Small sphincterotomy combined with endoscopic papillary large balloon dilation vs sphincterotomy alone for removal of common bile duct stones

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Author contributions: Guo SB and Duan ZJ designed the study; Meng H and Li CY collected and analyzed the data; Guo SB wrote the manuscript; Guo SB and Meng H contributed equally to the study; all authors read and approved the final manuscript.

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Received: April 23, 2014 Revised: July 13, 2014 Accepted: August 13, 2014 Published online: December 21, 2014

Abstract

AIM: To evaluate the efficacy and safety of endoscopic papillary large diameter balloon dilation (EPLBD) following limited endoscopic sphincterotomy (EST) and EST alone for removal of large common bile duct (CBD) stones.

METHODS: We retrospectively compared EST + EPLBD (group A, n = 64) with EST alone (group B, n = 89) for the treatment of large or multiple bile duct stones. The success rate of stone clearance, procedure-related complications and incidents, frequency of mechanical lithotripsy use, and recurrent stones were recorded.

RESULTS: There was no statistically significant difference between the two groups regarding periampullary diverticula (35.9% vs 34.8%, P > 0.05), pre-cut sphincterotomy (6.3% vs 6.7%, P > 0.05), size (12.1 ± 2.0 mm vs 12.9 ± 2.6 mm, P > 0.05) and number (2.2 ± 1.9 vs 2.4 ± 2.1, P > 0.05) of stones or the diameters of CBD (15.1 ± 3.3 mm vs 15.4 ± 3.6 mm, P > 0.05). The rates of overall stone removal and stone removal in the first session were not significantly different between the two groups [62/64 (96.9%) vs 84/89 (94.4%), P > 0.05; and 58/64 (90.6%) vs 79/89 (88.8%), P > 0.05, respectively]. The rates of post-endoscopic retrograde cholangiopancreatography pancreatitis and hyperamylasemia were not significantly different between the two groups [3/64 (4.7%) vs 4/89 (4.5%), P > 0.05; 7/64 (10.9%) vs 9/89 (10.1%), P > 0.05, respectively]. There were no cases of perforation, acute cholangitis, or cholecystitis in the two groups. The rate of bleeding and the recurrence of CBD stones were significantly lower in group A than in group B [1/64 (1.6%) vs 5/89 (5.6%), P < 0.05; 1/64 (1.6%) vs 6/89 (6.7%), P < 0.05, respectively].

CONCLUSION: EST + EPLBD is an effective and safe endoscopic approach for removing large or multiple CBD stones.

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Key words: Choledocholithiasis; Endoscopic retrograde cholangiopancreatography; Endoscopic papillary balloon dilation; Endoscopic sphincterotomy

Core tip: Endoscopic papillary large diameter balloon dilation (EPLBD) after limited endoscopic sphincterotomy (EST) is an effective and safe endoscopic approach to remove large or multiple common bile duct stones. Compared with EST alone, the rate of bleeding and recurrence of CBD stones were significantly lower in the EST + EPLBD group (1.6% vs 5.6%, P < 0.05; 1.6% vs 6.7%, P < 0.05, respectively). While the rates of overall stone removal and stone removal in the first session (96.9% vs 94.4%, P > 0.05; 90.6% vs 88.8%, P > 0.05,
respectively) and the rates of post-endoscopic retrograde cholangiopancreatography pancreatitis and hyperamylasemia were not significantly different between the two groups (4.7% vs 4.5%, P > 0.05; 10.9% vs 10.1%, P > 0.05, respectively).

Guo SB, Meng H, Duan ZJ, Li CY. Small sphincterotomy combined with endoscopic papillary large balloon dilation vs sphincterotomy alone for removal of common bile duct stones. World J Gastroenterol 2014; 20(47): 17962-17969. Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i47/17962.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i47.17962

INTRODUCTION

Although endoscopic sphincterotomy (EST) has been widely accepted as the standard therapy for removing common bile duct (CBD) stones, this procedure is associated with serious complications such as hemorrhage, pancreatitis, perforation, and recurrent infection of the bile duct caused by permanent functional loss of the sphincter of Oddi[1].

Endoscopic papillary balloon dilation (EPBD) of the biliary sphincter was introduced as an alternative to EST, especially for patients with small or moderate CBD stones[2]. By using the wire-guided method, EPBD could be easily performed. Because EPBD does not involve cutting the biliary sphincter, it possesses the advantages of preserving papillary sphincter function and reducing the chance of hemorrhage and perforation[3-4]. However, this procedure is associated with a high risk of pancreatitis[5] and with more frequent application of mechanical lithotripsy[6-8].

To overcome these disadvantages, endoscopic papillary large diameter balloon dilation (EPLBD) after limited EST was introduced for the removal of large (≥ 10 mm) or multiple bile duct stones[9-22]. This method combines the advantages of EST and EPBD by increasing the efficacy of stone extraction while minimizing complications of EST and EPBD when used alone[9,21].

This retrospective study aimed to evaluate the efficacy and safety of EPLBD after limited EST compared with EST alone for the removal of large (≥ 10 mm) or multiple CBD stones.

MATERIALS AND METHODS

Patients
A total of 153 patients with large (≥ 10 mm) or multiple CBD stones treated from January 2009 to December 2012 were retrospectively reviewed. Patients were excluded if they had a history of EST, a surgical history involving the gastrointestinal tract, co-existing bile leakage or choledochoduodenal fistula, bleeding tendency, intrahepatic stone diseases, or concomitant pancreatic or biliary malignant disorders. The patients were divided into two groups according to the order of the procedure. Sixty-four patients underwent EST + EPLBD (group A, from September 2011 to December 2012), and 89 patients underwent EST alone (group B, from January 2009 to September 2011). The study was approved by the Institutional Review Board of our hospital.

Methods

Prior to endoscopic retrograde cholangiopancreatography (ERCP), blood samples were obtained for a complete blood count, liver-function tests (bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and γ-glutamyl transpeptidase) before and the morning after the procedure, coagulation profiles, and serum amylase before and after the procedure (4 h and 24 h, respectively).

Written Informed Consent was obtained from all of the patients or from their relatives before the procedure. Local anesthesia of the pharynx was obtained using tetraaine. The patients were sedated with diazepam (5 mg) supplemented by an intramuscular injection of 50 mg of meperidine. To halt duodenal peristalsis, 20 mg of butyl scopalamine bromide was administered intramuscularly immediately prior to the start of ERCP. ERCP was performed by experienced endoscopists at a single center using side-viewing endoscopes (TFJ-240; Olympus Optical Corporation, Tokyo, Japan).

After selective cannulation of the CBD using a triple lumen sphincterotomy (Papillotome, ENDO-FLEX GmbH, Germany) with a guide wire (Hydra Jagwire 0.035 inch, Boston Scientific Microvasive, Cork, Ireland), a diagnostic cholangiogram was obtained, and the stone size and number were documented (Figure 1A). If cannulation of the CBD was not possible, a needle-knife sphincterotomy was performed to gain access. In group A, limited EST was performed (Figure 2A) for easy insertion of the balloon catheter and control of the direction of the balloon dilation during EPBD; then, a CRE wire-guided balloon catheter (5.5 cm in length, 1.0-1.2 cm/1.2-1.5 cm in diameter) (Boston Scientific Microvasive, Cork, Ireland) was passed over the guide wire and was positioned at the center of the balloon across the ampullary orifice. The balloon was gradually inflated with diluted contrast material to 12-15 mm at a pressure of 3-8 ATM, depending on the stone size and the diameter of the CBD (Figure 2B) as measured by cholangiography. The sphincter was adequately dilated when the waist of the balloon had disappeared completely (Figure 1B). The fully inflated balloon was maintained in its position for 2 min and then deflated and removed (Figure 2C). Following EPLBD, the stones were retrieved using a Dormia basket (Web™ extraction basket, Wilson-Cook Medical Inc. Winston-Salem, NC, United States) and/or a retrieval balloon catheter (Extractor Three Lumen Retrieval Balloon, Boston Scientific Microvasive. Cork, Ireland) (Figure 2D). When the stones were too difficult to remove intact, mechanical lithotripsy (BML-4Q; Olympus Optical, Tokyo, Japan) was performed to fragment the
Figure 1  Fluoroscopic view of large-balloon dilatation following limited sphincterotomy. A: Cholangiogram demonstrating two large stones within the dilated bile duct; B: A large balloon inflated across the papilla over the guidewire; C: The cholangiogram following complete stone removal showed no residual filling defect in the bile duct; D: The placement of a nasobiliary drainage tube.

Figure 2  Endoscopic view of large-balloon dilation following limited sphincterotomy. A: Endoscopic small sphincterotomy; B: A large balloon inflated across the papilla; C: Markedly dilated papilla following large-balloon dilation; D: A large stone extracted using a retrieval balloon catheter through the dilated papilla.
stones prior to extraction from the bile duct, and a naso-biliary drainage tube (nasobil.Sonde, ENDO-FLEX GmbH, Germany) was placed to prevent cholangitis (Figure 1D). In group B, EST was performed with a pull-type sphincterotomy as the standard method. Following EST, the stones were removed in the same manner as in group A. Complete stone removal was verified either by the final cholangiogram (Figure 1C) or by the follow-up cholangiogram obtained 3 d after the initial procedure through a nasobiliary drainage tube. If remnant stones were found, a second ERCP procedure with or without repeated EPLBD was performed for the retrieval of bile duct stones.

The outcomes measured were the number of therapeutic ERCP procedures required for complete stone removal, the frequency of use of mechanical lithotripsy, associated complications, including bleeding, pancreatitis, perforation during and after ERCP, and the recurrence of bile duct stones within one year. Post-ERCP pancreatitis was defined as persistent abdominal pain for more than 24 h associated with a serum amylase level of more than three times the upper limit of normal. Hyperamylasemia was defined as a serum amylase level exceeding three times the normal upper limit without any abdominal pain. Post-ERCP bleeding was classified as major or minor based on the amounts of hemorrhage. Major bleeding was defined as severe hemorrhage necessitating transfusion or interventions, and minor bleeding was defined as self-limited or endoscopically controlled mild hemorrhage not requiring transfusion. Cholangitis was defined as a fever accompanied by leukocytosis and right upper quadrant pain after the procedure\(^{[1]}\). Clinical and endoscopic factors (e.g., periampullary diverticula) were retrospectively evaluated.

**Statistical analysis**

The data analyses were performed using the Statistical SPSS 10.0 software (Chicago, IL, United States). Categorical parameters were compared using the chi-square test or Fisher's exact test, and continuous variables were compared using the Student’s t-test. All of the measurements in this study are expressed as mean ± SD. A value of \( P < 0.05 \) was considered statistically significant.

### RESULTS

The demographic characteristics of the 153 patients (81 men, 72 women; age range from 39 to 87 years) are presented in Table 1. The incidence of periampullary diverticula (PAD) was 35.3% (54/153). There was no statistically significant difference between the two groups in terms of the age and gender. The mean stone size in the 153 patients was 12.6 ± 2.4 mm (range, 10-27 mm), and the mean bile duct diameter was 15.2 ± 3.4 mm (range, 10-28 mm). There was no statistically significant difference between the two groups in terms of PAD (35.9% vs 34.8%, \( P > 0.05 \)), pre-cut sphincterotomy (6.3% vs 6.7%, \( P > 0.05 \)), size (12.1 ± 2.0 mm vs 12.9 ± 2.6 mm, \( P > 0.05 \)) or number (2.2 ± 1.9 vs 2.4 ± 2.1, \( P > 0.05 \)) of stones, or diameters of CBD (15.1 ± 3.3 mm vs 15.4 ± 3.6 mm, \( P > 0.05 \)).

Of the 153 patients, stone removal was completed in 95.4% (146/153). The rates of overall stone removal and stone removal in the first session were not significantly different between the two groups [62/64 (96.9%) vs 79/89 (88.8%), \( P > 0.05 \), and 58/64 (90.6%) vs 77/89 (88.8%), \( P > 0.05 \), respectively]. The patients in group A required less mechanical lithotripsy compared with those in group B [5/64 (4.7%) vs 9/89 (7.9%), \( P < 0.05 \)] (Table 2).

The procedure-related complications are listed in Table 3. The rates of post-ERCP pancreatitis and hyperamylasemia were not significantly different between the two groups [3/64 (4.7%) vs 4/89 (4.5%), \( P > 0.05 \), and 7/64 (10.9%) vs 9/89 (10.1%), \( P > 0.05 \), respectively]. All of the cases of pancreatitis were mild, and they were treated conservatively. There were no perforations or cases of acute cholangitis or cholecystitis in the two groups. The rate of bleeding was significantly lower in group A than in group B [1/64 (1.6%) vs 5/89 (5.6%), \( P < 0.05 \)]. There were 2 cases of major bleeding in group B; these patients later died from multi-organ failure. Regarding long-term complications, the recurrence of CBD stones was significantly higher in group B compared with group A [1/64 (1.6%) vs 6/89 (6.7%), \( P < 0.05 \)].

**DISCUSSION**

EST, which was first introduced by Classen et al\(^{[2]}\), remains the standard therapy for the treatment of CBD stones. Although EST has been proven to be safe in many studies, there are several complications, including pancreatitis (5.4%), hemorrhage (2.0%), perforation (0.3%), cholangitis (1.0%), cholecystitis (0.5%), and pro-

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**Table 1 Baseline characteristics of the patients**

| Variable         | Group A (\( n = 64 \)) | Group B (\( n = 89 \)) | \( P \) value |
|------------------|------------------------|------------------------|--------------|
| Mean age (yr)    | 68.5 ± 10.9 (39-87)    | 67.3 ± 9.8 (42-82)     | > 0.05       |
| Sex (male/female)| 33:31                  | 48:41                  | > 0.05       |
| CBD stones       |                        |                        |              |
| Mean diameter of stones (mm) | 12.1 ± 2.0 (10-25) | 12.9 ± 2.6 (10-27) | > 0.05       |
| Number of stones (1/2/3) | 34/11/19 | 47/15/27 | > 0.05       |
| Mean diameter of CBD (mm) | 15.1 ± 3.3 (10-26) | 15.4 ± 3.6 (10-28) | > 0.05       |
| Periampullary diverticula | 23 (35.9%) | 31 (34.8%) | > 0.05       |
EVLBD has become an alternative to EST for the treatment of CBD stones. EVLBD has several advantages over EST. First, EVLBD results in less trauma to the ampullary sphincter. Second, EVLBD might preserve the function of the biliary sphincter, reducing late complications such as the recurrence of biliary stones. Third, EVLBD has the advantage of less bleeding and is safer for patients with bleeding tendency. Finally, EVLBD is recommended for patients with abnormal anatomy, such as periampullary diverticula and Billroth II gastrojejunostomy, in which the margin for cutting is limited or the appropriate cutting direction is not clear. However, a meta-analysis demonstrated that post-ERCP pancreatitis occurred more commonly in the EVLBD group than in the EST group. The balloon dilation of the sphincter of Oddi might cause spasm, compression and edema of the distal pancreatic duct, which could result in the restriction of pancreatic juice flow and the occurrence of pancreatitis. Another disadvantage of conventional EVLBD is that it is difficult to remove larger stones because the biliary opening is not enlarged to the same degree as with EST. Therefore, the application of EVLBD is restricted to patients with small stones less than 10 mm in diameter.

EVLBD combined with limited EST, which was first proposed to facilitate the removal of large or multiple bile duct stones, has been proven safe and effective in patients with large bile duct stones. EVLBD combined with limited EST enlarged the biliary orifice enough to remove multiple or larger bile duct stones, resulting in an increased success rate of stone removal and in decreased use of mechanical lithotripsy. In our study, compared with EST alone, the efficacy of stone removal was similar in EVLBD following limited EST. The rates of overall stone removal and stone removal in the first session were not significantly different between the two groups (96.9% vs 94.4%, P > 0.05, 90.6% vs 88.8%, P > 0.05, respectively). Periampullary diverticula, which are known to be associated with an increased frequency of pancreatobiliary diseases, could influence endoscopic outcomes because the ampillary area in patients with periampullary diverticula is composed of thin mucosa without sphincter muscle, which increases the potential risks of perforation and bleeding. In this case, mechanical lithotripsy is a necessary technique for removing large stones. However, the combination of EVLBD with limited EST provided spacious opening of the bile duct, reducing the need for mechanical lithotripsy (4.7% vs 7.9%, P < 0.05) in our study, which is consistent with previous reports. For patients with difficult stones that are not suitable for extraction at the first attempt, the temporary placement of a stent might be an alternative method, and the plastic stents are able to fragment large CBD stones.
hyperamylasemia, including 7 cases in group A and 9 cases in group B. The elevated serum amylase level also normalized within 72 h after the procedure and did not affect the clinical course of the patients. There was no statistically significant difference between the two groups regarding post-ERCP pancreatitis and hyperamylasemia.

Regarding the risk of hemorrhage, we determined that limited EST prior to EPBD with a large balloon could reduce procedure-related hemorrhage. In our study, bleeding occurred less frequently in group A than in group B (1.6% vs 5.6%, P < 0.05). There were 2 cases of major bleeding in group B, and these patients later died from multi-organ failure. The other 4 cases had minor bleeding that was stopped by the administration of hemostatic agents. Limited EST and effective compression by a balloon are effective methods for the prevention of hemorrhage. Therefore, the combination of EST with EPLBD could be recommended for the removal of bile duct stones in patients who require anticoagulation[40]. Although there were some reports that EPLBD following limited EST resulted in a higher rate of bleeding, we attributed those results to the moderate degree of EST.

Another fatal complication during ERCP is perforation of the duodenum. However, during the ballooning after limited EST, the endoscopist could observe the dilatation status of the ampulla using a sideview endoscope and fluoroscopy. Therefore, the risk of duodenal perforation during EST + EPLBD is lower than during EST alone, and the technique of EST + EPLBD is typically recommended in patients with periampullary diverticula. In our study, there were no cases of perforation in either group. To minimize the risk of perforation, the size of the dilated balloon should not exceed the size of the CBD.

Previous reports show that procedure-related acute cholangitis developed more often in the EST group than in the EPBD group. This result might be explained by the loss of sphincter function after EST, which allows bacterial colonization from the intestine into the biliary system[40]. In our study, there were no cases of acute cholangitis in either group, which could be attributed to application of endoscopic nasobiliary drainage.

The recurrence of stones and chronic biliary inflammation are long-term complications after bile duct stone extraction, especially in patients who undergo a large sphincterotomy. Mechanical lithotripsy might be another risk factor for stone recurrence because remnant stone fragments after lithotripsy could act as nidi for stone recurrence[31]. In our study, there were 7 cases of CBD stone recurrence; group A had 1 case, and group B had 6 cases. The results showed that EPLBD combined with limited EST decreased the recurrence of CBD stones compared with EST alone (1.6% vs 6.7%, P < 0.05). This decrease could be attributed to the preservation of the sphincter of Oddi, which prevents the chronic reflux of duodenal contents and bacteria into the biliary tree and to the lower frequency of mechanical lithotripsy. There were no cases of chronic biliary inflammation in either group; this might have been because of the short follow-up time.

EPLBD with limited EST is an effective and safe endoscopic approach for removing large or multiple CBD stones. However, this was a retrospective study, and the decision to perform EST alone or EPLBD with limited EST was made on an individual basis at the time of each examination. Further large randomized prospective case-controlled studies might be needed to confirm the efficacy and safety of EPLBD plus limited EST.

Acknowledgments
The authors thank Professor Ai-Xia Gong for performing the ERCP procedures.

Comments
Background
Endoscopic sphincterotomy (EST) has been widely accepted as the standard therapy for removing common bile duct (CBD) stones; however, this procedure is associated with serious complications such as hemorrhage, pancreatitis, perforation, and recurrent infection of the bile duct. Endoscopic papillary balloon dilation of the biliary sphincter (EPBD) was introduced for patients with small or moderate CBD stones. This procedure has the advantages of preserving papillary sphincter function and reducing the chance of hemorrhage and perforation. However, it is associated with a high risk of pancreatitis and with more frequent application of mechanical lithotripsy.

Research Frontiers
Recently, endoscopic papillary large diameter balloon dilation after limited endoscopic sphincterotomy (EST + EPLBD) was introduced for removing large (>10 mm) or multiple bile duct stones. This method combines the advantages of EST and EPBD by increasing the efficacy of stone extraction while minimizing complications of EST and EPBD when used alone.

Innovations and Breakthroughs
The study showed that compared with EST alone, the patients in the EST + EPLBD group had lower rates of bleeding and recurrences of CBD stones, whereas the rates of overall stone removal and stone removal in the first session and the rates of post-ERCP pancreatitis and hyperamylasemia were not significantly different between the two groups. EST + EPLBD is a good alternative to conventional endoscopic sphincterotomy for the removal of large common bile duct stones. However, a larger study is required to clarify the advantages and disadvantages of this treatment.

Applications
Endoscopic papillary large diameter balloon dilation following limited sphincterotomy is effective and safe. An improved understanding of the advantages and disadvantages of the treatment for the removal of common biliary duct stones allows clinicians to make appropriate choices for patients.

Terminology
EST + EPLBD is defined as endoscopic papillary large diameter balloon dilation after limited endoscopic sphincterotomy. The balloon is positioned across the orifice of the ampulla and then is gradually inflated to an appropriate size.

Peer Review
This paper compares the curative effect and safety of EST and EST + EPLBD for the treatment of bile duct stones. The authors concluded that EST + EPLBD is a good alternative to conventional endoscopic sphincterotomy for the removal of large or multiple common bile duct stones. This result provides valuable information for other researchers.

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