

# Endoscopic sphincterotomy with balloon dilatation versus sphincterotomy alone for common bile duct stones removal: a randomised controlled trial

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## ABSTRACT

**Introduction:** Endoscopic sphincterotomy (EST) plus endoscopic papillary large balloon dilatation (EPLBD) has been reported as a valid alternative to EST alone in removing common bile duct (CBD) stone. The aim of this study is to compare efficacy, and safety of these two groups of patients in removing CBD stone in Hospital Universiti Sains Malaysia (HUSM).

**Materials and Methods:** This is a prospective single centre randomised single blinded comparative study conducted in HUSM. The primary endpoints for this study are the overall complete stone clearance rate and complication rate, while the secondary outcome for this study are duration of procedure and rate of usage of adjunct methods. Objective data analysis is conducted using independent sample t-test and chi-squared test.

**Results:** A total of 66 patients underwent endoscopic retrograde cholangiopancreatography (ERCP) for choledocholithiasis which is CBD stone. 34 patients were allocated to EST plus EPLBD arm (n=34), and 32 patients were in EST alone arm (n=32) using randomisation method. For intention to treat, patients from EST alone arm that unable to achieve complete stone clearance will be switched to EST plus EPLBD arm. The overall complete stone removal rate for both groups were comparable (EST plus EPLBD: 100% versus EST alone: 93.8%; p= 0.139). The two patients from EST alone group (6.2%) that unable to achieve complete stone clearance were converted to EST plus EPLBD group for intention to treat and able to achieve complete stone clearance by EST plus EPLBD. For procedural time, both arms are comparable as well (EST plus EPLBD: 15.8 minutes vs EST alone: 15.5 minutes; p= 0.860). Complications such as pancreatitis occurred in one patient in EST plus EPLBD arm (EST plus EPLBD: 2.9 % vs EST alone: 0 %; p= 0.328), and bleeding occurred in one patient in EST alone arm (EST plus EPLBD: 0 % vs EST alone: 3.1 %; p= 0.299) , but it is not statistically significant. No perforation or cholangitis complication occurred in both groups. No adjunct usage was observed in both groups.

**Conclusion:** In this study with limited sample size, both EST plus EPLBD and EST alone are effective and has comparable procedural time in removing CBD stone. Even though both

methods are equally effective, EPLBD plus EST is an alternative solution if complete stone clearance is unable to achieve via EST alone.

## KEYWORDS:

*Endoscopic sphincterotomy; balloon dilation; common bile stone; choledocholithiasis*

## INTRODUCTION

Endoscopic sphincterotomy (EST) is the most widely used procedure during endoscopic retrograde cholangiopancreatography (ERCP) to remove the common bile duct (CBD) stone and considered as a standard therapy for treatment of choledocholithiasis. However, in view of EST requires an adequate incision on major duodenal papilla to achieve biliary cannulation, it can potentially cause damage to biliary sphincter during the procedure and potentially increased risk of some complications such as bleeding and biliary reflux.<sup>1</sup> This procedure carries risk of complications such as haemorrhage, perforation and long-term effect like sphincter dysfunction.<sup>2</sup>

Staritz et al.<sup>3</sup> introduced a method called endoscopic papillary large balloon dilatation (EPLBD) in 1983 as an alternative to EST in clearing CBD stone. EPLBD can reduced the risk of bleeding and perforation post procedure, but it carries higher risk of post-ERCP pancreatitis.<sup>4,6</sup>

About 10 to 15% of CBD stone are unable to be extracted by both EST or EPLBD alone, especially in those patients with big and difficult stone (size bigger than 10 to 15mm, numerous, barrel-shaped, and impacted stones).<sup>7</sup> Besides that, other factors that can contribute to failure of stone extraction are periampullary diverticulum or post operative variation, tortuosity and tightening of distal common bile duct.<sup>8</sup>

In 2003, combination of EST and EPLBD was introduced as an alternative method.<sup>9</sup> It can reduce the risk of complications through avoiding a complete sphincterotomy, shortened procedure time and reducing the need of usage of mechanical lithotripsy.<sup>10</sup>

A study in 2007 showed that EST plus EPLBD had comparable efficacy and safety when compared to conventional EST

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alone and both groups had similar complication rate.<sup>10</sup> Besides that, in a recent study in 2020, it was shown that EST plus EPLBD had a comparable efficacy when compared with EST alone in clearing CBD stones and EST plus EPLBD required shorter procedural time when compared with EST alone.<sup>11</sup> While, a randomised controlled study in 2017 showed that EST plus EPLBD is more effective than the EST alone in clearing large CBD stones and is equally safe compared to EST alone.<sup>12</sup> In another randomised controlled trial in 2013, the study showed that the success rate for complete CBD stone removal in first session is higher in EST plus EPLBD group than the EST alone and it was statistically significant.<sup>13</sup> Apart from that, there are many other studies have suggested EST plus EPBD as a safe and promising alternative to conventional EST or EPLBD.<sup>14-16</sup> In a published meta-analysis, accumulated data showed that EST plus EPLBD is a safe and effective procedure in removing large or difficult CBD stone without any additional risk of complications.<sup>17</sup>

There is still no definite conclusion in evaluating superiority of EST plus EPLBD vs EST alone in term of efficacy in removing CBD stone.

Thus, in this study, our primary outcome is to compare the overall complete stone clearance rate and complication rate for both arms, while the secondary outcomes are the duration of procedure and rate of usage of adjunct methods.

## MATERIALS AND METHODS

This is a single centre, randomised controlled trial that was conducted in Hospital Universiti Sains Malaysia (HUSM). Patient with CBD stone who seek treatment at HUSM from June 2021 to June 2022 and fulfilled the inclusion criteria will be recruited into the study.

This study had obtained approval from ethical committee board (JEPPEM) from Universiti Sains Malaysia.

The inclusion criteria for this trial are patients with CBD stone as evidenced on imaging studies who are more than 18 years old. While the exclusion criteria are CBD stone size exceeding 15mm, number of CBD stone exceeding three, concurrent hepatobiliary tumour, patient with intrahepatic stone, patient with bleeding tendencies (coagulopathy, thrombocytopenia, patient on anticoagulant medication), patient in sepsis, cholangitis patient, patient with concurrent acute pancreatitis and history of patient with Bilroth II or Roux-en-y surgery.

### Sample Size Estimation

Assuming a 22.1% difference in CBD stone clearance rate in one endoscopic session with 74% in conventional group (EST alone) and 96.1% in EST plus EPLBD based on the previous positive series by Karsenti et al.<sup>12</sup> in 2017, with the usage of power and sample size programme, under Dichotomous test for sample size Design: independent, prospective, two proportion study, uncorrected chi-square test, with type 1 error of 0.05 (2-sided) and a power of 80%, PO of 0.74, P1 of 0.961 and m=1, the sample size needed is 40 for each arm. Add on 10% dropout :  $40 + 4 = 44$  for each arm.

Final sample size = 88

### Randomisation and Data Collection

Based on the sample size calculation, our required sample size was 88. But we were not able to achieve sample size of 88 on designated timeline (June 2021 to June 2022) due to inadequate number of patients undergone elective ERCP for choledocholithiasis in view of Malaysia movement control order (MCO) due to Covid-19 pandemic situation in Malaysia during that time. We managed to recruit 66 patients with CBD stone who meet all the inclusion criteria from period of June 2021 to June 2022. Written consent was taken from each of the patient.

A computer software for sequence generation was used and applied with 1:1 allocation using random block sizes of 6 and 8 to Group A: EST plus EPLBD or Group B: EST alone. The allocation concealment mechanism was developed by preparing equal numbers of sealed and opaque envelopes. Each envelop contain one allocation sequence which is generated by computer software. Data collection officer will randomly open one of the envelop each time one patient recruited and will need to follow the allocation sequences inside the envelop to determine whether the patient to be Group EST plus EPLBD or Group EST alone. This is single blinded study whereby the participant is blinded but the endoscopist is not blinded.

On the designated timeline, we are only able to recruit 66 patients out of 88 patients. As randomisation were already completed previously using computer software for sequence generation and allocation concealment mechanism for 88 patients with 88 sealed opaque envelopes, there were only 66 envelopes used. Thus, based on the randomisation method used above, there were 34 patients in EST+EPLBD arm and 32 patients in EST alone arm.

There is possibility of crossover of both arm in this study in which failure to clear all stone in EST alone will be proceeded with EST+EPLBD.

Participants were admitted 1 day prior to the procedure and were monitored in ward for at least 1 day after the procedure for any complication post procedure. Total duration of involvement were at least 72 hours.

### Procedure/Intervention

All the cases were done by one consultant hepatobiliary surgeon, with more than 5 years of experience in the field. ERCP was achieved with endoscopic side-viewing (Olympus Optical Co). Medications was given according to type of anaesthesia (local anaesthesia/monitored anaesthesia care/general anaesthesia) with or without the help of anaesthetist. In case of patient for ERCP under local anaesthesia, midazolam and pethidine and/or fentanyl were the preferred medications in our centre.

The initial cholangiogram was taken after cannulation of CBD.

**In EST alone group:** EST was extended to the full length of major duodenal papilla, but not exceeding the major duodenal horizontal fold avoiding crossing the intramural part of the CBD.

**In EST plus EPLBD group:** The length of the sphincterotomy was limited to one third the length of sphincterotomy of EST alone group. EPLBD with a balloon catheter (controlled radial expansion (CRE) wire-guided biliary dilation balloon catheter, Boston Scientific) was performed. The extent of balloon dilation was determined according to the size of the stones. The balloon was inflated slowly (1 – 2 minutes) under endoscopic and fluoroscopic guidance and was deflated immediately after the disappearance of the balloon waist.

After intervention done in both groups, conventional extraction balloon was trawled, and stone was removed from the bile duct.

#### *Operational Definition*

**CBD complete stone clearance:** no residual stone on cholangiogram in one endoscopic session (either via EST alone or EST plus EPLBD)

**Duration of procedure:** Defined as the duration of time from starting of intervention (EST alone or EST +EPLBD) until complete stone clearance as evidenced in cholangiogram.

**Number of attempts:** Defined as number of attempts of trawling that conventional retrieval balloon needed after intervention done (EST alone or EST +EPLBD) to remove CBD stone.

**Post ERCP pancreatitis:** Persistent abdominal pain more than 24 hours after ERCP and associated with rise of serum amylase more than three times of the upper normal limit.<sup>18</sup>

**Haemorrhage:** Evidence of bleeding such as melena or hematemesis with drop in at least 2g/dl of haemoglobin concentration or need for a blood transfusion.<sup>1</sup>

**Cholangitis:** Fever in which temperature > 38°C accompanied by leucocytosis and right upper quadrant abdominal pain after the procedure, without concomitant evidence of acute cholecystitis.<sup>1</sup>

#### *Statistical Analysis*

Statistical analysis was performed using SPSS version 26.0. Comparison of primary and secondary endpoints was done using independent t test and chi-square test. P-value of <0.005 is considered significant.

## **RESULTS**

A total of 66 patients were recruited and successfully randomised using computer software into two groups, group A for EST+EPLBD arm and group B for EST alone arm.

For baseline characteristics and demographic date of patient, mean age of study participants was 46.7 years, with group A patients had mean age of 45.5 years, while group B had mean age of 48 years. In term of gender, group A: EST+EPLBD arm included 24 female patients (70.6%) and 10 male patients (29.4%), while for group B: EST alone arm included 23 female patients (71.9%) and 9 male patients (28.1%). In group A, 15 patients (44.1%) had history of laparoscopic cholecystectomy, while, in group B, 16 patients

(50%) had history of laparoscopic cholecystectomy. In term of previous history of ERCP, in group A, 28 patients (82.4%) had previously undergone ERCP, while in group B, 23 patients (71.9%) had previously undergone ERCP.

The demographic data of all the participants are summarised in Table I.

For pre-ERCP blood investigations, both arms of patients had normal blood investigations in full blood count, renal function test, coagulation profile and liver function test. The pre-ERCP blood investigations result is summarised in Table II.

For the post ERCP data, 44 study participants (66.7%) had procedure (EST plus EPLBD or EST alone) done via local anaesthesia, while 22 study participants (33.3%) had procedure done via general anaesthesia. In terms of ampulla anatomy, 27 patients (79.4%) in group A: EST plus EPLBD had normal ampulla anatomy, while 26 patients (81.3%) in group B: EST alone arm had normal ampulla anatomy (p: 0.524). In terms of mean common bile duct (CBD) diameter, there is no statistically difference in mean CBD diameter in both groups. Group A patients had mean CBD diameter of 9.4 mm as compared to group B patient which had mean CBD diameter of 9.6 mm (p = 0.862). In terms of number of CBD stone, 55.9% of patients in group A had three CBD stone, while 40.6% of patients in group B had two CBD stone (p = 0.113). In addition, there is not statistically difference in largest size of CBD stone in both groups. Group A patients had largest CBD stone size of 7.6mm while group B patients had largest CBD stone size of 7.0 mm (p = 0.445).

#### **Comparison of overall complete stone clearance rate in Group A: EST plus EPLBD versus Group B: EST alone arm**

Group A patients achieved overall 100% complete stone clearance rate (n = 34), while group B patients achieved 93.8% overall stone clearance rate (n = 32), but it is not statistically significant (p = 0.139). Two patients from group B: EST alone arm unable to the had complete stone clearance thus, was being converted to EST plus EPLBD with intention to treat and able to achieve complete stone clearance. In term of number of attempts of trawling for conventional balloon retrieval needed for complete stone clearance, 41.2% of patient from group A required single trawling attempt of conventional balloon retrieval while 28.1% of patients from group B required two trawling attempts of conventional balloon retrieval to remove the CBD stone completely after the intervention (p = 0.523).

#### **Comparison of Duration of Procedure in Group A: EST plus EPLBD versus Group B: EST Alone Arm**

The duration for both procedures is almost similar, with 15.8 minutes for EST+ EPLBD and 15.5 minutes for EST alone (p= 0.860).

#### **Comparison of Rate of Adjunct Usage Among Patients in Group A: EST plus EPLBD versus Group B: EST Alone**

There was no usage of adjunct in both groups of study. Post ERCP data of both groups of study are summarised in Table III.

**Table I: Demographic data among patients with common bile duct stone in Hospital Universiti Sains Malaysia (n=66)**

Characteristics	Frequency (%)			p-value <sup>a</sup>
	All (n=66)	Group A EST + EPLBD (n=34)	Group B EST only (n=32)	
Age (years)*	46.7 ± 13.57	45.5 ± 12.64	48.0 ± 14.46	0.462 <sup>b</sup>
Gender				
Male	19 (28.8)	10 (29.4)	9 (28.1)	0.908
Female	47 (71.2)	24 (70.6)	23 (71.9)	
Ethnicity				
Malay	62 (93.9)	31 (91.2)	31 (96.9)	0.332
Chinese	4 (6.1)	3 (8.8)	1 (3.1)	
History of cholecystectomy				
Yes	31 (47.0)	15(44.1)	16 (50.0)	0.632
No	35 (53.0)	19 (55.9)	16 (50.0)	
History of ERCP				
Yes	51 (77.3)	28 (82.4)	23 (71.9)	0.310
No	15 (22.7)	6 (17.6)	9 (28.1)	

\*Presented in mean ±SD, SD= standard deviation

<sup>a</sup>Chi-square test was applied, <sup>b</sup>Independent t test was applied, significant set at 0.05

**Table II: Pre-ERCP lab investigation among patients with CBD stone in HUSM (n=66)**

Characteristics	Mean (SD)			p-value <sup>a</sup>
	All (n=66)	EST + EPLBD (n=34)	EST only (n=32)	
TWC	8.6 ±2.15	8.6 ±2.13	8.5 ±2.21	0.966
Platelet	269.2±78.78	283.0 ±74.56	254.9 ±81.61	0.152
INR	1.1 ±0.35	1.0 ±0.08	1.1 ±0.50	0.142
APTT	38.1 ±7.50	38.7 ±10.04	37.4 ±3.16	0.515
Serum urea	7.0 ±15.35	7.1 ±19.28	7.0 ±9.92	0.983
Serum creatinine	69.6 ±17.48	70.7 ±15.34	68.3 ±19.67	0.578
Total bilirubin	15.4 ±18.80	12.8 ±13.05	18.2 ±23.51	0.267
Albumin	41.2 ±3.79	41.5 ±4.29	40.8 ±3.22	0.466
ALP	125.8 ±63.8	126.6 ±59.63	125.0 ±68.96	0.920
AST	38.8 ±44.26	41.6 ±51.95	35.7 ±34.86	0.588
ALT	60.3 ±97.88	71.1 ±118.14	48.7 ±70.44	0.357

All data presented in mean± SD, SD= standard deviation

<sup>a</sup> Independent t test was applied, significant set at 0.05

**Table III: Post-ERCP among patients with CBD stone in HUSM (n = 66)**

Characteristics	Frequency (%)			p-value <sup>a</sup>
	All (n=66)	EST + EPLBD (n=34)	EST only (n=32)	
Type of anaesthesia				
LA	44 (66.7)	22 (64.7)	22 (68.8)	0.728
GA	22 (33.3)	12 (35.3)	10 (31.3)	
Ampulla anatomy				
Normal	53 (80.3)	27 (79.4)	26 (81.3)	0.524
Floppy	12 (18.2)	7 (20.6)	5 (15.6)	
Diverticulum	1 (1.5)	0 (0.0)	1 (3.1)	
CBD diameter (mm)*	9.5 ±3.49	9.4 ±3.66	9.6 ±3.36	0.862 <sup>b</sup>
Number of stones				
1	16 (24.2)	9 (26.5)	7 (21.9)	0.113
2	19 (28.8)	6 (17.6)	13 (40.6)	
3	31 (47.0)	19 (55.9)	12 (37.5)	
Largest size of stone (mm)*	7.3 ±2.78	7.6 ±2.61	7.0 ±2.97	0.445 <sup>b</sup>
Stone clearance				
Complete	64 (97.0)	34 (100.0)	30 (93.8)	0.139
Incomplete	2 (3.0)	0 (0.0)	2 (6.3)	
Number of attempts				
1	22 (33.3)	14 (41.2)	8 (25.0)	0.523
2	15 (22.8)	6 (17.6)	9 (28.1)	
3	14 (21.2)	7 (20.6)	7 (21.9)	
More than 3	15 (22.7)	7 (20.6)	8 (25.0)	
Duration of the procedure (minutes)*	15.6 ±6.75	15.8 ±5.58	15.5 ±7.89	0.860 <sup>b</sup>

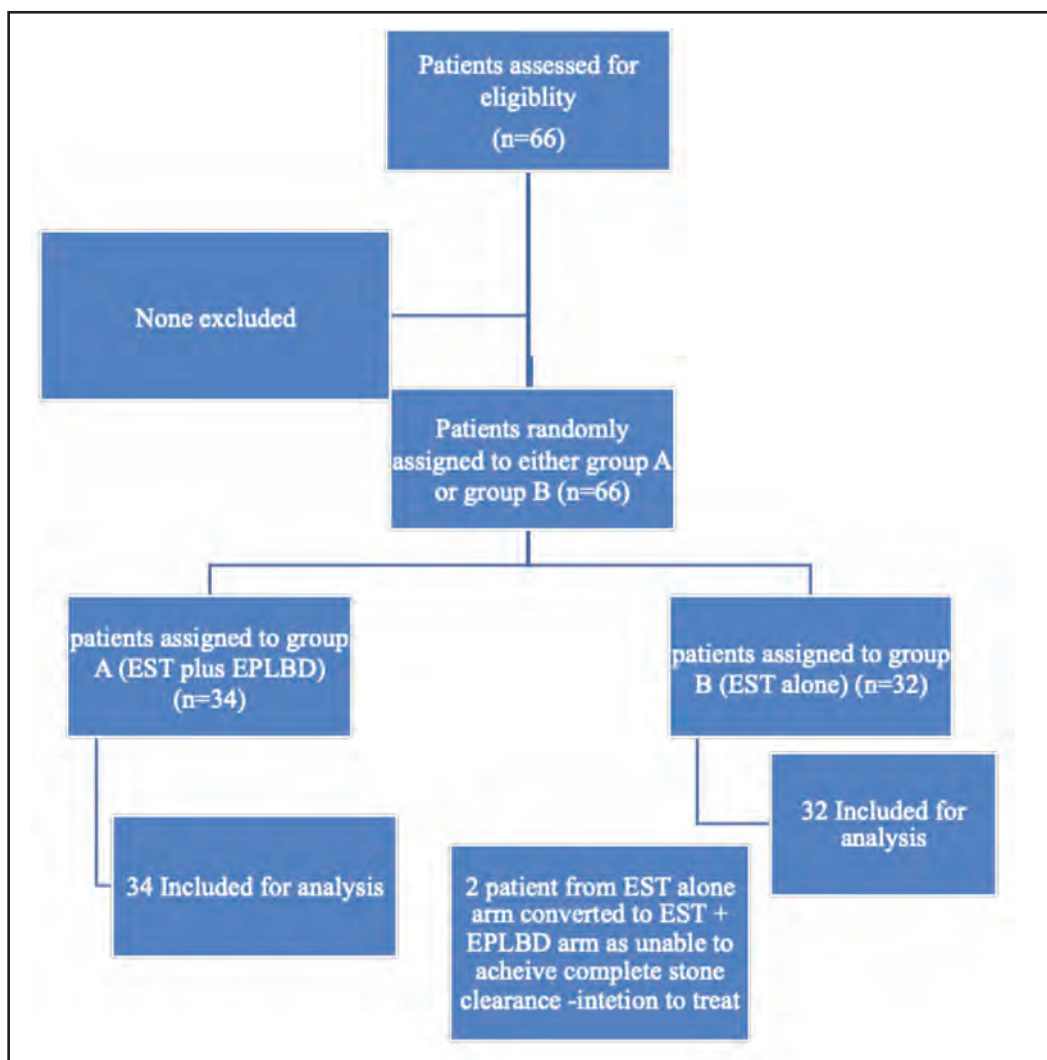
\*Presented in Mean ±SD, SD= standard deviation

<sup>a</sup>Chi-square test was applied, <sup>b</sup>Independent t test was applied, significant set at 0.05

**Table IV: Complications Among Patients with CBD stone in HUSM (n=66)**

Complications	Frequency (%)		p-value <sup>a</sup>
	EST + EPLBD (n = 34)	EST only (n = 32)	
Pancreatitis			
Yes	1 (2.9)	0 (0.0)	0.328
No	33 (97.1)	32 (100.0)	
Bleeding			
Yes	0 (0.0)	1 (3.1)	0.299
No	34 (100.0)	31 (96.9)	

<sup>a</sup>Chi-square test was applied, significant set at 0.05



**Fig. 1:** Consort flowchart

**Comparison of complications among patients in Group A: EST plus EPLBD versus Group B: EST Alone**

In general, there were only two cases of complication reported among patients in both groups of study. One patient from group A (2.9%) developed pancreatitis, while one patient from group B (3.1%) developed bleeding post procedure. There was no significant difference of complication between EST+ EPLBD and EST alone (p value >0.05).

There was no cholangitis or perforation complication happened in both groups.

Complications rate of both groups of study are summarised in Table IV.

**DISCUSSION**

Gallstone is a worldwide clinical problem which is affecting most of the populations with incidence of 15 to 20% in west

and 10% in Asians.<sup>19</sup> About 5 to 15% of patients with gallstones will go on to develop bile duct calculi.<sup>20</sup> Complications of bile duct stone can be devastating including pain, complete or partial biliary obstruction leading to obstructive jaundice, cholangitis, hepatic abscess, pancreatitis, and secondary biliary cirrhosis.<sup>21</sup> Thus, due to these serious complications, there are several endoscopic strategies developed for treatment of common bile duct stone that are EST alone, EPLBD and combination of EST plus EPLBD.

The development of EST occurred in 1974.<sup>22</sup> It is the most common procedure used during ERCP to remove CBD stone and is considered as standard therapy for treatment of choledocholithiasis.

EST requires an adequate incision on major duodenal papilla to achieve biliary cannulation and thus it can potentially cause damage to biliary sphincter during the procedure and can increase risk of some complications such as bleeding and biliary reflux.<sup>1</sup> Apart from that, it can potentially carry long term effect like sphincter dysfunction.<sup>2</sup> With the loss of sphincter function, it can cause enteric biliary reflux with bacterial colonisation and thus lead to cholangitis and stone formation.<sup>4</sup>

In 1983, a method called EPLBD was introduced and it is an alternative to EST in clearing CBD stone.<sup>3</sup> EPLBD can reduce the risk of bleeding and perforation post procedure, but it carries higher risk of post-ERCP pancreatitis.<sup>4,6</sup> EPLBD is usually only useful in extracting small to moderate sized stone which is less than 10mm.<sup>6</sup> About 10 to 15% of CBD stone was unable to be extracted by either EST nor EPLBD alone, especially in patients with large and difficult stone.<sup>7</sup>

In 2003, another method called combination of EST plus EPLBD was introduced as an alternative method to EST alone and EPLBD.<sup>9</sup> It can reduce the risk of complications through avoiding a complete sphincterotomy, shortening procedural time, and reducing the need of usage of mechanical lithotripsy.<sup>10</sup>

As mentioned above, EPLBD alone carries higher risk of post-ERCP pancreatitis.<sup>4,6</sup> EST alone carries higher risk of post-ERCP bleeding.<sup>1</sup> While EST plus EPLBD is useful in dealing with patient with flat ampulla where small sphincterotomy only can be performed.<sup>10</sup>

A meta-analysis done at 2013 to compare efficacy and safety of EST plus EPLBD and EST alone in removing large CBD stone (>15 mm in size), and this study had shown that EST plus EPLBD is equally effective as EST alone in removing large CBD stone and at the same time had lesser perforation risk.<sup>23</sup> However, in this meta-analysis, one of the limitations is this study included two low quality trials and thus vulnerable to bias. Apart from that, one systemic review and network meta-analysis done on 2020, comparing efficacy and safety of EST alone, EST plus EPLBD and EPLBD alone in managing CBD stone and the result showed that EPLBD has highest successful rate in removing CBD stone.<sup>24</sup> So, there is still no definite conclusion based on these two meta-analyses. Thus, in our study, we aim to compare effectiveness and

safety of both arm in removing CBD stone (<15mm in size) as previous meta-analysis only conducted for large CBD stone and still no definite conclusion whether both method is equally effective, or one arm is more effective than another arm.

In our study, EST plus EPLBD group had higher percentage of overall complete stone clearance rate when compared to EST alone group (100% vs 93.8%), but it is not statistically significant ( $p = 0.139$ ). Our study is in agreement in many other studies in which both EST plus EPLBD groups and EST alone groups have comparable efficacy in removing CBD stone.

In a study conducted in 2007, it was found that EST plus EPLBD had comparable efficacy and safety when compared to conventional EST alone.<sup>10</sup> In another study in 2020 by Mustafa et al,<sup>11</sup> it was found that EST plus EPLBD had a comparable efficacy when compared with EST alone. While in another study in 2017 by Karsenti et al,<sup>12</sup> it was found that EST plus EPLBD groups had higher success rate of complete CBD stone removal in first session when compared to EST group alone, but the overall complete stone clearance rate and complication rate were similar in both groups. In our study, those patients who failed to achieve complete stone clearance via EST alone were converted to EST plus EPLBD arm and able to achieve complete stone clearance.

While in terms of procedural time, our study showed that there is no difference in duration of procedure for both EST plus EPLBD and EST alone groups ( $p = 0.860$ ). This contrasts with the study in 2020 by Mustafa et al,<sup>11</sup> in which in the study, EST plus EPLBD required shorter procedural time.

For this study, it was noted that 77.3% of patient had previous ERCP before, which indicate likely sphincterotomy done during previous ERCP. There is no study done to compare the efficacy of EST plus EPLBD or EST alone in removing CBD stone for patients with prior sphincterotomy versus patient with no prior history of sphincterotomy. However, another study done in 2022 to quantify the effect of previous sphincterotomy on post-ERCP pancreatitis, showed that that the risk of post-ERCP pancreatitis is halved by prior sphincterotomy.<sup>25</sup> In our study, there is one patient from EST plus EPLBD group (2.9%) developed post-ERCP pancreatitis while there is no patient from EST alone group developed post ERCP pancreatitis, however it is not statically significant (2.9% vs 0 ;  $p = 0.328$ ). This is same with the study by Mustafa et al,<sup>11</sup> in which EST plus EPLBD group did not have increased risk of post-ERCP pancreatitis. In fact, EST plus EPLBD may have a lower chance of post ERCP pancreatitis as EST done prior to EPLBD will cause the separation of biliary orifice from pancreatic duct and can lead the path of balloon dilatation towards CBD rather than pancreatic duct.<sup>26,27</sup>

In addition, none of our patients from EST plus EPLBD group developed post-ERCP bleeding complications as compared to EST alone group in which one patient developed post-ERCP bleeding (0 vs 3.1%;  $p = 0.299$ ). However, it is not statically significant. In recent randomised controlled trial in 2019, the trial showed that EST alone group have higher post-ERCP bleeding rate compared to EST plus EPLBD.<sup>28</sup> In the EST

group, the bleeding rate was like the 1 to 3.0% rates reported by Cotton et al.<sup>1</sup> We believe that the decrease in bleeding episodes in EST plus EPLBD group may be caused by the balloon tamponade placed at the sphincterotomy site during EPLBD.

There is no cholangitis/perforation complication occurred in both groups of study.

#### LIMITATIONS

One of the limitations of our study is the small sample size that might be too small to detect difference in clinical outcomes such as total procedural time and stone extraction between endoscopic sphincterotomy (EST) plus endoscopic papillary large balloon dilatation (EPLBD) group and EST alone group. Small sample size might also decrease the validity of the study.

Another limitation is the single-centre clinical trial design may produce potential bias.

Besides that, another limitation in the study is only short-term complications was being studied, but not long-term complications such as recurrent common bile duct stone.

Another limitation of this study is cost of study. The cost of EPLBD is higher than EST alone as EPLBD will need a balloon catheter (Controlled Radial expansion (CRE) wire-guided biliary dilation balloon catheter, Boston Scientific).

Perhaps a future study with larger sample size and focusing of comparing long term complications such as recurrent CBD stone in both groups of patients should be carried out.

#### CONCLUSION

In summary, endoscopic sphincterotomy (EST) plus endoscopic papillary large balloon dilatation (EPLBD) had comparable efficacy rate of removing common bile duct stones when compared with EST alone group, without increasing the procedural time and adverse events. EPLBD plus EST should be considered as an alternative solution if complete stone clearance unable to achieve via EST alone.

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