Detection and management of bile duct stones

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Gallstones do not induce symptoms (eg, biliary pain) in the majority of cases, but 2% to 4% of patients become symptomatic each year.1 Gallstones are incidentally found during routine abdominal US, and the prevalence ranges from 10% in men older than 65 years of age to 20% in women older than 65 years of age. The prevalence of bile duct stones (BDSs) in patients with symptomatic gallstones varies from 10% to 20%.2,3 Gallstones should be managed by observation alone because asymptomatic gallstone disease has a benign natural course.4 BDSs should be removed because of an increased risk of the development of gallstone-related complications including biliary obstruction, acute pancreatitis, and cholangitis.4,5 BDSs can be suspected preoperatively by symptoms and abnormal liver test and imaging study results. Unfortunately, as many as 25% of BDSs are still discovered unexpectedly at surgery,6 and the question remains as to what to do in such cases: intraoperative choledochotomy and manual extraction of stones by using either the same surgical approach (laparoscopy) or conversion of a laparoscopic approach to an open laparotomy or perioperative endoscopic retrograde cholangiography (ERC) (Fig. 1). This article reviews the recent literature regarding the diagnostic modalities of BDSs, defining who should be screened for BDSs before a planned cholecystectomy and identifying the current treatments when stones are detected in the bile duct. To this end, we searched the PubMed database by using the terms “bile duct stone,” “biliary stone,” and “biliary pancreatitis” together with “complications,” “sphincterotomy,” “laparotomic,” and “laparoscopic bile duct stone clearance.” We selected citations from articles in English from the past 10 years, but did not exclude commonly referenced and frequently cited older publications. Several systematic reviews on the topic were also included.

Abbreviations: BDS, bile duct stone; EHL, electrohydraulic lithotripsy; ERC, endoscopic retrograde cholangiography; ILL, intraductal laser lithotripsy; LCBDE, laparoscopic common bile duct exploration; MRC, magnetic resonance cholangiography.

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NATURAL HISTORY OF BDSs

Although the majority of BDSs migrate from the gallbladder to the bile duct, some stones may form in the bile duct even in patients with their gallbladder in situ, including patients with hemolytic disorders or intraductal parasites.7,8 When assessed by intraoperative cholangiography, stone migration from the gallbladder to the bile duct is a frequent event. The prevalence of BDSs in patients undergoing cholecystectomy for symptomatic gallstones varies from 4% to 20% of all cases.2,3 As many as 21% of patients with BDSs found at EUS will spontaneously pass their stones in 4 weeks after the initial diagnosis of biliary colic or biliary pancreatitis.9 A rate of 3.4% of BDSs was reported in 997 patients undergoing laparoscopic cholecystectomy. More than one third of the patients passed the stones spontaneously within 6 weeks of operation.10 Although patients with large stones may remain asymptomatic, small gallstones may migrate from the gallbladder to the bile duct and increase the chance of symptoms and complications, such as cholangitis, hepatic abscesses, and acute pancreatitis.11 The incidence of acute pancreatitis associated with gallstone disease is low, ranging from 0.05% to 1% in uncomplicated disease, whereas the incidence increases to 3% to 8% in symptomatic gallstone disease.12,13 Stones are suspected of causing acute pancreatitis when serum alanine aminotransferase activity is 3 times or more of the upper normal limit and when stones are visualized on US.14 Of note, chronic obstruction by BDSs may lead to secondary biliary cirrhosis.

WHO SHOULD BE EVALUATED FOR THE PRESENCE OF BDSs?

The presence of BDSs should be evaluated in patients with symptomatic cholelithiasis before a planned laparoscopic cholecystectomy (Fig. 1).5,15 BDSs can be suspected preoperatively by symptoms (eg, cholangitis) and abnormal liver test and imaging study results.9,16-20 Several clinical and biochemical findings have been shown to greatly increase the probability of stones being found in the bile duct on further investigation. Although many predictive models exist, none are perfect. By using factors such as age, serum liver test results, and US findings, patients are categorized as having a low (<5%), intermediate (5%-50%), or high (>50%) probability of BDSs (Table 1). Normal liver test results may help to
exclude the presence of BDSs with a negative predictive value of 97%. Abnormal liver test results have only a 15% positive value in predicting BDSs. Cholestatic liver test results usually correlate with the duration and severity of biliary obstruction. US is recommended as the first line of investigation, but is not particularly sensitive in detecting BDSs caused by duodenal air interference. A dilated bile duct revealed by US, cholangitis, and bilirubin level higher than 1.7 mg/dL are strong predictors of BDSs. For example, the presence of cholangitis has a sensitivity and specificity of 11% and 99%, respectively, whereas the presence of a dilated bile duct on US has a sensitivity and specificity of 42% and 96%, respectively. In patients with a gallbladder in situ, the combination of both a normal bile duct on US and normal liver test results indicates a very low probability of BDSs, ranging from 0% to less than 5%. Conversely, the combination of an age of 55 years or older, bilirubin level 4 mg/dL or higher, and bile duct dilation on US increases the probability of BDSs to more than 70%.

Therefore, patients with symptomatic cholelithiasis for whom surgery is planned who have a low probability of BDSs should undergo cholecystectomy without further investigations. Patients with a high probability of BDSs should be sent for preoperative ERC or intraoperative cholangiography. Patients with an intermediate risk of BDSs after the initial evaluation need further evaluation before surgery, including EUS, magnetic resonance cholangiography (MRC), and preoperative ERC.

**TABLE 1. Risk factors for CBD stones in patients awaiting cholecystectomy**

<table>
<thead>
<tr>
<th>Low risk (0%-5%)</th>
<th>Intermediate risk (5%-50%)</th>
<th>High risk (&gt;50%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal liver tests</td>
<td>Age &gt;55 y</td>
<td>Cholangitis</td>
</tr>
<tr>
<td>Normal CBD size on US</td>
<td>Cholecystitis</td>
<td>Dilated CBD: &gt;6 mm</td>
</tr>
<tr>
<td>No further evaluation; intraoperative cholangiogram to be discussed</td>
<td>Dilated CBD: &gt;6 mm</td>
<td>CBD stone on US</td>
</tr>
<tr>
<td></td>
<td>Bilirubin: 1.8-4 mg/dL</td>
<td>Bilirubin: &gt;4 mg/dL</td>
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<tr>
<td></td>
<td>Abnormal liver biochemical test results other than bilirubin</td>
<td>First-line ERC</td>
</tr>
<tr>
<td></td>
<td>Cholangitis</td>
<td>Cholangitis</td>
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<td></td>
<td>Dilated CBD: &gt;6 mm</td>
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<td>CBD stone on US</td>
<td>CBD stone on US</td>
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<td>Bilirubin: &gt;4 mg/dL</td>
<td>Bilirubin: &gt;4 mg/dL</td>
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<td></td>
<td>First-line ERC</td>
<td>First-line ERC</td>
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</table>

**CBD, Common bile duct; ERC, endoscopic retrograde cholangiography.**

**HOW TO EVALUATE FOR THE PRESENCE OF BDSs IN INTERMEDIATE-PROBABILITY PATIENTS**

Although ERC is not recommended for use solely as a diagnostic test in patients with low or intermediate prob-
ability of BDSs, ERC is the preferred diagnostic test in patients with a high probability, even if no direct evidence of BDSs is documented. EUS and MRC are the best imaging modalities and have replaced ERC in patients presenting with an intermediate probability of BDSs. CT has a lower rate of detection of BDSs with a sensitivity of 85% to 88%, a specificity of 88% to 97%, and diagnostic accuracy of 86% to 94% compared with the rates achieved by EUS or MRC. However, CT can identify indirect signs of BDSs, such as a dilation of the bile duct. The accuracy of EUS is better than that of ERC for the detection of small BDSs, and the specificity of EUS to rule out the presence of BDSs is as high as 91% to 98% in some series (Fig. 2A). However, EUS is not better than diagnostic ERC for BDS detection when ERC includes sphincterotomy and balloon sweeping. MRC is a completely noninvasive imaging technique and is more accurate than CT in the detection of BDSs (Fig. 2B). This technique is contraindicated in patients with a pacemaker or cerebral aneurysm clips. EUS offers better spatial resolution than MRC, with values ranging between 0.1 mm and 1 to 1.5 mm, explaining why stones that are not diagnosed by MRC are often smaller than 10 mm in size and why EUS is able to identify stones impacted in the papilla (Fig. 3).

Studies examining MRC compared with ERC have used ERC as the criterion standard method. MRC has a sensitivity and specificity of 90% or more compared with ERC. Although there is no statistically significant difference in performance when EUS and MRC are compared, EUS is more sensitive for small stones. EUS cannot image the intrahepatic ducts and cannot easily be performed in patients with altered surgical anatomy (eg, gastrectomy).

Whether initial EUS or MRC is more cost-effective than ERC has been the subject of several recent cost-effectiveness analyses. ERC is the most cost-effective strategy within a patient population, with a probability of therapeutic ERC in 50% of the patients. However, in a patient population with a low probability of BDSs, EUS is superior to MRC for detecting BDSs. EUS is useful for confirming a normal biliary tract and should be considered a low-risk alternative to ERC. Patients suspected of having BDSs who previously underwent cholecystectomy should be evaluated by EUS or MRC when findings on the initial evaluation, including liver test and imaging study results, are abnormal. Diagnostic ERC and its related complications can be spared in 75% of the patients when EUS is used as a triage tool. EUS as the first strategy was cost-effective for patients with a probability of BDSs of less than 61%, with the ERC first-line strategy proving to be the prominent strategy for patients at higher risk. Performing EUS with or without ERC and sphincterotomy depending on the EUS findings during the same endoscopic procedure might be an appropriate approach in patients scheduled to undergo laparoscopic cholecystectomy. First-line ERC was performed in high-risk patients, whereas EUS with or without ERC (when a stone was demonstrated) was performed in intermediate- and low-risk patients. As a result, a BDS was identified in 79% of high-risk patients and in 19% of intermediate-risk patients. Although the concept of EUS-guided ERC makes sense, the number of well-trained and well-equipped gastroenterologists able to perform it is unknown. When

Figure 2. A, EUS image of a stone retained in the intrapancreatic part of the common bile duct (CBD). Note the postacoustic shadow produced by the stone (arrow). B, Magnetic resonance imaging of a stone appears in black located in the lower third part of the common bile duct.

Figure 3. EUS image of a stone (arrow) impacted into the papilla of Vater, a finding that magnetic resonance imaging cannot easily demonstrate.
one has to choose among the various bile duct imaging modalities and treatments, patient suitability and local expertise are the most important considerations.

**BDSs FOUND DURING SURGERY**

During the era of open cholecystectomy, BDSs were usually all removed surgically, although a minority were retrieved by intraoperative or postoperative ERC. When laparoscopic cholecystectomy started being performed, intraoperative clearance of BDSs was not technically feasible. As the laparoscopy technique improved with the introduction of laparoscopic common bile duct exploration (LCBDE), clearance of BDSs became possible in cases of undetected or unexpected BDSs. Nowadays, intraoperative cholangiography is recommended for patients with an intermediate to high risk of BDSs and for those in whom the diagnosis was not confirmed before surgery by other imaging modalities. Although LCBDE is attractive, the number of surgeons who can perform a laparoscopic choledochotomy is probably much lower than the number of gastroenterologists who are competent at ERC stone extraction. As a result, we must keep in mind that LCBDE has very limited availability worldwide.

**ENDOSCOPIC VERSUS LAPAROSCOPIC BILE DUCT CLEARANCE OF BDSs**

Studies comparing open bile duct exploration with postoperative ERC data are probably irrelevant in 2010. Five trials (4 published studies and 1 unpublished study) were reported on laparoscopic surgery including a total of 591 patients. In the largest study consisting of 471 patients scheduled to undergo cholecystectomy, 80 patients were found to have BDSs at surgery and were randomized to either LCBDE or postoperative ERC. In the laparoscopic group, duct clearance was successful in 30 patients (75%) (transcystic extraction in 23 cases and laparoscopic choledochotomy in 7 cases). The procedure in 1 patient was converted to open choledochotomy, and 9 had postoperative ERC for subsequent stone removal. In the endoscopic group, duct clearance was successful in 30 patients (75%) on first attempts at ERC. Five patients required 2 ERCs and 2 patients required 3 ERCs, whereas the remaining 3 patients had a long-term stent placed and the stones were left in situ. Even if these 3 patients did not meet satisfactory endpoints, there was no statistical difference in the rate of bile duct clearance when both groups were compared. Hospital stay was significantly shorter in the laparoscopic group than in the postoperative ERC group. However, this endpoint of longer hospital stay is a bit artificial because of the unnecessary delay between cholecystectomy and ERC. Table 2 summarizes the main data of the 4 randomized, controlled studies and gives bile duct clearance rates on an intent-to-treat basis. Regarding 3 other randomized studies, conversion rates for LCBDE to open surgery were 2.4%, 3.5%, and 7.4%, whereas the need for postoperative ERC was 0% and 2.8% to 11%. Based on the available literature, there is no evidence of a difference in performance, morbidity, or mortality when LCBDE and perioperative ERC are compared, although hospital stay is shorter for patients treated by LCBDE. As a result, patients with BDSs at the time of surgery may be treated by LCBDE or undergo peri- or postoperative ERC.

**ENDOSCOPIC TREATMENT OF BDSs: WHICH METHOD TO USE?**

Since its introduction, ERC has greatly evolved, with an expansion of indications and with several therapeutic developments, including stenosis dilation, stent placement, and large stone fragmentation. ERC carries a 0.6% to 5% risk of infection, a 0.3% to 2.0% risk of hemorrhage, a 0.1% to 1.1% risk of perforation, and a 1.3% to 6.7% risk of acute pancreatitis. However, prevention of post-ERC pancreatitis in high-risk patients might be achieved by placing a temporary pancreatic stent. Balloon sphincteroplasty was introduced as a sphincter-preserving alternative to sphincterotomy because concerns had been raised that

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**TABLE 2. Summary of the four randomized controlled studies comparing endoscopic versus laparoscopic bile duct clearance of bile duct stones**

<table>
<thead>
<tr>
<th>Author/year</th>
<th>n</th>
<th>Extraction rate, %</th>
<th>Morbidity rate, %</th>
<th>Mortality rate, %</th>
<th>Hospital stay, d</th>
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<tr>
<td></td>
<td>ERC</td>
<td>LCBDE</td>
<td>ERC</td>
<td>LCBDE</td>
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<tr>
<td>Rhodes et al55/1998</td>
<td>80</td>
<td>75</td>
<td>75</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Cuschieri et al56/1999</td>
<td>300</td>
<td>83</td>
<td>84</td>
<td>12.5</td>
<td>15.7</td>
</tr>
<tr>
<td>Sgourakis and Karaliotas,57 2002</td>
<td>78</td>
<td>84</td>
<td>86</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Nathanson et al58/2005</td>
<td>86</td>
<td>95</td>
<td>98</td>
<td>13</td>
<td>17</td>
</tr>
</tbody>
</table>

ERC, Endoscopic retrograde cholangiography; LCBDE, laparoscopic common bile duct exploration.
ablation of the sphincter may facilitate access of bacteria to the bile duct and cause cholangitis. Long-term follow-up studies have not confirmed this. The major drawbacks of sphincteroplasty compared with sphincterotomy include the limited size of the papillary opening and the high rate of postdilation pancreatitis.

Approximately 90% to 95% of BDSs can usually be accessed and removed after endoscopic sphincterotomy by using balloon-tipped catheters or baskets (Fig. 4A). When biliary access is difficult, precut papillotomy is proposed as an alternative. This technique carries a substantial rate of complications, ranging from 5% to 30% (eg, post-ERC pancreatitis, perforation), and its performance should be restricted to well-trained gastroenterologists because operator skill seems to be the most important factor to reduce the risk associated with the precut papillotomy.

When previous attempts at biliary cannulation have failed, the rendezvous technique combining endoscopy with percutaneous transhepatic cholangiography can be proposed. This technique is recommended for patients who are not candidates for surgery when ERC is unsuccessful and when it is impossible to resolve biliary obstruction by percutaneous transhepatic cholangiography. EUS-guided transhepatic cholangiography has also become an alternative to percutaneous transhepatic cholangiography or surgery in patients with obstructive jaundice after failed ERC. Although appealing, this new technique should be reserved for tertiary centers with advanced training in both EUS and ERC.

Patients with Roux-en-Y enteroanastomosis or modified Billroth II surgery are challenging because of the lack of access to the biliary anastomosis. Using double-balloon enteroscopy for ERC allows biliary access and cannulation as well as stone extraction. To circumvent the altered anatomy in patients with gastric bypass, laparoscopy-assisted ERC through the gastric remnant was developed. Thus, surgical gastrostomy allows pancreatobiliary and duodenal access to treat BDSs and cholangitis.

An anticipated “difficult stone” can be managed by mechanical lithotripsy, a method aimed at fragmenting the stones into small pieces. This technique uses a mechanical lithotripter that consists of a stronger basket with a spiral sheath, against which the stone is crushed by

Figure 4. A, A conventional open basket (left) and a fully inflated balloon (right). Both tools are used to remove common bile duct stones. B, Single-use mechanical lithotripter Lithocrush that is used for anticipated large and difficult stones.
The use of a crushing sleeve may facilitate the extraction of very large stones. Technically, this flexible spiral metal sleeve is advanced over the basket wires to the papilla by pulling on the basket wires. The wire is finally pulled by an external cranking handle leading to either a crushed stone or basket rupture.

Two types of lithotripters are used, depending on whether lithotripsy is being performed on an emergency or scheduled basis. The emergency lithotripter (eg, Cook Endoscopy, Inc, Winston-Salem, NC) requires more experienced endoscopists because it is not a single assembly device. The elective lithotripter consists of a single assembly device used when the need for lithotripsy is anticipated in documented large stones (usually >15-20 mm). Mechanical lithotripsy has a 90% success rate and carries a 9% complication rate compared with 3% in patients who did not undergo lithotripsy (hemobilia, cholangitis). The success rate varies from 68% to 90% when the stone diameter is larger than 3 cm.

Shock wave lithotripsy may replace mechanical lithotripsy when it fails because the stone is impacted in the bile duct or is too large to be captured by the basket. BDSs are fragmented by using shock waves delivered either with a conventional extracorporeal lithotripter or with an intraductal shock wave device. The extracorporeal system has major drawbacks because several sessions are needed to achieve complete stone fragmentation, each session being followed by endoscopic stone removal. Moreover, the logistics of the system are demanding and expensive. The largest published study using the extracorporeal shock wave lithotripsy (Lithostar Plus; Siemens, Erlangen, Germany) followed by endoscopic removal reported a bile duct clearance rate of 90% after a mean of 3.7 sessions per patient and with a 9% complication rate including cardiac arrhythmia, cholangitis, and hemobilia. The intraductal system consists of a cholangioscope inserted in the bile duct through the working channel of the duodenoscope. It is then advanced until it reaches the stone surface, where it delivers shock waves generated by electrical (electrohydraulic lithotripsy [EHL]) or light energy (intraductal laser lithotripsy [ILL]). Stone clearance after EHL or ILL with or without additional ERC varies from 77% to 90% after failure of conventional endoscopic fragmentation of BDSs. Although visual control can be achieved by peroral cholangioscopy by using a mother–baby endoscopic system, this procedure is difficult and requires the presence of 2 skilled endoscopists. To circumvent these disadvantages, direct peroral cholangioscopy by using an ultrathin upper endoscope (performed by a single endoscopist) and a single-operator peroral cholangiopancreatoscopy system have been proposed as a solution for direct visual examination of the biliary tree. In this setting, the overall success rate of bile duct clearance reached 89% by using either EHL or ILL. Laser lithotripsy is effective in a small number of clinical trials, but radiolucent laser fibers make accurate fragmentation difficult and require continuous visual control.

When a stone remains impacted in the basket or bile duct despite all the endoscopic attempts to remove it, biliary drainage to prevent acute cholangitis by inserting a nasobiliary catheter or percutaneous decompression or even biliary surgery is indicated in the following hours. A plastic stent can be considered instead of a nasobiliary catheter in a stable patient waiting for further attempts at another institution. For frail elderly patients with large impacted BDSs, long-term treatment with biliary stenting has been reported to provide palliation, but this definitive measure has been fraught with complications. The association of temporary biliary stenting with daily choleretic agents (ursodeoxycholic acid and terpene preparations) promotes BDS size reduction and results in bile duct clearance by ERC in 93% of 28 cases after 6 months of treatment.

**CONCLUSIONS**

The prevalence of BDSs in patients undergoing cholecystectomy for symptomatic gallstones varies from 4% to 20%. Detection of BDSs and their extraction, if any, should be considered before a planned cholecystectomy. Initial evaluation of a patient with gallstones should comprise complete medical history, liver biochemical tests, and an abdominal US scan. The results can serve as a strategy to assess the risk of BDSs in patients with symptomatic cholelithiasis and to give them the most appropriate additional evaluation and treatment.

Conventional endoscopic stone removal is possible in the vast majority of cases. Newly introduced endoscopic techniques are proposed in failed conventional ERC and are available in tertiary centers.

When a BDS is incidentally found during surgery, several options exist (Table 3). LCBDE is as effective and safe as ERC. No benefit was observed in terms of primary treatment failure, morbidity, and mortality when the 2 procedures were compared, whereas more procedures had to be undertaken and sometimes longer hospital stays were reported in the ERC arm. No cost-effectiveness data are available so far.

These results are from experienced laparoscopic centers and may not be applicable to all hospitals, although experience in the laparoscopic era is growing. Therefore, one may choose the best skilled procedure available at each center until surgeons are properly trained and experienced in LCBDE.

Further studies aimed at evaluating delayed complications of LCBDE (eg, rate of stenosis) and differences in the efficacy of either transcystic clearance versus true chole-
dochootomy are needed. Finally, improvement in techniques in the near future in both the endoscopic and laparoscopic fields will evolve and therefore may change the current conclusions.

REFERENCES


