Review Article

Is Endoscopic Papillary Large Balloon Dilation Safe for Treating Large CBD Stones?

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ABSTRACT

In recent years, endoscopic papillary large balloon dilation (EPLBD) with endoscopic sphincterotomy (EST) has been shown to be an effective technique for the removal of large or difficult common bile duct (CBD) stones, as an alternative to EST. Reviewing the literature published since 2003, it is understood that EPLBD has fewer associated overall complications than EST. Bleeding occurred less frequently with EPLBD than with EST. There was no significant difference in postendoscopic retrograde cholangiopancreatography pancreatitis or perforation. Recent accumulated results of EPLBD with or even without EST suggest that it is a safe and effective procedure for the removal of large or difficult bile duct stones without any additional risk of severe adverse events, when performed under appropriate guidelines. Since use of a larger balloon can tear the sphincter as well as the bile duct, possibly resulting in bleeding and perforation, a balloon size that is equal to or smaller in diameter than the diameter of the native distal bile duct is recommended. The maximum transverse diameter of the stone and the balloon-stone diameter ratio have a tendency to affect the success or failure of complete removal of stones by large balloon dilation to prevent adverse effects such as perforation and bleeding. One should take into account the size of the native bile duct, the size and burden of stones, the presence of stricture of distal bile duct, and the presence of the papilla in or adjacent to a diverticulum. Even though the results of EPLBD indicate that it is a relatively safe procedure in patients with common duct stones with a dilated CBD, the recommended guidelines should be followed strictly for the prevention of major adverse events such as bleeding and perforation.

Key Words: Adverse events, common bile duct, endoscopic papillary large balloon dilation, endoscopic sphincterotomy

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Endoscopic sphincterotomy (EST) has become the procedure of choice for removal of stones from the bile duct, especially in patients who have had a cholecystectomy.[1,2] The procedure is successful in 90%–98% of patients, and 86%–91% of all bile duct stones can be extracted using this technique.[3-5]

To overcome the limitations of conventional endoscopic papillary balloon dilation (EPBD), "large balloon dilation after minor biliary sphincterotomy" has been devised. Large balloon dilation after minor EST is effective for retrieving large biliary stones without the use of mechanical lithotripsy [Figures 1 and 2]. Although EST with a large incision may be effective in reducing the need for mechanical lithotripsy, a large incision has a higher risk of perforation and possibly a higher risk of bleeding than standard EST. This innovative, novel method incorporating slow dilation of the papilla to a large diameter can provide a larger opening than a large EST, and prevents perforation and bleeding. This method of stone retrieval is easy to perform and can effectively treat large or multiple bile duct stones.

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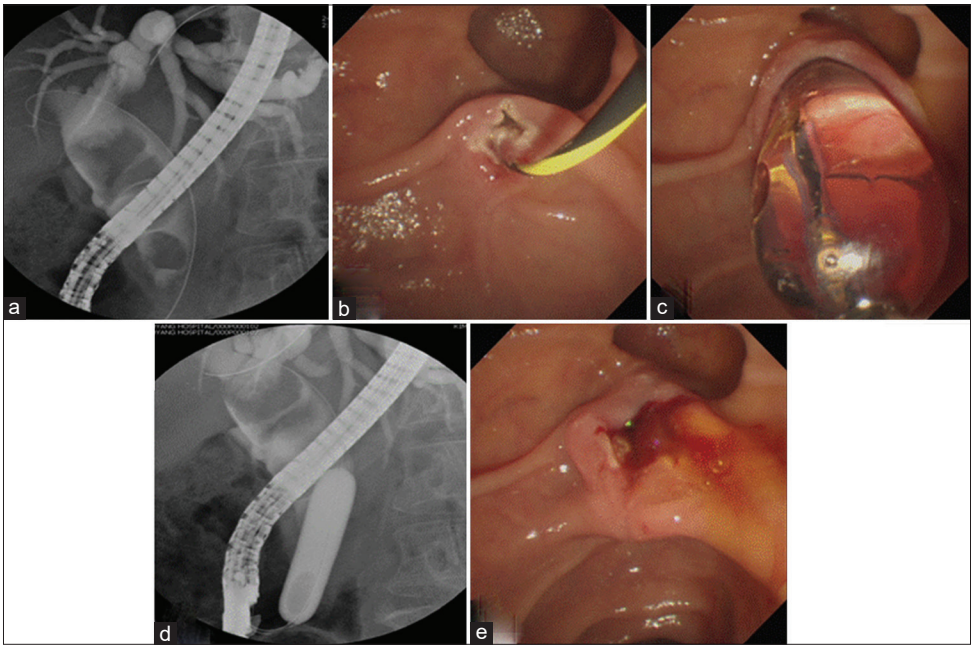

Figure 1: A case of large balloon dilation after minor endoscopic biliary sphincterotomy (ES) in a patient with multiple large extrahepatic bile duct stones. (a) Retrograde cholangiogram shows multiple large stones that completely fill the extrahepatic bile duct. (b-d) After minor ES, a large balloon is inflated up to 15 mm over the guidewire and through the sphincterotomized papilla. (e) The papillary orifice is dilated fully and the bile duct mucosa is readily seen

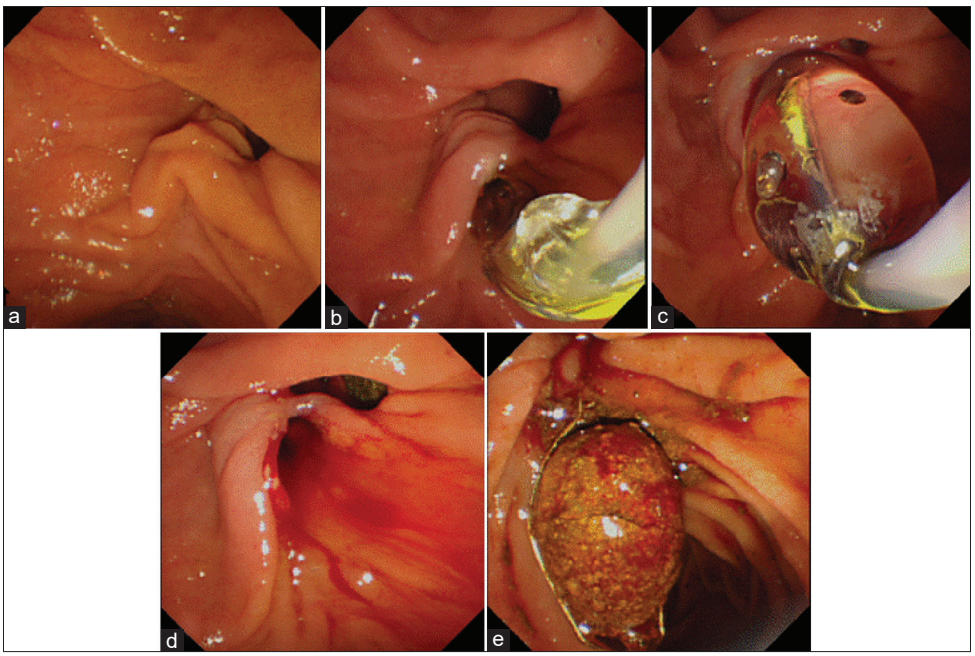

Figure 2: A huge stone is impacted at the bile duct bifurcation. Removal with a large basket catheter and mechanical lithotripter fails, and retrieval of a large stone is attempted with a retrieval balloon catheter. (a-d) After sphincterotomy, large balloon dilation is performed up to 18 mm. (e) The stone is pulled out with a large basket and extracted from the papilla. A huge stone (4.5 × 2.0 cm) is finally evacuated without crushing

However endoscopic papillary large balloon dilation (EPLBD) is still not fully accepted as some endoscopists are concerned about potentially serious adverse events (AEs), such as pancreatitis and bile duct perforation. However, recent data from a number of multicenter studies in both Eastern and Western countries[6-20] suggest that EPLBD with EST is safe and effective.

Over the past 10 years, the technical methods and safety of EPLBD have been established and the indication has been expanded. Development of guidelines for the application of EPLBD has been an ongoing effort to minimize the occurrence of potential serious AEs.

HISTORICAL REVIEW

EPBD is an alternative to EST for removing bile duct stones.[21-24] 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 Buschenfelde, who first reported it in 1983.[21] 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 AEs such as bleeding and perforation should be less likely, and the function of the biliary sphincter is also preserved.[22]

Previously, a Japanese group published a well-designed controlled prospective trial enrolling —282 patients with choledocolithiasis from 11 national institutions. Patients were randomized in an EST group and an EPBD without prior EST. The authors compared the two techniques and reported almost similar results regarding successful stone extraction and complication rate. They have therefore suggested EPBD without prior EST as an alternative option to EST.[23]

Studies from Western countries revealed completely opposite results. In a randomized controlled multicenter trial, Disario *et al*.[25] compared primary EPBD with EST in patients with choledocolithiasis. The reported outcome was that EPBD was associated with increased short-term morbidity, whereas two deaths were reported due to severe pancreatitis. This study was stopped at the first analysis, suggesting that EPBD for stone extraction should be avoided in every day clinical practice.

The enthusiasm for the potential advantages of EPBD over EST for the avoidance of short-term AEs of bleeding and perforation, while preserving the biliary sphincter and possibly reducing the long-term sequelae of EST, was soon dampened by reports of serious postprocedure pancreatitis.[25]

The final success rates for EST and EPBD are comparable. The reported success rates of stone removal are 81%–99% for EPBD[21,24,26,27] and 85%–98% for EST.[24,26] Randomized trials comparing EPBD with EST suggest that EPBD is at least as effective as EST in patients with small to moderate-sized bile duct stones.[22,24,27,28]

The lower rate of stone clearance, along with a higher usage of mechanical lithotripsy in EST is most likely because EST does not enlarge the bile duct opening to the same extent as EPBD. Erosz *et al*.[29] reported the use of large balloon dilation after EST for removal of bile duct stones that were difficult to extract by conventional sphincterotomy and extraction devices. EPLBD has been introduced as an adjunctive tool to EST for removing large or difficult common bile duct (CBD) stones.

The concept is to combine the advantages of sphincterotomy with those of balloon dilation. Theoretically, the risk of perforation or bleeding would be reduced by performing a less than maximal sphincterotomy, and risk of pancreatitis from balloon dilation would be reduced by first separating the biliary and pancreatic orifices with EST.

In EPLBD, limited (small) EST is generally recommended before balloon dilation, because the prior EST may shift the radial force of balloon along the cutting direction toward the bile duct rather than the pancreatic duct. EPLBD may have the advantages of a lower risk of overall AEs and pancreatitis compared with a large EST.[30] As an alternative method, Jeong *et al*. have reported that EPLBD without EST is safe and effective for managing large CBD stones without increasing the risk of pancreatitis in normal anatomy.[16] Skipping the sphincterotomy can simplify this procedure compared with EPLBD with EST.

OPTIMAL LARGE BALLOON DILATION TECHNIQUE FOR POSTSPHINCTEROTOMY PAPILLA

Why do we perform minor EST before dilation?

The therapeutic duodenoscope is advanced to the duodenum. It is important to use a duodenoscope with a large working channel (4.2 mm in diameter) to facilitate the passage of large balloons. The difference from conventional EPBD is that endoscopic biliary sphincterotomy (EST) is performed before the balloon catheter is inserted. In most cases, a minor EST is sufficient and a major EST is not required. This is because the purpose of the EST is not to dilate the sphincter of Oddi (SO), but to direct the orientation of SO dilation. When using a large balloon catheter to dilate the SO without an EST, it is difficult to predict the direction in which the SO will dilate. Therefore, by performing a minor EST, the direction of papilla dilation can be predicted. Another reason for a minor EST is to prevent postprocedure pancreatitis by minimizing the peripapillary edema after dilating the papilla.

After the EST, a guidewire is inserted into the bile duct and a balloon catheter is guided over the wire. The diameter of

the balloon catheter should be 12–20 mm. A balloon catheter that was initially developed for dilation in pyloric stenosis, such as a CRE™ wire-guided balloon (Boston Scientific, Natick, MA), can be useful.

The extent of sphincterotomy before performing EPLBD

The extent of the ampullary incision is another important predictor of AEs, such as bleeding and perforation. Theoretically, EPLBD with a limited EST has the combined advantages of minimizing the major AEs of both EST alone and EPBD alone, such as bleeding and perforation (mainly with a large EST) and pancreatitis (mainly in EPBD).[11] A comparison of EPLBD procedures based on the extent of the ampullary incision of the preceding EST, which was classified as large, limited, and no EST, showed no significant differences among them in the rates of overall AEs, pancreatitis, perforation, and other AEs. However, the rate of bleeding was significantly higher in EPLBD with a large EST when compared to others, whereas there was no significant difference between EPLBD with a limited or without an EST.[30]

OPTIMAL EPLBD TECHNIQUE WITHOUT A SPHINCTEROTOMY

Recent studies have shown that EST followed by large balloon dilation,[10,31] or large balloon dilation only,[16] for the removal of large or difficult stones from the CBD has good efficacy and acceptable rates of AEs. Theoretically, EPLBD without EST is easier to perform than the combined method and is also more suitable for patients with concomitant large stones and bleeding tendencies. In addition, the main purpose of EPLBD for large bile duct stones is to preclude additional endoscopic procedures, such as endoscopic mechanical lithotripsy (EML), to simplify the process of stone extraction and reduce AEs.

When the major papilla is accessed, the bile duct is cannulated and a cholangiogram is obtained. The bile duct and stone diameters are measured during endoscopic retrograde cholangiopancreatography (ERCP) and corrected for magnification using the 13.5-mm external diameter of the distal end of the duodenoscope as a reference. If the maximum transverse diameters of the largest stone and extrahepatic bile duct are ≥10 mm and ≥15 mm, respectively, a balloon catheter with a diameter >15 mm is used and EPLBD is performed without a preceding EST. After the diagnostic ERCP is performed, a 0.035-in guidewire is passed through the cannula into the bile duct. A 7.5-Fr over-the-guidewire type of hydrostatic balloon catheter for esophageal and pyloric dilation (CRE balloon; Microvasive, Boston Scientific, Natick, MA) is passed over the guidewire and placed across the ampulla. Then, the balloon is inflated gradually up to at least 15 mm with diluted contrast using an inflation device. The sphincter is considered to be adequately dilated if the waist of the balloon disappears completely on fluoroscopic examination. The fully expanded balloon is maintained in position for 30–60 s and then deflated and removed.

Determination of the diameter of dilating balloon

Dilation with large-diameter balloons is performed during the same session as the EST. The balloon catheter is passed over a guidewire and positioned at the biliary orifice; the middle portion of the balloon is filled gradually with diluted contrast medium under endoscopic and fluoroscopic guidance to maintain the correct position and to observe the gradual disappearance of the waist in the balloon, which is taken to indicate progressive dilation of the orifice.

The intended maximum target diameter of a dilating balloon for EPLBD should be determined based on the size of the stone and the size of the distal CBD proximal to the tapered segment,[6,32,33] but must never exceed the diameter of the distal CBD to prevent bile duct perforation.[34,35] A 12- to 20-mm-diameter balloon for pyloric use (CRE™ wire-guided balloon dilator; Boston Scientific, Natick, MA) is used most frequently to dilate the duodenal ampulla during EPLBD. These inflate gradually in three different diameter steps by increasing the balloon inflation pressure. The balloon used should be selected such that the second or third diameter step is the intended maximum target diameter, and it should be inflated gradually, starting from a diameter step of the balloon smaller than the intended maximum target diameter. The balloon is dilated slowly until it reaches its first diameter step by gradually increasing the balloon pressure to prevent sudden tearing of the ampullary roof. If the balloon is dilated without any difficulty and the central waist disappears, it is then dilated gradually to its second diameter step and then to its third diameter step until the intended maximum target diameter is reached.

Optimal duration of balloon inflation

One prospective randomized study revealed no difference in AEs between balloon inflation for 30 and 60 s, including pancreatitis, bleeding and perforation, in EPLBD with EST.[36] The longer duration of inflation did not seem to be related to an increased risk of AEs, and the shorter duration of inflation seemed to be related to an increased risk of serious bleeding due to insufficient compression by the balloon. Further studies should determine the optimal duration of balloon inflation during EPLBD. The standard duration of balloon dilation is 30-60 s after disappearance of the waist. In 24 studies describing the duration of balloon dilation using a dilating balloon with a diameter of 12–20 mm, inflation

varied from 10 to 180 s; in all but three studies, the duration was <60 s.[34,36,37]

ADVERSE EVENTS

Since 2003, there have been many reports on the outcomes and of EPLBD. Fortunately, most AEs are mild and few serious AEs have been reported. However, these results do not mean that EPLBD is completely safe for treating large bile duct stones, considering the lack of large-scale multicenter randomized studies.

A meta-analysis of randomized controlled trials that compared EPLBD and EST for the extraction of choledocholithiasis showed that EPLBD was associated with fewer overall complications than EST [5.8 vs 13.1%, odds ratio (OR) 0.41, 95% confidence interval (CI) 0.24-0.68, $P < 0.01$].[38]

Another meta-analysis comparing adverse events between EST alone and EPBD alone and EPLBD with EST showed that the rate of overall AEs was significantly lower in EPLBD with EST than EST alone ($P < 0.01$, OR = 1.60) or EPBD alone ($P < 0.01$, OR = 1.51).[30]

Concerning post-ERCP pancreatitis, there was no significant difference between EPLBD and EST (OR = 1.80, 95% CI 0.58-2.36, $P = 0.66$).[39] There was no difference in the rates of pancreatitis between EPLBD and EST (5.0% vs 7.0%).[35] From these reports, EPLBD itself might not increase the risk of pancreatitis, although further multicenter randomized trials of EPLBD without EST are warranted.

Interestingly, a multicenter study by Park *et al*.[34] reported that balloons larger than 14 mm in diameter were independently associated with a decreased risk of pancreatitis, implying that simple stretching of the ampullary orifice or direct blockage of the pancreatic orifice by compression with a large-diameter balloon is not a major etiological factor in pancreatitis following EPLBD. A probable mechanism of the reduced pancreatitis rate in EPLBD with EST is believed to be that the radial force exerted by the dilating balloon shifts toward the direction of the cut made during EST along the bile duct and away from the pancreatic orifice, resulting in less periampullary injury around the pancreatic duct, with a decreased risk of pancreatitis.[22,29,34,40] However, EST might have a limited role in preventing pancreatitis in EPLBD because there is no evidence in this review suggesting that EPLBD without EST increased the risk of pancreatitis. To explain this, Kim *et al*. postulated that pancreatitis after EPLBD can be reduced because the manipulation of Dormia basket and retrieval balloon catheter as well as frequency of EML, in EPLBD with or even without EST, can be reduced due to a sufficiently widened ampullary orifice, resulting in less periampullary trauma or edema that occurs during stone extraction and ultimately leading to a lower risk of pancreatitis.[30]

Recent data have shown that EPLBD without EST does not cause an excessive increase in pancreatitis,[16] which might be explained by the inherently lower risk of pancreatitis in patients with large CBD stones. Further prospective studies are needed to confirm whether EPLBD without EST is associated with a lower risk of pancreatitis.

A stratified subgroup analysis showed that EPLBD might reduce the risk of bleeding. A meta-analysis indicated a significant reduction in bleeding in the EPLBD group (OR 0.15, 95% CI 0.04-0.50, $P < 0.01$).[38] The rate of bleeding was not significantly different between EPLBD with EST vs. EST alone ($P = 0.164$), but was significantly lower in EPBD alone than in EPLBD with EST ($P < 0.01$, OR = 25.27) or EST alone ($P = < 0.01$, OR = 33.75).[30]

Kim *et al*.[30] compared the rates of AEs among EPLBD procedures that they classified based on the extent of ampullary incision of the EST: Large EST, limited EST, and no EST. There were no significant differences among the three groups of EPLBD procedures in the rates of overall AEs, pancreatitis, perforation, adverse events related to surgery or death, but the rate of bleeding was significantly higher in EPLBD with a large EST, compared with EPLBD with a limited EST ($P < 0.01$, OR = 3.33) or without EST ($P = 0.049$, OR = 2.17), but there was no significant difference between EPLBD with a limited EST and without an EST ($P = 0.35$).

A multicenter study by Park *et al*.[34] reported that cirrhosis, full-EST, and a stone size ≥16 mm were independent predictors of bleeding. Although there were few patients with cirrhosis, the majority of bleeding that occurred in these patients was mild to moderate in severity, and they recommended that caution should be taken when using EPLBD with EST in patients with cirrhosis. In one series, a small EPBD alone resulted in significantly less bleeding compared with EST alone in patients with cirrhosis, particularly Child–Pugh class C cirrhosis.[41] Further studies should examine whether EPLBD with mid-EST or no-EST decreases bleeding in cirrhotic patients. Although post-ERCP complications occur less frequently in EPLBD, EPLBD might cause marked bleeding.[42]

The rates of perforation and adverse event-related death did not differ significantly among EST alone, EPBD alone, or EPLBD with EST ($P = 0.941$ and 0.152, respectively).[30] The size of the balloon is the most important factor for ensuring the success of EPLBD and a reduction in AEs.[35]

How to predict and prevent fatal adverse events?

One recent interesting multicenter retrospective review of the predictors of AEs following EPLBD showed that 95 of 946 patients (10%) suffered an AE: The AEs were mild in 78 (82.1%), moderate in 12 (12.6%), and severe in 5 (5.3%), of which four were fatal [Table 1].[34]

The direct or indirect causes of death were perforation in three patients and delayed massive bleeding in one. Of the three patients with perforations, two died of septic shock and multiorgan failure, and the other died of cardiogenic shock [Table 2].[34]

Factors predictive of adverse events after EPLBD

Multivariate analysis using logistic regression analysis indicated that larger stone size (maximum size ≥16 mm; OR 4.26; 95% CI 2.30-7.88, $P < 0.01$), underlying cirrhosis (OR 4.05; 95% CI, 1.15 - 14.27, $P = 0.03$), and longer-length EST (full-EST; OR 3.40; 95% CI 1.75 - 6.59, $P < 0.01$) were independently associated with an increase in AEs. Larger balloon size was independently associated with a decrease in AEs (maximum size ≥14 mm: OR 0.36; 95% CI 0.20 - 0.67, $P < 0.01$). Cirrhosis (OR 8.03; 95% CI 2.02-31.88, $P < 0.01$), length of the EST (full-EST: OR 6.22; 95% CI 2.37-16.31, $P < 0.01$), and stone size (maximum size ≥16 mm: OR 4.00; 95% CI 1.98 - 8.07, $P < 0.01$) were independent predictors of bleeding after EPLBD, whereas a distal CBD stricture (OR 17.08; 95% CI 3.94-74.13, $P < 0.01$) was an independent predictor of perforation. Larger balloon size was independently associated with a decreased risk of pancreatitis (maximum size ≥14 mm; OR 0.27; 95% CI 0.10 - 0.78, $P = 0.02$).[34]

In one perforation patient, the CBD was uniformly dilated in caliber without an obvious stricture. In this patient, a full-EST was performed and the waist of the balloon was not effaced during inflation of 20 mm at 75% of the recommended maximum balloon pressure. The balloon was inflated to the maximum recommended pressure. The following day, perforation and postprocedural pancreatitis occurred. In the second case of perforation, persistent resistance was encountered during inflation of the balloon. Complete stone removal was achieved and the procedure was completed uneventfully. Unfortunately, the patient subsequently developed a retroperitoneal perforation and pancreatitis. In the third case of perforation, a tight balloon waist was noted in the distal CBD during dilation. The balloon pressure was increased to 90% of the maximum pressure, as recommended by the manufacturer, to resolve the balloon waist. Perinephric free air was noted immediately. In the last fatal case, stone removal using EPLBD and full-EST were performed in a patient with thrombocytopenia. No intraprocedural bleeding occurred, but massive bleeding developed 6 h later.

Table 1: Types and severity of adverse events following endoscopic papillary large balloon dilation[34]

Severity of AEs	Total	Mild	Moderate	Severe	*P* value
N (%)	95 (100)	78 (82.1)	12 (12.6)	5 (5.3)[a]	<0.001*
Types of AEs					
Bleeding	56 (58.9)	51 (53.7)	4 (4.2)	1 (1.1)	
Pancreatitis	24 (25.3)	20 (21.1)	4 (4.2)	0 (0)	
Perforation	9 (9.5)	1 (1.1)	4 (4.2)	4 (4.2)	
Cholangitis	6 (6.3)	6 (6.3)	0 (0)	0 (0)	

AE: Adverse event. *Significant difference with Fisher's exact test among mild, moderate, and severe adverse events groups. [a]Unfortunately four out of five severe cases were fatal, one from bleeding and three from perforation

Table 2: Characteristics and causes of death in four patients following endoscopic papillary large balloon dilation

Characteristics	Case 1	Case 2	Case 3	Case 4
Size of CBD (mm)	26	28	22	12
Size of distal CBD[a] (mm)	17.0	14.2	19.8	11
Shape of distal CBD	Occult stricture	Tapered CBD	Visible stricture[c]	No stricture
Length of EST	Full	Mid	Full	Full
Size of balloon (mm)	20	18	18	12
Balloon waist	Yes	NA[b]	Yes	No
Adverse events				
Bleeding	-	Mild	-	Severe
Pancreatitis	Mild	Mild	-	-
Perforation	Severe	Severe	Severe	-
Causative factors related to adverse event	Full-EST overinflation of balloon	Overinflation and rapid inflation of balloon	Full-EST and overinflation of balloon	Full-EST and thrombocytopenia
Causes of death	Perforation/MOF	Perforation/MOF	Perforation/cardiogenic shock	Delayed massive bleeding

EST: Endoscopic sphincterotomy, MOF: Multiorgan failure. [a]Diameter of distal CBD measured at the 1 cm-proximal portion from the opening of the major ampulla. [b]NA: Not available: The identification of balloon waist in case 2 was not available because of rapid forcible inflation of the balloon during ERCP. [c]Occult stricture indicated that no obvious distal CBD stricture was identified before balloon inflation and the balloon waist did not disappear after inflating the balloon. Visible stricture indicated that obvious distal CBD stricture was identified even before balloon inflation

Lessons from these fatal cases

In a multivariate analysis, a distal CBD stricture was an independent predictor of perforation, and Park *et al*.[34] suggest that the presence of a distal CBD stricture should be considered a relative contraindication to EPLBD. In addition, they recommended gradual inflation and that caution be taken when a persistent waist at the distal CBD is identified after inflation to 75% of the manufacturer's recommended maximum inflation pressure.[6]

If strong resistance is encountered during balloon inflation, additional pressure should not be applied. In such cases, converting to alternative stone retrieval methods or providing drainage with plans for repeat ERCP are recommended.[34]

Large balloon dilation should not be performed if the entire extrahepatic duct is small or normal in size. However, in all patients with large stones, the bile duct is dilated to at least the size of the stone.[34]

How can we detect invisible strictures during the ballooning to prevent fatal perforation?

Even if there is no obvious distal CBD stricture or tapered distal CBD after a cholangiogram, any marked resistance during balloon inflation or a distinct waist or severe pain during balloon inflation at any step should suggest an invisible stricture. Based on their experience, Lee *et al*.[36] recommended that balloon inflation be discontinued if the balloon waist does not disappear once 75% of the recommended maximum inflation pressure is reached. In patients who are known to have obvious distal CBD strictures, EPLBD should be avoided to prevent bile duct perforation. When a tapered distal CBD or invisible stricture is identified, we should pay attention during balloon inflation to avoid fatal bile duct perforation.

Recommendations for safe, successful EPLBD

No guidelines or consensus recommendations to avoid AEs such as perforation following EPLBD have been developed. Three published articles have proposed recommendations for safe EPLBD and the prevention of fatal adverse events.[6,30,34]

Park *et al*.[34] proposed the following guidelines for safe EPLBD: (1) Selection of suitable candidates; that is, EPLBD should be reserved for patients with a dilated CBD, but avoided in patients with distal CBD strictures; (2) avoidance of full-EST immediately before large balloon dilation to prevent perforation and bleeding; (3) gradual inflation of the dilating balloon to recognize a narrow distal CBD indicated by a lack of disappearance of the balloon waist; (4) discontinuation of inflation when resistance is encountered in the presence of a persistent balloon waist; (5) not inflating the balloon beyond the maximum upstream size of the dilated CBD; and (6) conversion to alternative stone removal or drainage methods when difficulty in removal of a stone is encountered.

Lee *et al*.[6] also recommended the almost same guidelines for EPLBD in 2012 and recommended that inflation be stopped if the balloon waist persists before applying more than 75% of the recommended maximum inflation pressure and to inflate the balloon gradually to recognize occult or undetermined strictures of the distal CBD shown by persistence of a waist during balloon dilation.

Kim *et al*.[30] also reported recommendations for successful EPLBD that are fundamentally similar to the previous recommendations,[6,34] but added the following details:

- In patients with obvious distal CBD strictures, EPLBD should be avoided. If there is a suspicion of strictures, they recommended using the pulling method with a large inflated retrieval balloon through the through the suspected area of narrowing to confirm its existence.
- Further balloon inflation must be ceased, if the central waist of the balloon does not disappear or the patient indicates severe pain during balloon inflation at any step.
- EPLBD without EST might be useful in some patients with coagulopathy, periampullary diverticulum, or surgically altered anatomy.

Patient-related factors related to adverse events

These include a periampullary diverticulum, surgically altered anatomy, and a bleeding tendency.

Patients with a periampullary diverticulum were suitable for EPLBD. A retrospective comparison of patients with and without a periampullary diverticulum showed similar stone clearance rates and AEs in both, following EPLBD with a limited EST.[39] Several studies reported that the presence of a periampullary diverticulum was not associated with a significantly increased rate of adverse events, such as pancreatitis, bleeding, or perforation.[34,36,43,44] There have been six clinical trials of EPLBD on patients with surgically altered anatomy, such as Billroth II surgery[18,45-48] and Roux-en-Y anastomosis.[49] In these, there was a complete stone clearance in all patients with a low incidence of pancreatitis and bleeding. In patients with coagulopathy, EPLBD without EST might be useful, but should be undertaken cautiously,[33,34] although further studies are warranted.

CONCLUSION

Recent accumulated results of EPLBD with or without EST suggest that it is a safe and effective procedure for

the removal of large or difficult bile duct stones without any additional risk of severe AEs, when performed under appropriate guidelines.

Further studies are necessary to determine whether EPLBD with EST is safer than EPLBD without EST, particularly in patients with coaguolopathy. And further large scale prospective randomized controlled studies will be warranted to assess the facts that affect AEs of EPLBD.

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Conflicts of interest
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