitis than dilation of long duration (2 minutes), and no significant difference (96.6% vs 96.6%) in the efficacy of bile duct stone extraction. Other studies^[11–13,16] also recommend dilation of short duration (≤ 1 minute) to reduce EPBD-associated complications. In contrast, no pancreatitis cases were observed in the studies with dilation of long duration (3 and 5 minutes) conducted by Sato et al^[8] and Lin et al.^[17] Indeed, those studies showed that there was no consensus regarding balloon dilation time in EPBD. In fact, only one

network meta-analysis^[18] has focused on the balloon dilation time (dilation of long [>1 minute] and short duration [≤ 1 minute]) by comparing the EST-associated pancreatitis and overall complication rates reported in randomized controlled trials (RCTs). Only one RCT compared dilation of short (1 minute) and long duration (5 minutes) in the meta-analysis.^[18] Thus, we conducted a systematic review and meta-analysis to compare the stone removal and overall complication rates of short versus long dilation times. According to the previous studies, dilation <1 minute and ≥ 1 minute were defined as short and long duration, respectively, in our study.

2. Methods

All analysis results of this study were based on previously published literature and therefore did not require ethical approval or patient consent.

2.1. Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; Cochrane Library), Web of Science, EMBASE Databases, and PubMed from the time of inception to December 1, 2019 for all articles using the following terms in the keyword lists, titles, and abstracts: "endoscopic papillary balloon dilation"; "papillary balloon dilation"; "balloon dilation"; "bile duct stones"; "choledocholithiasis"; and "cholelithiasis" without language restriction. The reference lists of the included articles and key reviews were manually searched for additional citations. We attempted to contact the first or corresponding author to obtain additional information if necessary.

2.2. Inclusion criteria

We defined inclusion criteria according to (PICOS), as follows^[19]: participants, all patients with bile duct stones who underwent EPBD; interventions and comparisons—comparing dilation of short versus long duration; outcomes—complete stone removal, mechanical lithotripsy, post-ERCP pancreatitis (PEP), perforation, biliary tract infection, and hemorrhage; study design, RCTs, or comparative studies. If the duplicate publication reported by the same authors or same population was analyzed in multiple or duplicate studies, the study of higher quality or the most recent study was included; and conference abstracts were excluded because the data between publication of the full paper and the data presented in a previous conference abstract may be different.^[20]

2.3. Data extraction and quality assessment

Two of the current study authors independently evaluated the studies retrieved from the database. We excluded apparently

irrelevant studies by scrutinizing the titles, abstracts, and full text according to the abovementioned criteria. Disagreements were resolved by discussion or consulting a third author until consensus was achieved.

Two reviewers (QW and TW) independently extracted and summarized the information of the studies, including the following: name of first author, country of origin, year of publication, age and sex of patients, and number of patients; and stone size, complete stone removal, stone removal in the first session, use of mechanical lithotripsy, and complications.

The Cochrane collaboration tool,^[21] which includes the adequacy of sequence generation, allocation concealment, binding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other bias for assessing risk of bias, was used for assessing each RCT (Table 1). Two reviewers (QW and TW) independently assessed the quality score of primary trials according to the Jadad scale.^[22] Total scores ranged from 0 to 5. We defined studies as high quality with a Jadad score \geq 3 points. The Newcastle-Ottawa Scale (NOS)^[23] was used to assess the quality of non-RCTs. Each study was assigned a score ranging from 1 to 9 points. The study with \geq 6 points was considered high quality.

2.4. Data synthesis and statistical analysis

The dichotomous outcomes are reported as the odds ratio (OR) between the experimental and control groups with 95% confidence intervals (CIs). Heterogeneity between the included studies was qualitatively evaluated using I^2 and Cochran Q.^[24] A *P*-value <.1 or $I^2 > 50\%$ showed that there was statistically significant heterogeneity across the studies.^[24,25] We used a random effect model for calculations of summary estimates and the 95% CIs unless there was no significant heterogeneity, in which case results were confirmed using a fixed effects statistical model. If significant heterogeneity was detected, subgroup and sensitivity analyses were used to explore important clinical differences. Publication bias was evaluated by visual inspection of funnel plot asymmetry as described by Egger et al^[26] if necessary. The meta-analysis was performed using Review Manager software (version 5.3; The Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark).

3. Results

3.1. Search results and article review

A total of 504 articles were retrieved. After the duplicates were excluded, 310 articles remained. We excluded reviews, systematic reviews, meta-analyses, case reports, and irrelevant studies based on the title or abstract; thus, 40 articles remained. Among the remaining 40 articles, 36 were excluded for the following reasons: not relevant (n = 30); long-term outcomes of 1- versus 5-minutes EPBD (n=1)¹²⁷¹; dilation of short versus long duration

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Characteristics of	f included RCT	Γ.				
Ref.	Sequence generation	Allocation concealment	Blinding of participants	Incomplete outcome	Selective outcome	Other sources of bias
Bang BW (2010) ^[31]	Unclear	Unclear	Blinded	No missing outcome data	All prespecified outcomes reported	No
Bang BW (2015) ^[32]	Unclear	Unclear	Blinded	No missing outcome data	All prespecified outcomes reported	No

RCT = randomized controlled trails.



after sphincterotomy $(n=3)^{[28-30]}$; 1 minute versus 5 minutes $(n=1)^{[14]}$; <5 minutes versus >5 minutes (n=1).^[35] Finally, 4 studies^[15,31-33] were included. The detailed process of selecting relevant articles is shown in Fig. 1.

3.2. Study characteristics

Two of the 4 included studies were RCTs.^[31,32] These 2 RCTs compared the efficacy and safety of dilation of short (20 seconds) and long duration (60 seconds). The remaining 2 studies, which compared the efficacy and safety of dilation of short (15 seconds) and long duration (2 or 5 minutes) were non-RCTs.^[15,33] Both RCTs and non-RCTs were analyzed separately as subgroups. The quality assessment of 2 RCTs and 2 non-RCTs are shown in Tables 1 and 2, respectively. The detailed outcome data derived from the included studies are shown in Table 3.

3.3. Efficacy

3.3.1. Complete stone removal. Four studies reported complete stone removal. No apparent heterogeneity ($I^2 = 33\%$, P = .22 and $I^2 = 0\%$, P = .97) was detected based on a metaanalysis of the 2 groups. Therefore, the fixed effects model analysis was used. No statistical difference existed between the 2 different dilation groups with respect to complete stone removal (RCTs: OR=3.29, 95% CI=0.79–13.75, P=.10; non-RCTs: OR=0.63, 95% CI=0.19–2.10, P=.45; Fig. 2).

3.3.2. Stone removal in the first session. Four studies reported stone removal in the first session. Heterogeneity $(I^2 = 63\%, P = .10)$ was shown based on a meta-analysis of the RCT group, thus a random-effect model was used. No heterogeneity $(I^2 = 18\%, P = .27)$ was demonstrated in the non-RCT group. No significant difference existed in the stone removal rate in the first session for the RCT group (OR=1.81, 95% CI=0.34–9.52, P = .49). In contrast, the stone removal rate in the first session was greater with dilation of long duration than short duration in the non-RCT group (OR=0.54, 95% CI=0.39–0.74, P = .0001; Fig. 3).

3.3.3. Mechanical lithotripsy requirement rate. Four studies reported the use of mechanical lithotripsy in the process of stone removal. Heterogeneity ($I^2 = 90\%$, P = .001) was demonstrated based on a meta-analysis of the non-RCT group, thus a random-effect model was used. No heterogeneity ($I^2 = 0\%$, P = .96) was shown in the RCT group. No significant difference existed between the different dilation duration groups with respect to use

Table 2

Characteristics of included studies.

Ref.	Site	Time of EPBD	Number Short Long	M/F Short Long	Mean age (y) Short Long	Stone size(mm) Short Long	Score
Bang BW (2010) ^[31]	Korea	20.s	35	19/16	66.2+17.4	8.2+3.3	Jadad: 3
Bally BTT (2010)	norod	1 min	35	16/19	63.3 + 13.6	8.1 + 3.5	buddar b
Bang BW (2015) ^[32]	Korea	20 s	109	58/51	62.0 ± 16.9	6.5 ± 2.7	Jadad: 3
		1 min	119	74/45	63.7 ± 16.6	6.9 ± 2.9	
Takeshi T (2008) ^[15]	Japan	15s	324	191/133 191/133	70	7.1	NOS: 6
		2 min	324		70	7.2	
Hakuta R	Japan	15s	450	272/178	73.5	5	NOS: 7
(2017) ^[33]		5 min	157	106/51	75	5	

EPBD = endoscopic papillary balloon dilation.

Table 3

Outcome data derived from the included studies n (%).

		Complete	Stone removal	Mechanical	Overall			Infection	
Ref.	EPBD	stone removal	in the first session	lithotripsy	complications	Pancreatitis	Bleeding	of biliary	Perforation
Bang BW (2010) ^[31]	20 s	35/35(100)	31/35(88.6)	1/35(2.9)	2/35(5.7)	2/35(5.7)	0/35(0)	0/35(0)	0/35(0)
	1 min	34/35(97.1)	32/35(91.4)	1/35(2.9)	4/35(11.4)	4/35(11.4)	0/35(0)	0/35(0)	0/35(0)
Bang BW (2015) ^[32]	20 s	107/109(98.1)	106/109(97.2)	3/109(2.7)	10/109(9.2)	7/109(6.4)	1/109(0.9)	3/109(2.7)	0/109
	1 min	112/119(94.1)	107/119(89.9)	3/119(2.5)	13/119(10.9)	9/119(7.5)	1/119(0.9)	2/119(1.7)	2/119(1.7)
Takeshi T (2008) ^[15]	15s	313/324(96.6)	203/324(62.6)	78/324(24.1)	26/324(8)	13/324(4)	1/324(0.3)	11/324(3.4)	1/324(0.3)
	2 min	314/324(96.9)	238/324(73.5)	86/324(26.5)	40/324(12.3)	24/324(7.4)	0/324(0)	14/324(4.3)	2/324(0.6)
Hakuta R	15s	438/450(97.3)	327/450(72.7)	90/450(20)	59/450(13.1)	40/450(8.9)	1/450(0.2)	18/450(4)	1/450(0.2)
(2017) ^[33]	5 min	156/157(99.4)	135/157(86)	13/157(8.3)	21/157(13.4)	13/157(8.3)	0/157(0)	9/157(5.7)	1/157(0.6)

EPBD = endoscopic papillary balloon dilation.

of mechanical lithotripsy (RCTs: OR=1.07, 95% CI=0.26–4.36, *P*=.92; non-RCTs: OR=1.52, 95% CI=0.49–4.70, *P*=.47; Fig. 4).

3.4. Safety

3.4.1. Overall complications. Four studies reported the overall complication rate (pancreatitis, bleeding, biliary tract infection, and perforation). No significant heterogeneity existed in the 2 groups (RCTs: $I^2=0\%$, P=.58; non-RCTs: $I^2=49\%$, P=.16). Therefore, we used a fixed-effects model to pool the data. There

was no significant difference in the overall complication rate between the 2 different dilation duration groups (RCTs: OR = 0.73, 95% CI=0.34 to 1.60, P=.44; non-RCTs: OR=0.77, 95% CI=0.51-1.16, P=.21; Fig. 5).

3.4.2. Pancreatitis. Four studies reported the pancreatitis rate. No significant heterogeneity ($I^2 = 0\%$, P = .58) existed in the RCT group; however, heterogeneity ($I^2 = 55\%$, P = .14) was demonstrated in the non-RCT group. A random-effect model was used to pool the data. There was no statistical difference between the 2



Figure 2. Forest plot on the complete stone removal comparing short dilation group and long dilation group.



Figure 3. Forest plot on the stone removal in the first session comparing short dilation group and long dilation group.



Figure 4. Forest plot on mechanical lithotripsy comparing short dilation group and long dilation group.

different dilation duration groups with respect to the postpancreatitis rate (RCTs: OR = 0.73, 95% CI = 0.30–1.76, P = .48; non-RCTs: OR=0.76, 95% CI=0.37-1.55, P=.45; Fig. 6).

3.4.3. Bleeding. No significant heterogeneity $(I^2 = 0\%, P = .65)$ existed in the non-RCT group, thus a fixed-effects model was used. There was no significant difference between the 2 different dilation duration groups in the bleeding rate (RCTs: OR = 1.09, 95% CI=0.07-17.68, P=.95; non-RCTs: OR=1.84, 95% CI= 0.19-17.66, P = .60; Fig. 7).

3.4.4. Biliary tract infection. Four studies reported biliary tract infections. No significant heterogeneity $(I^2 = 0\%, P = .83)$ existed in the non-RCT group, thus a fixed-effects model was used. There was no significant difference between the 2 different dilation duration groups in the biliary tract infection rate (RCTs: OR = 1.66, 95% CI=0.27-10.1, P=.58; non-RCTs: OR=0.73, 95% CI=0.41-1.31, P=.29; Fig. 8).

3.4.5. Perforation. Four studies reported perforation rates. No significant heterogeneity ($I^2=0\%$, P=.85) existed in the non-RCT group, thus a fixed-effects model was used. There was no significant difference between the 2 different dilation duration groups in the perforation rate (RCTs: OR = 0.21, 95% CI = 0.01-4.52, P=.32; non-RCTs: OR=0.43, 95% CI=0.07-2.73, P = .37; Fig. 9).

3.5. Assessment of risk of bias and publication bias

Only 4 studies (<10) were included in this meta-analysis. Thus, we did not assess publication bias using a funnel plot. Therefore, publication bias could not be completely excluded.

4. Discussion

Both EST and EPBD are well-established methods for expanding papillary openings during therapeutic ERCP.^[34] In addition,



	short El	PBD	long EP	BD		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl
1.5.1 RCT								
Bang BW 2010 [32]	2	35	4	35	5.6%	0.47 [0.08, 2.75]		
Bang BW 2015 [33]	7	109	9	119	16.8%	0.84 [0.30, 2.33]		
Subtotal (95% CI)		144		154	22.4%	0.73 [0.30, 1.76]		-
Total events	9		13					
Heterogeneity: Tau ² =	0.00; Chi ²	= 0.31	df=1 (P	= 0.58); I ² = 0%			
Test for overall effect:	Z = 0.71 (F	P = 0.48	3)					
1.5.2 non-RCT								
Hakuta R 2017 [34]	40	450	13	157	41.1%	1.08 [0.56, 2.08]		
Takeshi T 2008 [31]	13	324	24	324	36.5%	0.52 [0.26, 1.05]		
Subtotal (95% CI)		774		481	77.6%	0.76 [0.37, 1.55]		-
Total events	53		37					
Heterogeneity: Tau ² =	0.15; Chi2	= 2.23	df=1 (P	= 0.14); I ² = 559	6		
Test for overall effect:	Z = 0.76 (F	P = 0.45	5)					
Total (95% CI)		918		635	100.0%	0.76 [0.50, 1.15]		•
Total events	62		50					
Heterogeneity: Tau ² =	0.00; Chi ²	= 2.56	df = 3 (P	= 0.47); I ² = 0%			
Test for overall effect.	Z= 1.30 (F	= 0.19	3)				0.01	U.1 1 10 10
Test for subaroup diff	erences: C	hi ² = 0	.01. df = 1	(P = 0	.94). = (0%		Favours (short EFBD) Favours (long EFBD)
restion suburbub uni	Figure 6	Fore	et plot o			comparing short dilat	on ar	iroun and long dilation group

some systematic reviews have shown that EPBD and EST have similar efficacies with respect to stone clearance.^[35] Moreover, some previous studies^[8,36] indicated that sphincter of Oddi pressure recovers after EPBD alone; however, the current consensus is that EPBD is associated with a lower risk of bleeding and is preferred over EST in patients with a bleeding diathesis^[6,13,17,37] because a higher risk of pancreatitis has been reported.^[11,16] Recently, some studies compared the risk of pancreatitis at dilation of different duration during EPBD; short dilation (≤ 1 minute) is recommended because of the lower risk of pancreatitis.^[6,11,38] Dilation of different duration (15, 20 seconds, ≥ 1 , 2, <5, and ≥ 5 minutes) was performed in previous studies; however, additional studies with a focus on a dilation duration <1 and ≥ 1 minute are warranted.

This is the first meta-analysis involving the efficacy and safety of different dilation duration in EPBD. EPBD in the studies included in our meta-analysis was used alone. Our meta-analysis of 2 RCTs and 2 non-RCTs showed that there was no significant difference in the rate of stone clearance between the 2 different dilation duration groups. Currently, when bile duct stones cannot be removed after balloon dilation, mechanical lithotripsy is required for treatment; however, mechanical lithotripsy is a challenging technique^[39,40] because it is difficult to capture stones inside the lithotripter basket in most cases.^[41] As a result, the stone fragments created by mechanical lithotripsy are difficult to clear.^[39] Therefore, it is necessary to reduce mechanical lithotripsy in ERCP. In our meta-analysis no significant difference was shown in the utility of mechanical lithotripsy in RCTs and non-RCTs. Our meta-analysis of RCTs suggested that dilation of short and long duration achieved equivalent success in stone removal during the first session. There was heterogeneity ($I^2 = 63\%$, P = .10) in the RCT group. Because only 2 studies were









Figure 9. Forest plot on perforation comparing short dilation group and long dilation group.

included in this group, subgroup analysis for heterogeneity could not be performed. A lower rate of stone removal in the first session (88.6% vs 91.4%, P=.48) in the short EPBD group was demonstrated in the study conducted by Bang et al.^[31]A higher rate of stone removal during the first session (97% vs 89.9%, P=.052) was reported in the study conducted by Bang et al.^[32] The heterogeneity could have originated from the above discrepancy, although this difference was not statistically significant; however, non-RCT studies showed that long EPBD had a significantly high rate of stone removal in the first session with a short dilation duration. According to the non-RCTs, there were 2 possible reasons to account for this difference. First, a sufficiently enlarged orifice of the bile duct potentially eases insertion of endoscopic devices and subsequent stone removal.^[33] Second, Tsujino et al^[15] attempted to place a biliary stent at the time of lithotripsy. In the meta-analysis of the non-RCT group, significant heterogeneity $(I^2=90\%, P=.001)$ was found. The mechanical lithotripsy rate requirement in the long EPBD group was lower than the short EPBD group in the study conducted by Tsujino et al^[15] (8.3% vs 20%, P < .001); however, no significant difference was found in the study conducted by Hakuta et al.^[33] This discrepancy may be the main cause of the heterogeneity; however, no significant difference in the rate of stone clearance between the dilation of short and long duration in non-RCTs. Based on our meta-analysis, the efficacy between short and long EPBD was equivalent.

Pancreatitis is a severe complication of ERCP. Previous studies have suggested that dilation duration should be short because direct pancreatic duct compression during balloon dilation leads to pancreatitis.^[11,38] Other studies concluded that short dilation duration increases the risk of pancreatitis due to the higher risk of inadequate sphincter loosening.^[14,42] Indeed, inadequate sphincter loosening may extend the cannulation and stone removal times, which aggravate papillary edema. In contrast, our metaanalysis indicated that no significant difference in the pancreatitis rate between the dilation of short (RCTs: 6.25%; non-RCTs: 6.06%) and long duration (RCTs: 8.4%; non-RCTs: 7.07%). Unfortunately, only one study^[32] involved the cannulation time in our meta-analysis. In this study, the cannulation time was not different between the 2 dilation duration groups (4.6 ± 4.1) minutes vs 4.3 ± 3.4 minutes P = .302). We could not evaluate the effect of cannulation time on the risk of pancreatitis. Heterogeneity $(I^2 = 55\%, P = .14)$ was found in the non-RCT group. The stone diameter between the short and long EPBD groups was different (P=.005) in the study conducted by Hakuta et al.^[33] This discrepancy may be the main cause of heterogeneity.

Bleeding is one of the most common severe adverse events of ERCP.^[43] A previous meta-analysis and systematic review suggested that EPBD likely reduces post-ERCP hemorrhage.^[41] Although dilation has a risk of tearing the papilla, compression by the balloon may stanch bleeding. In our meta-analysis the rate of bleeding was low in the dilation of short (RCTs: 1/144; non-RCTs: 2/774) and long duration groups (RCTs: 1/154; non-RCTs: 0/481). In addition, no significant difference existed between the 2 dilation duration groups. Biliary tract infection is one of the complications of EPBD. No significant difference existed between the 2 dilation duration groups in our metaanalysis. Perforation is uncommon during balloon dilatation, but can present as a severe and fatal adverse event of ERCP. Our meta-analysis showed that the perforation rate was low in both the dilation of short (RCTs: 0/144; non-RCTs: 2/774) and long duration groups (RCTs: 2/154; non-RCTs: 3/481) and no

statistical difference was found between the 2 groups. In general, the safety between dilation of short and long duration was equivalent.

5. Limitations

There were several limitations in our meta-analysis, which should be taken into consideration when interpreting our results. First, the cannulation time was reported in only one study. Thus, we could not evaluate the effect of cannulation time on the risk of pancreatitis. Second, it is unclear whether dilation of short (15 and 20 seconds) and long duration groups (1, 2, and 5 minutes) influenced our results. Third, publication bias, which may influence the reliability of our results, could not be completely excluded. Finally, the small number of RCTs (2) and non-RCTs (2) with a small sample size (RCTs: 144 vs 154; non-RCTs: 774 vs 481) may have led to inherent biases and decreased the robustness of the analysis. Therefore, additional high quality RCTs are needed to assess the efficacy and safety of balloon dilation of different duration during EPBD.

6. Conclusion

There was no significant difference in the efficacy and safety of dilation of short (<1 minute) and long duration (\geq 1 minute) for removal of bile duct stones with EPBD; however, due to the limited quality of the included studies, additional studies with a large sample size are needed to confirm the above conclusion.

Author contributions

Data curation: Qiang Wang, Luyao Fu. Formal analysis: Tao Wu, Xiong Ding. Methodology: Tao Wu. Software: Xiong Ding. Writing – original draft: Qiang Wang. Writing – review & editing: Tao Wu.

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