Large Balloon Dilation versus Mechanical Lithotripsy for Large Bile Duct Stones: A Systematic Review & Meta-Analysis

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Abstract

Introduction: Common bile duct stone (CBDS) is a common disorder of the biliary tract and often necessitates intervention to prevent biliary complications. Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and balloon stone extraction remain to be the standard treatment for CBDS. For large stones (>12mm), removal may be challenging. After sphincterotomy, use of mechanical lithotripsy (ML) has been widely used for clearance of large stone in the last 3 decades. Large balloon dilatation (LBD) is also established as a highly successful method of removing CBDS. This present study aims to determine which procedure is more effective and safer in clearing common bile duct stones.

Methodology:
A literature search of randomized controlled trials (RCTs) comparing balloon dilatation and mechanical lithotripsy up to April 2020 in electronic databases including Cochrane Library, MEDLINE (PubMed), Google Scholar, Herdin.ph and Clinicaltrials.gov as well as hand-search of publications was done. Primary outcome was stone clearance rate. Secondary outcomes include overall complication rate and specific rates for pancreatitis, cholangitis, perforation and bleeding.

Results: Three RCTs (enrolling 273 patients) met our inclusion criteria. No significant difference observed in stone clearance rate between the two groups (OR 1.44, 95% CI 0.68 to 3.87, P=0.34, moderate certainty). The overall complication rate was significantly higher in the ML group (RR 0.45, 95% CI 0.24 to 0.82, P=0.01, high certainty). Post-ERCP cholangitis did not occur in the LBD group. Six percent of the patients in the ML group developed cholangitis and was statistically significant (RR 0.11, 95% CI 0.01 to 0.86, P=0.04, high certainty). No difference in post-ERCP pancreatitis, perforation and bleeding observed. No significant heterogeneity was seen in the studies included.

Conclusion: Balloon dilatation is a safer and effective alternative to mechanical lithotripsy in the removal of large common bile duct stones in terms of developing cholangitis. There was no difference in rate of pancreatitis, perforation and bleeding observed in both interventions. A higher risk of cholangitis is observed with the use of mechanical lithotripsy.

Keywords: common bile duct stone, mechanical lithotripsy, balloon dilatation, balloon dilation, balloon sphincteroplasty

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Introduction

Background. The presence of common bile duct stones (CBDS) is a common disorder of the biliary tract which is associated with many complications and frequently necessitates intervention. It is usually brought about by gallstone migration from the gallbladder into the biliary tree. Endoscopic retrograde cholangiopancreatography or ERCP with sphincterotomy and balloon stone extraction remain to be the standard treatment for extraction of CBDS. Albeit minimally invasive, it is a relatively complex procedure and is associated with complications such as bleeding, perforation, and pancreatitis in up to 15% of cases [1]. Estimates of nearly 85-90% of all CBDS can be successfully cleared by subsequent conventional balloon or basket extraction [2]. However, in a small percentage of patients, stone extraction may prove to be difficult, of which, one of the main reasons is stone size (>1cm). Increasing the stone size decreases the rate of successful stone extraction. There is no clear definition of a "large stone". Available literatures would define it as larger than 10-15mm in diameter. Otherwise, a retrospective study showed that a disproportionate CBD size should be considered in defining a large stone. Other factors of difficult stone extraction include an irregular stone shape, multiple stones, difficult location, presence of CBD strictures, and/or surgically altered enteral anatomy [3,4,5].

Since its introduction in the 1980s, mechanical lithotripsy (ML) has been widely used for stone fragmentation to facilitate stone clearance. Lithotripter devices have a high breaking point resulting to increased success of ML even for larger CBDS (>2 cm) [6]. Stones over 15mm in diameter can be successfully removed in 90% of cases. ML is readily available, cost-effective, and simple to operate. However, failure rates have also been reported ranging from 20-30% associated with stones larger than 25mm. And although relatively safe, complication may arise in 3-6% of cases. A main complication during ML is basket impaction or fracture of the basket wires. Perforation, bleeding, or injury to the bile duct may also occur and cholangitis is common [7,8,9,10]. Hence, other methods have been resorted for subsequent stone removal.

The use of a balloon to dilate the papilla was also introduced in the 1980s as an alternative to endoscopic sphincterotomy (EST). In 2003, large balloon dilation (LBD) following EST, by using a 20mm-diameter papillary balloon was utilized for difficult-to-remove stones and reported a high success rate [11]. Further studies using a controlled radial expansion balloon (CRE) resulted into stone clearance of up to 95% of cases [12]. Several studies showed that LBD was comparable to EST in the removal of large CBDS and appears to lower the subsequent use of ML as compared to doing EST alone [13,14]. Complications common to LBD include bleeding, pancreatitis, and perforation but nevertheless, it has an acceptable complication profile for the removal of large CBDS [15].

Description of the intervention. The technique for balloon dilatation in this review were as follows: all studies did an initial sphincterotomy and made use of a contrast-filled dilating balloon of varying sizes (12, 15, 18, and 20mm). The balloons were inflated to its designated diameter for 10-60secs and was observed via fluoroscopy guidance [7,16,17].

The technique for mechanical lithotripsy in this review were as follows: all studies did an initial sphincterotomy and made use of a mechanical lithotriptor to capture and fragment the stone. The stone were then retrieved via basket or balloon extraction [7,16,17].

Why is it important to do this review? Several endoscopy units in the country are capable of performing these techniques. Successful stone clearance and safety remain a priority in the management of CBDS. In the local setting, the use of a mechanical lithotriptor is a common practice by experts in the field. Balloon dilation, a technique also available in the country, has been studied and utilized as well for removal of CBDS. In addition, both interventions may be used as an alternative rescue therapy, when stone extraction is a failure by the initial procedure of choice [8,17].

As previously mentioned, both procedures have inherent procedural and safety concerns. Considering the risks involved, an up-to-date look on the evidence on the choice procedure for removal of large CBDS is valuable. To date, there is no systematic review nor meta-analysis published nor ongoing that directly compare the two procedures.

Objectives. The general objective of this review is to compare sphincterotomy with balloon dilatation versus sphincterotomy with mechanical lithotripsy, in terms of successful stone clearance and safety, among adult patients with large common bile duct stones.

Specific objectives are as follows:

1. To compare stone clearance rate of patients who underwent ERCP with sphincterotomy and balloon dilatation versus sphincterotomy with mechanical lithotripsy.
2. To compare the overall complication rates, and specific complications, namely, post-ERCP pancreatitis, cholangitis, bleeding, and perforation between the two modalities.

Methodology

Types of Studies. St*udies* included will be randomized controlled trials (RCTs) comparing balloon dilatation and mechanical lithotripsy in removing large common bile duct stones. Full-text articles will be included. Correspondence with the primary author will be done if only abstracts are available. The inclusion of studies was independently decided upon by two reviewers and disagreements were resolved by a third independent reviewer and co-author. Excluded studies would be: (1) case reports; (2) trials comparing LBD with a different intervention other than ML and vice versa; (3) trials focusing on either LBD or ML alone; (4) review articles; (5) retrospective studies and; (6) non-randomized trials.

Types of Participants. The study participants will include adult patients with clinical, laboratory, and imaging-confirmed presence of large CBDS measuring ≥12mm in diameter, undergoing ERCP wherein the stones cannot be extracted using standard balloon catheter. Exclusion criteria include: concomitant presence of intrahepatic duct stones, patients with altered enteral anatomies, anticoagulant or antiplatelet use, shock, and acute pancreatitis.

Types of Interventions. Interventions were: ERCP with sphincterotomy then subsequent balloon dilatation versus ERCP with sphincterotomy then subsequent mechanical lithotripsy.

Types of Outcome Measures. The primary outcome measured is stone clearance rate (solely using the investigated interventions without rescue therapy). Secondary outcomes include overall complication rate, and specific rates for post-ERCP pancreatitis (PEP), cholangitis, bleeding, and perforation.

Search Methods for Identification of Studies. Published literature was searched through electronic databases including PubMed, MEDLINE, EMBASE, Herdin, Clinicaltrials.gov, LILACS (Latin American and Caribbean Health Sciences Literature) and the Cochrane Library up to April 2020. The following keywords were used for the search: "endoscopic sphincterotomy," "balloon dilation," "balloon dilatation", "balloon sphincteroplasty", "mechanical lithotripsy," and "choledocholithiasis" or "common bile duct stone." Abstracts were also hand-searched from the ASGE journal Gastrointestinal Endoscopy (GIE). To avoid redundancy, the study is registered at the International Prospective Register of Systematic Reviews (PROSPERO) as an ongoing review.

Data Collection and Analysis. Two reviewers will independently identify eligible studies. Demographic data, data on the intervention and outcomes were extracted. The study authors were consulted for any discussion and disagreements. Software used is RevMan 5 (Review Manager version 5.3.5 - Cochrane Collaboration Copyright). For the primary outcome of stone clearance rate, pooled odds ratio (OR) with 95% confidence interval was used. For the secondary outcome, relative risks (RR) with 95% confidence intervals were used. The quality of the included studies was also assessed using

GRADEpro GDT in order to evaluate the level of evidence.

Assessment of Risk of Bias in Included Studies. The Cochrane Collaboration Tool was used to assess risk of bias and identify if the study included is of low, high or unclear risk. Selection bias, performance bias, attrition bias and reporting bias were assessed.

Measurement of Treatment Effect. The measures of treatment effect were odds ratio and risk ratio at 95% confidence interval.

Assessment of Heterogeneity. Heterogeneity was assessed using the chi-squared test, assessing whether the observed differences in results are compatible with chance alone. A p-value of less than 0.10 is considered to be significant. I2 statistic which quantifies inconsistencies will also be used. Heterogeneity will be considered when I2 statistic is greater than 50%.

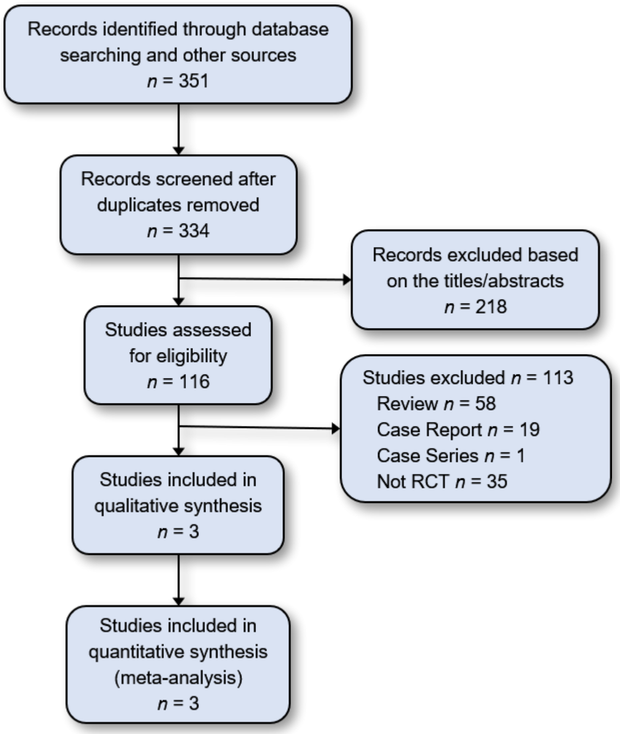
Data Synthesis. The meta-analysis procedure used the fixed effects model.

Results

Description of studies. A total of 351 related studies were found from PubMed, MEDLINE, EMBASE, Herdin, Clinicaltrials.gov, LILACS and the Cochrane Library. No related studies were found from hand-searched journals. After screening by reviewing titles, abstracts, full texts, and excluding review articles, case series, case reports and non-randomized studies, 3 RCTs were eventually included [7,16,17]. The detailed selection process is shown in **Figure 1**.

A total of 273 patients with large CBDS who underwent ERCP were included with 138 patients in the LBD group and 135 in the ML group. The device used for LBD and ML were specified in 2 studies [7,17]. All studies included had CBDS more than 12mm. The study by Netinatsunton et al, had a larger mean diameter of stones compared to the other 2 trials. All patients were subjected to EST prior to either LBD or ML. Complications were reported in the 3 trials. Additional complication of oxygen desaturation was reported in one study [17] and was not included in the analysis. Characteristics and summary of the included studies are summarized in **Table 1**. The mean age was similar in the included studies. The study by Radwan et al involved cirrhotic patients. Subgroup analysis was done for procedure-related bleeding with and without the study by Radwan et al, to consider the potential effect of inherent coagulopathy in cirrhotic patients on the analysis (**Figure 8**).

Figure 1. PRISMA flow diagram showing selection of articles for meta-analysis. RCT, randomized controlled trial



Risk of bias in included studies. In general, the included studies were assessed to be of low risk of bias. Details of the assessment is shown in **Figure 2** and **3**. Randomization in all studies made use of computer-generated numbers or sequence. Sealed envelopes were also used. Performance bias was eliminated in two studies by having only experienced endoscopists doing the intervention while in the study by Netinatsunton, et al, trainees were also doing the procedure. Blinding of the outcome assessors were not mentioned in all studies. All patients were included in the analysis.

Table 1. Summary of included clinical trials

Study	Study type	Balloon Diameter	ML Device	Intervention	Mean age		Sample size, n		Stone size, mm (mean)		Complications Reported
					LBD	ML	LBD	ML	LBD	ML	
Stefanidis 2011	RCT	15-20mm (CRE, Boston Scientific Corp. USA)	Mechanical lithotriptor (BML 4Q, Lithocrush 201 or 202Q; Olympus Optical)	EST-LBD vs EST-ML	69.4 ± 17.8	68.2 ± 18.9	45	45	12 to 20	12 to 20	PEP, Cholangitis, Bleeding, Perforation
Netinatsunton 2017	RCT	Up to 20mm (CRE, Boston Scientific Corp. USA)	3 × 6 cm Trapezoid® (Boston Scientific Corp. USA)	EST-LBD vs EST-ML	66.4 ± 15.2	68.7 ± 15.5	44	41	≥15 (25.96 ± 9.80)	≥15 (24.75 ± 8.30)	PEP, Cholangitis, Bleeding, Perforation, Desaturation
Radwan 2019	RCT	12-18mm (Not specified)	Standard Mechanical lithotriptor device (Not specified)	EST-LBD vs EST-ML	53.8±10.84	53.9±11.25	49	49	≤20 (17.1 ± 2.2)	≤20 (17.2±1.53)	PEP, Cholangitis, Bleeding, Perforation

Figure 2. Risk of bias graph

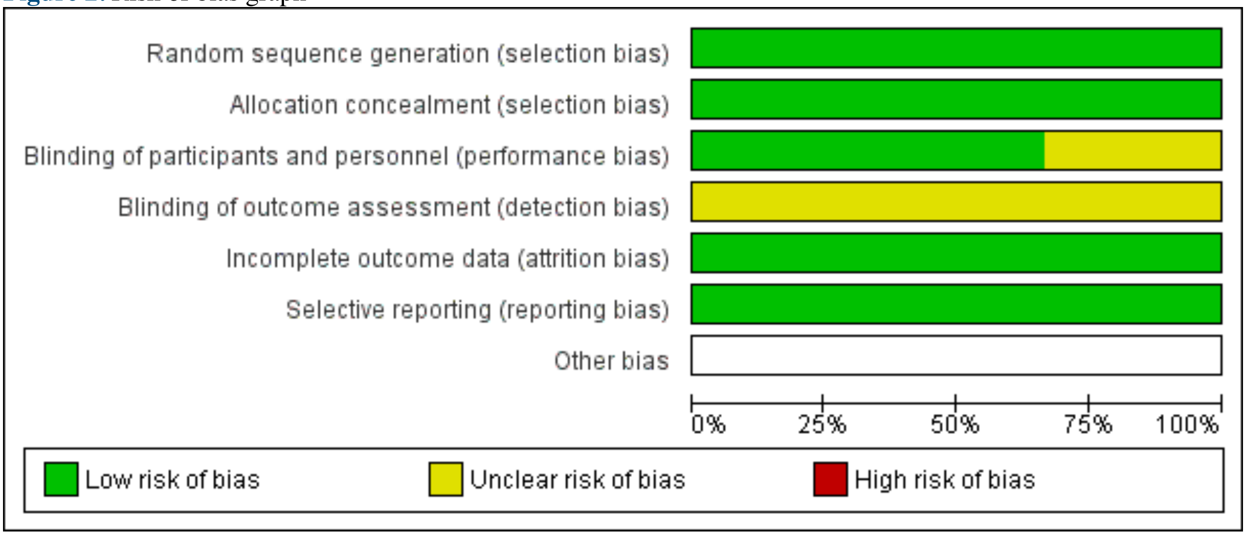
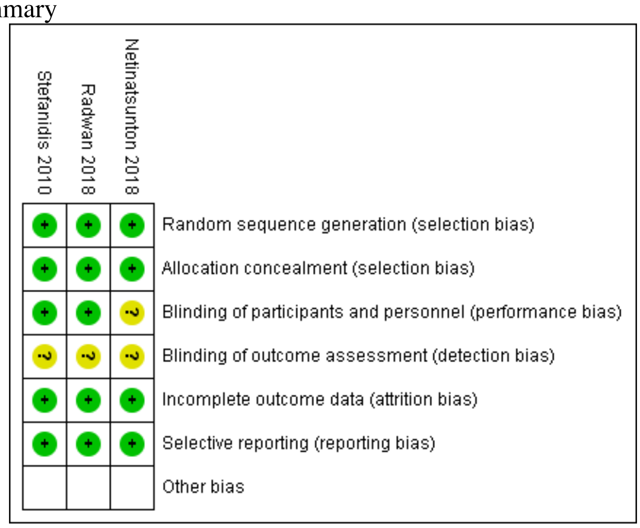


Figure 3. Risk of bias summary

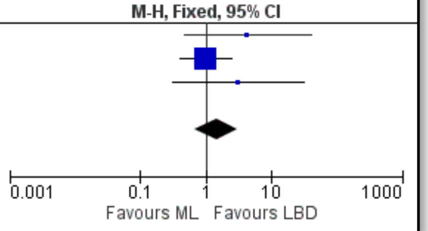


Results of research. We first compared the stone clearance rate between the LBD and ML group (**Figure 4**). The crude total stone clearance rate was 87.7% for the LBD group (95%CI 0.41 to 1.33) and 84.4% for the ML group (95%CI 0.45 to 1.22). Although a trend favoring LBD was shown, there was no statistically significant difference in stone clearance (p=0.34). Netinatsunton and colleagues [17] provided data on overall stone clearance after cross over treatment (37 out of 44 for LBD; 33 out of 41 for ML). This same study was also observed to have a lower rate of stone clearance, likely due to larger stone sizes (mean=25.36mm).

All studies were used to compare overall complication rate (**Figure 5**). The LBD group was associated with a significantly lower risk of overall complications (pooled RR 0.45, 95%CI 0.24-0.82, p=0.01), and with non-significant or low level of heterogeneity (p=0.19, I^2=39%). The risk of cholangitis was significantly decreased in the LBD group (pooled RR 0.11, 95%CI 0.01-0.86, p=0.04, **Figure 6**). No significant heterogeneity was observed (p=0.72, I^2=0%).

Although, there was a trend favoring LBD observed in 3 outcomes, no statistically significant difference was shown in the rate of pancreatitis (p=0.44), bleeding (p=0.42), and perforation (p=0.59) as shown in **Figure 7, 8,** and **10** respectively. A subgroup analysis for bleeding was done among the non-cirrhotic population (**Figure 9**) which also showed no significant difference (p=0.88). No mortality was reported in all 3 trials.

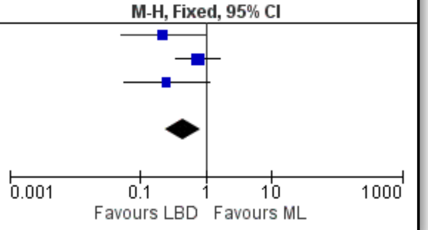
Figure 4. Forest plot comparing Stone clearance between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	44	45	41	45	8.0%	4.29 [0.46, 40.01]	2011
Netinatsunton 2017	29	44	27	41	83.7%	1.00 [0.41, 2.46]	2017
Radwan 2019	48	49	46	49	8.2%	3.13 [0.31, 31.19]	2019
Total (95% CI)		**138**		**135**	**100.0%**	**1.44 [0.68, 3.07]**	
Total events	121		114				

Heterogeneity: Chi² = 1.98, df = 2 (P = 0.37); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)

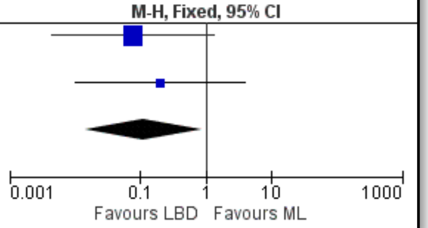
Figure 5. Overall Complication Rate between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	2	45	9	45	31.7%	0.22 [0.05, 0.97]	2011
Netinatsunton 2017	9	44	11	41	40.1%	0.76 [0.35, 1.65]	2017
Radwan 2019	2	49	8	49	28.2%	0.25 [0.06, 1.12]	2019
Total (95% CI)		**138**		**135**	**100.0%**	**0.45 [0.24, 0.82]**	
Total events	13		28				

Heterogeneity: Chi² = 3.28, df = 2 (P = 0.19); I² = 39%
Test for overall effect: Z = 2.59 (P = 0.010)

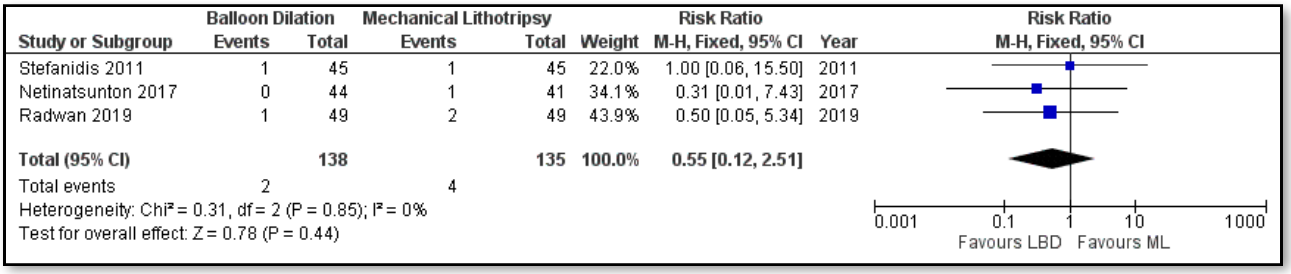
Figure 6. Rate of Cholangitis between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	0	45	6	45	72.2%	0.08 [0.00, 1.33]	2011
Netinatsunton 2017	0	44	0	41		Not estimable	2017
Radwan 2019	0	49	2	49	27.8%	0.20 [0.01, 4.06]	2019
Total (95% CI)		**138**		**135**	**100.0%**	**0.11 [0.01, 0.86]**	
Total events	0		8				

Heterogeneity: Chi² = 0.21, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 2.10 (P = 0.04)

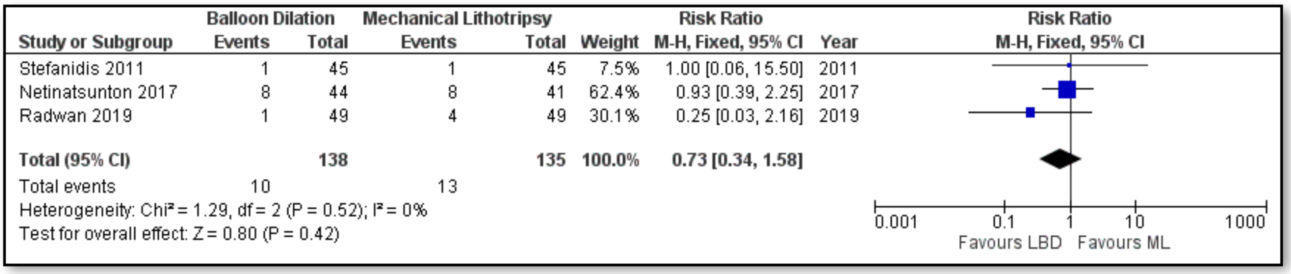
Figure 7. Post-ERCP Pancreatitis Rates between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	1	45	1	45	22.0%	1.00 [0.06, 15.50]	2011
Netinatsunton 2017	0	44	1	41	34.1%	0.31 [0.01, 7.43]	2017
Radwan 2019	1	49	2	49	43.9%	0.50 [0.05, 5.34]	2019
Total (95% CI)		**138**		**135**	**100.0%**	**0.55 [0.12, 2.51]**	
Total events	2		4				

Heterogeneity: Chi² = 0.31, df = 2 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.78 (P = 0.44)

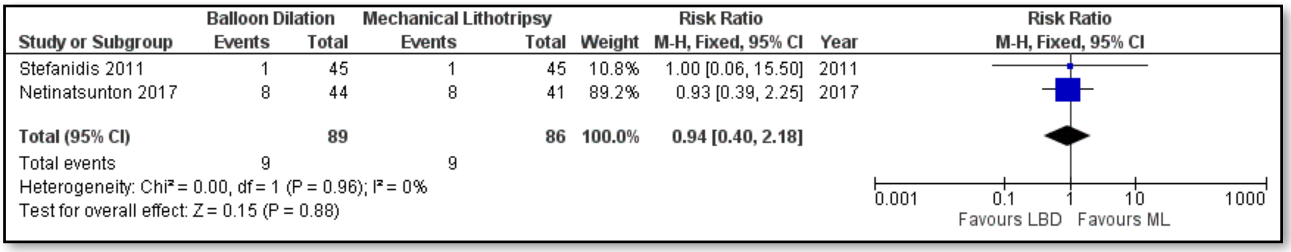
Figure 8. All Procedure-Related Bleeding Rates between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	1	45	1	45	7.5%	1.00 [0.06, 15.50]	2011
Netinatsunton 2017	8	44	8	41	62.4%	0.93 [0.39, 2.25]	2017
Radwan 2019	1	49	4	49	30.1%	0.25 [0.03, 2.16]	2019
Total (95% CI)		**138**		**135**	**100.0%**	**0.73 [0.34, 1.58]**	
Total events	10		13				

Heterogeneity: Chi² = 1.29, df = 2 (P = 0.52); I² = 0%
Test for overall effect: Z = 0.80 (P = 0.42)

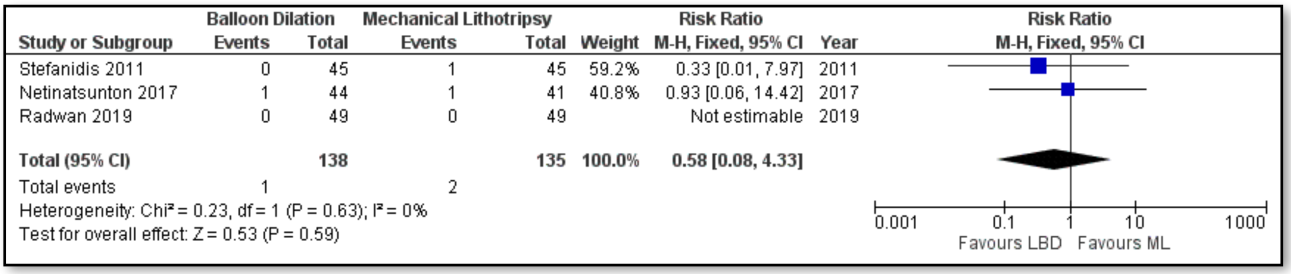
Figure 9. Procedure-Related Bleeding Among Non-Cirrhotics between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	1	45	1	45	10.8%	1.00 [0.06, 15.50]	2011
Netinatsunton 2017	8	44	8	41	89.2%	0.93 [0.39, 2.25]	2017
Total (95% CI)		**89**		**86**	**100.0%**	**0.94 [0.40, 2.18]**	
Total events	9		9				

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.15 (P = 0.88)

Figure 10. Perforation between Balloon Dilation versus Mechanical Lithotripsy



Study or Subgroup	Balloon Dilation Events	Balloon Dilation Total	Mechanical Lithotripsy Events	Mechanical Lithotripsy Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Stefanidis 2011	0	45	1	45	59.2%	0.33 [0.01, 7.97]	2011
Netinatsunton 2017	1	44	1	41	40.8%	0.93 [0.06, 14.42]	2017
Radwan 2019	0	49	0	49		Not estimable	2019
Total (95% CI)		**138**		**135**	**100.0%**	**0.58 [0.08, 4.33]**	
Total events	1		2				

Heterogeneity: Chi² = 0.23, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.53 (P = 0.59)

Table 2. Summary of Quality of Evidence of Included Trials using GRADEpro GDT

Certainty assessment							Summary of findings				
№ of participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%) With mechanical lithotripsy	With balloon dilatation	Relative effect (95% CI)	Anticipated absolute effects Risk with mechanical lithotripsy	Risk difference with balloon dilatation
Stone clearance rate											
273 (3 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	114/135 (84.4%)	121/138 (87.7%)	**OR 1.44** (0.68 to 3.07)	844 per 1,000	**42 more per 1,000** (from 58 fewer to 99 more)
Over-all complication rate											
273 (3 RCTs)	not serious	not serious	not serious	not serious	none	⊕⊕⊕⊕ HIGH	28/135 (20.7%)	13/138 (9.4%)	**RR 0.45** (0.24 to 0.82)	207 per 1,000	**114 fewer per 1,000** (from 158 fewer to 37 fewer)
Post-ERCP pancreatitis											
273 (3 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	4/135 (3.0%)	2/138 (1.4%)	**RR 0.55** (0.12 to 2.51)	30 per 1,000	**13 fewer per 1,000** (from 26 fewer to 45 more)
Cholangitis											
273 (3 RCTs)	not serious	not serious	not serious	not serious	none	⊕⊕⊕⊕ HIGH	8/135 (5.9%)	0/138 (0.0%)	**RR 0.11** (0.01 to 0.86)	59 per 1,000	**53 fewer per 1,000** (from 59 fewer to 8 fewer)
Bleeding											
273 (3 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	13/135 (9.6%)	10/138 (7.2%)	**RR 0.73** (0.34 to 1.58)	96 per 1,000	**26 fewer per 1,000** (from 64 fewer to 56 more)
Bleeding among non-cirrhotics											
175 (2 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	9/86 (10.5%)	9/89 (10.1%)	**RR 0.94** (0.40 to 2.18)	105 per 1,000	**6 fewer per 1,000** (from 63 fewer to 123 more)
Perforation											
273 (3 RCTs)	not serious	not serious	not serious	serious [a]	none	⊕⊕⊕◯ MODERATE	2/135 (1.5%)	1/138 (0.7%)	**RR 0.58** (0.08 to 4.36)	15 per 1,000	**6 fewer per 1,000** (from 14 fewer to 50 more)

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **OR:** Odds ratio; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Discussion

This meta-analysis compared the efficacy and safety of LBD versus ML for the removal of large CBDS. No meta-analysis nor review is presently published or registered. Several published studies have compared LBD to EST alone, with one large meta-analysis of 18 studies (n=2789) concluding that LBD is superior to EST in terms of removing stones of ≥10mm diameter and lesser complications [18]. In our study, we found that LBD was comparable to ML in the removal of large CBDS. Although not statistically significant, LBD may even appear to be more effective. Larger studies may still be necessary to strengthen this observation.

Our results showed that LBD had a significant lower risk of overall complications compared to ML. Low level of heterogeneity was observed, probably because of the overall complication rates in the study by Netinatsunton, et al. In this study, complication rates between LBD and ML group were comparable in contrast to the other trials wherein complication rates were consistently lower in the LBD group. A factor that may have possibly affected this outcome was the participation of trainees in the performance of ERCP in this study. Previous literature has shown that ERCP complications relatively increase when performed by a trainee [19]. On the contrary, experienced endoscopists performed the procedure in the other two studies.

Compared with the ML group, the risk of cholangitis was significantly decreased in the LBD group. Cholangitis events only occurred among the ML group, in the studies by Stefanidis, et al and Radwan, et al. Cholangitis did not occur in the LBD group; a finding similar in another RCT studying LBD [20]. A possible explanation for ML having a higher risk of cholangitis is that small fragments of stones after ML may still lead to stasis and subsequent cholangitis [21]. To reiterate, no difference was observed in the other outcomes measured including the subgroup analysis on bleeding rates in non-cirrhotics. Though a potential underlying bleeding diathesis may be present in the cirrhotic population, the study exclusion criteria by Radwan et al (severe coagulopathy, Child-Pugh C cirrhosis, and marked thrombocytopenia <50,000/mL) may have contributed to the consistent outcome of no difference in bleeding rates.

Summary of main results. No significant difference observed in stone clearance rate between the two groups (OR 1.44, 95% CI 0.68 to 3.87, P=0.34). The overall complication rate was significantly higher in the ML group with low heterogeneity (RR 0.45, 95% CI 0.24 to 0.82, P=0.01, I^2=39%). There was a significant difference in the rate of cholangitis in favor of balloon dilatation, with no significant heterogeneity (RR 0.11, 95% CI 0.01 to 0.86, P=0.04). No difference in post-ERCP pancreatitis, perforation and bleeding observed.

Overall completeness and applicability of evidence. The evidence available is sufficient to answer the objectives of the review. However, limitation of this review is that only three studies were qualified to be included with 273 participants in the comparison of LBD and ML in the management of large CBDS. Due to the limited available studies, the power of this study might be decreased. An update to this review might be done in the future if there would be new prospective trials comparing the two interventions. In addition, an interesting area of subgroup analysis and further research is on the effect of intervention on stone clearance with respect to size. This was not done due to inconsistent reporting in the included trials.

Quality of the evidence. The quality of evidence was high for overall complication rate and risk of cholangitis. While the quality of evidence was moderate for stone clearance rate, pancreatitis, bleeding, and perforation. The details on the quality assessment using GradePro GDT are outlined in **Table 2**.

Potential biases in the review process. No potential bias was noted in the review process.

Conclusion

Implications for practice. There is evidence that the use of balloon dilatation is safer in terms of less cholangitis compared to mechanical lithotripsy. In addition, the success of stone clearance is equivalent in both groups. For patients with large CBDS, balloon dilatation is a safer and an equally effective modality for stone removal.

Implications for research. Future randomized controlled trials may be done in specific populations. Short term outcomes such as length of hospital stay, mortality, and the additional use of a rescue intervention may be measured. Analysis on the effect of differing stone sizes and form of intervention may also be studied. Long term outcomes such as timing of subsequent surgery, and CBD stone recurrence rate may be included to increase the validity and clinical significance of this review. Subsequently, a more extensive systematic review and meta-analysis may be done.

Disclosure

The authors have no disclosure.

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