TECHNICAL REVIEW

International consensus guidelines for endoscopic papillary large-balloon dilation

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Common bile duct stones are frequently diagnosed throughout the world. Endoscopic sphincterotomy (EST) has been used for the removal of bile duct stones for the past 40 years. The purpose of EST is to provide an opening to allow bile duct stone extraction. However, adverse events such as bleeding, perforation, pancreatitis, and cholangitis occur in 5% to 10% of patients who undergo EST.[1-4] Additionally, endoscopic mechanical lithotripsy (EML) may be required as an adjunctive procedure in patients with large bile duct stones to facilitate clearance.[5-9] Endoscopic papillary balloon dilation (EPBD) was first proposed as an alternative to EST in 1982.[10] Because the extent of orifice dilation with EPBD is limited to a diameter of $\leq$10 mm, it is less successful than EST in removing bile duct stones.[11,12] Endoscopic papillary large balloon dilation (EPLBD) combined with EST was introduced in 2003 to facilitate the removal of large or difficult bile duct stones,[13] and the size of the large-diameter balloons used was 12 to 20 mm. Since then, EPLBD with limited or large EST has become rapidly and widely adopted, mainly in Asia. As an alternative method, EPLBD without a preceding EST was introduced as a simplified technique in 2009.[14] Several studies have reported that this technique is safe and effective in patients with large bile duct stones without an increased risk of severe pancreatitis or bile duct perforation. Nevertheless, it is difficult to precisely analyze the outcomes of EPLBD because the techniques and definitions are used differently among studies. To date, there is no published consensus of guidelines on the techniques and indications for EPLBD. The consensus guidelines in this report will help provide a framework to improve the outcome of EPLBD.

Abbreviations: CI, confidence interval; EML, endoscopic mechanical lithotripsy; EPBD, endoscopic papillary balloon dilation; EPLBD, endoscopic papillary large-balloon dilation; EST, endoscopic sphincterotomy; OR, odds ratio; PAD, periampullary diverticulum.

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METHOD FOR PREPARING THE GUIDELINES

The literature on EPLBD was initially reviewed by searching titles and abstracts with the search terms "large balloon," "balloon dilation," "sphincteroplasty," and "endoscopic papillary large balloon dilation" in MEDLINE, the Cochrane Library, and Embase. After reviewing the corresponding abstracts of the retrieved articles, the full text of the articles relevant to this review were downloaded. Additional articles were then searched by reviewing the references of these articles.

Before the consensus meeting, the Korean co-authors created first draft statements. The statements for EPLBD were divided into the following topics: definition, indication, technique, outcomes, adverse events, and specific cases such as periampullary diverticulum, surgically altered anatomy, and previous EST. These topics were determined according to their perceived clinical importance. These statements were provided by e-mail to the consensus group panel. A face-to-face meeting of the consensus group was held on February 14, 2014, in Seoul, Republic of Korea, to review and discuss the evidence for all statements. All statements were revised and finally agreed on at the concluding plenary session. Thereafter, the evidence level and recommendation grade were rated using the evidence leveling system of Scottish Intercollegiate Guidelines Network Grading Review Group (Table 1),[15] and the voting system used was a 5-point Likert scale (Table 2). The first vote was conducted in this meeting, and the second voting was conducted electronically by e-mail. Consensus was considered to be achieved when 80% or more of voting members indicated "accept completely" or "accept with some reservation." A statement was refused when 80% or more of voting members "reject completely" or "reject with some reservation" (Table 2). Commentaries on statements

TABLE 1. Definitions of categories for evidence levels and recommendation grades used in these guidelines[15]

Evidence level:

- 1++: High-quality meta-analyses; systematic reviews of randomized, controlled trials; or randomized, controlled trials with a very low risk of bias
- 1+: Well-conducted meta-analyses; systematic reviews of randomized, controlled trials; or randomized, controlled trials with a low risk of bias
- 1−: Meta-analyses, systematic reviews, or randomized, controlled trials with a high risk of bias
- 2++: High-quality systematic reviews of case-control or cohort studies; high-quality case-control studies or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
- 2+: Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
- 2−: Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
- 3: Nonanalytic studies (eg, case reports, case series)
- 4: Expert opinion

Recommendation grade:

- A: At least 1 meta-analysis, systematic review, or randomized, controlled trial rated as 1++ and directly applicable to the target population or a systematic review of randomized, controlled trials or a body of evidence consisting principally of studies rated 1+ directly applicable to the target population and demonstrating overall consistency of results
- B: A body of evidence including studies rated 2++ directly applicable to the target population and demonstrating overall consistency of results or extrapolated evidence from studies rated 1++ or 1+
- C: A body of evidence including studies rated 1− or 2+ directly applicable to the target population and demonstrating overall consistency of results or extrapolated evidence from studies rated 2++
- D: Evidence level 2−, 3, or 4 or extrapolated evidence from studies rated 2+

were written by T.H. Kim and J.H. Kim and all co-authors were involved in the final editing of the commentaries.

In this report, we first discuss the definition, indication, and technique of EPLBD with or without EST. We then focus on the best indications, followed by a discussion of safe techniques and outcomes of EPLBD. Each section of this report includes the key recommendations related to the section topic followed by a summary of the supporting evidence (Table 3).

1. DEFINITION

1.1. EPLBD is used to dilate the biliary orifice with a large-diameter balloon (≥12 mm) and can be performed with or without EST.

EPBD involves dilation of the biliary sphincter with a small-diameter balloon (≤10 mm) and is usually performed without EST. When large bile duct stones are extracted by using EPBD, a great number of EMLs is needed because of the small biliary opening created after EPBD. EPLBD is an extension of EPBD, which is used to create a larger biliary opening with a large diameter balloon (≥12 mm). The intended purpose of EPLBD is to simplify removing large or difficult bile duct stones without additional adverse events of EST alone or EPBD alone. EST has been generally recommended before EPLBD because it was believed to be associated with a decreased risk of postprocedure pancreatitis.[16,17] EPLBD was initially performed when the standard balloon and basket extraction techniques failed after large EST, but recently it has been performed after limited EST or sometimes without EST to minimize the risk of adverse events of large EST, even before attempting trials of the standard extraction techniques. A recent systematic review of EPLBD concluded that EPLBD with EST has similar outcomes in terms of stone clearance and the advantage of a lower risk of overall adverse events and pancreatitis compared with EST alone.[18] As an alternative method, Jeong et al[14] reported that avoiding EST during EPLBD can simplify the procedure and that this technique is safe and effective for managing large bile duct stones without increasing the risk of pancreatitis. Although the initial success rate of EPLBD without EST was significantly lower than that of EPLBD with EST, there were no significant differences in the overall success rates in the systematic review.[18] However, only a few reports regarding EPLBD without EST have been published. Accordingly, large-scale prospective, multicenter studies would be ideal to verify the effectiveness of EPLBD without EST.

TABLE 2. Voting on recommendation

- A: Accept completely
- B: Accept with some reservation
- C: Accept with major reservation
- D: Reject with reservation
- E: Reject completely

2. INDICATION

2.1. In the removal of large or difficult bile duct stones, EPLBD can be used as an alternative to EML.

Evidence level: 1+

Recommendation level: B

Level of agreement: A, 70.6%; B, 29.4%; C, 0%; D, 0%; E, 0%

Bile duct stones may be difficult to remove endoscopically by using standard balloon and basket extraction

TABLE 3. Summary statements of EPLBD

1. Definition:
- 1.1. EPLBD is used to dilate the biliary orifice with a large-diameter balloon (≥12 mm) and can be performed with or without EST.

2. Indication:
- 2.1. In the removal of large or difficult bile duct stones, EPLBD can be used as an alternative to EML (evidence level: 1+, recommendation level: B).
- 2.2. EPLBD can be used as the initial method when large bile duct stones have been identified on endoscopic retrograde cholangiography or cross-sectional imaging (evidence level: 1+, recommendation level: B).
- 2.3. When conventional stone removal after EST fails, EPLBD can be considered (evidence level: 1+, recommendation level: B).
- 2.4. In patients with obvious distal bile duct strictures or a nondilated bile duct, EPBLD is not recommended because of the increased risk of perforation (evidence level: 2+, recommendation level: C).
- 2.5. EPLBD without EST is preferred over EPLBD with EST in patients with coagulopathy (evidence level: 4, recommendation level: D).

3. Techniques:
- 3.1. The maximal diameter of the balloon should not exceed the diameter of the distal bile duct (evidence level: 3, recommendation grade: D).
- 3.2. The balloon should be inflated slowly in gradual steps (evidence level: 3, recommendation grade: D).
- 3.3. The usual duration of balloon dilation is approximately 30 to 60 seconds after disappearance of the waist (evidence level: 1−, recommendation grade: C).

4. Outcomes:
- 4.1. The initial and overall success rates of EPLBD with EST are comparable to those of EST alone (evidence level: 1+, recommendation grade: A).
- 4.2. Overall success rates of EPLBD with and without EST for bile duct stone clearance are comparable (evidence level: 2++, recommendation grade: B).
- 4.3. EPLBD with EST can reduce the need for EML (evidence level: 1+, recommendation grade: B).

5. Specific cases:
- 5.1. The presence of a periampullary diverticulum may not increase the risk of adverse events in patients who undergo EPLBD (evidence level: 2++, recommendation grade: B).
- 5.2. In patients with surgically altered anatomy, EPLBD may be an effective and safe procedure to remove bile duct stones (evidence level: 3, recommendation grade: D).
- 5.3. In patients with a previous EST, EPLBD without repeated EST may be effective and safe for the removal of recurrent stones (evidence level: 2−, recommendation grade: D).

6. Adverse events:
- 6.1. The rate of overall adverse events for EPLBD with EST is lower than that for EST alone in patients with large or difficult stones (evidence level: 1−, recommendation grade: C).
- 6.2. EPLBD may not increase the risk of pancreatitis (evidence level: 1+, recommendation grade: B).
- 6.3. EPLBD with large EST may increase the risk of bleeding (evidence level: 2++, recommendation grade: C).
- 6.4. EPLBD with EST has a perforation rate similar to that of EST. A distal CBD stricture is a major risk factor for perforation (evidence level: 1+, recommendation grade: B).

EML, Endoscopic mechanical lithotripsy; *EPLBD*, endoscopic papillary large-balloon dilation; *EST*, endoscopic sphincterotomy.

techniques after mainly large EST in the setting of large stones (>15 mm), multiple stones, barrel-shaped stones, and tapering or tortuosity of the distal common bile duct.[19,20] In such situations, additional endoscopic procedures, mainly EML, are usually required.[5-9] However, EML is a time-consuming procedure, raising problems such as impaction and fracture of the Dormia basket, and increases the risk of adverse events ranging from 6% to 13%.[9,21-24] The frequency of the use of EML when performing EST or EPBD is related to various factors such as the diameter of the dilating balloon, a discrepancy in the size between the stone and ampullary orifice or distal bile duct, and the shape of the stone and bile duct. EPLBD combined with EST or without a preceding EST can be used as the alternative to EML after EST for the removal of large or difficult bile duct stones, reducing the need for EML because it allows a larger biliary orifice to be achieved than full-incision EST or EPBD. A number of case series; retrospective cohort studies; randomized, controlled trials; and meta-analyses supported the fact that EPLBD was a safe and useful alternative technique to EML without causing any additional risk of severe adverse events when removing large or difficult bile duct stones.[16,20,25-36]

2.2. EPLBD can be used as the initial method when large bile duct stones have been identified on endoscopic retrograde cholangiography or cross-sectional imaging.

Evidence level: 1+

Recommendation level: B

Level of agreement: A, 70.6%; B, 23.5%; C, 5.9%; D, 0%; E, 0%

In early trials of EPLBD, a supplementary EPLBD was performed when the standard balloon and basket extraction technique failed after large EST.[13,37] However, preemptive EPLBD has recently been performed after limited EST or sometimes without EST in patients with large bile duct stones that are suspected to be difficult to remove by using standard extraction techniques even after large EST, because EPLBD after large EST may increase the risk of adverse events such as bleeding and perforation. Abdominal CT with coronal reconstruction and MRCP can be used to measure the number and size of bile duct stones and to determine the shape of the bile duct. Accordingly, this allows endoscopists to decide on the method to use for bile duct stone removal even before endoscopic retrograde cholangiography is

performed. All recent studies that were conducted to compare the clinical outcomes of EPLBD with limited EST with EST alone as an initial stone extraction technique in patients with large bile duct stones, constituting 2 retrospective cohort studies[25,26] and 5 randomized, controlled trials,[27-30,35] showed similar or even better initial and overall success rates of stone clearance and rates of adverse events. In addition, 2 retrospective case series reported that initial EPLBD without a preceding EST could be safely and effectively used as an alternative stone extraction technique to EST alone in patients with large bile duct stones.[14,38] Therefore, if large or difficult bile duct stones are seen on endoscopic retrograde cholangiography or cross-sectional imaging, initial EPLBD before attempting trials of the standard extraction techniques can be performed after limited EST or sometimes without EST to facilitate effective stone removal, minimizing the risk of adverse events of large EST.

2.3. When conventional stone removal after EST fails, EPLBD can be considered.

Evidence level: 1+

Recommendation level: B

Level of agreement: A, 88.2%; B, 11.8%; C, 0%; D, 0%; E, 0%

In 2003, Ersoz et al[13] were the first to report successfully performing EPLBD as an alternative technique to EML as a means of removing difficult or large bile duct stones in patients in whom standard extraction techniques after large EST failed. Thereafter, a number of case series supported the finding that supplementary EPLBD after mainly large EST was a feasible and useful technique in similar situations.[37,39-43] However, several severe to fatal adverse events (1 case of fatal pancreatitis,[42] 2 cases of severe bleeding,[39,40] 1 case of fatal bleeding,[43] and 1 case of severe perforation[40]) have been described in published reports. One well-conducted randomized, controlled trial reported that full-incision EST followed by EPLBD was equally as effective as full-incision EST followed by EML for the removal of large bile duct stones, but associated with fewer adverse events (4.4% vs 20%, $P = .049$).[29] However, further large-scale randomized, controlled trials are needed to verify the effectiveness of supplementary EPLBD in patients in whom standard extraction techniques after mainly large EST failed.

2.4. In patients with obvious distal bile duct strictures or a nondilated bile duct, EPLBD is not recommended because of the increased risk of perforation.

Evidence level: 2+

Recommendation level: C

Level of agreement: A, 64.7%; B, 35.3%; C, 0%; D, 0%; E, 0%

In a well-conducted case-control multicenter study for the analysis of adverse events in 946 patients who underwent EPLBD, a distal bile duct stricture was found to be the independent risk factor for perforation (odds ratio [OR] 17.083; 95% confidence interval [CI], 3.936–74.132; $P < .001$), which was known as the most serious adverse event of EPLBD.[17] In this study, perforation-related deaths occurred only in 3 patients with a distal bile duct stricture, and suspected causative factors of perforation in these patients were overinflation of the balloon in all 3 patients as well as full-incision EST in 2.[17] Therefore, EPBLD is not recommended in patients with obvious distal bile duct strictures or a nondilated bile duct because of the increased risk of perforation due to excessive dilation of the bile duct with a balloon.[17,18] Obvious strictures of the distal bile duct can be detected easily on cholangiography, whereas obscure strictures may not. The speed and degree of balloon inflation should be carefully controlled to avoid adverse events in view of such obscure strictures of the distal bile duct.[44] If there is a suspicion of distal bile duct strictures during ERCP, especially in patients with a tapered distal bile duct, use of the pulling method of a large inflated retrieval balloon through the suspected site is recommended to confirm a suspected existence.[18]

2.5. EPLBD without EST is preferred over EPLBD with EST in patients with coagulopathy.

Evidence level: 4

Recommendation level: D

Level of agreement: A, 58.8%; B, 35.3%; C, 5.9%; D, 0%; E, 0%

The risk of bleeding with EST depends on the extent of the ampullary incision and underlying conditions such as coagulopathy, use of antithrombotic and antiplatelet medications, cirrhosis, thrombocytopenia, and chronic renal failure.[6,45] Therefore, endoscopic balloon dilation is the preferred strategy in patients with coagulopathy. In fact, in a retrospective cohort study of bleeding risk in patients with cirrhosis and coagulopathy, the bleeding rates for EST and EPBD with a small-diameter balloon ($\leq$10 mm) were 30% and 0%, respectively.[46] Several randomized, controlled trials have shown that EPBD might significantly reduce the risk of bleeding compared with EST.[47-49] However, there is not enough evidence supporting the advantages of EPLBD without EST in patients with coagulopathy. Based on the results of a number of EPBD studies, it is suggested that EPLBD without EST may theoretically minimize bleeding. In a well-conducted case-control multicenter study for the analysis of adverse events in 946 patients who underwent EPLBD, underlying liver cirrhosis was found to be an independent predictor of bleeding after EPLBD (OR 8.028; 95% CI, 2.022–31.883; $P = .003$).[17] In the systematic review of 32 EPLBD studies, cases of serious bleeding, including severe and fatal bleeding, were not noted in all 413 patients who underwent EPLBD without EST, whereas it was noted in 4 of 2503 patients who underwent EPLBD with EST, although there was no significant difference in the overall rate of bleeding between EPLBD with and without EST.[18] Therefore, EPLBD without EST is preferred over EPLBD with EST if EPLBD must be performed in patients with coagulopathy.

3. TECHNIQUES

3.1. The maximum diameter of the balloon should not exceed the diameter of the distal bile duct.

Evidence level: 3

Recommendation grade: D

Level of agreement: A, 70.6%; B, 29.4%; C, 0%; D, 0%; E, 0%

Major procedure-related risk factors that seem to be related to adverse events during EPLBD include the extent of EST, the diameter of the balloon, and the method of balloon inflation. The size of the bile duct stones and the diameter of the distal bile duct are crucial factors when selecting the diameter of the balloon. Although the balloon diameter for EPLBD ranges from 12 mm to 20 mm, a balloon with a diameter of 15 mm or less is frequently used to prevent serious adverse events, even if the bile duct stones are larger than 15 mm in diameter. Therefore, the diameter of the distal bile duct may be regarded as a more important factor when selecting the balloon rather than the size of bile duct stones because excessive balloon dilation beyond the diameter of the distal bile duct may increase the risk of perforation. A large-scale retrospective, multicenter EPLBD study of 946 patients with large bile duct stones (>10 mm) noted that the diameter of the inflated balloon used was larger than that of the distal bile duct in 2 of 3 patients with fatal perforation.[17] Although further studies are still needed, the maximal inflated diameter of the balloon should not exceed the diameter of the distal bile duct to prevent the risk of perforation due to overinflation of the balloon.

3.2. The balloon should be inflated slowly in gradual steps.

Evidence level: 3

Recommendation grade: D

Level of agreement: A, 58.8%; B, 41.2%; C, 0%; D, 0%; E, 0%

During EPLBD, the rapid and forcible inflation of the balloon across a tight distal bile duct stricture can lead to perforation and bleeding. Obvious bile duct strictures are easily visible on cholangiography, whereas obscure bile duct strictures are sometimes difficult to diagnosed. In a multicenter retrospective EPLBD study of 946 patients, the central waist of the balloon did not disappear during EPLBD in 2 of 3 patients who experienced bile duct perforation that resulted in death, whereas it could not be identified in the third patient because of rapid forcible inflation of the balloon during EPLBD.[17] Therefore, if the central waist of the balloon does not disappear, obscure strictures of the distal bile duct stricture should be strongly considered and further balloon inflation must be ceased at any step to avoid perforation.[17] The balloon should always be inflated slowly and gradually, starting from a smaller diameter than the intended maximal target, to recognize obscure bile duct strictures with attention paid to the balloon shape under fluoroscopy.[44]

3.3. The usual duration of balloon dilation is approximately 30 to 60 seconds after disappearance of the waist.

Evidence level: 1−

Recommendation grade: C

Level of agreement: A, 41.2%; B, 41.2%; C, 5.9%; D, 5.9%; E, 5.9%

The duration of balloon dilation in 24 studies of EPLBD with EST, which were included in the systematic review, varied from 10 seconds to 180 seconds; the duration of every study was <60 seconds with the exception of 3 studies.[18] One randomized, controlled trial reported that a 30-second duration of balloon dilation was not different from a 60-second duration with regard to adverse events, including pancreatitis, bleeding, and perforation in EPLBD with EST.[42] One randomized, controlled study on the duration of balloon dilation by using a small-diameter balloon reported that 5-minute EPBD improved the efficacy of stone extraction and reduced the risk of pancreatitis compared with conventional 1-minute EPBD.[50] When studies were stratified by different durations of balloon dilation in a meta-analysis of EPLBD studies by Feng et al,[31] the rates of bile duct stone clearance were not significantly different between EPLBD and EST alone, despite EPLBD being performed with either short duration (<1 minute) (OR 2.77; 95% CI, 0.80–9.61; $P = .11$) or long duration (≥1 minute) (OR 0.56; 95% CI, 0.18–1.78; $P = .33$). In a large-scale retrospective case series of 247 patients who underwent EPLBD without EST for the treatment of large bile duct stones (>10 mm), there were only 3 adverse events (1.2%) comprising 2 cases of mild pancreatitis (0.8%) and 1 case of mild cholangitis (0.4%), after inflating a large balloon up to the mean diameter of 13.2 mm (range 11-20 mm) over a mean duration of 4.7 minutes (range 2-6 minutes).[51] Therefore, a longer duration of balloon dilation does not seem to be related to an increased risk of adverse events, even in patients who undergo EPLBD without EST. However, further studies are warranted to determine the optimal duration of balloon dilation during EPLBD.

4. OUTCOMES

4.1. The initial and overall success rates of EPLBD with EST are comparable to those of EST alone.

Evidence level: 1+ (systemic review and prospective studies, meta-analysis)

Recommendation grade: A

Level of agreement: A, 47.1%; B, 47.1%; C, 5.9%; D, 0%; E, 0%

The initial success rate, which was defined as the rate of successful stone removal during the first ERCP session, of EPLBD with EST in the systematic review[18] was comparable to that of EST alone (84.0% vs 80.8%, $P = .131$) in a meta-analysis by Weinberg et al.[11] The initial

success rate in EPLBD with EST was similar to that of EST alone in 1 retrospective cohort study,[20] in 4 of the 6 randomized, controlled trials[27-30]; and in all 5 meta-analyses[16,31-33,36]; whereas it was significantly higher in EPLBD with EST than that in EST alone in another 2 retrospective cohort studies by Kim et al[25] and Rosa et al[26] and the remaining 2 randomized, controlled trials by Li at al[34] and Jun et al.[35] The overall success rate of EPLBD with EST in the previously mentioned systematic review[18] was comparable to that of EST alone (96.5% vs 95.3%, P = .141) in a previous meta-analysis.[11] The overall success rate of EPLBD with EST was similar to that of EST alone in 2 of 3 retrospective cohort studies[20,25]; in all 6 randomized, controlled trials[27-30,34,35] and in all 5 meta-analyses,[16,31-33,36] whereas it was significantly higher in EPLBD with EST than in EST alone in the remaining retrospective cohort study by Rosa et al.[26] Based on these results, the initial and overall success rates of EPLBD with EST are comparable to, or somewhat better than, those of EST alone.

4.2. Overall success rates of EPLBD with and without EST for bile duct stone clearance are comparable.

Evidence level: 2++

Recommendation grade: B

Level of agreement: A, 70.6%; B, 29.4%; C, 0%; D, 0%; E, 0%

After EPLBD with EST was introduced in 2003, EPLBD without EST was formally incorporated as a simplified alternative technique in 2009.[14] There are not enough comparison studies to investigate the clinical outcomes between EPLBD with and without EST in patients with large bile duct stones. A retrospective cohort study that compared stone clearance between EPLBD without and with EST showed similar outcomes in overall successful stone removal (96.8% vs 95.7%; P = .738) and complete stone removal without EML (80.6% vs 73.9%; P = .360).[38] In the systematic review of 32 EPLBD studies, the initial success rate of EPLBD without EST was significantly lower than that of EPLBD with EST (76.2% vs 84.0%; P < .001).[18] This was most likely due to the opening of the orifice retracting almost immediately to its original size, which is commonly seen with EPBD alone. However, there was no significant difference in the overall success rate between the 2 procedures (97.2% vs 96.5%; P = .432).[18] Therefore, it can be concluded that the overall success rates of EPLBD with and without EST are comparable.

4.3. EPLBD with EST can reduce the need for EML.

Evidence level: 1+

Recommendation grade: B

Level of agreement: A, 76.5%; B, 23.5%; C, 0%; D, 0%; E, 0%

EML is usually required as an adjunctive procedure of EST to facilitate complete clearance of large bile duct stones.[5-9] However, EML has proven to be a time-consuming and a challenging technique,[21,22] and EML-related adverse events such as basket impaction and bile duct injury can occur. EPLBD can be used as the main alternative to EST followed by EML for the removal of large or difficult bile duct stones. The widened ampullary orifice made by EPLBD facilitates easier extraction of relatively large bile duct stones and may reduce the need for EML. However, the frequency of EML use with EPLBD might be related to various factors such as the diameter of the dilating balloon used, a discrepancy in the size between the stone and the ampullary orifice or the distal bile duct, and the shape of the stone and the bile duct.

There are some conflicting results concerning the need for EML for the removal of large or difficult bile duct stones in several studies comparing EPLBD with EST and EST alone. In 2 of 3 retrospective cohort studies[20,26] and 3 of 5 randomized, controlled trials,[30,34,35] EPLBD with EST showed a reduced need for EML over EST alone. However, in the remaining 3 studies,[25,27,28] the need for EML was similar that for EST alone. One retrospective study in these 3 studies reported a reduced need for EML in EPLBD with EST, when confined to patients with large CBD stones (≥15 mm).[25] In 4 meta-analyses,[16,31-33] it was evident that EPLBD with EST reduced the need for EML compared with EST alone, although one of them, a meta-analysis by Yang and Hu[16] reported no significant difference between the 2 groups when conducting a sensitivity analysis by including only high-quality full-text studies, which was 4 of the total 6 studies of this meta-analysis. Based on these results, there is speculation that EPLBD with EST can reduce the need for EML in patients with large bile duct stones.

5. SPECIFIC CASES

5.1. The presence of a periampullary diverticulum may not increase the risk of adverse events in patients who undergo EPLBD.

Evidence level: 2++

Recommendation: B

Level of agreement: A, 76.5%; B, 23.5%; C, 0%; D, 0%; E, 0%

The prevalence of periampullary diverticula (PAD) increases with age, and PAD are found in as many as 65% of elderly patients.[52,53] PAD tend to distort the anatomy of the duodenum and the sphincter, making a controlled EST more difficult and possibly increasing the risk of adverse events.[4] Also, when EPLBD is performed in patients with PAD, the potential risk of perforation is of particular concern due to lack of sphincter muscle components around the ampulla. In 3 retrospective comparison studies in patients with and without PAD, there were no significant differences in overall success rates of bile duct stone removal and rates of adverse

events in both, after EPLBD with limited EST or EPLBD alone.[54-56] When comparing each subtype of PAD with the controls or between subtypes of PAD in these studies, the rates of adverse events were not significantly different,[54,56] whereas the frequency of pancreatitis was significantly higher in PAD type A than controls (14.3% vs 3.0%, $P = .047$) in 1 study.[55] In addition, several studies, including a well-conducted case-control, multicenter study for the analysis of adverse events in 946 patients who underwent EPLBD, reported that the presence of PAD did not significantly increase the risk of adverse events such as pancreatitis, bleeding, and perforation after EPLBD, even with large EST.[17,54-56] Nevertheless, EPLBD without EST is generally considered to avoid serious adverse events such as perforation and bleeding in patients with PAD. Randomized, controlled trials for comparing outcomes of patients with and without PAD warrant further investigative studies, especially based on the type of PAD.

5.2. In patients with surgically altered anatomy, EPLBD may be an effective and safe procedure to remove bile duct stones.

Evidence level: 3

Recommendation: D

Level of agreement: A, 88.2%; B, 5.9%; C, 5.9%; D, 0%; E, 0%

It is well known that EST is usually difficult and may require special techniques or devices in patients with surgically altered anatomy. Despite the development of specific sphincterotomes, EST in patients who have undergone Billroth II gastrectomy is more difficult than in patients with unaltered anatomy because the papilla now has to be approached from an inverted anatomic structure. In such a situation, balloon dilation may be particularly suitable instead of EST. Six case series of EPLBD with limited EST, mainly using a needle-knife or a rotatable papillotome in patients with a surgically altered anatomy such as Billroth II surgery and Roux-en-Y anastomosis, reported relatively high rates of complete stone clearance (96.7%–100%)[57-62] compared with 81.3% to 100% in other studies using adjusted EST techniques to suit the surgically altered anatomy.[63-65] In all of these EPLBD studies in patients with a surgically altered anatomy, only mild pancreatitis and mild to moderate bleeding were noted without any perforation or serious adverse events. Jang et al[66] reported complete CBD stone removal after EPLBD without EST in all Billroth II gastrectomy patients with large or difficult CBD stones without any serious adverse events. However, to date, there are still no randomized, controlled trials of EPLBD and EST alone in Billroth II gastrectomy patients. Nonetheless, EPLBD is still regarded as an effective and safe procedure and is commonly used to remove bile duct stones in patients with surgically altered anatomy.

5.3. In patients with previous EST, EPLBD without repeated EST may be effective and safe for the removal of recurrent stones.

Evidence level: 2−

Recommendation: D

Level of agreement: A, 82.4%; B, 11.8%; C, 5.9%; D, 0%; E, 0%

In recurrent bile duct stones, extended incision of a previous EST site is sometimes required to remove large and difficult stones. However, it can increase the risk of adverse events such as bleeding and perforation.[1,4,6] In such cases, EPLBD can be safely and effectively used to widen the ampullary orifice without performing a repeat EST. There have been 3 case series and 1 retrospective cohort study of EPLBD in patients who underwent previous EST.[67-70] In the 3 case series involving 146 patients, complete stone removal was achieved in all patients with 1 case of mild pancreatitis being the only procedure-related adverse event.[67,68,70] In a retrospective cohort study of EPLBD without repeated EST and standard balloon and basket extraction techniques in patients with a history of EST and large bile duct stones (>10 mm), the total procedure time was significantly shorter and the frequency of EML use was significantly lower in EPLBD without repeated EST than when performing standard extraction techniques, whereas the rates of complete stone clearance and the procedure-related adverse events were similar in both.[69] Therefore, in patients with previous EST, EPLBD without repeated EST may be effective and safe for the removal of recurrent stones.

6. ADVERSE EVENTS

6.1. The rate of overall adverse events for EPLBD with EST is lower than that for EST alone in patients with large or difficult stones.

Evidence level: 1−

Recommendation grade: C

Level of agreement: A, 41.2%; B, 41.2%; C, 17.6%; D, 0%; E, 0%

Major adverse events typically related to both EST and EPLBD are pancreatitis, bleeding, and perforation. In the systematic review, which included 30 studies conducted in patients with EPLBD with EST, the rate of overall adverse events was significantly lower for EPLBD with EST than that for EST alone (8.3% vs 12.7%, OR 1.60, $P < .001$).[18] The rate of overall adverse events was similar in 5 of all 6 randomized, controlled trials between the 2 groups,[27,28,30,34,35] whereas it was significantly lower for EPLBD with EST than that for EST alone in the remaining study by Stefanidis et al.[29] In contrast, in 4 of 5 meta-analyses that evaluated a comparison of EPLBD with EST and EST alone in the removal of large bile duct stones, the rate of overall adverse events was significantly lower for EPLBD with EST than that for EST alone.[16,31,33,36] In a

large-scale multicenter case-control study that investigated 946 patients, a subgroup analysis showed that stones larger than 16 mm, cirrhosis, and full-length EST were independently associated with an increase in overall adverse events.[17]

6.2. EPLBD may not increase the risk of pancreatitis.

Evidence level: 1+

Recommendation grade: B

Level of agreement: A, 70.6%; B, 11.8%; C, 11.8%; D, 5.9%; E, 0%

Two meta-analyses of EPBD by using small-diameter balloons (<10 mm) showed a significantly higher rate of pancreatitis than EST (8.6% vs 4.3%, $P = .0005$ and 7.4% vs 4.3%, $P = .05$).[11,71] Based on this evidence, many concerns have been raised about pancreatitis after balloon dilation with increasing balloon size. However, Youn et al[72] reported that EPLBD with a large balloon of more than 15 mm with EST is safe with a very low rate of severe pancreatitis. In the systematic review of EPLBD studies using large-diameter balloons (12-20 mm), pancreatitis occurred in 2.4% (61/2511) of patients who underwent EPLBD with EST; almost all cases of pancreatitis were of mild to moderate severity (98.4%) with the exception of 1 fatal case of severe pancreatitis.[18] Furthermore, this systematic review reported that only mild to moderate pancreatitis after EPLBD without EST occurred in 3.9% of 413 patients.[18] In the comparison of adverse events between results of a previous meta-analysis by Weinberg et al[11] of EST alone and those of this systematic review in EPLBD with EST, the rate of pancreatitis in patients who underwent EPLBD with EST was significantly lower than that in patients who underwent EST alone (4.3% vs 2.4%, $P = .006$).[18] In all 6 randomized, controlled trials[27-30,34,35] and all 5 meta-analyses[16,31-33,36] that were conducted to compare the clinical outcomes of EPLBD with EST and of EST alone, the rate of pancreatitis showed no statistical difference between them. Furthermore, the systematic review of 3 studies reported that only mild to moderate pancreatitis after EPLBD without EST occurred in 3.9% of 413 patients.[18] Based on these results, acute pancreatitis associated with EPLBD with or even without EST may occur at a lower incidence rate and is less severe than that associated with EPBD alone and may occur with a similar incidence to that associated with EST alone. Therefore, there is no doubt that the mechanism of pancreatitis differs between EPLBD and EPBD, although it still remains unclear.

Interestingly, in a multicenter study, balloons larger than 14 mm in diameter were independently associated with a lower risk of pancreatitis, suggesting that only simple stretching of the ampullary orifice or direct blockage of the pancreatic orifice by compression of large-diameter balloons is not a major mechanism for pancreatitis after EPLBD.[17] A possible mechanism of the reduced pancreatitis rate for EPLBD with EST is that the radial force exerted by the dilating balloon shifts along the cutting direction made during EST toward the bile duct and away from the pancreatic orifice, resulting in less periampullary injury around the pancreatic duct.[16,17] However, EST may have a limited role in preventing pancreatitis in EPLBD because patients undergoing EPLBD without EST did not have an increased risk of pancreatitis.[18] Therefore, the other hypothesis about the mechanism of pancreatitis after EPLBD was suggested: the manipulation frequency of the Dormia basket and retrieval balloon catheter in EPLBD both with and without EST can be reduced due to a sufficiently widened ampullary orifice, resulting in less periampullary trauma or edema and a lower risk of pancreatitis. On the contrary, the risk of injury to the ampullary orifice in EPBD by using small-diameter balloons may be increased because instruments for stone removal are passed through an inadequately widened ampullary orifice.

6.3. EPLBD with large EST may increase the risk of bleeding.

Evidence level: 2++

Recommendation grade: C

Level of agreement: A, 76.5%; B, 11.8%; C, 5.9%; D, 5.9%; E, 0%

EPLBD with EST would theoretically combine the advantages of EST and EPBD by increasing the efficacy at stone extraction all the while minimizing their major adverse events.[73] In all 6 randomized, controlled trials[27-30,34,35] and 3 of 4 meta-analyses[16,32,33], which were conducted to compare the clinical outcomes between EPLBD with EST and EST alone, the rate of bleeding was similar, whereas the remaining meta-analysis by Feng et al[31] found that the rate of bleeding was significantly lower for EPLBD with EST than that for EST alone. However, the incision extent of the ampulla is one of several major factors that induce serious bleeding, although EPLBD itself may lead to bleeding due to blood vessel injury. In a systematic review of 32 EPLBD studies, the rate of bleeding was significantly higher for EPLBD with large EST than for EPLBD with limited EST (OR 3.33, $P < .001$) and without EST (OR 2.17, $P = .049$).[18] However, no significant difference in the bleeding rate was noted between EPLBD with limited EST and without EST ($P = .35$).[18] In this systematic review, 4 cases of serious bleeding, including 2 severe and 2 fatal cases, were noted only in patients who underwent a full-incision or large EST before EPLBD.[18] Serious bleeding may occur if a large blood vessel located at the proximal part of the ampullary roof is severed during full-incision or large EST, not by injury caused by the balloon itself.[17,18] Based on these results, EPLBD after large EST should be cautiously performed to prevent serious bleeding, and EPLBD after limited EST or sometimes without EST can be initially recommended even before attempting standard

extraction techniques with large EST when the stone is seen to be too large on cholangiography or cross-sectional imaging.

6.4. EPLBD with EST has a rate of perforation similar to that of EST alone. A distal bile duct stricture is a major risk factor for perforation.

Evidence level: 1+

Recommendation grade: B

Level of agreement: A, 82.4%; B, 11.8%; C, 5.9%; D, 0%; E, 0%

The most serious adverse event of EPLBD with EST is bile duct perforation. In the systematic review of EPLBD studies, the rates of perforation were 0.6% (range 0%–2.8%) for EPLBD with EST.[18] Six problematic perforations after EPLBD with EST were reported: 2 duodenal perforations that were successfully managed with surgery, 1 cystic duct perforation managed with percutaneous drainage, and 3 fatal perforations from either septic shock or cardiogenic shock. In all 6 randomized, controlled trials[27-30,34,35] conducted to compare the clinical outcomes between EPLBD with EST and EST alone, the rate of perforation was similar. Among 4 meta-analyses of the clinical outcomes between EPLBD with EST and EST alone, 2 meta-analyses by Feng et al[31] and Jin et al[32] showed no significant difference between them; a meta-analysis by Yang and Hu[16] found a lower perforation rate only in EPLBD with EST, but no significant difference between them when excluding 2 low-quality abstracts of all 6 studies; the last meta-analysis by Madhoun et al[33] showed no estimable results between them, but no significant difference when excluding guidewire-related perforations. The extent of ampullary incision may not be a major cause of perforation because there was no difference in the perforation rate between EPLBD with large EST and EPLBD with limited EST (0.4% vs 0.5%, $P = 1.00$) in the systematic review,[18] but it is well known that the diameter of the balloon is the most important major factor in ensuring the success of EPLBD and minimizing adverse events.[74] The wider the ampullary orifice is dilated with the balloon, the more easily removal of the stone can be achieved. However, choosing an inappropriately oversized balloon increases the risk of perforation. Also, the large-scale multicenter case-control EPLBD study of 946 patients showed that a distal bile duct stricture was noted in 7 of a total of 9 perforations, consisting of 3 perforations of moderate severity and all 4 perforations of severe severity and was an independent predictor of perforation (OR 17.08, $P < .001$).[17]

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REFERENCES

1. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991;37:383-93.
2. Sherman S, Ruffolo TA, Hawes RH, et al. Complications of endoscopic sphincterotomy. A prospective series with emphasis on the increased risk associated with sphincter of Oddi dysfunction and nondilated bile ducts. Gastroenterology 1991;101:1068-75.
3. Boender J, Nix GA, de Ridder MA, et al. Endoscopic papillotomy for common bile duct stones: factors influencing the complication rate. Endoscopy 1994;26:209-16.
4. Leung JW, Chan FK, Sung JJ, et al. Endoscopic sphincterotomy-induced hemorrhage: a study of risk factors and the role of epinephrine injection. Gastrointest Endosc 1995;42:550-4.
5. Bergman JJ, Rauws EA, Fockens P, et al. Randomised trial of endoscopic balloon dilation versus endoscopic sphincterotomy for removal of bileduct stones. Lancet 1997;349:1124-9.
6. Freeman ML, Nelson DB, Sherman S, et al. Complications of endoscopic biliary sphincterotomy. N Engl J Med 1996;335:909-18.
7. Higuchi T, Kon Y. Endoscopic mechanical lithotripsy for the treatment of common bile duct stone. Experience with the improved double sheath basket catheter. Endoscopy 1987;19:216-7.
8. Moriai T, Hasegawa T, Fuzita M, et al. Successful removal of massive intragastric gallstones by endoscopic electrohydraulic lithotripsy and mechanical lithotripsy. Am J Gastroenterol 1991;86:627-9.
9. Hintze RE, Adler A, Veltzke W. Outcome of mechanical lithotripsy of bile duct stones in an unselected series of 704 patients. Hepatogastroenterology 1996;43:473-6.
10. Staritz M, Ewe K, Meyer zum Buschenfelde KH. Endoscopic papillary dilatation: an alternative to papillotomy? (author's transl). Dtsch Med Wochenschr 1982;107:895-7.
11. Weinberg BM, Shindy W, Lo S. Endoscopic balloon sphincter dilation (sphincteroplasty) versus sphincterotomy for common bile duct stones. Cochrane Database Syst Rev 2006:CD004890.
12. Zhao HC, He L, Zhou DC, et al. Meta-analysis comparison of endoscopic papillary balloon dilatation and endoscopic sphincteropapillotomy. World J Gastroenterol 2013;19:3883-91.
13. Ersoz G, Tekesin O, Ozutemiz AO, et al. Biliary sphincterotomy plus dilation with a large balloon for bile duct stones that are difficult to extract. Gastrointest Endosc 2003;57:156-9.
14. Jeong S, Ki SH, Lee DH, et al. Endoscopic large-balloon sphincteroplasty without preceding sphincterotomy for the removal of large bile duct stones: a preliminary study. Gastrointest Endosc 2009;70:915-22.
15. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. BMJ 2001;323:334-6.
16. Yang XM, Hu B. Endoscopic sphincterotomy plus large-balloon dilation vs endoscopic sphincterotomy for choledocholithiasis: a meta-analysis. World J Gastroenterol 2013;19:9453-60.

17. Park SJ, Kim JH, Hwang JC, et al. Factors predictive of adverse events following endoscopic papillary large balloon dilation: results from a multicenter series. Dig Dis Sci 2012;58:1100-9.
18. Kim JH, Yang MJ, Hwang JC, et al. Endoscopic papillary large balloon dilation for the removal of bile duct stones. World J Gastroenterol 2013;19:8580-94.
19. Kim HJ, Choi HS, Park JH, et al. Factors influencing the technical difficulty of endoscopic clearance of bile duct stones. Gastrointest Endosc 2007;66:1154-60.
20. Itoi T, Itokawa F, Sofuni A, et al. Endoscopic sphincterotomy combined with large balloon dilation can reduce the procedure time and fluoroscopy time for removal of large bile duct stones. Am J Gastroenterol 2009;104:560-5.
21. Leung JW, Tu R. Mechanical lithotripsy for large bile duct stones. Gastrointest Endosc 2004;59:688-90.
22. Shaw MJ, Mackie RD, Moore JP, et al. Results of a multicenter trial using a mechanical lithotripter for the treatment of large bile duct stones. Am J Gastroenterol 1993;88:730-3.
23. Garg PK, Tandon RK, Ahuja V, et al. Predictors of unsuccessful mechanical lithotripsy and endoscopic clearance of large bile duct stones. Gastrointest Endosc 2004;59:601-5.
24. Chang WH, Chu CH, Wang TE, et al. Outcome of simple use of mechanical lithotripsy of difficult common bile duct stones. World J Gastroenterol 2005;11:593-6.
25. Kim TH, Oh HJ, Lee JY, et al. Can a small endoscopic sphincterotomy plus a large-balloon dilation reduce the use of mechanical lithotripsy in patients with large bile duct stones? Surg Endosc 2011;25:3330-7.
26. Rosa B, Moutinho Ribeiro P, et al. Endoscopic papillary balloon dilation after sphincterotomy for difficult choledocholithiasis: a case-controlled study. World J Gastrointest Endosc 2013;5:211-8.
27. Heo JH, Kang DH, Jung HJ, et al. Endoscopic sphincterotomy plus large-balloon dilation versus endoscopic sphincterotomy for removal of bile-duct stones. Gastrointest Endosc 2007;66:720-6; quiz 68, 71.
28. Kim HG, Cheon YK, Cho YD, et al. Small sphincterotomy combined with endoscopic papillary large balloon dilation versus sphincterotomy. World J Gastroenterol 2009;15:4298-304.
29. Stefanidis G, Viazis N, Pleskow D, et al. Large balloon dilation vs. mechanical lithotripsy for the management of large bile duct stones: a prospective randomized study. Am J Gastroenterol 2011;106:278-85.
30. Teoh AY, Cheung FK, Hu B, et al. Randomized trial of endoscopic sphincterotomy with balloon dilation versus endoscopic sphincterotomy alone for removal of bile duct stones. Gastroenterology 2013;144:341-5.e1.
31. Feng Y, Zhu H, Chen X, et al. Comparison of endoscopic papillary large balloon dilation and endoscopic sphincterotomy for retrieval of choledocholithiasis: a meta-analysis of randomized controlled trials. J Gastroenterol 2012;47:655-63.
32. Jin PP, Cheng JF, Liu D, et al. Endoscopic papillary large balloon dilation vs endoscopic sphincterotomy for retrieval of common bile duct stones: a meta-analysis. World J Gastroenterol 2014;20:5548-56.
33. Madhoun MF, Wani S, Hong S, et al. Endoscopic papillary large balloon dilation reduces the need for mechanical lithotripsy in patients with large bile duct stones: a systematic review and meta-analysis. Diagn Ther Endosc 2014;2014:309618.
34. Li G, Pang Q, Zhang X, et al. Dilation-assisted stone extraction: an alternative method for removal of common bile duct stones. Dig Dis Sci 2014;59:857-64.
35. Jun Bo Q, Li Hua X, Tian Min C, et al. Small endoscopic sphincterotomy plus large-balloon dilation for removal of large common bile duct stones during ERCP. Pak J Med Sci 2013;29:907-12.
36. Liu Y, Su P, Lin Y, et al. Endoscopic sphincterotomy plus balloon dilation versus endoscopic sphincterotomy for choledocholithiasis: a meta-analysis. J Gastroenterol Hepatol 2013;28:937-45.
37. Maydeo A, Bhandari S. Balloon sphincteroplasty for removing difficult bile duct stones. Endoscopy 2007;39:958-61.
38. Hwang JC, Kim JH, Lim SG, et al. Endoscopic large-balloon dilation alone versus endoscopic sphincterotomy plus large-balloon dilation for the treatment of large bile duct stones. BMC Gastroenterol 2013;13:15.
39. Misra SP, Dwivedi M. Large-diameter balloon dilation after endoscopic sphincterotomy for removal of difficult bile duct stones. Endoscopy 2008;40:209-13.
40. Attasaranya S, Cheon YK, Vittal H, et al. Large-diameter biliary orifice balloon dilation to aid in endoscopic bile duct stone removal: a multicenter series. Gastrointest Endosc 2008;67:1046-52.
41. Poincloux L, Rouquette O, Privat J, et al. Large-balloon dilation of the sphincter of Oddi after sphincterotomy or infundibulotomy to extract large calculi or multiple common bile duct stones without using mechanical lithotripsy. Scand J Gastroenterol 2012;48:246-51.
42. Paspatis GA, Konstantinidis K, Tribonias G, et al. Sixty- versus thirty-second papillary balloon dilation after sphincterotomy for the treatment of large bile duct stones: a randomized controlled trial. Dig Liver Dis 2013;45:301-4.
43. Ghazanfar S, Qureshi S, Leghari A, et al. Endoscopic balloon sphincteroplasty as an adjunct to endoscopic sphincterotomy in removing large and difficult bile duct stones. J Pak Med Assoc 2010;60:1039-42.
44. Lee DK, Han JW. Endoscopic papillary large balloon dilation: guidelines for pursuing zero mortality. Clin Endosc 2012;45:299-304.
45. Huibregtse K. Biliary sphincter balloon dilation; who, when and how? Can J Gastroenterol 1999;13:499-500.
46. Park DH, Kim MH, Lee SK, et al. Endoscopic sphincterotomy vs. endoscopic papillary balloon dilation for choledocholithiasis in patients with liver cirrhosis and coagulopathy. Gastrointest Endosc 2004;60:180-5.
47. Fujita N, Maguchi H, Komatsu Y, et al. Endoscopic sphincterotomy and endoscopic papillary balloon dilatation for bile duct stones: a prospective randomized controlled multicenter trial. Gastrointest Endosc 2003;57:151-5.
48. Disario JA, Freeman ML, Bjorkman DJ, et al. Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. Gastroenterology 2004;127:1291-9.
49. Watanabe H, Yoneda M, Tominaga K, et al. Comparison between endoscopic papillary balloon dilatation and endoscopic sphincterotomy for the treatment of common bile duct stones. J Gastroenterol 2007;42:56-62.
50. Liao WC, Lee CT, Chang CY, et al. Randomized trial of 1-minute versus 5-minute endoscopic balloon dilation for extraction of bile duct stones. Gastrointest Endosc 2010;72:1154-62.
51. Chan HH, Lai KH, Lin CK, et al. Endoscopic papillary large balloon dilation alone without sphincterotomy for the treatment of large common bile duct stones. BMC Gastroenterol 2011;11:69.
52. Shemesh E, Klein E, Czerniak A, et al. Endoscopic sphincterotomy in patients with gallbladder in situ: the influence of periampullary duodenal diverticula. Surgery 1990;107:163-6.
53. Zoepf T, Zoepf DS, Arnold JC, et al. The relationship between juxtapapillary duodenal diverticula and disorders of the biliopancreatic system: analysis of 350 patients. Gastrointest Endosc 2001;54:56-61.
54. Kim KH, Kim TN. Endoscopic papillary large balloon dilation in patients with periampullary diverticula. World J Gastroenterol 2013;19:7168-76.
55. Kim HW, Kang DH, Choi CW, et al. Limited endoscopic sphincterotomy plus large balloon dilation for choledocholithiasis with periampullary diverticula. World J Gastroenterol 2010;16:4335-40.
56. Lee JW, Kim JH, Kim YS, et al. The effect of periampullary diverticulum on the outcome of bile duct stone treatment with endoscopic papillary large balloon dilation. Korean J Gastroenterol 2011;58:201-7.
57. Itoi T, Ishii K, Itokawa F, et al. Large balloon papillary dilation for removal of bile duct stones in patients who have undergone a Billroth II gastrectomy. Dig Endosc 2010;22(Suppl 1):S98-102.
58. Kim GH, Kang DH, Song GA, et al. Endoscopic removal of bile-duct stones by using a rotatable papillotome and a large-balloon dilator in patients with a Billroth II gastrectomy (with video). Gastrointest Endosc 2008;67:1134-8.

59. Kim TN, Lee SH. Endoscopic papillary large balloon dilation combined with guidewire-assisted precut papillotomy for the treatment of choledocholithiasis in patients with Billroth II gastrectomy. Gut Liver 2011;5:200-3.
60. Choi CW, Choi JS, Kang DH, et al. Endoscopic papillary large balloon dilation in Billroth II gastrectomy patients with bile duct stones. J Gastroenterol Hepatol 2011;27:256-60.
61. Kim KH, Kim TN. Endoscopic papillary large balloon dilation for the retrieval of bile duct stones after prior Billroth II gastrectomy. Saudi J Gastroenterol 2014;20:128-33.
62. Itoi T, Ishii K, Sofuni A, et al. Large balloon dilatation following endoscopic sphincterotomy using a balloon enteroscope for the bile duct stone extractions in patients with Roux-en-Y anastomosis. Dig Liver Dis 2011;43:237-41.
63. van Buuren HR, Boender J, Nix GA, et al. Needle-knife sphincterotomy guided by a biliary endoprosthesis in Billroth II gastrectomy patients. Endoscopy 1995;27:229-32.
64. Bergman JJ, van Berkel AM, Bruno MJ, et al. A randomized trial of endoscopic balloon dilation and endoscopic sphincterotomy for removal of bile duct stones in patients with a prior Billroth II gastrectomy. Gastrointest Endosc 2001;53:19-26.
65. Siegel JH, Cohen SA, Kasmin FE, et al. Stent-guided sphincterotomy. Gastrointest Endosc 1994;40:567-72.
66. Jang HW, Lee KJ, Jung MJ, et al. Endoscopic papillary large balloon dilatation alone is safe and effective for the treatment of difficult choledocholithiasis in cases of Billroth II gastrectomy: a single center experience. Dig Dis Sci 2013;58:1737-43.
67. Yoon HG, Moon JH, Choi HJ, et al. Endoscopic papillary large balloon dilation for the management of recurrent difficult bile duct stones after previous endoscopic sphincterotomy. Dig Endosc 2014;26:259-63.
68. Kim KO, Kim TN, Lee SH. Endoscopic papillary large balloon dilation for the treatment of recurrent bile duct stones in patients with prior sphincterotomy. J Gastroenterol 2010;45:1283-8.
69. Harada R, Maguchi H, Takahashi K, et al. Large balloon dilation for the treatment of recurrent bile duct stones prevents short-term recurrence in patients with previous endoscopic sphincterotomy. J Hepatobiliary Pancreat Sci 2013;20:498-503.
70. Kurita A, Maguchi H, Takahashi K, et al. Large balloon dilation for the treatment of recurrent bile duct stones in patients with previous endoscopic sphincterotomy: preliminary results. Scand J Gastroenterol 2010;45:1242-7.
71. Baron TH, Harewood GC. Endoscopic balloon dilation of the biliary sphincter compared to endoscopic biliary sphincterotomy for removal of common bile duct stones during ERCP: a metaanalysis of randomized, controlled trials. Am J Gastroenterol 2004;99:1455-60.
72. Youn YH, Lim HC, Jahng JH, et al. The increase in balloon size to over 15 mm does not affect the development of pancreatitis after endoscopic papillary large balloon dilatation for bile duct stone removal. Dig Dis Sci 2011;56:1572-7.
73. Attam R, Freeman ML. Endoscopic papillary large balloon dilation for large common bile duct stones. J Hepatobiliary Pancreat Surg 2009;16:618-23.
74. Oh MJ, Kim TN. Prospective comparative study of endoscopic papillary large balloon dilation and endoscopic sphincterotomy for removal of large bile duct stones in patients above 45 years of age. Scand J Gastroenterol 2012;47:1071-7.

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