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ERCP Stone Extraction: Complex

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INTRODUCTION

Choledocholithiasis remains the most common indication for ERCP. The management of choledocholithiasis has evolved substantially in the last three decades, with ERCP-based therapies centered around endoscopic stone extraction replacing open common bile duct exploration surgery and percutaneous biliary drainage. National registries show that 96.1% of interventions for the management of choledocholithiasis were performed during ERCP,[1] reaffirming ERCP as the gold-standard approach for the management of biliary stone disease. ERCP is safe, minimally-invasive and effective for the management of choledocholithiasis. The vast majority of biliary stones are readily extracted by ERCP with the conventional techniques of endoscopic sphincterotomy and balloon extraction; however, extraction may be challenging in approximately 10%-15% of cases in which the stone disease is designated to be complex.[2] This article will focus on defining complex stone disease and reviewing best practices in the evaluation and management of complex choledocholithiasis.

Complex biliary stone disease arises due to characteristics of the stone itself and the characteristics of the biliary tree and patient's surrounding biliary and small bowel anatomy. Broadly defined, complex choledocholithiasis

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requires more than conventional ERCP with endoscopic sphincterotomy and balloon extraction approaches. Alternatively, stone extraction requiring more than one ERCP for complete stone clearance may be considered complex.[5] Stone extraction can be challenging for numerous reasons (Table 1), including large stone size (>10mm), the presence of multiple stones, difficult location of stones (intrahepatic duct, cystic duct, impacted stones, stones proximal to a biliary stricture or a combination thereof), irregular stone morphology (triangular or tubular stones) and the presence of altered anatomy from prior surgical intervention or underlying disease such that access to the ampulla or bile duct is limited and/or technically challenging.[2,3] Examples of anatomical factors that lead to difficult ERCP include an ampulla within a periampullary diverticulum and surgically altered anatomy such as gastrojejunostomy with Roux-en-Y reconstruction, or a history of Bilroth II surgery. In these cases, the main challenge is access to, and deep cannulation of, the bile duct. In some cases, multiple factors, including patient/anatomic and stone characteristics may contribute to complex stone disease and technically challenging stone extraction. Tailoring the approach to endoscopic stone extraction to address these specific factors that contribute to stone extraction complexity and utilizing a combination of equipment and techniques can overcome the challenge of achieving complete stone clearance in these cases.

Prospective studies have identified a variety of factors that predict the difficulty of stone extraction by ERCP (Table 2), including a very elevated direct bilirubin, low CBD/stone diameter ratio, a short distal common bile duct (CBD) segment defined as <36mm in length and angulation of the distal CBD measuring ≤135 degrees.[3,4,5]

Table 1.

Characteristics of Complex Biliary Stone Disease
Large stone size (>10mm)
Multiple stones
Stone morphology (tubular, triangular or irregular shape)
Difficult stone location (intrahepatic or cystic duct location, proximal to a biliary stricture)
Altered patient enteral anatomy due to prior foregut surgery

Techniques for Complex Biliary Stone Extraction

The most common obstacle to clearance of choledocholithiasis is the presence of large stones.[4] In general, stones greater than 10mm in diameter can be considered large, however, varying definitions exist in the literature. Some studies refer to large stones as those with a diameter >15mm, others focus on the size ratio between the stone and bile duct diameter, considering a stone 'large' when it is larger than the diameter of the bile duct.[8,9] Regardless of the size threshold used to define large choledocholithiasis, studies demonstrate that larger stone size is inversely correlated with successful clearance of the bile duct in a single ERCP.[4,5,10]

When a large stone is encountered, a range of techniques may be employed to maximize the success of clearance of large and complex biliary stones. These techniques include extended endoscopic biliary sphincterotomy, mechanical lithotripsy, endoscopic papillary large balloon dilation and cholangioscopy-assisted lithotripsy and will each be reviewed in detail in this chapter. Figure 1 illustrates a case wherein multiple techniques were used to perform complex stone extraction.

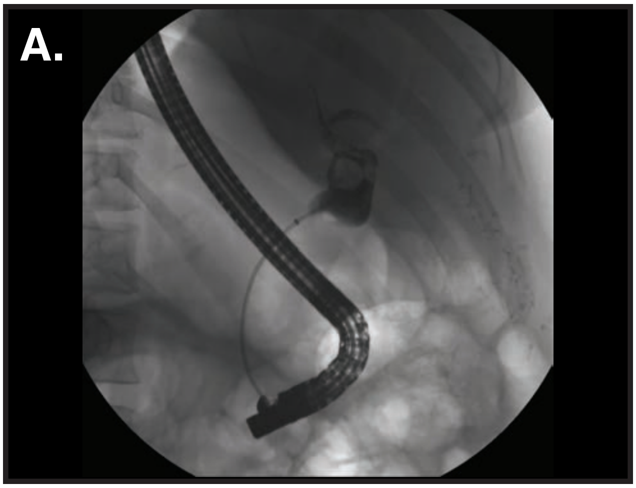
Endoscopic Biliary Sphincterotomy

The mainstay of biliary stone extraction is endoscopic biliary sphincterotomy (ES), by which the opening of the bile duct, the sphincter choledochus, at the ampulla, is incised to allow access to the bile duct and passage of stones out of the bile duct. Understanding key features of the ampulla and sphincter of Oddi is integral to understanding the techniques that facilitate complex stone management. Successful ERCP

Table 2. Factors that predict difficult stone extraction by ERCP

Markedly elevated direct bilirubin
Low CBD/stone diameter ratio
Short distal CBD (<36mm)
Acute angulation of the distal CBD (≤135 degrees)

Figure 1. Large choledocholithiasis managed with cholangioscopy-assisted EHL and balloon extraction of fragments.



1.A. Cholangiogram revealing a large biliary stone in the distal bile duct.

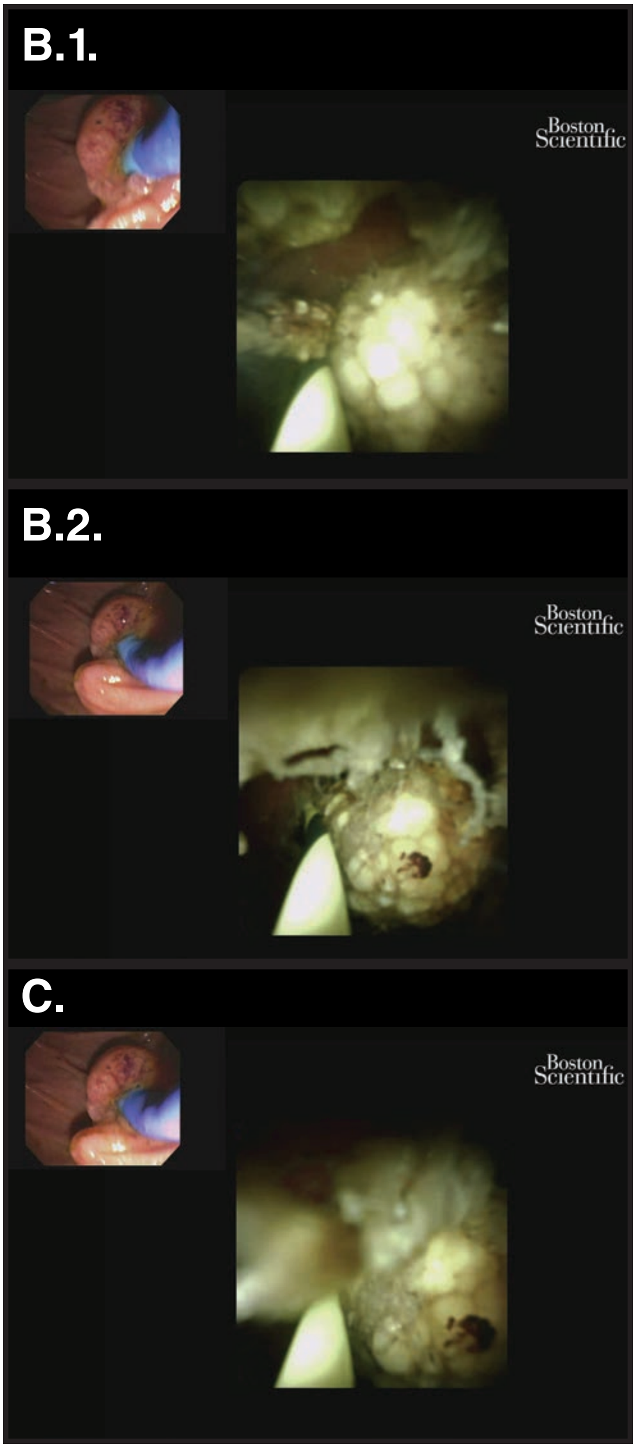


Figure 1. B1.The biliary stone after extraction with a balloon extractor. B2. Biliary stent placement after incomplete clearance of the bile duct. C. Bile flow through the stent despite incomplete clearance of the bile duct.

first relies on identification of the ampulla and the surrounding sphincter of Oddi in the second portion of the duodenum. For this reason, we will briefly review relevant ampullary anatomy here. The ampulla appears as a nodular mound protruding from the lateral wall of the second duodenum, approximately 8cm distal to the pylorus.[6] It is composed of a complex network of muscular fibers termed the sphincter of Oddi, which is comprised of the sphincter choledochus, the opening to the bile duct, the sphincter pancreaticus, the opening to the pancreatic duct, and the sphincter ampullae.[7] The muscle fibres of the sphincter of Oddi are thick and dense, acting as the main barrier to stone expulsion. The principle of sphincterotomy is to cut through those dense fibers at the sphincter choledochus using an electrocautery current, which reduces the resistance of the biliary outflow tract by effectively shortening the sphincter length and markedly widens the biliary orifice. The decrease in resistance of the biliary outflow tract enables the passage of stones, debris and biliary sludge and also allows for the introduction of an extraction balloon into the bile duct over a wire. A balloon catheter can then be advanced over the guidewire to a point proximal to the biliary stone, inflated and withdrawn to sweep the stone and any associated debris, out of the bile duct. For stones less than 10mm, balloon extraction by this method is highly effective, however, the efficacy of this technique

Figure 1.
Continued

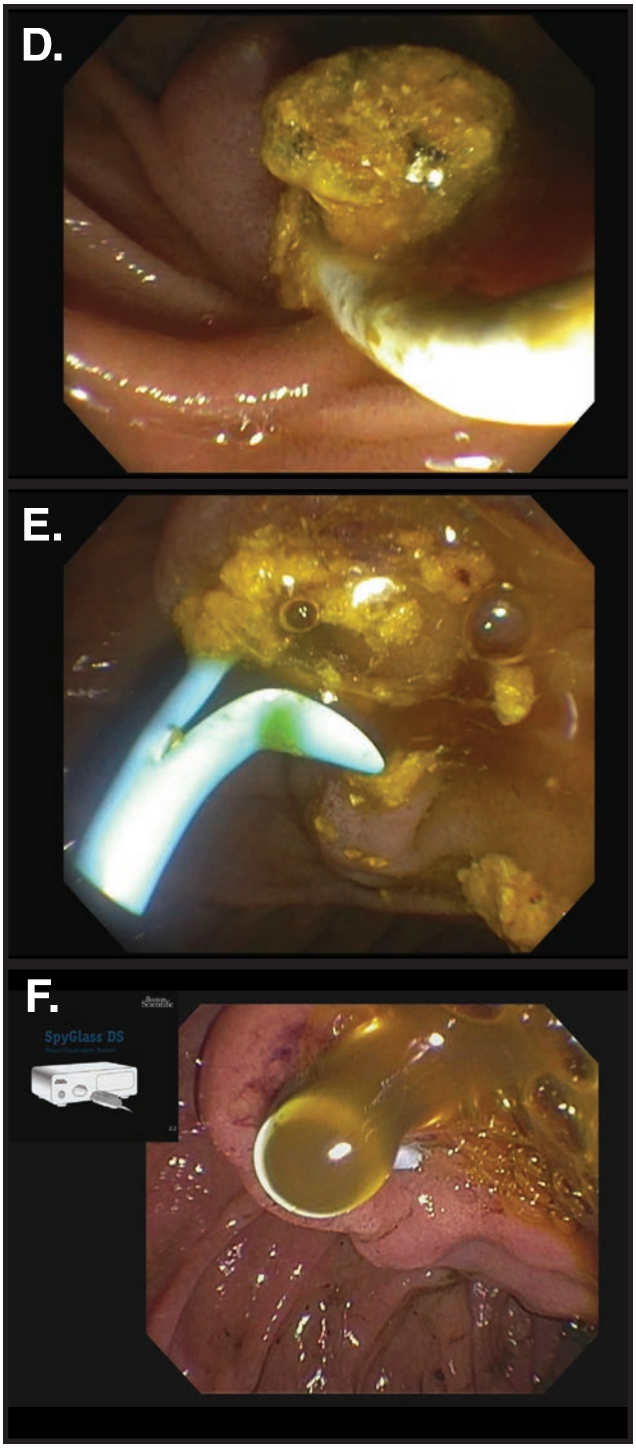


Figure 1.D. The biliary stone after extraction with a balloon extractor. E. Biliary stent placement after incomplete clearance of the bile duct. F. Bile flow through the stent despite incomplete clearance of the bile duct.

declines as the size of the stone increases and in cases where the stone size is larger than the size of the distal CBD diameter, dropping to a success rate of 12% for stones larger than 15mm in diameter.[10] As described further in this article, additional techniques are often necessary if balloon extraction is incomplete or ineffective.

When large stones are encountered, the first consideration is often whether the size of the sphincterotomy is adequate for stone extraction. This can be assessed, armed with the anatomical knowledge described above, by determining whether each of these sphincters has been adequately incised to maximize the size of the extraction orifice. Extension of the sphincterotomy as possible, often facilitates extraction of large stones that might otherwise require advanced approaches. Utilization of advanced stone extraction approaches such as mechanical lithotripsy with a small or inadequate biliary sphincterotomy may lead to increased trauma to and edema of the ampulla, which could become another barrier to extraction of stone fragments and may increase a patient's risk for developing post-ERCP pancreatitis. In these cases, the next reasonable steps in management include decreasing the size of the stone(s) by fragmenting them and/or increasing the size of the biliary orifice to decrease resistance to extraction, or a combination thereof. Increasing the size of the biliary orifice beyond that of conventional endoscopic sphincterotomy can be accomplished by endoscopic papillary balloon dilation (EPBD) and endoscopic papillary large balloon dilation. Fragmentation of large stones can be achieved by various lithotripsy techniques, including mechanical, electrohydraulic and laser lithotripsy.

Endoscopic Papillary Balloon Dilation

EPBD was first described in 1982 as an alternative technique to biliary stone extraction with sphincterotomy.[11] EPBD is performed by inserting and inflating a concentric dilation balloon up to 10mm in diameter at the ampullary orifice to dilate the biliary outflow tract and reduce the resistance to flow by dilating the entire length of the sphincter choledochus. Whereas endoscopic sphincterotomy cuts through the sphincter mechanism to shorten the sphincter length and may rarely lead to complications such as bleeding and perforation,

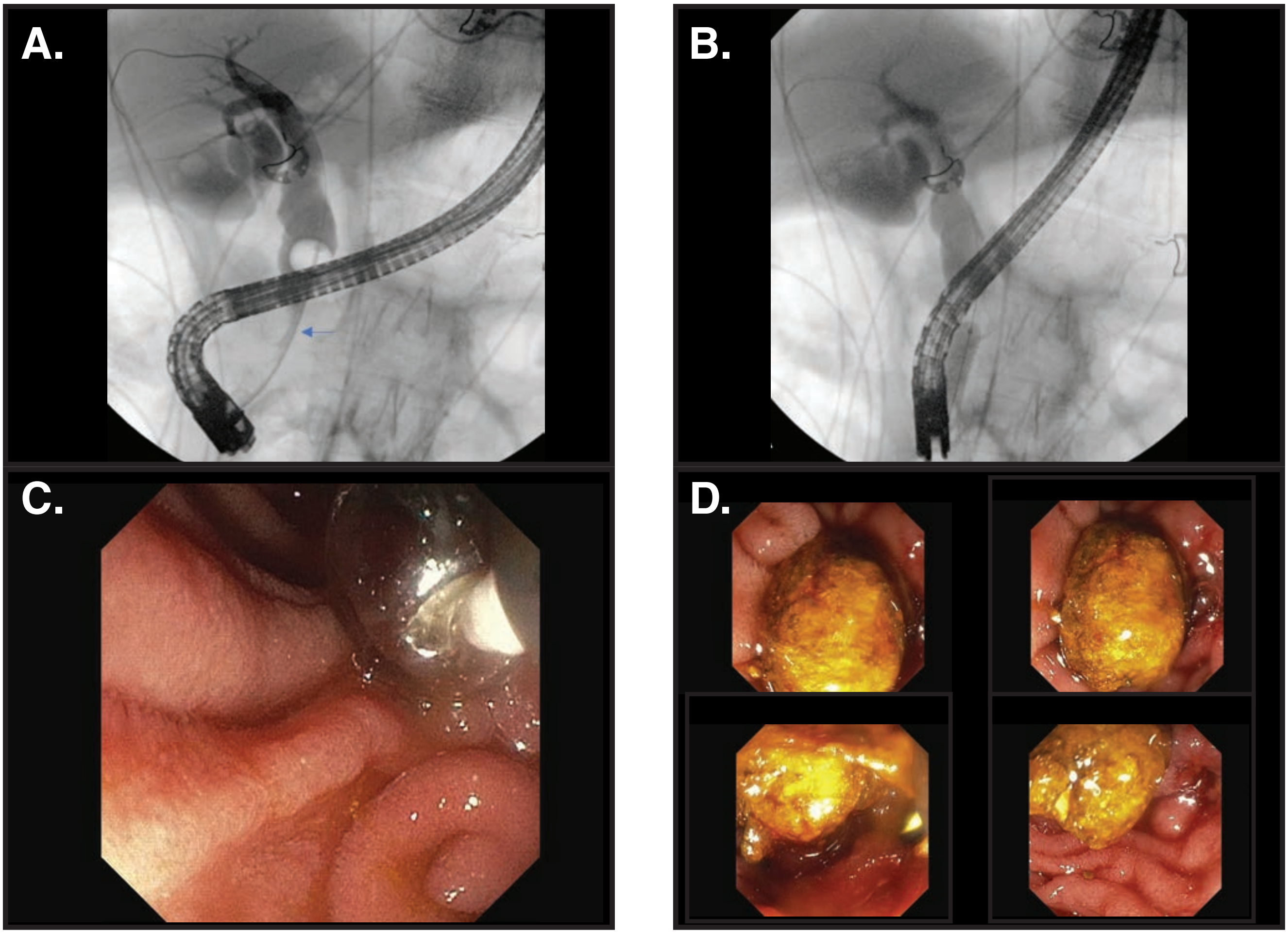


Figure 2. Impacted choledocholithiasis managed with endoscopic balloon papillary dilation followed by extraction balloon sweeps when mechanical lithotripsy failed.
A. Cholangiogram showing a biliary stone impacted in the distal bile duct (arrow) below the level of the extraction balloon. B. Cholangiogram during endoscopic papillary balloon dilation using a 10mm x 4cm dilation balloon. C. Endoscopic view of endoscopic papillary balloon dilation D. Large biliary stone extracted after endoscopic papillary balloon dilation and balloon extraction with a 15mm extractor balloon.

EPBD stretches the sphincter, preserving the integrity of the sphincter mechanism, theoretically reducing the risk of bleeding, perforation and long-term reflux of intestinal contents into the biliary tract. However, the use of EPBD in stone extraction has been controversial.

Studies initially showed that EPBD and ES techniques for choledocholithiasis were equally effective, with some studies showing higher rates of post-ERCP pancreatitis in cases where EPBD was employed, and increased rates of bleeding in cases where ES was used.[12-15] A subsequent multicenter randomized control trial in the US showed that EPBD without ES was associated with significantly higher rates of adverse events compared to ES alone for stones less than 10mm in diameter. These adverse events that occurred most often in patients undergoing EPBD without ES were a higher rate of post-ERCP pancreatitis (15.4% vs. 0.8%) and two mortalities in the EPBD group.[16] The postulated reason for the higher rates of pancreatitis after EPBD is that the radial force exerted by the dilation balloon extends to the sphincter pancreaticus, which may lead to subsequent pancreatic outflow obstruction from tissue edema leading to functional obstruction of the sphincter. Meta-analyses align with the multicenter randomized controlled trial data, finding that EPBD alone, specifically in the absence of sphincterotomy, is associated with higher rates of post-ERCP pancreatitis and, in some cases, lower success rates compared to ES.[17,18] Newer data suggest that longer dilation times up to five minutes vs. one minute may reduce adverse events associated with EPBD.[19,20] While the risk of EPBD may appear to outweigh the benefits of using EPBD, it may have a role in patients with uncorrected coagulopathy, where the risk of bleeding from ES is high. Still, EPBD may cause local tissue trauma that can result in bleeding for these high bleeding risk patients as well. When ampullary bleeding is encountered in post-EPBD patients who do not have a prior sphincterotomy, endotherapy for hemostasis may be relatively limited as most hemostasis techniques rely upon access to the actual sphincterotomy site itself.

Sphincterotomy with Papillary Balloon Dilation

Although the risk profile of EPBD without sphincterotomy is unfavorable in most cases of choledocholithiasis, papillary balloon dilation is still a relevant technique for endoscopic biliary stone clearance and is a useful technique in the management of complex stone disease. A significant limitation to EPBD is the ability to dilate the biliary orifice only up to limited sizes, i.e. 10mm, therefore the technique has been innovated over the years to overcome that with a technique called endoscopic papillary large balloon dilation (EPLBD). EPLBD is a technique whereby a limited or incomplete ES is performed, immediately followed by a large balloon dilation (to >12mm) of the biliary orifice. It was first described in 2003 by Ersoz et al.[21] The rationale for this method is that large balloon dilation can stretch the biliary orifice to diameters larger than 12mm, facilitating large stone extraction. Furthermore, performing the dilation after an ES reduces the radial force and associated trauma of the balloon dilation to the ampulla and sphincter pancreaticus when subsequent additional techniques (e.g. Lithotripsy, balloon extraction) are performed, thereby decreasing the risk of pancreatitis. Figure 2 illustrates a case wherein EPBD was used successfully as an adjunct to sphincterotomy for complex stone extraction.

Since the advent of EPLBD, multiple studies have demonstrated that EPLBD with a limited ES is equally effective as standard ES with conventional stone extraction techniques, with decreased costs, decreased need for mechanical lithotripsy and lower rates of cholangitis.[22-24] Subsequent systematic reviews have demonstrated that EPLBD is effective and associated with lower risks of bleeding, perforation and overall complications.[25-29]

Large balloon dilation alone may be an appropriate approach to large stones in patients who have an increased risk of bleeding or perforation from sphincterotomy, but in practice this is rarely performed.[30,31]

With data supporting the use of EPLBD, international consensus guidelines were published in 2016.[32] The consensus statements from the guidelines based on level 1 evidence is presented in Table 3 below.

While these consensus statements serve as a general guide of how to apply EPLBD, there are several details about the technique in complex biliary stone disease that remain unaddressed in the

Table 3. Level 1 Evidence-Based Consensus Statements from the International Consensus Guidelines for Endoscopic Papillary Large Balloon Dilation

1.	EPLBD can be used as an alternative to mechanical lithotripsy for removal of large or difficult bile duct stones.
2.	When large bile duct stones are identified on ERCP or cross-sectional imaging, EPLBD can be used as the initial method of stone removal.
3.	EPLBD can be considered when conventional stone removal after endoscopic sphincterotomy fails.
4.	The usual duration of balloon dilation is approximately 30 to 60 seconds after disappearance of the waist.
5.	EPLBD with endoscopic sphincterotomy can reduce the need for mechanical lithotripsy.
6.	In patients with difficult or large biliary stones, the overall rate of adverse events for EPLBD with endoscopic sphincterotomy is lower than that for endoscopic sphincterotomy alone.
7.	EPLBD may not increase the risk of post-ERCP pancreatitis.
8.	EPLBD with endoscopic sphincterotomy has a perforation rate similar to that of endoscopic sphincterotomy alone. A major risk factor for perforation is a distal CBD stricture.

literature, such as the duration of balloon dilation and optimal size of balloon inflation/dilation, the level at which dilation should ideally occur (e.g., ampulla, distal CBD and ampulla) and whether ES is necessary prior to EPBLD. General rules of thumb are to avoid EPLBD in cases where there is a CBD stricture and to size the balloon to no more than the maximal diameter of the bile duct just proximal to the ampulla to avoid complications such as perforation and bile duct injury. From the evidence thus far, it appears that EPLBD is a technique that is especially useful in situations where ES may be high risk, for instance in cases where the patient is coagulopathic, there is the presence of a peri-ampullary diverticulum making the risk of perforation with ES high and in cases of surgically altered anatomy where a biliary anastomosis is present rather than an ampulla.

It is also worth noting that EPBD and EPLBD can be performed in patients with a prior *complete*, and not just a *limited*, biliary sphincterotomy. Many times, a patient is referred who has undergone a prior biliary sphincterotomy and may warrant a balloon dilation. It is fully within the standard of care to perform these balloon dilations even if the extent of the prior sphincterotomy is unknown as long as some degree of sphincterotomy has been performed.

Mechanical Lithotripsy

Along with balloon extraction, mechanical lithotripsy is one of the most frequently applied techniques for clearance of choledocholithiasis. It was first described in 1982[33] and, since its initial description, mechanical lithotripters have been continuously innovated to exert and withstand high tensile forces to fragment large biliary stones. In general, mechanical lithotripters are comprised of a metal basket (of various sizes and with several shapes available) in a plastic sheath within a metal sheath. The lithotripter is advanced over a guidewire into the bile duct and is then opened in the bile duct, maneuvered to capture biliary stones within the basket and then closed using external mechanical closure to crush the stones.

Mechanical lithotripsy is widely available, effective and inexpensive compared to other techniques for stone fragmentation and extraction; however, it does require skill and time to maneuver the stones within the basket wires to capture and crush them. Still, the success rates of bile duct clearance using mechanical lithotripsy is up to 84% at index ERCP (34-39) and up to a 90-98% cumulative success rate with multiple sequential ERCPs.[34,35,37]

Predictors of unsuccessful mechanical lithotripsy are large stone size, impacted stones and stones with a high stone/bile duct diameter ratio.[38,39] Each of these factors associated with unsuccessful mechanical lithotripsy is associated with potential difficulty maneuvering the basket around stones within the bile duct. Techniques to optimize the success of mechanical lithotripsy have been described and include opening the basket below the level of the stone, then advancing the basket to capture the stone, and using short-term biliary stents to potentially erode and fragment a large stone and render it more amenable to mechanical lithotripsy during a subsequent ERCP session. A randomized trial studying optimal basket technique showed that opening the basket below the stone instead of above it, increased the capture rates from 33.3% to 94.1%.[40]

While the adverse events associated with mechanical lithotripsy are similar to those associated with other stone extraction techniques, such as bleeding, perforation, pancreatitis and cholangitis, a complication specific to the use of mechanical lithotripsy is impaction. After stone capture, basket impaction can develop when the lithotripter handle is actuated to crush the stone; however, the basket ruptures at either the distal or the proximal end of the tool. If the basket ruptures at the distal end, it is retrievable as it remains connected to the sheath proximally. If the proximal end of the basket ruptures, or the basket fails to rupture but cannot crush or release the stone, special retrieval maneuvers such as using a second basket as a salvage device, extending the sphincterotomy and retrieving the basket using grasper forceps, laser or electrohydraulic lithotripsy, cholangioscopy and retrieval or using a large external lithotripter may be utilized, with varying rates of success for each approach.[42-45]

The rate of basket impaction was previously reported to be 5.9%,[46-48] however, with advances in lithotripter design, the incidence of basket impaction is now reported to be lower, approximately 0.8%

in one study.[49] Predictors of basket impaction and unsuccessful mechanical lithotripsy have been reported to be large stone size, typically over 25mm,[36,50] multiple stones[50] and impacted stones in the bile duct leading to inadequate space to manipulate the lithotripsy basket between the stones and the bile duct walls.[38]

Electrohydraulic and Laser Lithotripsy

In cases requiring fragmentation of biliary stones prior to extraction, electrohydraulic (EHL) and laser lithotripsy are alternatives to mechanical lithotripsy. Both of these lithotripsy approaches are accomplished via cholangioscopy. Cholangioscopy is a technique wherein direct visualization of the bile duct and management of intraductal pathology is possible using either direct peroral cholangioscopy (DPOC) with an ultraslim endoscope or as single-operator catheter-based digital cholangioscope (SpyGlass DS; Boston Scientific, Natick, MA, USA). While EHL and laser lithotripsy can be accomplished by either method of cholangioscopy, the more commonly applied method of direct intraductal visualization is via the single-operator digital cholangioscope, which has a 10Fr catheter containing a 1.2mm working channel and an irrigation port. This single operator digital cholangioscope can be inserted into the duodenoscope working channel and controlled by a single endoscopist using four-way steering knobs. The newer iterations of the system allow for high-resolution images and easy setup. Application of the technique, however, is limited by availability and cost. There is high biliary cannulation and intervention success rates with the use of this catheter-based system, as it is easier to manipulate and maintain positional stability relative to use of an ultraslim endoscope for direct peroral cholangioscopy. In the latter, there can be significant looping of the endoscope in the stomach, leading to limited mechanical advantage for maneuvering and resulting in a more challenging cannulation.[51,52] Various tools have been developed to facilitate direct peroral cholangioscopy, such as the use of overtubes and anchoring balloons to stabilize the endoscope and improve biliary cannulation rates,[53-56] however, this approach remains a cumbersome technique and carries a risk of gas embolism from insufflation of the biliary system, although it is felt that gas embolism is less like to occur when using carbon dioxide for insufflation. This rare but catastrophic adverse event associated with DPOC may be fatal.[57,58] For these reasons, DPOC has become a less commonly utilized technique.

Cholangioscope-facilitated lithotripsy using either the DPOC or the digital single-catheter based cholangioscope, involves the direct intraductal application of energy to fragment biliary stones. This is achieved by two modalities of energy application: electrohydraulic lithotripsy (EHL) and pulsed laser lithotripsy (LL).

Electrohydraulic Lithotripsy (EHL)

In EHL, a coaxial bipolar device generates sparks suspended in a liquid medium (saline) that, consequently, produces a hydraulic pressure wave that causes stone fragmentation. The EHL probe is advanced through either the working channel of the ultraslim endoscope in DPOC, or the working channel of the single-operator catheter-based cholangioscope. The tip of the probe should be approximately 2mm from the target stone to be effective, but ideally should not be in physical contact with the stone. EHL should be performed after saline instillation to facilitate conduction and optimal stone fragmentation. Contact of the catheter tip to the stone is unnecessary as it is the pressure waves generated in the medium that induce fragmentation (Figure 3).

Laser Lithotripsy (LL)

In LL, a quartz fiber is advanced through the working channel and a pulsed laser energy generator is used to deliver laser pulses at a specific wavelength, leading to creation of a mechanical shockwave adjacent to the stone. Contact between the laser tip and the stone is not necessary, as the shockwave is responsible for fragmentation.

In terms of efficacy, cholangioscope-facilitated laser lithotripsy by either the DPOC or digital cholangioscopy is successful in 78-100% of cases according to a recent meta-analysis, with an overall stone clearance rate of 88% and an adverse event rate of 7%.[59] In a large multicenter study of 407 patients using the digital cholangioscope (SpyGlass DS; Boston Scientific) with EHL and LL, index biliary clearance was achieved in 77.4% of cases

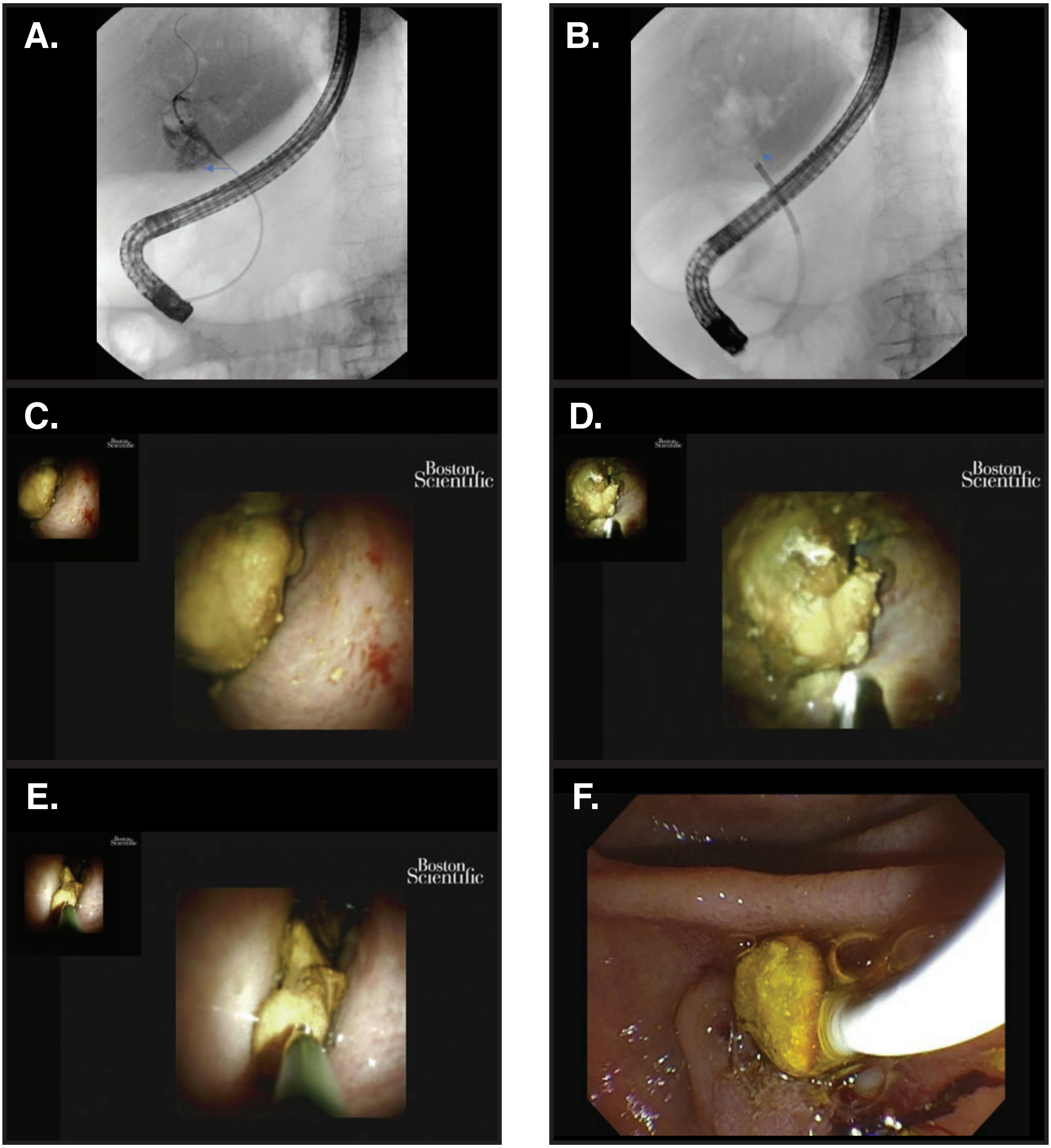


Figure 3. Biliary stones impacted in a recessed area of a capacious bile duct. Stones were fragmented with EHL and extracted using an extractor balloon. Panel A: Cholangiogram showing a biliary stone impacted in the proximal bile duct (arrow) below the level of the extraction balloon. Panel B: Cholangiogram during cholangioscopy with the SpyGlass system showing the EHL probe extruding from the working channel of the cholangioscope and directed at the intraductal stone (arrow). Panel C: Cholangioscopic view of large intraductal biliary stone. Panel D: Cholangioscopic view of EHL probe adjacent to large biliary stone after initial EHL fragmentation. Panel E: Cholangioscopic view of large biliary stone after further EHL fragmentation. Panel F: Large biliary stone extracted after endoscopic papillary balloon dilation and balloon extraction with a 15mm extractor balloon.

(74.5% EHL and 86.1% LL) and overall clearance achieved in 97.3% of cases (96.7% EHL and 99% LL).[60] In the latter study, EHL was used three times more frequently than LL, however, EHL required longer procedure times than LL (74 vs. 50 minutes).[60]

These lithotripsy modalities are useful in settings where ML is unlikely to provide adequate stone fragmentation or has been tried without success; for example, in patients with stone size over 2cm, impacted stones, stones in locations that are challenging for extraction such as in Mirizzi syndrome, stones proximal to biliary strictures or in intrahepatic or cystic ducts. Another advantage of EHL or LL over ML is that these approaches are performed under direct visualization, which may reduce the risk of bile duct wall damage which is, admittedly, rare.

There are a few maneuvers than can be employed to optimize the success of EHL or LL via cholangioscopy. First and foremost, patient safety is a key factor, and in cases where significant irrigation of the bile duct is necessary, airway protection with intubation should be considered. In addition, antibiotic prophylaxis to prevent cholangitis is recommended in all cases where cholangioscopy-facilitated lithotripsy is performed, due to the increased risk of cholangitis reported with the use of this modality.[61] This increased risk of cholangitis may relate to stone fragmentation, coupled with saline insufflation within the bile duct that raises intra-biliary pressures and increases the potential for bacterial translocation and bacteremia. Other technical tips include advancing the cholangioscope deep into the bile duct to provide a straighter passage for the lithotripsy catheter by decreasing pressure at the elevator of the duodenoscope, or inserting the catheter through the cholangioscope prior to insertion of the cholangioscope into the bile duct and minimizing contrast injection to improve direct visualization without the need for copious irrigation of the bile duct to clear injected contrast.

Extracorporeal shock wave lithotripsy can also be performed to assist with stone dissolution in addition to ERCP and may improve clearance at subsequent ERCP, though this approach is most commonly utilized for pancreatic duct stones that are refractory to EHL, however, biliary applications of this lithotripsy approach have been reported in a limited manner.[64-66]

Biliary Stenting

If there is evidence of residual stone disease or significant concern for incomplete clearance of stone fragments after lithotripsy, a biliary stent is typically placed to secure biliary drainage until complete eradication of choledocholithiasis can be performed, with the proximal end of the biliary stent extending above the stone/fragments to ensure ongoing drainage of bile from the duct. The rate of endoscopic clearance of complex stones at an index ERCP is 80% and approaches an overall success rate of 99%,[62] thus endoscopic management has largely replaced surgical and percutaneous management of biliary stone disease. However, endoscopists should recognize the limitations of endoscopic management and individualize the approach to patient-specific factors as well as recognizing and informing the patient that complete biliary clearance may not be achieved at an index procedure. In the setting of abundant or complex stone disease, in many cases it is reasonable to achieve partial stone clearance and place a biliary stent to ensure biliary drainage, with the intention of repeating the ERCP for full stone clearance. Such an approach may be the safest, most effective way to manage complex stone disease in patients who are elderly or have co-morbidities, or who may be at high risk of procedural complications. It also ensures drainage to prevent cholangitis and may improve changes of successful clearance at subsequent ERCP.

There are data suggesting that in the interim between procedures, biliary stenting along with ursodeoxycholic acid and terpene may lead to improved clearance compared to stenting alone,[63] however, in our experience this is rarely utilized in modern endoscopic practice

In general, plastic stents are placed for the purpose of maintaining biliary drainage between procedures. Anecdotal reports indicate that the presence of these plastic biliary stents may fragment and promote clearance of residual stones, however, data surrounding this theory are limited. There are, however, data that demonstrate some success with the placement of fully-covered self-expandable metal stents for a longer in-dwelling time (up to six months) for management of complex stone disease.[67,68] The placement of fully-covered metal stents for a longer in-dwelling time may be applicable in cases where a benign distal biliary stricture is present in addition to complex stone disease. In the end, the choice of stent type is left to the endoscopist.

Regardless of the specific endoscopic strategy used to manage complex biliary stone disease, maintenance of biliary drainage for patient safety is of critical importance. In some clinical scenarios, management of complex stone disease is optimally accomplished with multiple procedures, employing various techniques for bile duct clearance and minimizing the duration and anesthesia time of any single procedure.

Stone Eradication in Patients with Altered Anatomy

Complex biliary stone disease in patients with surgically altered anatomy poses a significant challenge to endoscopists. Obtaining access to the biliary tree in patients who have undergone prior Billroth 2, Whipple, Roux-en-Y hepaticojejunostomy and Roux-en-Y gastric bypass surgeries may be cumbersome due to the inability to use standard duodenoscopes, the need for deep enteroscopy, lower success rates of ampulla cannulation/biliary access and limitations on the use of standard equipment through enteroscopes. The first step in devising an endoscopic strategy for ERCP in the setting of surgically altered anatomy is to understand the details of the patient's history and anatomy in as much detail as possible and to correlate that with current imaging prior to undertaking the procedure.

Hepaticojejunostomy and Roux-en-Y gastric bypass anatomies are particularly challenging because they often require deep enteroscopy-assisted ERCP to reach the ampulla. In a multicenter study, the success rate is reported to be 63% in those cases and there was a relatively high adverse event rate of 12.4%.[69] Percutaneous biliary access and laparoscopy-assisted ERCP via a gastrostomy have higher success rates in such cases. However, they are fraught with other challenges, including long-term catheter-related complications in percutaneous therapy reported to be up to 25%[70,71] and the invasiveness of laparoscopy-assisted ERCP with adverse event rates of up to 36%.[72-74] Another consideration with respect to laparoscopy-assisted ERCP is whether or not repeat procedures will be necessary and the percutaneous access that will be necessary for these subsequent procedures.

Alternatives to laparoscopic and percutaneous biliary access in post-Roux-en-Y gastric bypass anatomy include EUS-guided biliary access. EUS-directed transgastric ERCP (EDGE) has been described as minimally-invasive technique for ERCP in this setting. It involves placing a lumen-apposing metal stent to create a gastro-gastric or gastro-jejunal fistula, effectively reversing the Roux-en-Y gastric bypass such that a standard duodenoscope can be used to access the bile duct. In a multicenter study, EDGE was shown to be non-inferior to laparoscopy-assisted ERCP in efficacy and safety and was associated with shorter lengths of hospital stay as well as procedure time.[75] A common concern with respect to EDGE is the potential for weight gain after reversal of the Roux-en-Y gastric bypass, however, there is data to suggest that patients actually lose weight after EDGE,[75] and the reversal is temporary. In general, weight gain has not proved to be a clinical issue of concern.

EUS-guided biliary access can also be applied to patients who have a hepaticojejunostomy. EUS can be used to localize and create a hepaticoenterostomy from the left intrahepatic biliary tree from either the stomach or jejunum, using a fully-covered metal stent, after which an ultraslim endoscope or cholangioscope can be used to access the bile duct from an antegrade approach and stones can be treated. Typically, this approach is performed at expert centers, however, it may become more widely applied in the future as experience with the technique increases. EUS-guided hepaticoenterostomy has been associated with improved clinical outcomes and fewer adverse events compared to percutaneous biliary drainage in meta-analysis.[76] In addition, EUS-guided approaches may offer a quality-of-life advantage over percutaneous biliary drainage.

In post-Whipple anatomy, the bilioenteric anastomosis can be accessed with a colonoscope in up to 84% of cases.[77] In patients with Billroth 2 anatomy, a duodenoscope can be used to reach

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the ampulla, however, the cannulation rate is variable, reported to be between 49-92%, which in some part is due to the inverted orientation of the ampulla in that scenario. Rotatable and straight catheters are usually used to access the ampulla from the inverted position. Once the biliary orifice is cannulated, sphincterotomy can be challenging but can usually be accomplished. EPLBD may be a useful technique to employ in these patients.[78] A major adverse event to consider in Billroth 2 anatomy is the risk of perforation at the gastrojejunal anastomosis, which reportedly occurs in up to 3.6% of cases.[79]

Endoscopic techniques for the management of choledocholithiasis in altered anatomy are ever-evolving and as EUS-guided approaches and devices designed for altered anatomy are further developed, endoscopic therapy will be more accessible to this patient population.

Endoscopic Management of Choledocholithiasis in Challenging Locations

Choledocholithiasis in the intrahepatic biliary ducts, around acute angulations in the bile duct or proximal to a biliary stricture pose a significant challenge to endoscopic stone removal by ERCP. Hepatolithiasis, or choledocholithiasis within the intrahepatic biliary tree, is arguably the most challenging type of complex stone disease to manage endoscopically, not only due to the proximal location of the choledocholithiasis, but also because in many cases these stones are associated with intrahepatic bile duct strictures. The presence of both stone disease and intrahepatic bile duct strictures are a main factor in endoscopic treatment failure due to inadequate access or inability to extract the stones. In these cases, management of the stricture through dilation or serial stent placement and dilation is often necessary to facilitate stone extraction. This can lead to the need for multiple ERCPs prior to even attempted stone extraction. Risk factors for hepatolithiasis include primary sclerosing cholangitis, hepatic artery ischemia, surgical bile duct injuries, foreign bodies, hemolytic disorders, prior liver transplantation, and gallstone disease. Stones in these locations may also form primarily within the liver. When choledocholithiasis in challenging locations is encountered, the standard tool kit for stone extraction, described early in this article, is typically applied; however, serial management of obstacles to stone clearance, such as strictures between the duodenoscope and the stone, must be managed first to accomplish stone clearance.

CONCLUSION

In conclusion, management of choledocholithiasis has evolved substantially in the last three decades, with endoscopic stone extraction replacing open bile duct exploration surgery and percutaneous biliary drainage. The vast majority of biliary stones are readily extracted by ERCP with the conventional techniques of endoscopic sphincterotomy and balloon extraction, however, extraction proves to be more challenging in approximately 10%-15% of cases in which the stone disease is complex.

As choledocholithiasis management further evolves, multi-center and population level analyses of complex stone disease management during ERCP will be informative and help guide the continued evolution of endoscopic biliary interventions. ■

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