

The outcomes and early complications of endoscopic partial sphincterotomy with, endoscopic papillary balloon dilatation versus, endoscopic sphincterotomy in patients with common bile duct stone disease

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ABSTRACT

Introduction: Choledocholithiasis refers to the presence of stone(s) within the common bile duct, most of cases of choledocholithiasis are secondary to the passage of gallstones from the gallbladder into the common bile duct. Endoscopic treatment by endoscopic retrograde cholangiopancreatography (ERCP) is the least invasive method and it's the procedure that should be primarily tried. EST is the gold standard procedure in the current endoscopic treatment. Endoscopic papillary balloon dilation (EPBD) it's an alternative to endoscopic sphincterotomy (EST) for removing bile duct stones. In an effort to avoid permanent destruction of the biliary sphincter, EPBD seemed to be an attractive alternative to early investigators. **Aim of study:** To evaluate the outcomes and early complications of endoscopic sphincterotomy with endoscopic papillary balloon dilatation versus endoscopic sphincterotomy alone in patients with common bile duct stone disease. **Patients & method:** One hundred forty patients with CBD stone disease were all treated by ERCP then studied, 100 patients of them were exposed to endoscopic sphincterotomy alone and 40 of them were exposed to EST with EPBD, Cotton's criteria were used to determine the incidence and severity of post EST with EPBD or post-EST pancreatitis. CBD stone extraction and other complications (bleeding, cholangitis and perforation) after each procedure were compared between the two groups. **Results:** The CBD stones were removed successfully in 91% (91/100) and 85% (34/40) of patients who underwent EST alone or EST with EPBD respectively ($p=1.075$). Acute Pancreatitis occurred in (6/100)6% of EST group compared with (2/40)5% of EST with EPBD group, $p=0.053$. Acute bleeding in form of mild bleeding which stopped spontaneously was occurred in (3/100)3% of EST group as compared with (1/40)2.5% of EST with EPBD group $p=0.026$. Perforation and acute cholangitis were not reported during the study in any patient. **Conclusion:** EST with EPBD can be used as safe and effective alternative to EST alone in CBD stone patients and it is comparable to EST alone for CBD stone extraction and post procedure pancreatitis risk.

Introduction:

Choledocholithiasis refers to the presence of stone(s) within the common bile duct (CBD), most cases of choledocholithiasis are secondary to the passage of gallstones from the gallbladder into the common bile duct¹. Primary choledocholithiasis (i.e., formation of stones within the common bile duct) is less common. Primary choledocholithiasis typically occurs in the setting of bile stasis (e.g., patients with cystic fibrosis), resulting in a higher propensity for intraductal stone formation, older adults with large bile ducts and periampullary diverticula are at elevated risk for the formation of primary bile duct stones, patients with recurrent or persistent infection involving the biliary system are also at risk¹.

CBD stones may be asymptomatic (up to half of cases), or associated with various symptoms and conditions, ranging from colicky pain to potentially life-threatening complications, such as ascending cholangitis or acute pancreatitis². Endoscopic treatment by endoscopic retrograde cholangiopancreatography (ERCP) is the least invasive method and it's the procedure that should be primarily tried. Recently, endoscopic treatment has made remarkable progress and it can be performed in most patients diagnosed with common bile duct stones³. As for the papilla, endoscopic sphincterotomy (EST) was first reported by the pioneers Kawai et al and Classen et al in 1974⁴⁻⁵.

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EST is the gold standard procedure in current endoscopic treatment. However, sometimes endoscopic papillary balloon dilation (EPBD) is performed because it can be used in patients with a bleeding tendency, those who have been subjected to Bill Roth-II reconstruction or surgery, and in patients in whom it is necessary to preserve papillary sphincter muscle function⁶.

Although these procedures are useful to treat bile duct stones, it is difficult to perform stone extraction in patients with stones ≥ 15 mm or with multiple stones, and it is reported that many patients require a lithotripsy procedure such as mechanical lithotripsy (ML) or electrohydraulic or laser lithotripsy^{7,8,9}. Currently, endoscopic papillary balloon dilation (EPBD), which consists of stone extraction without lithotripsy and dilation of the papilla using a large balloon, has been reported for large stones or multiple stones after performing EST¹⁰⁻¹¹.

Endoscopic sphincterotomy (EST):

The term sphincterotomy refers to severing of the deep muscle layers of the sphincter of Oddi¹². The goal of it is to overcome the principal anatomic barrier impeding stone passage and facilitating stone extraction¹².

Technique: Standard sphincterotomy involves the application of electrocautery to create an incision through the musculature of the biliary portion of the sphincter of Oddi. A number of different devices are available with that vary in design to facilitate the procedure depending upon specific anatomic considerations. In expert hands, a sphincterotomy is possible in 95 to 100 percent of patients¹². The length of the sphincterotomy should be tailored to the size of the stone and papilla. We prefer to create a sphincterotomy that completely unroofs the papilla, since this maximizes access to the common bile duct and decreases the risk of developing papillary stenosis¹². Sphincterotomy is usually performed after selective deep cannulation of the bile duct has been accomplished.

However, in some circumstances, this may not be possible. As an example, impaction of a stone within the papillary sphincter may prohibit advancement of a papillotomy or guidewire. In these patients, sphincterotomy can still be accomplished using a needle knife papillotomy, a technique known as precutting¹².

Indications of EST:

- 1 - Common bile duct stones.
- 2-Facilitation of biliary stent placement (especially multiple stents) for malignant or benign common bile duct obstruction or stricture.
- 3- Palliation of obstruction due to malignant ampullary neoplasm as alternative to stent placement.
- 4-Sphincter of Oddi dysfunction (SOD), benign papillary stenosis.
- 5- Biliary leaks.
- 6-Miscellaneous conditions (choledochocoele, sump syndrome, biliary parasites).
- 7- Access for peroral choledochoscopy.
- 8-Access for cannulation of the pancreatic duct after failure of standard cannulation techniques¹³.

Contraindications of EST:

Contraindications to ERCP and EST include an uncooperative or unstable patient, inability of the patient to provide informed consent, uncorrected coagulopathy, and a newly created gastrointestinal anastomosis. Contrast hypersensitivity is not considered a contraindication to EST, but prophylactic intravenous application of corticosteroids may be considered. Preprocedure coagulation studies are strongly recommended and coagulopathy must be corrected before sphincterotomy¹³.

The presence of liver cirrhosis and use of aspirin or other nonsteroidal anti-inflammatory drugs do not appear to be important predictors of bleeding. However, antiplatelet drugs such as Clopidogrel and Ticlopidine should be interrupted for at least 7 days before elective sphincterotomy depending on the individual clinical risks¹³.

Cutting should be avoided if the position of the cutting wire cannot be seen or if the tip of the sphincterotome is bowing in the wrong direction because of difficult anatomy¹³. If these problems cannot be resolved by changing the position of the device or through other maneuvers, then balloon dilation of the biliary sphincter should be considered as an alternative to EST¹³.

Complications of sphincterotomy:

A-Short-term complications:

- 1 -Acute pancreatitis which is the most frequent complication (5%).
- 2- Bleeding (2%).
- 3-Perforation (0.5-2.1%)¹⁴.

B-Long-term complications:

Long-term complications following endoscopic sphincterotomy include stone recurrence, papillary stenosis, and cholangitis, which occur in approximately 6 to 24 percent of patients¹⁵⁻¹⁶.

Endoscopic papillary balloon dilation (EPBD):

It's an alternative to endoscopic sphincterotomy (ES) for removing bile duct stones^{17,18,19,20}. In an effort to avoid permanent destruction of the biliary sphincter, EPBD seemed to be an attractive alternative to early investigators, such as Staritz and Meyer zum Buschen-felde, who first reported it in 1983²¹.

In this procedure a balloon is inflated to enlarge the opening of the bile duct at the level of the biliary sphincter. The main theoretical advantage of this technique is that it does not involve cutting the biliary sphincter. Therefore acute adverse events such as bleeding and perforation should be less likely, and the function of the biliary sphincter is also preserved¹⁸.

Indications for EPBD:

In the recent meta-analysis by Baron et al., the incidence of bleeding was significantly less after EPBD compared to EST²². Clinically significant post-ES bleeding occurs in 2% to 5% of ES patients^{14, 23}.

In addition, patients with coagulopathy and those requiring anticoagulation within 3 days of the procedure are at increased risk for bleeding¹⁴. Thus transient discontinuation of anticoagulation, correction of coagulopathy with fresh frozen plasma, or platelet transfusion are frequently used to avoid bleeding after ES, though these measures may be inadequate to prevent it. EPBD provides a useful alternative to ES in such cases no articles have described bleeding after EPBD^{17, 19, 20, 24}.

In light of this, EPBD should be considered a viable alternative to ES in patients with an underlying coagulopathy or the need for anticoagulation following ES, as such patients have a higher incidence of post-ES bleeding¹⁴.

EPBD may significantly reduce the risk of bleeding compared to EST in patients with advanced cirrhosis and coagulopathy. In these patients, EPBD is recommended over EST for treating choledocholithiasis²⁵.

Other populations in which EPBD may be an attractive option are those patients who refuse blood transfusion for religious reasons and patients with difficult anatomy that prevents safe orientation of the papillotomy for EST e.g., prior Billroth II gastrectomy, or intradiverticular location of the papilla²⁶.

Bergman et al reported a randomized trial of EPBD and EST for removing bile duct stones in patients with a prior Billroth II gastrectomy²⁶.

Compared to patients with a normal anatomy, patients with a prior Billroth II gastrectomy had a significantly increased risk of bleeding after EST. Early adverse events occurred in 19% of the patients who underwent EPBD as compared to 39% of the

patients who underwent EST²⁷. Endoscopic stone removal in patients with a prior Billroth II gastrectomy and Billroth II anastomosis poses one of the great challenges to the biliary endoscopist²⁷.

Compared to standard EST in the normal anatomic situation, all of these techniques are more demanding and probably associated with a smaller sphincterotomy incision, less successful stone removal, and a higher rate of acute adverse events²⁶. When EST is used for such patients, careful consideration must be given to the direction and length of the incision, and a high level of skill is required to avoid severe adverse events. With EPBD, however, once a catheter is inserted into the common bile duct, the balloon catheter is simply inserted and the balloon is inflated, therefore patients with Billroth II anatomy appear to be especially suited for stone removal using EPBD²⁸.

Adverse Events of EPBD:

1 -Acute pancreatitis, Bleeding ,Infection (cholangitis or cholecystitis) and Perforation²⁸.

Contraindications and limitations of EPBD:

1 -The presence of acute cholangitis.

2- History of previous or ongoing acute pancreatitis.

3- Difficult biliary cannulation²⁹.

Aim of study:

To evaluate the outcomes and early complications of endoscopic partial sphincterotomy with endoscopic papillary balloon dilatation versus endoscopic sphincterotomy in patients with common bile duct stone disease.

Design:

The research design was a prospective interventional analytical cohort single center study in which we evaluated the early complications and outcomes of EST versus EST with EPBD in patients with common bile duct stone disease.

Patients and methods: This study was done in the Gastroenterology and Hepatology teaching hospital in Baghdad (IRAQ), From January 2015 to January 2016.

One hundred forty patients with CBD stone disease were all treated by ERCP by different operators, 100 patients of them were treated by endoscopic sphincterotomy and 40 of them were treated by EST with EPBD, 52(37.1%) of them were male and 88(62.8%) were female patients.

All patients with common bile duct stone(s) treated by ERCP were included. They had underwent full history and clinical examinations , biochemical investigations and cross-sectional imaging (by

means of MRI,MRCP) and divided into two groups one with EST alone and the other with EST and EPBD(in those patients the indications to do EPBD were large stone and periampullary diverticula).

The caliber of common bile duct and stone size were taken in consideration. The yield and outcomes in form of complete clearance of common bile duct from stones in same session were assessed.

Early complications in form of 1 st day post ERCP bleeding, pancreatitis, acute cholangitis and perforation in both groups were assessed as well.

Patients in which we failed to extract their large stones were not exposed to mechanical lithotripsy and referred directly to surgery because of risk of intrabiliary entrapment of the lithotripsy basket.

Exclusion criteria:

(1)Patients with Bleeding diathesis, (2) previous EPBD (3) Bill Roth II or Roux-en-Y anatomy, (4) distal extrahepatic bile duct stenosis, (5) acute pancreatitis (6) intrahepatic bile duct stone. (7) Acute cholangitis (8) Current anticoagulation or Clopidogrel treatment. (9) Pregnancy (10) Inability to give informed consent.

Intervention:

All patients received standard method of sedation in form of combination of pethidine, diazepam and/or midazolam prior to ERCP with routine prophylactic intravenous Ceftriaxone 1gm once daily to prevent post ERCP biliary infection and prophylactic Indomethacin rectal suppositories was used to prevent post ERCP pancreatitis.

ERCP was done with side viewer endoscope Pentax (4.2) ED-3490TKEPKi-5000 guide wire-assisted selective cannulation of the CBD, using a sphincterotome (ERCP cannula; CT-30, Cannulotome II PC double lumen sphincterotome, COOK medical, USA), confirmation of the correct site of the catheter in CBD was performed by fluoroscopic imaging. For EST we used electrocautery method by ERBE system ICC200.

For EPBD, a triple-sized dilator balloon (Hercules 3 stage-wire guided esophageal/pyloric/colonic balloon dilation catheter; COOK medical,USA) was inserted into the bile duct, for dilating the papilla.

The balloon was inflated by dye in different steps up to 16mm and according to CBD size and stone: each for 1 min. Stones were removed with a multiple-sized TRI-EX extractor balloon (COOK medical, USA),then CBD stones were removed with the extractor balloon.

Post procedure evaluation:

After the procedure was completed the patients were observed in the ward for 24 hour for any complication in form of bleeding, pancreatitis (according to **Cotton *et al.*** criteria), perforation and acute cholangitis.

Severity classification of post ERCP pancreatitis by cotton *et al.*

mild moderate severe Hospitalization for more than 10 days, or hemorrhagic pancreatitis, necrosis or pseudocyst or intervention (percutaneous drainage or surgery). Pancreatitis requiring hospitalization of 4-10 days. Clinical pancreatitis, amylase at least 3times normal at more than 24 hr. After the procedure, requiring admission or prolongation of planned admission for 2-3 days.

Statistical analysis:

After collecting data it were analyzed using SPSS software for windows version 18, binary variables were compared using **chi-square** test and the difference was considered significant when *p* was <0.05.

RESULTS:

A total of 140 patients were studied their mean age was (55.35±16.86 SD) years, 52(37.14%) out of 140 were male patients, while 88(62.85%) were female patients.

All the studied patients were underwent ERCP in which they divided into 2 groups an EST group which included 100(71.4%) patients, 36(25.71%) male and 64(45.71%) female, the second group was those patients who underwent EST and EPBD they were 40 (28.6%) patients in which 16(11.42%) male and 24(17.14%) female. The mean age in males was (56.36±14.91 SD) year, while the female mean age was (54.76±17.98SD) year.

Twenty (14.2%) patients with periampullary diverticulum were reported, 9(6.4%) of them were male while 11 (7.8%) were female patients, 4(2.8%) of them in EST group and 16 (11.4%) in EST and EPBD group.

The mean CBD size was (11.01±3.57 SD) mm, the mean CBD size in EST group was (9.84±2.47 SD) mm while the EST and EPBD group was (13.95±4.19 SD) mm.

The size of CBD stones ranging from (4 to 21) mm, the mean stone size in all patients was (8.06±3.36 SD) mm, while the mean stone size in EST group was (6.67±1.74 SD) mm and the EST and

EPBD group was (11.32 ± 4.16 SD) mm.

The number of CBD stone(s) was ranging from (1 to 4) stones the mean stone number was (1.23 ± 0.58 SD), the mean stone number in EST group was (1.27 ± 0.64 SD) and in EST and EPBD was (1.15 ± 0.36 SD).

The mean balloon size was (12.77 ± 3.69), the mean in male was 12.87 ± 3.57 , while in female was 12.70 ± 3.82 .

Clinical Characteristics of the study: summarized in table no. 1 and 2

Table no. 1 clinical characteristics of patients

PROCEDURE TYPE	CBD CLEARANCE		TOTAL NO. (%)
	YES	NO	
EST GROUP. NO. (%)	91(91)	9(9)	100(100)
EST+EPLBD GROUP NO. (%)	34(85)	6(15)	40(100)
TOTAL NO. (%)	125(89.2)	15(10.8)	140(100)
P.VALUE	1.075		

Table no. 2 characteristics of patients

PARAMETER	OVERALL	EST GROUP	EST+EPLBD GROUP
Mean CBD size in Mm(SD)	11.01 (3.57)	9.84 (2.47)	13.95 (4.19)
Male(SD) Female(SD)	10.78(3.44) 11.14(3.65)	9.55(2.52) 10(2.44)	13.56(3.68) 14.20(4.55)
Mean stone size in Mm(SD)	8.06 (3.36)	6.67 (1.74)	11.32 (4.16)
Male(SD) Female(SD)	8.51(3.68) 7.79(3.15)	7.02(1.85) 6.6(1.67)	11.87(4.54) 10.95(3.95)
Mean stone no.(SD)	1.23 (0.58)	1.27(0.64)	1.15 (0.36)
Male(SD) Female(SD)	1.32 (0.73) 1.18 (0.46)	1.41(0.84) 1.18 (0.5)	(0.34) 1.16 (0.38)
Mean balloon size in Mm(SD)			12.77(3.69)
Male(SD) Female(SD)			12.87(3.57) 12.70(3.82)

The CBD stones were removed successfully in 91% (91/100) and 85% (34/40) of patients who underwent EST and EST and EPBD respectively ($p=1.075$).

Patients with CBD stone(s) larger than 10 mm were 31 out of 140 patient, 7(22.6%) of them were in EST group and all of them had successful stone removal.

The remaining 24(77.4%) patients were in EST and EPBD group in which 18(58.1 %) patients were had successful stone(s) clearance while 6 (19.3%) of them had failure of clearance, p value is 2.1.

Acute Pancreatitis occurred in 6% of EST group as compared with 5% of EST and EPBD group, $p=0.053$. severity of acute pancreatitis was determined as mild type according to criteria of cotton *et al.*

All patients were treated conservatively successfully with full recovery as no any type of intervention was needed.

Acute bleeding in form of mild bleeding which stopped spontaneously was occurred in 3% of EST group as compared with 2.5% of EST and EPBD group $p=0.026$.

Perforation and acute cholangitis were not reported during the study in any patient.

The procedure related outcomes and complications which are summarized in both table 3, 4 and 5 below.

TABLE 3. Comparison of CBD clearance in same session between EST and EST and EPBD groups

PROCEDURE TYPE	CBD CLEARANCE		TOTAL NO. (%)
	YES	NO	
EST GROUP. NO. (%)	91(91)	9(9)	100(100)
EST+EPLBD GROUP NO. (%)	34(85)	6(15)	40(100)
TOTAL NO. (%)	125(89.2)	15(10.8)	140(100)
P.VALUE	1.075		

Table.4 Comparison of procedure related adverse events between the EST+ EPLBD and EST group

Complication	EST Group (No.=100)	EST+EPLBD Group (No.=40)	P. value
Pancreatitis No. (%)	6(6)	2(5)	0.053
Bleeding No. (%)	3(3)	1(2.5)	0.026
Perforation No. (%)	0	0	
Acute cholangitis No. (%)	0	0	

Table no.5 CBD clearance in stones > 10mm

Procedure type.	CBD clearance		Total
	Yes	No	
EST group no. (%)	7(100)	0(0)	7(100)
EST+EPBD Group no. (%)	18(75)	6(25)	24(100)
Total	25(80.7)	6(19.3)	31(100)
P. value	2.1		

Discussion:

Since the introduction of EPBD as an alternative method for EST, several studies reported that it has some advantageous effects over the EST with regard to outcomes and short and long term complications^{22, 30, 31}.

EPBD is relatively easier to perform than EST, with less possibility of complications of bleeding and perforation. It also allows functional preservation of the papillary sphincter, one of the

major advantages of EPBD over EST, which in turn may result in a decrease in long term complication (liver abscess, cholangitis, abdominal pain, etc)²².

In the present study we achieved CBD stone clearance in 91% (91/100) versus 85% (34/40) of patients who underwent EST and EST and EPBD respectively, ($p=1.075$) which revealed insignificant difference between the 2 groups according to p value result.

Successful clearance of large CBD stone(s) with size more than 10 mm was in 100% of cases in EST group (7/7) versus 75% (18/24) of patient in of EST and EPBD group, p value is 2.1 which is statistically insignificant.

Heo JH et al found that EST plus EPBD compared with EST alone resulted in similar outcomes in terms of overall successful stone removal (97.0% vs 98.0%), and for large stones removal (94.4% vs 96.7%) which is statistically not significant³². The result of our study was in agreement with **Heo JH et al** study in which there is no significant difference in CBD stone clearance between the two groups.

The rate of post ERCP complications were compared between the two groups and we found that the incidence of post ERCP **pancreatitis** was 6% in EST group versus 5% in EST and EPBD group p value is 0.053 which is statistically insignificant.

Heo JH et al found that Complications were as follows: for the EST plus EPBD group and the EST group: pancreatitis, 4.0% and 4.0% which is statistically insignificant³².

Also our study is in agreement with **Heo JH et al** in which there is no significant difference in rate of post ERCP pancreatitis between the two groups.²²

This may be explained by the routine use of prophylactic Indomethacin suppositories with cautious use of guide wire assisted biliary duct cannulation, avoidance of needle Knife sphincterotomy, avoidance of pancreatic duct cannulation and contrast injection, and the use of different sizes of balloon.

Also Partial sphincterotomy separate the pancreatic orifice from the biliary one preserving it from injuries related to biliary dilation.

Perforation was not reported in any patient in both groups and Post ERCP. **acute cholangitis** was not reported also in both groups and this may be attributed to good prophylactic antibiotic treatment (Ceftriaxone 1gm/day) received by all patients prior to ERCP.

Post ERCP **bleeding** was found in 3% versus 2.5% in EST group and EST and EPBD group, respectively which is statistically significant as the p value is 0.026.

Heo JH et al found that EST plus EPBD compared with EST alone resulted in bleeding in 0% and 2.0%, respectively which is statistically not significant³².

Yang X, Hu B, they found There were no significant

differences between the two groups regarding complete stone removal in the first session, post-ERCP pancreatitis, bleeding, infection of biliary tract³³.

Lei Xu et al, they reported no significant difference of adverse events between the two interventions, such as post-ERCP pancreatitis, bleeding, infection, and perforation, with no difference in stones clearance rate³⁴.

Shi-Bin Guo et al reported that the rates of stone removal in the first session were not significantly different between the two groups and the rates of post ERCP pancreatitis were not significantly different between the two groups³⁵.

Shi-Bin Guo et al reported also that there were no cases of perforation, acute cholangitis, in the two groups but the rate of bleeding was significantly lower in EST and EPBD group than in EST group alone³⁵. Our study was in agreement with the results of **Yang X, Hu B** and **Lei Xu et al** studies apart from the difference in incidence of bleeding which was more in EST group and statistically significant.

Also our study was in agreement with all the results of **Shi-Bin Guo et al** study.

Limitations of the study:

1 -The number of patients included in this study is small.

2 -The balloon diameter(s) reported in the study were different, and this may affect the overall risk of pancreatitis and bleeding, in addition to other risk factors.

3 -The ERCP was operated by different operators which may affect the overall results.

Conclusion:

1 -EST with EPBD can be used as safe and effective alternative to EST alone in CBD stone patients and it is comparable to EST for CBD stone extraction.

2 -In our study the risk of bleeding is less in EPBD so it may outweigh EST for patients with coagulopathy, cirrhosis, patients with history of Billroth II surgery, patients with periampullary diverticulum and patients with large CBD stones.

3 -Partial sphincterotomy plus balloon dilation has a lower incidence of procedure related pancreatitis compared to dilation alone and has no significant difference of procedure related pancreatitis compared to ES alone.

Recommendations:

- 1 - Additional prospective study with larger sample of patients or even multicenter studies are needed to confirm and prove our results.
- 2- Encourage the use of mechanical lithotripsy for large CBD stones.
- 3- Encourage the use of EST and EPBD in patients with coagulopathy, cirrhosis, patients with history of Billroth II surgery, patients with periampullary diverticulum and patients with large CBD stones.
- 4- Encourage the use of EST with EPBD since it has a lower incidence of procedure related pancreatitis compared to dilation alone and has no significant difference of procedure related pancreatitis compared to ES alone.
- 5- We may need to review our use of EPBD in our hospital regarding its indications and the size used.

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