JGES guidelines for endoscopic papillary large balloon dilation

Takao Itoi1, Shomei Ryozawa1, Akio Katanuma1, Yoshinobu Okabe1, Hironori Kato1, Jun Horaguchi1, Takayoshi Tsuchiya1, Takuji Gotoda1, Naotaka Fujita1, Kenjiro Yasuda1, Yoshinori Igarashi1, Kazuma Fujimoto1

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Corresponding author: Takao Itoi, MD, PhD, FACG, FASGE

Department of Gastroenterology and Hepatology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan

Tel.: +81-(0)3-3342-6111, Fax: +81-(0)3-5381-6654, E-mail: itoi@tokyo-med.ac.jp

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ABSTRACT

The Japan Gastroenterological Endoscopy Society has developed the ‘EPLBD Clinical Practice Guidelines’ as fundamental guidelines based on new scientific techniques. EPLBD is a treatment method that has recently become widely used for choledocolithiasis. The evidence level in this field is usually low, and in many instances, the recommendation grading has to be determined on the basis of expert consensus. At this point, the guidelines are divided into the following 6 sections according to the ‘EST Clinical Practice Guidelines’: 1) Indications, 2) procedures, 3) special cases, 4) procedure-related adverse events, 5) treatment outcomes, and 6) postoperative follow up observation.

Key words: EPLBD, endoscopic papillary large balloon dilation, guidelines, endoscopic retrograde cholangiopancreatography, ERCP

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INTRODUCTION

Basic guidelines are needed to safely and accurately perform endoscopic papillary large balloon dilation (EPLBD), which has become widely used recently. However, there have been no guidelines for performing EPLBD to date. Therefore, the Clinical Practice Guidelines Committee of the Japan Gastroenterological Endoscopy Society (JGES) decided to develop the EPLBD clinical practice guidelines based on scientific techniques to serve as fundamental guidelines. The working committee established 6 sections as follows: 1) indications, 2) procedures, 3) special cases, 4) procedure-related adverse events, 5) treatment outcomes, and 6) postoperative follow up observation. Clinical questions (CQs) were developed for each item, which were evaluated and accordingly modified by the evaluation committee to finally come up with a total of 20 questions. Furthermore, reports in the literature from 1985 to 2013 regarding each CQ were systematically searched using the PubMed and JAMAS websites. A hand search was also performed for questions with insufficient supporting literature. The reports identified in our literature search were evaluated, and if deemed pertinent, a report was used to create statements and references for each CQ. Thereafter, the working committee established the evidence level of each report in each assigned field, and the grades of recommendations and evidence level for statements in accordance with the ‘Minds Handbook for Clinical Practice Guideline Development 2014’ \(^1\) (Table 1). For the created statements, 10 members of the Guidelines Creation Committee voted on them using the Delphi method, as reported previously.\(^2\)

1. INDICATIONS

Statement 1-1: EPLBD is indicated for large and multiple stones with bile duct dilatation that are difficult to treat by EST and EPBD alone.

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Endoscopic sphincterotomy (EST) was reported in 1974 as a transpapillary treatment method for bile duct stones [4-6]. At present, it has become one of the most widely used standard procedures. Similarly, endoscopic papillary balloon dilation (EPBD) is a transpapillary treatment method [7-9] and is performed as an option when the preservation of papillary function is important and when patients tend to bleed. The procedure involves dilation of the biliary orifice using a small balloon ($\leq 10$ mm). The procedure is generally performed without EST. On the other hand, endoscopic papillary large balloon dilation (EPLBD) is a procedure wherein the biliary orifice is dilated using a large balloon ($\geq 12$ mm). EPLBD was first reported in 2003 by Ersoz et al. [11]. As a large opening can be obtained following EPLBD, stone removal can be relatively easily performed for patients with bile duct dilatation, and for cases that are difficult to treat by EST and EPBD (e.g., large stones, multiple stones, and barrel-shaped stones) [12-15].

Ersoz et al. [11] performed EPLBD for 58 patients in whom stone removal was difficult using the standard basket catheter and balloon catheter following a large incision for EST. Of 18 patients with tapered distal bile ducts, the stone was successfully removed without using a mechanical lithotripter (ML) in 16 patients (89%). Furthermore, in 38 out of 40 patients with large stones $\geq 15$ mm, stacked stones, and barrel-shaped stones (95%), the stones were successfully removed without using ML. Maydeo et al. [12] reported a 95% success rate in stone removal without using ML for giant stones $\geq 12$ mm. In Japan, Minami et al. [13] reported a complete stone removal rate of 99% in subjects with large stones $\geq 12$ mm using a method that involved the use of a balloon with a maximum diameter of 20 mm, which was repeatedly inflated and deflated by hand. Itoi et al. [15] reported that the use of EPLBD reduced the procedural duration, leading to a shorter exposure time.

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With regard to stone diameter, EPLBD is indicated for stones $\geq 10\, \text{mm}^{14}$, $\geq 12\, \text{mm}^{12,13,16}$, and $\geq 15\, \text{mm}^{15,17}$. Many reports have described the application of EPLBD for 3 or more stones$^{15,18}$. In cases with a tapered or bent distal bile duct, stone removal can be difficult and EPLBD is considered to be well suited$^{11,15,18}$. EPLBD is also well suited for recurrent stones following EST$^{19,20}$. In patients with recurrent stones following EST, several required additional incision, posing the risk of bleeding and perforation. Harada et al.$^{20}$ compared the EPLBD group and the group without recurrent stones following EST. They reported that the rates of ML usage and recurrent stones within 2 years were significantly lower in the EPLBD group.

Statement 1-2: The contraindications of EPLBD include patients with distal bile duct stricture, patients without bile duct dilatation and patients with acute pancreatitis (strength of recommendation: 1); patients with coagulopathies and patients taking oral antithrombotic drugs (strength of recommendation: 2).

Strength of recommendation: 1 and 2 (patient selection described above), evidence level: C

Delphi scores: median = 8, lowest = 7, highest = 9

EPLBD is not recommended for patients with obvious stricture of the distal bile duct and with no bile duct dilatation$^{18,21}$. Such patients are thought to be at an increased risk of perforation resulting from dilation treatment by EPLBD.

Furthermore, EPLBD is contraindicated in patients in whom EST is contraindicated in the ‘EST Clinical Practice Guidelines’, that is, patients with coagulopathies, patients taking oral antithrombotic therapy, and patients with acute pancreatitis (excluding biliary pancreatitis).

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With regard to patients receiving oral antithrombotic therapy and EST, in the ‘Guidelines for Gastroenterological Endoscopy in Patients Undergoing Antithrombotic Treatment’ (22), EST is considered to carry a high risk of bleeding as well as EPLBD, and as a general rule, treatment based on the ‘EST Clinical Practice Guidelines’ (22) is recommended (refer to CQ 2 – 5).

Regarding biliary pancreatitis in acute pancreatitis, the ‘Clinical Practice Guidelines for Acute Pancreatitis, 2015 (4th ed.) strongly recommend performing ERCP/EST early in patients with acute biliary pancreatitis and concurrent cholangitis, and in whom jaundice appears or exacerbates. However, there has been no clear evidence for EPLBD to date, and more cases need to be evaluated in the future. For stones impacted at the papilla, when the stones cannot be removed from the papilla, EPLBD is not indicated because of the risk of bile duct perforation by balloon dilation, and precutting or EST should be attempted.

Statement 1-3: Regarding the prerequisites for practitioners performing EPLBD, it is recommended that practitioners are skilled in ERCP and undergo training to learn the basic technique for EST.

Strength of recommendation: 1, evidence level: D

Delphi scores: median = 8, lowest = 8, highest = 9

Presently, ERCP is increasingly being used as a therapeutic procedure rather than for diagnosis. Therefore, as with EST, EPLBD is a compulsory subject in ERCP training, and is a procedure that should be mastered before beginners can perform ERCP alone. EPLBD is not an alternative to EST but a procedure to supplement EST. Therefore, EST skills should be mastered before acquiring EPLBD skills.

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For reference, the American Society for Gastrointestinal Endoscopy (ASGE) requires beginners to fully master the following basic ERCP and cannulation skills before performing EST: A) insertion of a duodenal scope, B) obtaining frontal view of the papilla, C) selective cannulation, and D) interpreting cholangiopancreatic findings\textsuperscript{24}. EST training should begin after mastering these skills. Furthermore, the principles of high-frequency generators and the difference between each mode, as well as between various sphincteromes and guidewires should be thoroughly understood. Practitioners should also understand EST indications and basic procedures, as well as procedural accidents and associated risk factors. ASGE has stated that until a beginner is able to perform ERCP alone, training should include approximately 200 ERCPs including 40 EST procedures and 10 stent placements\textsuperscript{25}. In addition to hands-on training with an instructor, various useful models for EST training have been recently developed\textsuperscript{26 – 28}.

2. PROCEDURES

Statement 2-1: EPLBD following EST improves the stone removal rate in the first session, and it might reduce the frequency of mechanical lithotripsy usage.

**Strength of recommendation: 2, evidence level: C**

**Delphi scores: median = 9, lowest = 8, highest = 9**

EPLBD was reported in 2003 as a procedure for obtaining a large bile duct aperture using a large balloon following EST\textsuperscript{11}. In 2009, a simplified method for the procedure was reported whereby EST is not performed, and the papilla is dilated using a large balloon only\textsuperscript{29}. The conventional EPBD using a 6-8 mm balloon has a higher rate of concurrent pancreatitis than EST\textsuperscript{8, 9, 30}. There is a concern that the procedure involving dilation without EST using a larger balloon would also lead to pancreatitis. However, in the preliminary study conducted by Jeong et al.\textsuperscript{29}, they showed that of 38

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patients who underwent EPLBD without EST, only 1 patient (2.6%) had moderate pancreatitis. Thus, it was reported that EPLBD without EST was a safe and useful procedure. According the results of a randomized controlled trial (RCT) of 131 patients (62 patients without EST; 69 patients with EST) by Hwang et al.\textsuperscript{31)}, there was no significant difference in the rate of complications according to the presence or absence of EST, including pancreatitis (without EST 6.5% vs. with EST 4.3%, \( p = 0.593 \)), basket impaction (without EST 0% vs. with EST 1.4%, \( p = 0.341 \)), and perforation (without EST 0% vs. with EST 1.4%, \( p = 0.341 \)). In a retrospective analysis conducted in Japan, there was no difference in the incidence of procedural accidents according to the presence or absence of EST\textsuperscript{32), 33)}. Park et al.\textsuperscript{21)} examined the risk factors for procedural adverse events in 946 patients who underwent EPLBD at 12 institutions in Japan and Korea. They concluded that the absence of EST was not a risk factor for procedural adverse events. Furthermore, Kim et al.\textsuperscript{34)} conducted a meta-analysis of 30 articles regarding EPLBD with EST, and 3 articles regarding EPLBD without EST. They found no significant difference in the incidence of procedural accidents (8.6%, 7.5%, 7.0%, \( p = 0.568 \)) and the onset of pancreatitis (2.1%, 3.1%, 3.9%, \( p = 0.349 \)) in 756 patients who underwent EPLBD with large EST, in 946 patients who underwent EPLBD with limited EST, and in 416 patients who underwent EPLBD without EST. Similar reports have been published\textsuperscript{35), 36)}. Thus, performing EST before EPLBD is considered to have a slight effect from the perspective of procedural adverse events. However, attention should be drawn to the fact that these reports included patients with bile duct dilatation and large stones.

To compare the outcomes of stone removal by EPLBD with EST and EPLBD without EST, retrospective outcomes have been reported in Japan, in which no difference in the stone removal and ML usage rates was observed\textsuperscript{32), 33)}. Furthermore, in 2 RCTs of EPLBD with EST and EPLBD without EST, reports of both trials indicated no difference in the rate of stone removal or ML usage. It was concluded that EST was not necessary before EPLBD\textsuperscript{31), 35)}. However, according to the meta-analysis conducted by Kim et al.\textsuperscript{34)}, the stone removal rate in the first session was significantly higher.
higher with EST (with EST 84.0% vs. without EST 76.2%, \( p < 0.001 \)), and the rate of ML usage was significantly lower with EST (with EST 14.1% vs. without EST 21.6%, \( p < 0.001 \)). Thus, performing EPLBD with EST might help improve the initial stone removal rate and reduce the rate of ML usage. However, in this meta-analysis, there were few studies that conducted prospective comparisons, and there were 30 reports of EPLBD with EST (2511 patients) and 3 reports of EPLBD without EST (414 patients), which could have caused a bias. Therefore, additional large-scale comparative studies are needed.

Statement 2-2: The recommended EST incision direction is towards the 11 o’clock to 12 o’clock position. The cutting range is up to a medium incision.

**Strength of recommendation: 1, evidence level: B**

**Delphi scores: median = 9, lowest = 8, highest = 9**

There is presently no study comparing the risk of hemorrhage and perforation according to the cutting direction. Cutting in the 11 o’clock to 12 o’clock direction is considered to be safe and is therefore recommended by many experts\(^{37} - 40\). With regard to hemorrhage, Mirjalili et al.\(^{41}\) identified 98 arteries near the major papilla in 19 autopsy cases, and reported the blood vessel distribution in the endoscopy screen. According to their report, the blood vessel distribution in the 10 to 11 o’clock region was low at 10%-11%, thus they noted that cutting in this region has a low risk of hemorrhage. However, considering the bile duct position, it is thought that cutting towards the 11 to 12 o’clock position is valid. Regarding the cutting range, in a multicenter collaborative
analysis of 946 patients by Park et al.\textsuperscript{21}, liver cirrhosis (OR 8.03, p = 0.003), EST length (full-EST: OR 6.22, p < 0.001), and stone diameter (≥ 16 mm: OR 4.00, p < 0.001) are considered the risk factors of hemorrhage. In their previous meta-analysis, Kim et al.\textsuperscript{34} reported that large EST carried a higher rate of hemorrhage than limited EST (OR 3.33, p < 0.001) and without EST (OR 2.17, p = 0.049). Thus, many are of the opinion that large incisions should be avoided.\textsuperscript{42} There is currently no evidence whether a small incision or a medium incision should be selected. In a comparison of 55 patients who underwent small EST + EPLBD (n = 27) and conventional EST (n = 28) for stones ≥ 15 mm, there was no significant difference in the complete stone removal rate (85% vs. 86\textsuperscript{p} = 0.473) and ML usage rate (33% vs. 32\textsuperscript{p}, p = 0.527). Thus, it was reported that small EST had a minimal effect on the therapeutic outcomes compared with EST.\textsuperscript{43} However, the report involved a small sample. For patients with parapapillary diverticulum, small incision with balloon dilatation can be performed safely.\textsuperscript{44}

**Statement 2-3:** The distal bile duct diameter and the short diameter of the stone are taken into consideration when selecting the balloon diameter.

*Strength of recommendation: 2, evidence level: C*

**Delphi scores:** median = 9, lowest = 7, highest = 9

In Japan, there are 4 types of large balloon catheters available for EPLBD. These include the CRE dilatation balloon catheter (Boston Scientific), Kaneka EPBD catheter DI-WI Giga (Kaneka Medix), Kaneka biliary dilation balloon REN (Kaneka Medix), and the disposable balloon dilator V-system

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(with knife) ‘Stone Master V’ (Olympus), which has the same form as the sphincterotome. There are currently no reports comparing the procedure according to the instrument used.

With regard to the balloon diameter, Hisatomi et al.\textsuperscript{45}) conducted a study using a live porcine model and reported that dilatation using a balloon $\geq 12$ mm and $\geq 15$ mm caused bile duct wall injury and bile duct perforation, respectively. However, the anatomical structure of the bile duct wall in pigs differs from that in humans in that it is thinner and that the area of the lower bile duct is not surrounded by the pancreas. Therefore, the results cannot be necessarily applied to humans. Although there are currently no reports comparing balloon diameter, the report by Park et al.\textsuperscript{21}) based on their multicenter collaborative study regarding procedural accidents in EPLBD does not include balloon diameter as a risk factor for perforation. In their retrospective study of 101 patients who underwent EPLBD with dilatation using a balloon $\geq 15$ mm in diameter, Youn et al.\textsuperscript{46}) reported that the only procedural adverse events were pancreatitis (5%) and perforation (1%). Thus, there is presently no clear evidence regarding the incidence of procedural events and balloon diameter. In reference to an expert opinion based on animal experiments, it has been suggested that the use of a balloon $\geq 15$ mm in diameter should be avoided as much as possible as it increases the risk of perforation\textsuperscript{47}). However, many experts\textsuperscript{48}–\textsuperscript{50}) advocate selecting a balloon diameter that does not exceed the range of the bile duct diameter and the short diameter of the stone. Regarding the measurement of the bile duct diameter, the distal bile duct is narrow in some patients\textsuperscript{48}) and therefore the diameter of the distal bile duct should be measured.

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Statement 2-4-1: The maximum diameter of the balloon should not exceed the diameter of the distal bile duct.

**Strength of recommendation: 2, evidence level: D**

**Delphi scores: median = 9, lowest = 7, highest = 9**

In their multicenter collaborative study regarding procedural accidents in EPLBD, Park et al. observed perforation in 9 out of 946 patients who underwent EPLBD, 3 of whom were fatal with excessive balloon dilation as the underlying cause. Furthermore, distal bile duct stricture was extracted by multivariate analysis as a risk factor for perforation (OR 17.083, 95% CI 3.963-74.132; p < 0.001). Cheng et al. retrospectively examined EPLBD performed under double-balloon enteroscopy to treat bile duct stones in patients with Billroth-II anatomy. They observed perforation in 2 out of 48 patients, both of whom underwent dilation using a balloon that had the same size as the distal bile duct (case 1: balloon caliber of 12 mm/ distal bile duct caliber of 12 mm; case 2: balloon caliber of 18 mm/ distal bile duct caliber of 18 mm). The international guidelines for EPLBD recommend that dilation should not exceed the bile duct diameter. Therefore, it is considered important for balloon dilatation not to exceed the distal bile duct diameter.

When performing dilation, a balloon waist (narrow part of the balloon) develops at the site corresponding to the sphincter of Oddi, and in the event of EPLBD, dilation is generally performed until disappearance of the notch is confirmed. Disappearance of the notch is often confirmed in EPLBD. However, when the notch does not disappear even with the application of a maximum dilatation pressure of 75% or greater, it is possible that there is distal bile duct stricture and it is safer to refrain from applying further pressure.

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Statement 2-4-2: The balloon should be inflated slowly; however, there is no clear evidence as to the optimal length of time for balloon dilation.

Strength of recommendation: 2, evidence level: D

Delphi scores: median = 9, lowest = 9, highest = 9

Although there are currently no studies examining the speed of balloon dilation, it is recommended that balloon inflation should be performed slowly to prevent perforation caused by excessive dilatation\textsuperscript{11, 48, 52}. With regard to the required time for maintaining balloon dilation, there are no clear lines of evidence and reports vary from those indicating dilation in a short time of 5-15 sec, or until immediately after the waist disappears\textsuperscript{53}, to reports indicating that dilation should be performed over a long period of 2-6 minutes\textsuperscript{36}. Comparative trials of the length of time for dilation include only the RCT of Paspati et al.\textsuperscript{54} who compared dilation time between over 30 sec and over 60 sec, and in 64 patients with dilation time over 30 sec and in 60 patients with dilation time over 60 sec. They observed no significant difference in the rate of stone removal (86% vs. 85%, \( p = 0.5 \)) and complications (hemorrhage: 3.1\% vs 6.7\%, \( p = 0.2 \); perforation: 1.6\% vs. 1.7\%, \( p = 0.9 \); and pancreatitis: 3.1\% vs. 3.3\%, \( p = 0.9 \)). Furthermore, Feng et al.\textsuperscript{55} conducted a meta-analysis comparing EPLBD and EST. Upon comparing the stone removal rate of EST against that of EPLBD with dilation time \( \geq 60 \) sec, and EPLBD with dilation time \( < 60 \) sec, they found no significant difference in both conditions (EPLBD with dilation time \( < 60 \) sec vs. EST, OR = 2.77, 90\% CI 0.80 – 9.61, \( p = 0.11 \); EPLBD with dilation time \( \geq 60 \) sec vs. EST, OR = 0.56, 90\% CI 0.18 – 1.78, \( p = 0.33 \)). The international guideline recommends a dilation time over 30-60 sec after notch

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disappearance\textsuperscript{18}, and although it is suggested that dilation does not necessarily require a long time, we believe that additional lines of evidence need to be accumulated.

Statement 2-5: EPLBD in patients using antithrombotic agents should be managed in accordance with the JGES guidelines.

Strength of recommendation: 2, evidence level: D

Delphi scores: median = 9, lowest = 9, highest = 9

The meta-analysis of Kim et al.\textsuperscript{34} showed that the risk of bleeding was comparable between EPLBD with EST and EPLBD without EST (limited EST + EPLBD 1.3% vs. EPLBD without EST 1.9%, $p = 0.35$). Cases with severe hemorrhage as complication have also been reported\textsuperscript{56, 57}. Therefore, it is thought that EPLBD is an endoscopic procedure that is associated with the risk of hemorrhage, irrespective of EST.

With regard to EPLBD with EST, the guidelines for gastroenterological endoscopy\textsuperscript{22} indicate that EST is an endoscopic procedure with a high risk of hemorrhage, thus treatment should be managed in accordance with the guidelines. Of particular note in reference to the multicenter collaborative study of procedural accidents in EPLBD conducted by Park et al.\textsuperscript{21}, they reported that a large incision was a significant risk factor for hemorrhage (OR 6.2, 95% CI 2.374 – 16.307; $p < 0.001$), and that it should be avoided.

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For EPLBD without EST, there are currently no reports of EPLBD in patients with coagulopathy and in patients taking antithrombotic agents. In a retrospective cohort study comparing EST and EPLBD as papillary treatment in patients with coagulopathy and liver cirrhosis conducted by Park et al.\(^\text{58}\), they observed no bleeding in the 21 patients who underwent EPLBD, but observed bleeding in 6 out of the 20 patients who underwent EST (30%). Thus, EPLBD is more preferable than EST in patients with coagulopathy. The International consensus guidelines for EPLBD recommends EPLBD without EST when it is difficult to suspend anticoagulant therapy. However, there is no clear evidence for the management of antithrombotic agents when performing EPLBD without EST, and additional studies are needed with regard to safety.

**Statement 2-6:** When performing EPLBD with EST for patients with pacemakers and implanted defibrillators, high-frequency surgical devices can affect such patients and therefore a cardiologist should be consulted. During the procedure, electrocardiogram, blood pressure, and oxygen saturation should be monitored as in the case of normal patients.

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Strength of recommendation: 2, evidence level: D

Delphi scores: median = 9, lowest = 9, highest = 9

Balloon dilation does not have an electrical mechanism and is therefore thought to have no effect on cardiac pacemakers and implanted defibrillators. However, when performing balloon dilation after EST, there is a concern that high-frequency generators will cause interference, and it cannot be stated that their safety has been fully established. High-frequency current is an external source of interference for pacemakers. It is considered dangerous as it can damage the inner part of the pacemaker and impair the demand mechanism. To date, there have been reports of cases in which the intraoperative use of high-frequency generators caused pacemaker failure and death\(^{59}\). However, there are also reports of cases of colon polypectomy completed safely using high-frequency generators\(^{60},^{61}\). Other reports have indicated that EST can be performed safely in cooperation with a cardiologist\(^{62}\).

According to an expert opinion and the ASGE guidelines, in the event of a complete atrioventricular block, it is recommended to change the pacemaker setting to an asynchronous setting (VOO or DOO mode)\(^{63},^{64}\). However, the circumstances differ according to the type of pacemaker, and a cardiologist should be adequately consulted regarding the patient’s condition, pacemaker type, and the management method. There are currently no reports on the use of high-frequency devices for ICD patients, thus procedures should be determined after consulting a cardiologist.

3. SPECIAL CASES

Statement 3-1: In patients with periampullary diverticulum, EPLBD can be performed (strength of recommendation: 2). When performing EPLBD with EST, it can be difficult to determine the incisional length and direction; therefore, a more careful procedure is required (strength of recommendation: 1)
Strength of recommendation: 2/1, evidence level: C

Delphi scores: median = 9, lowest = 8, highest = 9

The prevalence of periampullary diverticulum increases with age, and it has been reported to be found in as many as 65% of elderly people\(^{65,66}\). Periampullary diverticulum can make a controlled EST more difficult and possibly increase the risk of adverse events\(^{67}\). Regarding retrospective studies that have been conducted to date which compared the usefulness of EPLBD according to the presence or absence of periampullary diverticulum, there was no significant difference observed between the two conditions in terms of the stone removal rate and procedural adverse events including perforation and bleeding\(^{44,68,69}\). In a multicenter study involving 946 EPLBD patients, it was reported that patients with periampullary diverticulum did not have an increased incidence of procedural adverse events including pancreatitis, bleeding, and perforation\(^{21}\). However, in EPLBD with periampullary diverticulum, there is the possibility of perforation owing to the anatomical fragility of the sphincter of Oddi, thus the procedure should be performed carefully with slow dilation. The frequency of post-ERCP pancreatitis was reported to be significantly higher when the papilla is located within or on the margin of the diverticulum than when the papilla is located near the diverticulum (14.3% vs. 3.0%, \(p = 0.047\))\(^{44}\). When performing EPLBD with EST, a wire-guided sphincterotome should be used to perform the incision safely. As the sphincterotome blade comes into contact with the duodenal mucosa on the oral side, which can cause unnecessary cutting, it is advantageous to use a sphincterotome with an insulating coating at nearside of the blade\(^{70}\). Furthermore, in patients with periampullary diverticulum, if the oral protrusion is unclear and the papilla is tilted, it can be difficult to determine the incisional direction. To verify the oral protrusion and incision direction, inflating the balloon catheter for stone removal inside the papilla\(^{71}\), and inserting and withdrawing the sphincterotome with the blade extended are useful.
Statement 3-2: EPLBD can be performed in patients with surgically altered anatomy. However, the difficulty of the procedure depends on each reconstruction method.

Strength of recommendation: 2, evidence level: C

Delphi scores: median = 9, lowest = 9, highest = 9

EPLBD can be performed in patients with surgically altered anatomy, and is an effective and safe procedure for removing bile duct stones. For patients with surgically altered anatomy, EST is usually difficult and may require special techniques or devices. On the other hand, EPBD and EPLBD use the same device for patients with normal anatomy and they can be relatively easily performed. Therefore, when EST is difficult, stone removal can be achieved by EPLBD alone. Jang et al.\textsuperscript{72} reported complete CBD stone removal after EPLBD without EST in all 40 Billroth II gastrectomy patients with large or difficult CBD stones without any serious adverse events. The indications of EPLBD in patients with surgically altered anatomy are the same as those in the patients with normal anatomy. With regard to the procedure, in patients with Billroth I reconstruction and jejunal interposition after proximal gastrectomy/jejunal interposition after total gastrectomy, the procedure is the same as the usual EPLBD. However, in patients with Billroth II reconstruction and Roux-en-Y reconstruction following (sub) total gastrectomy, a colonoscope and balloon enteroscope are required to reach the papilla. Therefore, when using an enteroscope, the device used can be limited owing to the effective length\textsuperscript{73, 74}. For papillary dilatation after the endoscope reaches the papilla, unlike with conventional ERCP, the papilla is identified from an inverted anatomic structure. Therefore, it can be somewhat difficult to cut in the bile duct direction using a normal sphincterotome. In such instances, a needle knife or a rotatable sphincterotome is useful. Although based on case reports and case series, in patients with surgically altered anatomy such as Billroth II surgery and Roux-en-Y anastomosis, relatively high rates of complete stone clearance have been reported (96.7%-100%)\textsuperscript{73–78}. This rates were better than the success rates for stone clearance.
removal (81.3%-100%) using EST for similar patients with surgically altered anatomy. In these EPLBD studies in patients with surgically altered anatomy, only mild pancreatitis and mild-to-moderate bleeding were noted without any perforation or serious adverse events. On the other hand, in EPLBD without EST, case reports of severe acute pancreatitis can be found. The onset of severe acute pancreatitis is caused by EPLBD of the oral protrusion fistula, thus caution should be exercised. Although EPLBD is useful in patients with surgically altered anatomy, there are still no RCTs of EPLBD and EST alone; thus, we cannot conclusively say that the safety has been established.

4. PROCEDURE-RELATED ADVERSE EVENTS

Statement 4-1: The incidence of early adverse events caused by EPLBD is in the range of 0%-22.5%, including bleeding, perforation, pancreatitis, and cholangitis.

Strength of recommendation: 2, evidence level: C

Delphi scores: median = 9, lowest = 9, highest = 9

The incidence of early procedural accidents associated with EPLBD is reported to range from 0% to 22.5%. The primary procedural accidents and associated incidences include acute pancreatitis at 0%-13.2%, bleeding at 0%-10%, perforation at 0%-2.5%, and cholangitis at 0%-5.0%. The incidences are listed in Table 3. In the systematic review of 32 articles by Kim et al., they reported that EPLBD with EST had a significantly lower incidence of procedural accidents than EST alone (8.3% vs. 12.7%, OR 1.60, p < 0.001). Moreover, many other meta-analyses reports indicate that EPLBD with EST has comparable or lower incidence of procedural accidents than EST.

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In their study of EPLBD with EST for patients with parapapillary diverticula, Kim et al.\textsuperscript{44} reported that there was no significant difference in the presence or absence of parapapillary diverticula. Kim et al.\textsuperscript{68} also reported that there was no difference in the incidence of procedural accidents between EPLBD with EST and EPLBD without EST according to the presence or absence of parapapillary diverticula.

In recent years, reports of EPLBD without EST have appeared. Hwang et al.\textsuperscript{31} reported that there was no significant difference in the rate of procedural accidents observed and related incidences between EPLBD with EST and EPLBD without EST (7.2\% vs. 6.5\%, \( p = 0.858 \)). Furthermore, Kogure et al.\textsuperscript{33} reported that there was no significant difference in the incidence of procedural accidents (7\% vs. 8\%) and the incidence of PEP (7\% vs. 4\%, \( p = 0.9999 \)) for both procedures; however, severe pancreatitis developed in 1 patient in the EPLBD without EST group. Guo et al.\textsuperscript{106} conducted a prospective RCT of 3 groups, which included the EPLBD with EST, EPLBD without EST, and EST alone groups, and found no significant difference in the procedural accidents observed and related incidences (5.9\% vs. 4.7\% vs. 4.7\%, \( p = 1.000 \)). Although several reports describing the safety of EPLBD without EST can be found, no consensus has been reached at this stage and further studies are anticipated. On the other hand, it has been reported that the incidence of procedural accidents in EPLBD in patients with previous EST, such as those with recurrent bile duct stones, is extremely low\textsuperscript{20, 100}, and it is possible that the incidence of procedural accidents is lower than that in the initial EPLBD. While carefully keeping the indications of EPLBD, practitioners should thoroughly understand the incidences of procedural accidents as well as the measures that need to be taken in the event that they occur. Practitioners must also obtain informed consent from the patient before surgery.

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Statement 4-2: The first-line treatment for bleeding following EPLBD is endoscopic hemostasis.

Strength of recommendation: 2, evidence level: C

Delphi scores: median = 9, lowest = 7, highest = 9

At present, the mechanism underlying bleeding following EPLBD is unclear. Feng et al.\textsuperscript{55} conducted a meta-analysis and reported that the rate of bleeding was significantly lower in EPLBD with EST than in EST alone (OR 0.15; \( p = 0.002 \)), whereas other reports indicate that the rate of bleeding is comparable\textsuperscript{98}, \textsuperscript{101}. However, there are also reports of deaths caused by bleeding following EPLBD\textsuperscript{101}, thus due care should be exercised.

Park et al.\textsuperscript{21} conducted a subanalysis and noted an increased risk of procedural accidents in large-incision EST. Kim et al.\textsuperscript{34} reported that EPLBD with large-incision EST had a significantly higher incidence of bleeding than EPLBD with limited EST (\( p < 0.001, \text{OR} = 3.33 \)) and EPLBD without EST (\( p = 0.049, \text{OR} = 2.17 \)). In their article, it was also reported that there was no difference in the incidence of bleeding between EPLBD with limited EST and EPLBD without EST. Therefore, many reports currently indicate that bleeding following EPLBD is caused by EST.

The treatment of bleeding following EPLBD is administered in accordance with the ‘EST Clinical Practice Guidelines’\textsuperscript{2}. When intraoperative bleeding occurs immediately after EPLBD at the EST incision site, spraying methods such as ice water spray or physiological saline spray containing epinephrine are used\textsuperscript{107}. In the event of postoperative bleeding, this can result in blood in the stool and anemia, as well as hemorrhagic shock several days after surgery. This condition is treated by systemic management similarly to normal gastrointestinal bleeding with emergency endoscopy as required.

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Methods of hemostasis include endoscopic hemostasis, angiographic embolization, and surgical hemostasis. The first choice is to attempt endoscopic hemostasis as in the case of EST. Although there are still no reports of hemostasis for bleeding following EPLBD, there are various options that can be selected at the discretion of the physician according to the situation. These include local epinephrine injection as in the case of bleeding following EST, the balloon pressure method, use of hemostatic forceps, and argon plasma coagulation (APC)\(^{108}\). As in the case of EST, the pressure method using a large balloon, a balloon catheter for EPBD, or a balloon catheter for stone extraction is relatively simple and effective\(^{109}, 110\).

In recent years, case reports of hemostasis achieved by the temporary placement of a covered metallic stent for bleeding following EPLBD have been reported\(^{56, 111}\). However, this procedure is not covered by health insurance in Japan. When endoscopic hemostasis is difficult, angiographic embolization and surgical hemostasis are considered depending on the situation.

**Statement 4-3:** In the event of suspected perforation associated with EPLBD, plain CT should be performed. When perforation is diagnosed, close cooperation with the surgeon to administer appropriate treatment in a timely manner is recommended.
Strength of recommendation: 2, evidence level: C

Delphi scores: median = 9, lowest = 7, highest = 9

Kim et al.\(^{34}\) conducted a systematic review and reported that EPLBD caused perforation at a rate of 0.6% (0%-2.8%), with no significant difference between the EPLBD with large EST group, EPLBD with limited EST group, and EPLBD without EST group (3% vs. 5% vs. 2%, \(p = 1.000\))\(^{34}\).

In a subanalysis examining procedural accidents in 946 patients from 12 institutions within Japan and Korea\(^{21}\), multivariate analysis identified lower bile duct stricture to be a significant risk factor for perforation (\(OR \, 17.08, \, p < 0.001\)). The article reported 4 fatal cases associated with EPLBD, among which perforation was the cause of death in 3 cases. Hisatomi et al.\(^{45}\) conducted an in vivo basic experiment using a porcine model and found that as the balloon diameter increased to more than the diameter of the bile duct, there was an increased incidence of damage to the bile duct mucous membrane and perforation. Park et al.\(^{21}\) noted that the bile duct diameter gradually increases when a bile duct stone is present for a long time. Thus, they recommend performing balloon dilation gradually. As possible means of preventing perforation, the indications for EPLBD must be carefully followed, and balloon dilation should not exceed the diameter of the lower bile duct.

At present, the diagnosis and treatment of perforation are performed in accordance with the ‘EST Clinical Practice Guidelines’\(^{2}\). The diagnosis of perforation is made by intraoperative endoscopic imaging or fluoroscopic imaging, and can be confirmed by the abnormal gas images (free air) surrounding the liver, leakage of contrast medium, and abnormal positioning of surgical instruments. However, free air can be difficult to confirm during the procedure; thus, in the event of suspected perforation based on postoperative physical findings and biochemical blood tests, CT should be actively performed. Retroperitoneal emphysema can develop into pneumothorax and subcutaneous emphysema, thus careful systemic management is needed\(^{122}\). Following perforation diagnosis (including suspected perforation), fasting with transfusion management should be adopted,
together with systemic management by antibiotic administration and gastric intubation. A surgeon should be consulted immediately.

EPLBD perforations are most commonly thought to occur near the papilla or bile duct. In the case of post-EST perforations, performing biliary drainage and gastric intubations is thought to minimize the subsequent activation of pancreatic fluid and the spread of infection to the retroperitoneum. Furthermore, intrabiliary emphysema tends to develop after EPLBD, thus it is recommended to perform the procedure under CO2 insufflation as a countermeasure for procedural accidents such as air embolism. Surgical treatment is indicated when no improvement is observed with conservative treatment and in the event of gastrointestinal perforation, taking into consideration that the prognosis becomes poor if diagnosis and treatment are delayed. Notably, there have only been few cases reported regarding the mechanism and treatment of perforation following EPLBD, and more cases should be evaluated.

Statement 4-4: Although the onset mechanism of post-EPLBD pancreatitis has not yet been established, prevention and treatment should be performed in accordance with the guidelines for the management of acute pancreatitis.

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In the systematic review by Kim et al.\textsuperscript{34}, the incidence of pancreatitis following EPLBD (balloon diameter: 12-20 mm) with EST was 2.4% (0%-13.2%), which included mild-to-moderate pancreatitis in 98.4% and severe pancreatitis in 1 patient who eventually died. Furthermore, in 6 RCTs\textsuperscript{16,43,85,92,94,99} and 5 meta-analyses\textsuperscript{55,97,98,122,123}, it was reported that there was no significant difference in the incidence of pancreatitis between EPLBD with EST and EST alone.

Also in the review by Kim et al., EPLBD without EST (retrospective studies: 413 patients) was also examined and it was reported that post-ERCP pancreatitis (PEP) occurred in 3.9% of cases (2.6%-6.4%), all of which were mild or moderate cases. Moreover, the incidence of PEP following EPLBD with EST was reported to be significantly lower than the incidences of post-EST pancreatitis and post-EPBD pancreatitis (2.4% vs. 4.3% vs. 8.6%, $p = 0.006$). There was also no significant difference in the incidence of PEP between the 3 groups, that is, EPLBD with large EST, EPLBD with limited EST, and EPLBD without EST (2.4% vs. 3.1% vs. 3.9%, $p = 0.349$).

Following analysis of the results of their multicenter study, Park et al.\textsuperscript{21} reported that the risks factors for pancreatitis onset included the use of a balloon catheter of 14 mm diameter or greater and the reduced onset of PEP (OR 0.272, 95% CI 0.095 – 0.778, $p = 0.015$).

At present, although the onset mechanism of post-EPLBD pancreatitis remains to be established, it is assumed that a large papillary aperture, reduced pressure on the papilla by the surgical instrument, and reduced PEP onset are involved\textsuperscript{18}.

There are no established preventive measures for pancreatitis following EPLBD. However, considering that ERCP is a factor involved in the onset of pancreatitis, treatment and preventive measures are performed in accordance with post-ERCP pancreatitis\textsuperscript{23}.
5. TREATMENT OUTCOME

Statement 5-1: The rate of stone removal in EPLBD for gallstones of the common bile duct is from 80.9% to 89% for the initial treatment and ultimately from 95.2% to 100% for the complete stone removal.

Strength of recommendation: N/A, evidence level: A

Delphi scores: median = 9, lowest = 9, highest = 9

In an RCT comparing EPLBD + EST and EST monotherapy for bile duct stones, it has been reported that the rate of complete stone removal by EPLBD was from 80.9% to 89% for the initial treatment, and ultimately from 95.2% to 100% (Table 4)\(^\text{16}, 43, 85, 92, 94, 99\). With regard to bile duct stone removal, some reports have indicated that the complete stone removal rate in the initial treatment was significantly higher in the EPLBD group than in the EST group\(^\text{94}, 99\); however, compared with the EST group, there was no difference in the initial and ultimate stone removal rates\(^\text{16}, 43, 85, 92\).

Similarly, in a meta-analysis of RCTs that involved bile duct diameter and stone diameter of 12 mm or greater, the stone removal rate was 85.5% in the EPLBD group and 86.9% in the EST group in the initial treatment (RR 0.98, 95%CI: 0.91 – 1.06), whereas the stone removal rates were 97.5% and 99.0%, respectively, in the ultimate treatment (RR 0.98, 95%CI: 0.91 – 1.01), with no significant difference found between the 2 treatments\(^\text{124}\). With regard to the use of ML for patients with large bile duct stones, 3 RCTs revealed a significantly lower rate of usage in the EPLBD group\(^\text{92}, 94, 99\).

Furthermore, a previous meta-analysis found that the rate of ML usage was significantly lower, particularly in patients with large stones exceeding 15 mm in diameter\(^\text{124}, 125\). In the case of relatively large stones, enlarging the bile duct aperture widely by EPLBD enables lithotomy without breaking the stone, which may result in a shorter procedure and fluoroscopic duration\(^\text{99}\).

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Although there are few reports of the stone removal rate in EPLBD with or without EST, a systematic review has compared EPLBD with EST and EPLBD without EST\(^{34}\). The review found no significant difference in the ultimate stone removal rate between EPLBD with EST and EPLBD without EST (96.5% vs. 97.2%, \(p = 0.432\)); however, the stone removal rate in the initial treatment was significantly lower in EPLBD without EST than in EPLBD with EST (76.2% vs. 84.0%, \(p = 0.001\)).

**Statement 5-2: The recurrent rate of bile duct stone after EPLBD is 4.4% to 14.5%**

**Strength of recommendation: N/A, evidence level: C**

**Delphi scores: median = 9, lowest = 9, highest = 9**

The incidence of stone recurrence following EPLBD varies according to different reports because of differences in the subjects and observation periods\(^{33}, 36, 105, 126-129\). However, when limited to reports describing a high follow-up rate and relatively long observation periods, the incidence of bile duct stone recurrence following EPLBD is reported to range from 4.4% to 14.5% (Table 5). Most reports of the long-term prognosis of EPLBD are retrospective studies, although 2 cohort studies have been reported in Japan. In a prospective follow-up study of 42 patients after EPLBD, it was reported that during the follow-up period of 22 months (median), the rate of stone recurrence was 14%, and that the accumulated recurrence rate was 6% at 1 year, and 15% at 2 years\(^{33}\). On the other hand, in a prospective cohort study with the largest sample size of 183 patients following EPLBD, during the mean observation period of 43 months, the rate of stone recurrence was 4.4%, which was lower than those of the other reports\(^{106}\). Most reports of long-term prognosis of EPLBD describe the therapeutic outcomes of EPLBD with EST, although there are also reports of the long-term treatment outcomes of EPLBD without EST. Chan et al. examined 172 consecutive patients with bile duct stones who underwent EPLBD monotherapy. They noted a stone recurrence rate of 14.5% and a mean period until recurrence of 27 months\(^{36}\). There are also reports comparing this article is protected by copyright. All rights reserved.
stone recurrence following EPLBD and EST monotherapy, with no significant difference in the rate of recurrence between the 2 treatment groups\textsuperscript{127}, \textsuperscript{128}. However, both studies were retrospective in nature and with different subject backgrounds. Thus, reports of long-term therapeutic outcomes following RCT are eagerly awaited. Although there is only 1 report of repeat stone recurrence, there are also reports of recurrence in 2.7\% of EPLBD patients overall, and in 62.5\% when limited to patients with recurrence\textsuperscript{105}. The risk factors associated with the recurrence of bile duct stones following EPLBD are similar to those associated with the recurrence of bile duct stones following EST, and include a large bile duct diameter\textsuperscript{33}, \textsuperscript{36}, \textsuperscript{127}. Reports of treatment progress following EPLBD are limited to cases of less than 5 years. Further examination is therefore needed regarding the effects of EPLBD on papillary function and delayed procedural accidents including stone recurrence.

**Statement 5-3**: Transpapillary endoscopic treatment is recommended for bile duct stone recurrence following EPLBD.

**Strength of recommendation: 2, evidence level: C**

**Delphi scores: median = 9, lowest = 8, highest = 9**

Although there are still no reports describing the treatment methods for bile duct stone recurrence following EPLBD, most patients undergo repeat endoscopic treatment at the time of stone recurrence\textsuperscript{33}, \textsuperscript{36}, \textsuperscript{105}. Although bile duct intubation is relatively easy, patients often present multiple stones and large stones at the time of recurrence\textsuperscript{105}, and additional EPLBD is performed as needed for patients in whom stone access and removal are difficult\textsuperscript{33}, \textsuperscript{36}, \textsuperscript{105}. In most patients with repeat This article is protected by copyright. All rights reserved.
stones, complete stone removal is achieved through endoscopic treatment. However, in the endoscopic treatment of resistant patients and patients with frequent recurrence, surgical treatments such as cholangiojejunostomy are an option as in the case of recurrent stones following EST\(^{130}\).

6. POST-OPERATIVE FOLLOW-UP OBSERVATION

Statement 6-1: Delayed adverse events other than recurrent stones of the common bile duct have an incidence of 0% to 10% and include cholecystitis and cholangitis.

**Strength of recommendation:** N/A, evidence level: C

**Delphi scores:** median = 9, lowest = 9, highest = 9

Some of the reported delayed complications of EPLBD other than recurrent stones of the bile duct include cholecystitis and cholangitis\(^{33}, 36, 128\). With regard to long-term follow-up observation following EPLBD, the shortest reported median observation period is 12 months, and the longest median observation period is 45 months\(^{33}, 36, 99, 100, 105, 127-129, 131\). Although most of these reports describe recurrent stones of the bile duct, many do not mention other complications. Reports of cholecystitis complications\(^{33}, 36, 128\) indicate that the associated incidence is in the range of 5%-10%, and reports of cholangitis complications indicate an incidence of 4%\(^{128}\). Of the reports describing cholecystitis and cholangitis complications, very few mention the presence or absence of cholecystolithiasis, and the presence or absence of recurrent bile duct stones\(^{33}\). Thus, the incidence of acalculous cholecystitis and cholangitis is unclear. Although bile duct stricture, pancreatitis, and This article is protected by copyright. All rights reserved.
bile duct cancer were not considered as delayed complications in some reports\(^9\(^9\(^9\)\), the median observation period was approximately 12 months. Further examination with a longer observation period is therefore needed.

With regard to EST, delayed complications other than recurrent bile duct stones include cholecystitis and cholangitis. Recurrent bile duct stones occur in cholecystitis at the rates of 3.6%-22% for calculous cholecystitis and 0%-11.9% for acalculous cholecystitis\(^2\). Cholangitis is often accompanied by recurrent bile duct stones; however, it has been reported that the incidence of cholangitis without recurrent bile duct stones is 2.8%\(^1\(^3\(^2\)\). Furthermore, papillary stenosis, bile duct stricture, and pancreatitis have also been reported as delayed complications. However, the reports remain few and the incidences are still unknown.

On the basis of these results, we cannot say that the observation period and sample size are adequate. However, it is assumed that compared with EST alone, EPLBD with EST does not clearly increase the risk of delayed complications. As noted above, further studies with a longer observation period are anticipated.

**Statement 6-2: The association between EPLBD and the onset of bile duct cancer is unclear.**

**Strength of recommendation: N/A, evidence level: D**

**Delphi scores: median = 9, lowest = 9, highest = 9**

At present, the concurrence of bile duct cancer as a delayed complication of EPLBD remains unclear as a sufficient observation period has not been established. The existing endoscopic papillary treatments include EST and EPBD. However, there is no evidence indicating a high incidence of bile duct cancer as a delayed complication of such treatments\(^1\(^3\(^2\), 133\). On the other hand, bile duct cancer is observed in 5.8%-7.4% of patients who undergo papilloplasty\(^1\(^3\(^4\), 135\). Depending on This article is protected by copyright. All rights reserved.
whether EPLBD progresses as in the cases of EST and EPBD, or surgical papilloplasty, the incidence of concurrent bile duct cancer can vary greatly. Thus, additional cases with long-term follow-up need to be evaluated.
ACKNOWLEDGEMENTS

We greatly appreciate the affiliated congress and the secretary of JGES for their cooperation. The guidelines committee was formed as shown in the table below. The JGES commissioned a committee consisting of 6 pancreatobiliary endoscopists to oversee the development of the guidelines. For the evaluation committee, 4 pancreatobiliary endoscopists were placed in charge of the evaluations.

Guidelines Committee, Japan Gastroenterological Endoscopy Society

Responsible director:

Kazuma Fujimoto (Department of Internal Medicine, Faculty of Medicine, Saga University)

Chairman:

Kazuma Fujimoto (Department of Internal Medicine, Faculty of Medicine, Saga University)

Working committee

Chairman:

Takao Itoi (Department of Gastroenterology and Hepatology, Tokyo Medical University)

Chairman in charge of guidelines creation:

Takao Itoi (Department of Gastroenterology and Hepatology, Tokyo Medical University)

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Members:

Shomei Ryozawa (Department of Gastroenterology, Saitama Medical University International Medical Center)

Akio Katanuma (Center for Gastroenterology, Teine-Keijinkai Hospital)

Yoshinobu Okabe (Division of Gastroenterology, Department of Medicine, Kurume University School of Medicine)

Hironori Kato (Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences)

Jun Horaguchi (Department of Gastroenterology, Natori-Chuo Clinic)

Takayoshi Tsuchiya (Department of Gastroenterology and Hepatology, Tokyo Medical University)

Chairman of the Evaluation Committee:

Naotaka Fujita (Miyagi Health Check-up Plaza)

Members:

Takuji Gotoda (Division of Gastroenterology and Hepatology, Nihon University School of Medicine)

Kenjiro Yasuda (Department of Gastroenterology, Kyoto Second Red Cross Medical Center)
Conflict of Interest

The authors declare that they have no conflicts of interest associated with The development of these guidelines.

References


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Table 1: Grades of recommendation and evidence level

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<td>1: Strong recommendation</td>
<td>A: Based on strong evidence</td>
</tr>
<tr>
<td>2: Weak recommendation (propose suggestion)</td>
<td>B: Based on moderate evidence</td>
</tr>
<tr>
<td>N/A: No clear recommendation, or recommendation grade cannot be determined</td>
<td>C: Based on weak evidence</td>
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<tr>
<td></td>
<td>D: Based on very weak evidence</td>
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Table 2: Members of the EPLBD Clinical Practice Guidelines Development Committee.

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<thead>
<tr>
<th>Committee members of the Japan Gastroenterological Endoscopy Society</th>
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<tr>
<td>Director</td>
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<td>Chairperson</td>
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<tr>
<td>Chair of the Editorial Committee</td>
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<tr>
<td>Committee members</td>
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<tr>
<td>Shomei Ryozawa</td>
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<tr>
<td>Akio Katanuma</td>
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<tr>
<td>Yoshinobu Okabe</td>
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<tr>
<td>Jun Horaguchi</td>
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<td>Hiroya Kato</td>
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<td>Takayoshi Tsuchiya</td>
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<tr>
<td>Kenjiro Yasuda</td>
</tr>
<tr>
<td>Yoshinori Igarashi</td>
</tr>
<tr>
<td>Takuji Gotoda</td>
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<td>Coordination committee</td>
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### Table 3: Overview of procedural accidents in EPLBD

<table>
<thead>
<tr>
<th>Author</th>
<th>Reference</th>
<th>Report year</th>
<th>Study design</th>
<th>Sample size</th>
<th>Adverse event</th>
<th>Pancreatitis</th>
<th>Bleeding</th>
<th>Cholangitis</th>
<th>Perforation</th>
<th>Other</th>
<th>Death</th>
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<td>0.00%</td>
<td>1.00%</td>
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<td>2013</td>
<td>Retro</td>
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<td>2.40%</td>
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<td>0.00%</td>
<td>1.6% (2: pneumonia)</td>
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Overview of procedural accidents in EPLBD (RCT only)

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<tr>
<th>Author</th>
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<th>Report year</th>
<th>Study design</th>
<th>Sample size</th>
<th>Adverse event</th>
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<th>Cholangitis</th>
<th>Perforation</th>
<th>Other</th>
<th>Death</th>
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<td>4.00%</td>
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<td>RCT</td>
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<td>0.00%</td>
<td>0</td>
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<td>RCT</td>
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<td>4.40%</td>
<td>2.20%</td>
<td>2.20%</td>
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<td>Oh MJ</td>
<td>21</td>
<td>2012</td>
<td>RCT</td>
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<td>Teoh AY</td>
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<td>2013</td>
<td>RCT</td>
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<td>6.80%</td>
<td>2.70%</td>
<td>1.40%</td>
<td>2.90%</td>
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<td>Jun Bo Q</td>
<td>25</td>
<td>2013</td>
<td>RCT</td>
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<td>7.94%</td>
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<td>0.00%</td>
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<tr>
<td>Hwang JC</td>
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<td>2013</td>
<td>RCT</td>
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<td>4.30%</td>
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<tr>
<td>Paspatis GA</td>
<td>30</td>
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<td></td>
<td></td>
<td></td>
<td>62</td>
<td>15.00%</td>
<td>3.30%</td>
<td>6.60%</td>
<td>3.30%</td>
<td>1.67%</td>
<td>0.00%</td>
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Table 4: EPLBD stone removal rate.

<table>
<thead>
<tr>
<th>Report year</th>
<th>Author</th>
<th>Study design</th>
<th>Subject sample</th>
<th>Initial stone removal rate (%)</th>
<th>Ultimate stone removal rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Heo</td>
<td>RCT</td>
<td>100</td>
<td>83.0</td>
<td>97.0</td>
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<tr>
<td>2009</td>
<td>Kim</td>
<td>RCT</td>
<td>27</td>
<td>85.5</td>
<td>100</td>
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<td>2011</td>
<td>Stefanidis</td>
<td>RCT</td>
<td>45</td>
<td>unknown</td>
<td>97.7</td>
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<tr>
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<td>Teoh</td>
<td>RCT</td>
<td>73</td>
<td>89.0</td>
<td>97.2</td>
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<td>Jun Bo</td>
<td>RCT</td>
<td>63</td>
<td>80.9</td>
<td>95.2</td>
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<td>Li</td>
<td>RCT</td>
<td>232</td>
<td>87.7</td>
<td>97.4</td>
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Table 5: The rate of stone recurrence following EPLBD

<table>
<thead>
<tr>
<th>Author</th>
<th>Report year</th>
<th>Sample size</th>
<th>Observation period</th>
<th>Recurrence rate (%)</th>
<th>Follow-up rate (%)</th>
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<tr>
<td>Chan</td>
<td>2011</td>
<td>172</td>
<td>Mean 30.2±20.2</td>
<td>14.5</td>
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<td>Kogure</td>
<td>2014</td>
<td>42</td>
<td>Median 22.0</td>
<td>14.0</td>
<td>100</td>
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<td>Itokawa</td>
<td>2015</td>
<td>183</td>
<td>Mean 43.5±19.7</td>
<td>4.4</td>
<td>84.3</td>
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</tbody>
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