INTRODUCTION AND OVERVIEW OF DIFFICULT BILE DUCT STONES

Choledocholithiasis has been primarily managed by therapeutic endoscopic retrograde cholangiopancreatography (ERCP) for decades with a very high success rate; however, occasionally, the endoscopist may encounter a so-called “difficult stone”. Although there is no consensus on what makes a stone difficult, most agree that stone size is an important factor. Stones greater than 10-15mm have typically been considered to be more difficult to remove. Stone size is an important variable, but the ratio of stone diameter to common bile duct (CBD) diameter may be more clinically relevant.\(^1\) Intrahepatic stones, and stones above strictures are also commonly considered to be “difficult stones”.

A prospective study by Kim et al. on factors influencing the technical difficulty of endoscopic stone clearance in 102 patients with difficult stones showed that age greater than 65, acute distal CBD angulation, previous gastrojejunostomy, and shorter length of distal CBD segment were independent contributors to situations that make stone removal problematic.\(^2\)

This review will describe the endoscopic therapeutic options that are currently used for the treatment of difficult CBD stones, with a focus on success rates and complication rates.

Endoscopic Sphincterotomy with Stone Clearance by Sweeping Basket and Balloons

Endoscopic sphincterotomy (ES) is widely accepted as the first step in CBD stone clearance. Endoscopic sphincterotomy was first performed in 1974 by Classen and Demling of Germany, and Kasai et al. of Japan.\(^3\,\text{and}\,4\) After localization of the papilla with a side viewing duodenoscope, the papilla is cannulated with the sphincterotome. The sphincterotome is equipped with a cutting wire that allows the actual sphincterotomy to be performed using electrocautery. The size of the sphincterotome can be tailored to the size of the stone, the duct diameter, and other factors.

The conventional method for removing CBD stones is by performing biliary sphincterotomy followed by simple extraction using occlusion balloons. Conventional techniques can usually remove small to medium sized stones in a single procedure. In a study of 100 patients with CBD stones, Lauri et al. found that 100% of stones less than 10mm in size were successfully cleared, while only 12% of stones greater than 15mm were cleared using conventional methods.\(^5\)
This emphasizes that as stone diameter increases past 15mm, clearance rates using conventional methods drop dramatically necessitating stone fragmentation techniques. The decision to stop simple stone clearance methods and move on to more aggressive treatments is made by the endoscopist on a case-by-case setting.

**Endoscopic Papillary Balloon Dilation**

Endoscopic papillary balloon dilation (ESPD) was first described in 1982 by Staritz et al. The goal is similar to ES, to dilate the sphincter of Oddi (SOD) for stone passage or for instrumentation of the bile duct. In modern practice, ESPD is almost always done after a biliary sphincterotomy. (Figure 1)

Following sphincterotomy, a dilating balloon is passed through the working channel and across the sphincter over a guidewire. The balloon is then inflated with water and/or contrast material. The size of the dilation balloon can be selected based on the size of the stone to be removed and the surrounding common duct. Various inflation times are used, and a study comparing inflation times of 30 and 60 seconds found no significant difference in stone clearance rates or complications. Some bleeding following ESPD in patients who have undergone ES is common, but is usually mild and self limited. Significant bleeding following ESPD is rare. The effect of the balloon dilation is usually relatively short lived, on the order of several minutes during which other tools and techniques can be used to remove stones through the dilated distal common bile duct.

A main advantage of ESPD following sphincterotomy is that it can often allow the rapid removal of very large CBD stones. The proposed advantages that ESPD has over ES in patients who do not undergo sphincterotomy first are preservation of the SOD function, decreased rates of stone recurrence, and reduced bleeding rates and severity when compared to sphincterotomy alone. The majority of the data that supports the safety and efficacy of ESPD comes from small retrospective studies conducted in North-East Asia where gabexate is widely used. Gabexate, which has been reported to reduce the incidence of post ERCP pancreatitis, is rarely used in North America; therefore, the generalization of these results to a North American population is controversial. Additionally, very little ESPD data has focused specifically on large or difficult CBD stones.

The significance of the abovementioned benefits is controversial. A small randomized prospective study conducted in Asia using manometry to measure the SOD function following either ESPD or ES showed only a marginal benefit with regards to preservation of SOD function. Another study that compared pancreatic enzyme levels drawn from the CBD before
and after ESPD or ES, found no significant difference between the two groups.\textsuperscript{14} An animal study by Mac Mathuna et al. examined SOD tissue 6-12 weeks after ESPD. They observed mild chronic inflammation with moderate to severe submucosal follicular hyperplasia but no smooth muscle disruption or fibrosis.\textsuperscript{15} A human study that examined surgical and postmortem biopsies from ten patients at 2-64 months after ESPD, found mild to moderate inflammation in nine patients and fibrosis in eight. No smooth muscle disruption or architectural distortion was observed.\textsuperscript{16} Whether or not fibrosis and inflammation following ESPD predisposes the patient to future papillary stenosis remains controversial.

Hemorrhage rates have been reported to be significantly lower with ESPD alone compared to ES. Lin et al. reported a single bleeding event in 48 cirrhotic patients who underwent ESPD for CBD stones, compared to 14 bleeding events in 53 patients treated with ES.\textsuperscript{17}

Stone recurrence rates were originally thought to be lower with ESPD; however, multiple studies have shown no difference in recurrence rates between ESPD and ES.\textsuperscript{18}

In 2006, a Cochrane review comparing ESPD to ES highlighted the lack of quality data on this topic. Of fifteen randomized trials that met their inclusion criteria, less than half reported adequate randomization, and only two trials were blinded. ESPD was statistically less successful for stone removal, required higher rates of mechanical lithotripsy, and had higher risk of pancreatitis but significantly lower hemorrhage rates than ES.\textsuperscript{19}

A novel technique uses large dilating balloons (up to 20mm) without preceding ES to remove difficult CBD stones. Although several studies report that this technique has similar outcomes to ES and has reduced bleeding rates,\textsuperscript{20,21,22,23,24} a study by Park et al. revealed four deaths and one delayed massive hemorrhage in a group of 946 patients who underwent large balloon dilation.\textsuperscript{25} In practice large balloon dilation without prior ES is not commonly performed in the west.

Endoscopic papillary balloon dilation is more often done following a limited ES. This technique has the theoretical advantage of dilating the CBD beyond what ES can achieve alone while potentially applying less trauma to the pancreatic duct. In this method, the balloon can be dilated up to 20mm (and sometimes even greater sizes). This method has been proposed as a safe and effective alternative treatment in patients with difficult CBD stones that are refractory to conventional stone removal methods, with final duct clearance rates of 94\% to 100\% and complication rates of 4\% to 7\%.\textsuperscript{26,27,28,29} Large balloon dilation with ES is being applied with increasing frequency in the west, with studies from referral centers in the US reporting similar outcomes as the abovementioned studies from Asia.\textsuperscript{30,31}

A landmark study comparing ESPD to ES for

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the extraction of CBD stones was published in 2004 by Disario et al. This was a blinded, randomized, prospective study of high quality conducted in North America. The authors reported significantly higher rates of overall morbidity (mainly due to pancreatitis) and severe morbidity (with death in two patients) in the ESPD group compared to the ES group (17.9% vs. 3.3%; and 6.8% vs. 0% respectively), and the study was stopped early due to the deaths. The authors recommended against the routine use of ESPD without a prior ES. As a result, many endoscopists in North America favor ES or ESPD following ES as opposed to ESPD alone.32

Mechanical Lithotripsy

Mechanical lithotripsy refers to a variety of techniques that utilize endoscopic devices to physically break and/or crush large stones into smaller pieces to facilitate removal. Mechanical lithotripsy was first described in 1982 by Riemann et al. to facilitate the removal of large CBD stones.33 Special wire baskets, referred to as lithotripter baskets (as opposed to simple retrieval baskets) were developed that feature stronger, braided wires and metallic sheaths to allow stones to be crushed in the CBD itself.

Mechanical lithotripsy is the first line therapy when conventional methods cannot extract stones. After endoscopic sphincterotomy is performed, a closed lithotripsy basket is passed through the working channel into the CBD (often over a guidewire) and past the stone. The basket is then opened and its position adjusted to capture the stone. It may be difficult to pass the basket beyond the stone, or to trap the stone within the basket in patients with impacted stones, but as a rule most stones can be captured in modern baskets. Twisting and vigorously shaking the basket are helpful techniques to enhance stone capture. Once the stone is captured a control knob is twisted or a handle is compressed to create tension on the basket wires, pulling the wires themselves into a metal sheath, (functionally reducing the volume created inside the wire basket) and the stone is crushed. The stone fragments can be swept out using the same lithotripter basket and/or a balloon. (Figure 2) Large stone fragments may require repeat lithotripsy to be performed in the same manner.

Several different mechanical lithotripter basket systems are available. Through the scope (TTS) single-piece disposable units offer ease of use and are available from several manufacturers; these are the most commonly used devices. These disposable lithotripter devices come in sizes up to 3cm in diameter and are usually of the 4-wire basket design with the wires themselves being braided for increased strength. The

![Figure 2c](image.png) Stone fragments in the duodenum following mechanical lithotripsy and stone clearance.

![Figure 2d](image.png) Final cholangiogram showing stone clearance and excellent drainage of bile and dye to the duodenum. There is some pneumobilia.
baskets are mounted in catheters with a metal external sheath.

The Soehendra lithotriptor device usually functions as a “rescue device” for several difficult situations. The device is most commonly employed when the physician has been able to capture a stone but cannot crush it or if the basket/stone complex has become trapped in the bile duct. In these situations, the basket’s overlying catheter is physically separated from the basket itself and its handle (usually with a wire cutter) and the duodenoscope is removed from the patient. This leaves only the basket/stone complex and the trailing wires of the basket device in the patient, with the wires exiting the patient’s mouth. The Soehendra lithotripter is a heavy-duty metal sheath that is affixed to a large mechanical crank. The basket wires are passed through the metal sheath and onto the main axle of the crank handle, which when turned, advances the sheath over the wires and eventually, down into the CBD to the level of the basket. When the device is fully deployed, the metal sheath is used to crush the stone/basket complex. In practice, this has the effect of both crushing the stone and destroying the basket itself. The basket can then usually be removed, which is especially helpful if the basket had previously been trapped in the duct. The physician can then re-intubate the patient with the duodenoscope and proceed with stone fragment removal using standard devices, including other baskets.34

When mechanical lithotripsy was initially being developed, it was frequently unsuccessful due to basket wire fracture. After the introduction of stronger (“hard wire”) baskets with breaking strengths of up to 125 kg, Schnieder et al. reported a 92% clearance rate for stones measuring 20 to 25 mm, and an 85% clearance rate for stones greater than 25 mm.35 Other studies report successful extraction of difficult stones in 92 to 94.4% of cases using mechanical lithotripsy.36,37

A single center study by Chang et al. in Taiwan enrolled 304 patients with difficult CBD stones (>15 mm) for mechanical lithotripsy using TTS lithotripters. The authors reported a stone clearance rate of 90%, with 22% of patients requiring multiple lithotripsy sessions. Pancreatitis, cholangitis, and bleeding complicated mechanical lithotripsy in up to 3.3%, 1.4% and 0.4% of the patients, respectively. These rates typically increase if repeat lithotripsy is required.38

Complications that are unique to mechanical lithotripsy include lithotripsy basket impaction or entrapment within the duct, fracture of the basket wires or the main lithotripsy cable, and gastric laceration from out-of-scope lithotripter metal catheters. Ductal injury, pancreatitis, cholangitis and bleeding can also occur. A retrospective review of 643 difficult CBD stone cases treated by mechanical lithotripsy reported

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Figure 3a. Cholangioscopic view of large stones seen in the CBD.

Figure 3b. The electrohydraulic lithotripsy probe (arrow) is advanced to level of CBD stones, after which shockwaves were applied to fracture the stone.
complications in 23 patients (3.6%). Basket impaction, traction wire fracture, broken handle, and duct injury occurred in 11 (1.7%), 8 (1.2%), 7 (1.08%), and 3 (0.4%) patients respectively.39

Endoscopic management techniques for the treatment of complications associated with mechanical lithotripsy, most notably basket entrapment within the duct, include electrohydraulic lithotripsy (to fracture the stone in the trapped basket), Soehendra lithotripsy (to crush the stone/basket complex), sphincterotomy extension (to help remove the stone/basket complex), extracorporeal shockwave lithotripsy or the placement of a biliary stent to allow for biliary drainage while other options are considered.40,41 Surgical excision may be required if endoscopic salvage techniques fail.42

In a retrospective study of 102 patients who underwent mechanical lithotripsy for difficult CBD stones, an impacted stone, stone size >30mm, and stone diameter to bile duct diameter ratio >1.0 were predictive of mechanical lithotripsy failure with odds ratios of 17.8, 4.3 and 5.4, respectively.43 Another study reported that impacted stones are the most relevant predictor for failed mechanical lithotripsy.44

Mechanical lithotripsy remains the “go-to” technique for difficult CBD stones that are refractory to conventional removal techniques and is widely employed in modern ERCP practice. When stones remain refractory to mechanical lithotripsy, laser lithotripsy or electrohydraulic lithotripsy can be considered.

**Laser Lithotripsy**

The use of endoscopic laser lithotripsy in humans was first described by Ell et al. in 1988 for the treatment of CBD stones that were refractory to mechanical lithotripsy.45 Laser lithotripsy applies pulsed laser energy via a fiber to the stone, resulting in its fragmentation and/or obliteration. The Nd:YAG laser, holmium laser, and pulsed dye laser are some of the available technologies that are used to fragment CBD stones, although the holmium laser is the most widely used. Laser lithotripsy is traditionally performed using a cholangioscope that is passed through the working channel of a duodenoscope for direct cholangioscopic visualization and control. Single and dual operator cholangioscopes are available, with the single operator device being the most commonly used in current practice.46 Alternatively, laser lithotripsy can also be done under fluoroscopy with a radio-opaque marker or balloon to guide the laser probe.47 Lasers have the technical capacity to differentiate tissue from stone, reducing the chance of damaging the duct.48

The lasers apply different techniques to fragment stones. The holmium laser, which was first used for CBD stones in 1998, creates a vapor bubble, which in turn vaporizes the stone.49 The Nd:YAG laser creates a shockwave that destroys the stone. A modified version of the Nd:YAG laser, called the frequency doubled, double pulsed Nd:YAG laser (FREDDY), creates a plasma bubble around the stone, that readily absorbs the lasers light resulting in a powerful shockwave. In comparison to FREDDY, the holmium laser has a longer pulse duration and higher pulse energy. This results in more energy being released into the bile duct, potentially causing thermal tissue damage. This theoretical advantage has not been defended in literature.

Laser lithotripsy has been shown to have good overall outcomes for treating refractory stones. Complications associated with laser lithotripsy include pancreatitis, cholangitis, duct trauma, hemobilia, fever, and pain. Successful stone extraction rates for holmium laser lithotripsy range from 83% to 90%, with most patients requiring 1-2 procedures to achieve duct clearance. Holmium laser complication rates range from 7%-13%.50,51,52,53 The success rate and mean number of interventions for FREDDY are comparable (88% to 92% and 1.4 to 1.7 respectively); however, the complication rate ranges from 6% to 23% which is slightly higher than holmium laser lithotripsy.54,55,56

**Electrohydraulic Lithotripsy**

Electrohydraulic lithotripsy (EHL) is an advanced therapeutic technique typically performed at referral centers. Electrohydraulic lithotripsy and laser lithotripsy share the same indications; the removal of stones refractory to mechanical lithotripsy, intrahepatic stones, and stones above a stricture. The same cholangioscopes that are used for laser lithotripsy are used for EHL. The development of single user cholangioscopes with irrigation channels and multiple working channels has greatly improved the feasibility of this technique. As with laser lithotripsy, the EHL probe is passed through one of the cholangioscope’s working channels and into the bile duct. The bile duct is then irrigated, and the EHL probe generates an electric spark that creates a shock wave that travels through the aqueous medium of the
duct and fractures the stone. (Figure 3)

Success rates with EHL are very similar to laser lithotripsy, making this technique a useful method for stone extraction. In general, stone extraction rates with EHL range from 77% to 98%. Complications associated with EHL are very similar to those associated with laser lithotripsy. Delayed ductal injury from EHL is always a possibility, but is relatively uncommon in practice.

Stenting

Biliary stents were first used in the early 1980s for the treatment of CBD stones that could not be removed by conventional techniques. Stenting is generally reserved for refractory stones and is not a first line therapy. This technique may also be used as a temporizing measure in high-risk patients. Stenting is usually done by placing a retrievable plastic stent into the CBD. The stent should be placed with its proximal end above the stone and the distal end in the duodenum. Metal stents can also be used in patients who wish to minimize future endoscopy as they have longer patency rates than plastic stents but this is an off-label use of these devices.

In addition to draining the CBD, biliary stents may also grind the stone down, thereby permitting stone passage. Chan et al. showed a significant reduction in stone size from 24.9mm to 20.1mm in 46 patients with a median stenting period of 63 days. Another study of 45 patients with difficult CBD stones refractory to conventional methods who underwent stenting for 3 to 6 months showed that stone size decreased from 23.1mm to 15.4mm. They also found that stones dissolved in 10 patients and that 43 patients underwent successful stone removal by conventional techniques after stenting. That being said, stents should generally not be placed to “grind” stones. If this occurs it should be viewed as a beneficial side effect.

Long-term placement of biliary stents has proven to be effective for the treatment of difficult CBD stones, with stone clearance rates ranging from 44% to 94.2%. However, the rates of cholangitis, stent migration and death are significantly higher than with conventional methods, limiting its widespread application. For example, in a prospective assessment of 49 patients with mean follow up time of 39 months, late complications occurred in 40.8% of cases, with 3 cases of biliary-related sepsis. Another study assessing 58 elderly patients who received permanent biliary stents for CBD stones revealed that over a 36-month period, 40% had complications (with cholangitis being the most frequent), and there were 9 deaths due to biliary related causes. The high complication rates associated with long term biliary stents for the treatment of CBD stones restricts the use of this therapy for high-risk patients with a short expected life span who cannot undergo surgical treatment.

The supplementary use of ursodeoxycholic acid with stenting offers minimal additional benefit compared with stenting alone. Therefore medical management of stones is, in general, not recommended.

CONCLUSION

Endoscopic management of CBD stones has been considered to be the first line therapy for decades. Occasionally, the endoscopist will encounter stones that are refractory to conventional techniques. Difficult stones are more than just large stones. Altered biliary anatomy, CBD angulation, and CBD to stone diameter ratio are factors that make stones more difficult to remove.

Conventional stone extraction methods (sphincterotomy and sweeping baskets or balloons) should be attempted before considering more advanced techniques. If conventional methods fail, additional, more aggressive endoscopic therapies should be attempted prior to consideration of surgery.

In patients who require anticoagulation or those at increased risk for bleeding (cirrhosis), ESPD can be considered to dilate the sphincter of Oddi without performing biliary sphincterotomy, although in North America this practice is relatively uncommon. Endoscopic papillary balloon dilation after sphincterotomy appears to be safe and is becoming more widely performed.

Mechanical lithotripsy is successful in 90% of cases and is the “go-to” method if conventional techniques fail. When stones cannot be removed via mechanical lithotripsy, either laser lithotripsy or electrohydraulic lithotripsy can be attempted. Both of these techniques have good success rates but are technically demanding and are therefore typically done at referral centers.

References


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