Gallstones have an estimated prevalence of 5.3 to 8.9% in men and 13.9 to 26.7% in women, making gallstone disease one of the most common problems encountered by general surgeons. Of all patients with gallstones, 1 to 3% will develop complications annually, and this increases to 30% in patients with biliary colic. The most common complications include acute cholecystitis, common bile duct (CBD) stones, and gallstone pancreatitis, with less common complications including choleodochoduodenal fistula and gallstone ileus. Acalculous cholecystitis, although not a complication of gallstones per se, can also arise in high-risk patients and is included in this discussion of complicated benign gallbladder disorders.

Acute Cholecystitis

Acute cholecystitis is the result of cystic duct obstruction leading to gallbladder edema, mucosal sloughing, and, potentially, ischemia. Signs and symptoms of acute cholecystitis include right upper quadrant pain, nausea, and vomiting. Unlike the self-limited pain associated with biliary colic, pain associated with acute cholecystitis generally lasts more than 6 to 8 hours. In addition to the signs of local inflammation (pain and tenderness in the right upper abdomen or epigastric area), patients also exhibit signs of systemic inflammation, including fever, leukocytosis, and elevated C-reactive protein. Mild elevations in bilirubin and liver enzymes may be present. A positive Murphy sign on physical examination is suggestive of a diagnosis of cholecystitis (likelihood ratio of 2.8). Necrosis of the gallbladder wall can occur due to prolonged inflammation and decreased gallbladder perfusion. Gallbladder perforation occurs in 5 to 10% of patients with acute cholecystitis.

Diagnostic Imaging

Ultrasoundography

Ultrasoundography is one of the most commonly used and practical diagnostic tests in confirming the diagnosis of acute cholecystitis. The sensitivity of ultrasonography in diagnosing acute cholecystitis is approximately 80%. Findings of acute cholecystitis by ultrasonography include gallbladder wall edema (thickening > 4 mm), pericholecystic fluid, a sonographic Murphy sign, and gallbladder distention [see Figure 1 and Table 1].

Cholescintigraphy

Cholescintigraphy (also known as hepatobiliary iminodiacetic acid [HIDA] scanning) has a limited role in the diagnosis of gallstones but is a reliable and highly sensitive test for diagnosing acute cholecystitis. In fact, it is more sensitive than ultrasonography, with an estimated sensitivity of greater than 90 to 95%. A HIDA scan is considered positive for acute cholecystitis if there is no visualization of the gallbladder at 30 minutes after intravenous injection along with hepatic clearance and biliary to bowel transit of the technetium 99m–iminodiacetic acid tracer [see Figure 2]. Visualization of the gallbladder implies a negative test as no obstruction of the gallbladder outlet is present. Although more accurate than ultrasonography, HIDA scanning involves ionizing radiation and is less readily available. Furthermore, tracer uptake, and therefore test accuracy, is compromised in the setting of cholestasis or impaired liver function. For these reasons, cholescintigraphy is generally used when ultrasonography is equivocal or limited due to a patient’s body habitus.

Magnetic Resonance Cholangiopancreatography

Magnetic resonance imaging (MRI) has a limited role in the diagnosis of acute cholecystitis given its limited availability, increased expense, and limited added benefit above ultrasonography or cholescintigraphy.

Computed Tomography

Computed tomography (CT) may be useful in the evaluation of a patient with suspected acute cholecystitis but in...
whom significant diagnostic uncertainty exists as CT provides a more comprehensive examination of the remainder of the abdomen. CT findings of acute cholecystitis include gallbladder distention, gallbladder wall edema, and pericholecystic fluid or fat stranding. Gangrenous cholecystitis can be seen on a CT scan as air in the gallbladder wall [see Figure 3] with or without evidence of perforation. Despite limitations in visualizing the actual gallstones, the sensitivity of CT in diagnosing acute cholecystitis is estimated to be as high as 95%.

TREATMENT

Cholecystectomy is the recommended treatment for acute cholecystitis. In the acute setting, laparoscopic cholecystectomy can be performed safely, with a low risk of complications. The risk of conversion to open surgery in the setting of acute cholecystitis is reported to be 5 to 35%. Patient factors such as older age, male gender, longer duration of symptoms, and a thickened gallbladder wall are associated with an increased likelihood of conversion. Bile duct injuries as a result of laparoscopic cholecystectomy are uncommon, with an incidence of less than 1%, whereas postoperative bile leaks occur in approximately 3% of patients.

The timing of surgery in acute cholecystitis was controversial for many years as surgeons were concerned that inflammation in the presence of acute cholecystitis increased the chance of converting to open surgery and the risk of serious complications such as bile duct injury. However, recent meta-analyses of large randomized trials reveal that early laparoscopic cholecystectomy (within 7 days of the

Table 1  Ultrasonographic Findings in Acute Cholecystitis

<table>
<thead>
<tr>
<th>Sonographic Murphy sign</th>
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<tbody>
<tr>
<td>Thickened gallbladder wall &gt; 4 mm</td>
</tr>
<tr>
<td>Distended gallbladder (&gt; 8 cm long axis, &gt; 4 cm diameter)</td>
</tr>
<tr>
<td>Pericholecystic fluid</td>
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<tr>
<td>Gallstones, incarcerated gallstone</td>
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Figure 2  Hepatobiliary iminodiacetic acid (HIDA) scan showing acute cholecystitis. At 2 minutes (a), uniform uptake into the liver parenchyma is seen, and at 1 hour (b), passage of contrast into the duodenum is seen. At 90 minutes (c) and 2 hours (d), there is still no filling or visualization of the gallbladder, consistent with cystic duct obstruction.
onset of symptoms) is not associated with any significant difference in the rates of bile duct injury or conversion to open surgery compared with delayed surgery. Furthermore, early intervention eliminates the risk of developing further gallstone-related complications (which occur in up to 20% of patients), return to the emergency department, or refractory symptoms while waiting for surgery. Early laparoscopic cholecystectomy is associated with decreased overall length of hospital stay as well, making it a safe and cost-effective treatment for patients with acute cholecystitis. If delayed treatment is chosen or required due to clinical circumstances, waiting 6 to 12 weeks is recommended to allow the inflammation to settle down before interval cholecystectomy.

In certain high-risk patients, it may be desirable to postpone surgery or potentially avoid surgery altogether. Nonoperative management of acute cholecystitis consists of decreasing gallbladder stimulation by keeping the patient fasting, rehydration with intravenous fluids, and appropriate analgesia. Antibiotics with adequate gram-negative and anaerobic coverage are given due to the risk of superimposed infection. The majority of patients respond to conservative management, but 20 to 25% of patients will require urgent or emergency surgery for either refractory symptoms or disease progression, including gallbladder empyema, perforation, and sepsis. In patients who are unfit or who present a very high risk for surgery, and in whom an effort at conservative management is unsuccessful, image-guided percutaneous cholecystostomy is a useful option. Percutaneous cholecystostomy tubes decompress the gallbladder, relieving the patient’s symptoms and controlling biliary sepsis. Treatment of acute cholecystitis with a percutaneous cholecystostomy tube is successful in the majority of patients (85% or greater). Tube complications may arise; blocked or dislodged tubes or bleeding during installation occurs in approximately 16% of patients. Recurrent symptoms following cholecystostomy tube removal are estimated to occur in 7 to 41% of patients. Patients who recover from critical illness and are fit to undergo surgery at a later date should do so. Complications at interval laparoscopic cholecystectomy following cholecystostomy do not appear to be substantially higher than in the acute setting, and conversion to open surgery is estimated to be in the very acceptable range of 10%.

Common Bile Duct Stones

Approximately 10 to 18% of patients undergoing laparoscopic cholecystectomy have CBD stones or choledocholithiasis. Clinical presentation, laboratory investigations, and imaging studies are essential for patient risk stratification, which then guides further investigation and treatment decisions. Multiple treatment options, each with high success rates, are available, and the choice of approach depends on patient factors, available equipment, and local expertise.

CBD stones can be asymptomatic but more commonly present with upper abdominal or back pain, nausea, vomiting, and jaundice. Asymptomatic stones are often found incidentally on abdominal imaging studies. Symptomatic stones cause pain due to obstruction of the duct.

Choledocholithiasis can lead to biliary or pancreatic obstruction and serious sequelae, including cholangitis and pancreatitis [see Gallstone Pancreatitis, below], both of which can range from mild to potentially life threatening and require prompt diagnosis and treatment. Patients with acute suppurative cholangitis often present with the Charcot triad of right upper quadrant pain, jaundice, and fever. In more severe cases, patients progress to also manifest hypotension and altered mental status, known as the Reynolds pentad.

Primary CBD stones develop spontaneously, usually due to biliary stasis, such as in cystic fibrosis, or due to chronic inflammation, such as in recurrent pyogenic cholangitis or parasitic infection. Secondary CBD stones are far more common, are due to stones in the gallbladder passing through the cystic duct into the CBD, and are the most common cause of CBD stones in Western countries.

Laboratory Studies for Suspected Choledocholithiasis

Serum liver enzymes, bilirubin, and alkaline phosphatase are often elevated in patients with obstructing CBD stones; however, the best biochemical test to predict CBD stones has been the subject of some debate. Elevated bilirubin has been shown to have a sensitivity and a specificity for CBD stones of 69% and 88%, respectively, by meta-analysis, and an elevated bilirubin greater than 30 µmol/L is an independent predictor of CBD stones. Moreover, biochemical predictors of CBD stones are stronger when combined with imaging and patient factors, including age over 55, CBD dilatation greater than 6 mm, and bile duct stones or sludge seen on a sonogram. For ruling out CBD stones, a normal β-glutamyl transpeptidase (GGT) has the highest negative predictive value (97.9%).
In summary, biochemical markers have high yield for ruling out CBD stones, with a normal GGT having the highest negative predictive value. However, elevated biochemical markers alone do not necessarily predict persistent CBD stones and are better combined with other modalities to avoid unnecessary invasive tests such as endoscopic retrograde cholangiopancreatography (ERCP) or CBD exploration.

**IMAGING STUDIES**

Numerous imaging studies can be used to diagnose CBD stones, including transabdominal ultrasonography (TUS), endoscopic ultrasonography (EUS), magnetic resonance cholangiopancreatography (MRCP), ERCP, intraoperative cholangiography (IOC) or intraoperative ultrasonography, abdominal CT, and percutaneous transhepatic cholangiography (PTC).

**Transabdominal Ultrasonography**

TUS is by far the most common primary imaging modality used to evaluate patients for CBD stones as it is readily available and noninvasive and can even be performed at the bedside if necessary. However, limitations of TUS include operator dependence, decreased sensitivity with increasing thickness of the abdominal wall, and difficulty in visualizing the distal CBD due to frequent obfuscation by bowel gas, although variations in technique can improve diagnostic yield. Reported sensitivity of TUS in detecting CBD stones ranges from 18% to 74%, and may depend greatly on equipment, patient factors, and operator experience. A prospective study of diagnostic accuracy of TUS for CBD stones by operator experience found that high-resolution TUS in experienced hands had an accuracy of 83% versus 64% when the operator was relatively inexperienced, highlighting the significance of operator skill in interpreting TUS results.

Although TUS can identify CBD stones, it is less sensitive than other imaging modalities (such as MRCP or diagnostic ERCP). A prospective study of 191 patients with suspected CBD stones referred for ERCP found that ultrasonography had a sensitivity of only 38%, compared with 91% for MRCP when cholangiography was used as the gold standard. However, ultrasonography was shown to have a specificity of 100% for CBD stones.

In summary, TUS is a good initial test for CBD stones when they are suspected and confirms the diagnosis when a stone is visualized, eliminating the need for further investigations with more costly and/or invasive diagnostic modalities such as MRCP and EUS. However, TUS is not therapeutic, and if stones are identified, ERCP, CBD exploration, or other invasive modalities are necessary for stone removal. In addition, a negative transabdominal sonogram does not rule out CBD stones with great accuracy, and further investigations should be done if the clinical suspicion is high.

**Endoscopic Ultrasonography**

EUS overcomes many of the limitations of TUS in that the probe is in closer proximity to the CBD compared with the transabdominal approach. However, this technique is invasive and requires specialized equipment and operator skill, which are not always readily available. In comparison with ERCP, however, EUS has the advantage of avoiding biliary instrumentation and thus avoids the potential risks of pancreatitis, bleeding, and CBD perforation.

Despite its limitations, the diagnostic accuracy of EUS for CBD stones is considerably higher than that of TUS, with reported sensitivities of 80 to 100% and specificities of 50 to 99%, although it has not been shown to significantly improve diagnostic yield over MRCP. Furthermore, EUS seems to offer equivalent specificity and increased sensitivity to CBD stones as ERCP while avoiding unnecessary bile duct cannulation.

**Magnetic Resonance Cholangiopancreatography**

As described above, MRCP has good sensitivity and specificity for detecting CBD stones, with sensitivity of 93% and specificity of 94%. It is advantageous in that it is a noninvasive test; however, it may be less accurate in diagnosing stones less than 6 mm in size in comparison with direct cholangiography, is time consuming, cannot be provided at the bedside, and is not always readily available. Furthermore, MRCP cannot be used in patients with contraindications to MRI, such as pacemakers and other embedded metal hardware incompatible with use in magnetic fields, and, if positive, does not provide the option for intervention as ERCP does.

MRCP and EUS have essentially equivalent performance in the diagnosis of cholecodocholithiasis compared with ERCP but are less invasive and avoid the risks of unnecessary bile duct cannulation. EUS may still have greater sensitivity to detect small stones and biliary sludge compared with MRCP but requires sedation and remains a somewhat invasive test. The selection of MRCP versus EUS as first-line imaging to diagnose cholelithiasis when TUS and biochemical studies suggest (but fail to confirm) a stone depends on the availability of resources and expertise, patient factors, and clinician preference. EUS should be considered an adjunct to MRCP when there is high clinical suspicion of biliary obstruction but MRCP fails to identify a cause.
Laparoscopic Intraoperative Ultrasonography

Laparoscopic ultrasonography (LUS) of the CBD has been proposed as an alternative to IOC for patients suspected of having CBD stones. An ultrasound probe is passed through a 10 to 12 mm trocar and is used to assess the CBD during laparoscopic cholecystectomy. The procedure is attractive as it obviates the risks of ionizing radiation, it avoids the need for cannulation of the biliary system, contrast agents are unnecessary, significantly less time is required, and disposable cholangiogram catheters are not needed. However, it is very operator dependent and requires specialized skills and equipment. In experienced hands, LUS can have sensitivity and specificity of up to 95 and 100%, respectively.\(^{36-38}\) One limitation of LUS is that, unlike cholangiography, it does not provide an anatomic map of the biliary tree.

Cholangiography

Direct cholangiography remains the gold standard for diagnosis of choledocholithiasis, although the invasiveness of such tests has limited their use when EUS and MRCP are available and able to rule out choledocholithiasis. Three techniques of cholangiography are well established: ERCP, PTC, and IOC.

Endoscopic Retrograde Cholangiopancreatography

ERCP requires endoscopic cannulation of the CBD under fluoroscopic guidance [see Figure 5]. It was previously the test of choice for CBD stones as it was both diagnostic and therapeutic and offered high sensitivity and specificity. However, EUS and MRCP have since replaced ERCP for first-line diagnostic biliary imaging due to their lower complication rates and equivalent diagnostic accuracy. Rates of ERCP complications were comprehensively reviewed in a systematic review of 21 studies including 16,855 patients. This study reported an overall complication rate of 6.85% and the following rates of individual complications: pancreatitis, 3.47%; bleeding, 1.34%; perforation, 0.6%; and mortality, 0.33%.\(^{39}\) Although the majority of events were of mild to moderate severity, ERCP remains a procedure with a significant complication rate, and care should be taken to limit this test to situations in which other modalities are unavailable and in patients who are most likely to experience benefit. Currently, ERCP remains useful as a first-line diagnostic test in patients with equivocal TUS, in patients with contraindication to MRCP, when EUS expertise or equipment are unavailable, or in patients at high risk for having CBD stones in whom therapeutic ERCP will most likely be necessary.

Percutaneous Transhepatic Cholangiography

PTC is done by cannulating the biliary tree within the liver under imaging guidance. These tests are usually limited to patients who cannot have ERCP for technical or anatomic reasons (e.g., patients with Roux-en-Y gastrojejunostomy) and when EUS, MRCP, and IOC are either unavailable or contraindicated. PTC is an invasive test and carries the risk of serious complications, such as severe hemobilia and CBD injury.\(^{40}\) Due to these risks and the availability of less invasive tests, PTC is largely reserved for emergent biliary decompression when other modalities fail and is rarely the diagnostic procedure of choice or first choice of treatment for CBD stones.

Intraoperative Cholangiography

In some institutions, IOC is done routinely in all patients undergoing cholecystectomy [see Figure 6]; however, in many centers, this practice has been largely replaced by a selective approach to IOC for patients at intermediate risk for CBD stones. A large series of 1,171 patients who underwent IOC found this test to have a sensitivity of 97% and a specificity of 99% when validated against the patient’s postoperative course, and IOC added an average of 16 minutes to the surgical time.\(^{41}\) However, IOC exposes the surgical team to ionizing radiation and may not be possible in some cases due to inability to cannulate the cystic duct as a result of inflammation, stones, angulation, or stenosis. It has been reported to be a rare cause of CBD injury.
TREATMENT

Once CBD stones are identified or if the operating surgeon has high suspicion, several treatment options exist for removal. These include endoscopic approaches of ERCP and sphincterotomy and surgical extraction of stones by direct cholecdocholeotomy or via the cystic duct. Each treatment option has its own efficacy and risk profile, and patients should undergo careful selection for the appropriate treatment option.

Risk Stratification and Patient Selection

Identification and risk stratification of patients suspected of having CBD stones are necessary to plan investigations and interventions. Although no consensus exists, several models have been suggested. In 1994, Barkun and colleagues used multiple regression analysis to identify factors that were independent predictors of choledocholithiasis and proposed a model that they then prospectively validated.21 They found four factors (age > 55, bilirubin > 30 µmol/L, CBD dilatation > 6 mm, and visible CBD stone on a transabdominal sonogram), which together conferred a 94% risk of CBD stones, compared with an 18% risk when all were absent, regardless of other biochemical or clinical findings. Liu and colleagues proposed a four-group stratification system from very high to low risk based on ultrasonography and clinical and biochemical markers,42 although the groupings have not been validated. More recently, the American Society for Gastrointestinal Endoscopy (ASGE) proposed a risk stratification system for patients suspected of having CBD stones.43 This included very strong predictors: CBD stone on a transabdominal sonogram, clinical cholangitis, and an elevated serum bilirubin level greater than 68 µmol/L. Strong predictors included a dilated CBD greater than 6 mm with gallbladder in situ and serum bilirubin of 31 to 68 µmol/L. Moderate predictors were abnormal liver chemistry other than bilirubin, age over 55, and clinical gallstone pancreatitis. Patients with none of these findings are considered to be at low risk [see Table 2].

In general, low-risk patients with normal biochemistry and ultrasound findings and no symptoms of CBD obstruction do not warrant further investigation; IOC is not routinely done in these cases. High-risk patients are referred for ERCP directly or undergo IOC and, when appropriate, intraoperative bile duct exploration. Moderate-risk patients require further investigation before determining the management course. At our institution, where EUS and MRCP are readily available and reliable, intermediate-risk patients are often referred for these investigations first. If these are inconclusive or unavailable due to circumstantial or patient factors, IOC is performed at the time of laparoscopic cholecystectomy. Otherwise, patients with normal EUS or MRCP are managed clinically without further CBD exploration or imaging, and those with positive studies undergo preoperative CBD clearance, usually by ERCP. At some institutions, IOC with laparoscopic CBD exploration if stones are identified has become the procedure of choice. These approaches are equally efficacious in the treatment of CBD stones, and the choice of procedure depends on local expertise.

Endoscopic Retrograde Cholangiopancreatography and Sphincterotomy

ERCP with sphincterotomy is commonly used for management of choledocholithiasis. In many centers, this technique has largely replaced open common bile duct exploration (OCBDE) in the era of minimally invasive approaches to biliary disease44 [see Figure 7]; however, laparoscopic common bile duct exploration (LCBDE) is being increasingly practiced as surgical expertise in this procedure increases, and the choice between ERCP or LCBDE depends on local expertise. The success rate of ERCP for CBD clearance is reported to be as high as 96%, regardless of whether sphincterotomy or papillary balloon dilatation is used.45 ERCP is, however, associated with some risks, most notably

| Very strong |
| CBD stone on U/S |
| Clinical cholangitis |
| Bilirubin > 68 µmol/L |

| Strong |
| Dilated CBD (> 6 mm if gallbladder in situ) |
| Bilirubin 31–68 µmol/L |

| Moderate |
| Abnormal liver tests other than bilirubin |
| Age > 55 |
| Clinical gallstone pancreatitis |

CBD = common bile duct; U/S = ultrasonography.
The risk of CBD stones is high in the presence of any very strong predictor or both strong predictors, low if no predictors are present, and intermediate for all other patients.

Table 2 Predictors of Choledocholithiasis43

Scientific American Surgery
acute pancreatitis, hemobilia (1.3%), and duodenal perforation (0.1 to 0.6%). In a large meta-analysis of 21 studies, the rate of postprocedure pancreatitis was 3.5%; however, this varies widely from 1.6 to 15.7%, likely due in part to variations in diagnosis and reporting. Known risk factors for post-ERCP pancreatitis include young age, suspected sphincter of Oddi dysfunction, pancreatic sphincterotomy and duct injection, normal bilirubin, balloon dilatation of biliary sphincter, and previous post-ERCP pancreatitis. Due to the risks of such complications, the use of ERCP as a diagnostic tool has largely been supplanted by less invasive measures, such as MRCP and EUS. However, it still plays a valuable role as a therapeutic tool for CBD clearance. ERCP is also used in the postoperative setting for stones identified during IOC or in patients who present with retained CBD stones after cholecystectomy.

Transcystic and Laparoscopic Common Bile Duct Exploration

Transcystic and laparoscopic CBD exploration are advanced laparoscopic techniques for CBD clearance at the time of cholecystectomy. This approach is increasingly practiced as skills in advanced laparoscopy have become more common. There are some data to suggest that this approach is more cost effective with shorter lengths of stay than laparoscopic cholecystectomy with routine perioperative ERCP, although other studies support the cost-effectiveness of ERCP over LCBDE. Transcystic CBD clearance is the preferred technique if the stones are small (< 10 mm) and located distal to the cystic duct–bile duct junction. Surgical CBD clearance is guided by imaging using fluoroscopy or choledochoscopy and is achieved usually by retrieving the stones with a wire basket and/or flushing of the CBD until complete clearance is achieved. In a large series of 372 patients with choledocholithiasis undergoing laparoscopic cholecystectomy, 77% of patients successfully underwent duct clearance by the transcystic approach, highlighting the high success rate of this technique. The transcystic approach to duct clearance also has several advantages over choledochotomy in that it is technically less challenging and avoids portal dissection, T tube insertion, and complications of choledochotomy such as stricture and bile leakage. The cystic duct must be dilated to the diameter of the largest stone to avoid basket impaction. The limitations of the transcystic approach include difficulty in reaching proximal stones and access issues in the case of small or obliterated cystic ducts. In cases of an unsuccessful transcystic approach, options include laparoscopic or open CBD exploration by choledochotomy or postoperative ERCP.

LCBDE is considerably more challenging than the transcystic approach as it requires laparoscopic suturing skills.

Figure 7 Endoscopic view of the ampulla of Vater showing a large, incarcerated stone in the common bile duct.
and dissection of the CBD. A dilated CBD facilitates the success of this procedure. In experienced hands, a large meta-analysis of five randomized controlled trials of LCBDE versus ERCP found that the laparoscopic approach was as efficient in achieving duct clearance, with no increased morbidity or mortality. Moreover, the laparoscopic approach was found to result in reduced length of stay and fewer overall procedures when compared with either pre- or postoperative ERCP.\(^{44}\) When experience permits, patients with intraoperatively discovered CBD stones not amenable to transcystic retrieval should preferentially undergo LCBDE versus postoperative ERCP.

Another option, when transcystic duct clearance fails, is intraoperative ERCP. This approach was found by a meta-analysis of nine studies to be as effective as LCBDE or postoperative ERCP.\(^{54}\) However, coordination of surgical and endoscopy personnel limits the practicality of this approach.

**Laparoendoscopic Rendezvous Procedure**

Frequently, patients with choledocholithiasis are treated in a two-stage manner: preoperative ERCP followed by laparoscopic cholecystectomy. Pancreatitis after ERCP in this setting is a possible complication. Moreover, patients have to undergo two procedures in this treatment model. To combat these limitations, a single-stage combined laparoscopic and endoscopic procedure known as the “rendezvous” technique has been developed in which a guide wire is advanced through the cystic duct as in IOC and is snared by an endoscope in the duodenum. The guide wire is then used to guide direct cannulation of the bile duct, and endoscopic sphincterotomy and duct clearance are performed as usual. The cholecystectomy is completed laparoscopically in the same sitting.

A recent systematic review analyzed the results of four randomized controlled trials comparing the two-stage versus the rendezvous procedure for endoscopic CBD clearance and cholecystectomy in 430 patients. The review found a decreased rate of overall complications (odds ratio [OR] 0.56, \(p = .04\)) and a lower pancreatitis rate (2.4% versus 8.4%, OR 0.33, \(p = .03\)) for the rendezvous patients compared with those undergoing two-stage treatment. Moreover, two of the included studies demonstrated a reduced length of stay for patients undergoing the one-stage procedure.\(^{55}\) Significant limitations of this approach are the necessity of coordinating two procedural teams and difficulties in patient positioning to accommodate both techniques. As a result, there has been limited use of this approach despite data suggesting that it may be preferable to a two-stage procedure. Further data are needed in this area, specifically comparing this approach with laparoscopic techniques to achieve duct clearance at the time of cholecystectomy.

**Open Common Bile Duct Exploration**

OCBDE was the procedure of choice for duct clearance before the era of ERCP and laparoscopic cholecystectomy. Several randomized controlled trials have compared OCBDE with ERCP and were the subject of a recent Cochrane review.\(^{44}\) Of the five randomized controlled trials included in the review, all of which were published in 1998 or earlier, there was no difference in morbidity between the surgical and endoscopic groups and a trend toward a higher mortality rate in the ERCP group, although this did not reach statistical significance (OR 2.01; \(p = .24\)). ERCP patients also underwent 0.62 more procedures on average than surgical patients (\(p = .009\)). Despite these findings, no recent randomized controlled trials of OCBDE versus ERCP have been reported in the modern era. In the era of minimally invasive approaches to biliary disease, no such trial will likely ever be completed. As such, despite older studies supporting OCBDE over ERCP, ERCP is presently practiced much more commonly than OCBDE due to the less invasive nature of this technique; OCBDE is now reserved for patients for whom ERCP and/or LCBDE is unavailable.

**Special Considerations**

**Inaccessible Papillae**

Patients with altered anatomy, such as after gastrectomy with Billroth II or gastric bypass Roux-en-Y reconstruction, present difficulties for cannulation of the papilla of Vater by standard endoscopy techniques. CBD stones in these patients pose significant management challenges and either warrant surgical CBD exploration (either open or laparoscopic, depending on the expertise available) or access via alternative techniques. Percutaneous transhepatic stone retrieval has been described with some success, although specialized equipment and expertise are required.\(^{56,57}\) An alternative that has been described for patients after gastric bypass surgery is transgastric ERCP via gastrotomy through the gastric remnant. This approach has been described with good success, although the results are limited to case series and animal studies.\(^{58–60}\)

**Cholecystectomy Deferral after Sphincterotomy**

Patients who have undergone duct clearance for choledocholithiasis are currently advised to undergo laparoscopic cholecystectomy to prevent further complications of gallstones. However, in patients who have undergone sphincterotomy and have otherwise asymptomatic gallstones, the necessity of cholecystectomy has been challenged. A recent Cochrane review of this issue found five randomized controlled trials that met their inclusion criteria for analysis. In the pooled data, patients who underwent a wait-and-see approach had higher mortality (relative risk [RR] 1.78, \(p = .010\)), more recurrent biliary pain (RR 14.56, \(p < .0001\)) or jaundice or cholangitis (RR 2.53, \(p = .03\)), and a greater need for repeat ERCP or cholangiography (RR 2.36, \(p = .005\)). Due to the clear improvement in outcomes with cholecystectomy versus leaving the gallbladder in situ, patients in this scenario should generally be offered surgery as soon as possible, ideally during the same hospitalization. However, the elderly and infirm patients who present a high surgical risk pose a difficult treatment challenge and should be treated on a case-by-case basis.

**Lithotripsy Techniques**

In rare cases, large and impacted CBD stones provide therapeutic challenges. The strategy to manage these unusual problems is to try to fragment the large stone into multiple smaller components that can then be removed using conventional baskets. Lithotripsy techniques can be
carried out using extracorporeal techniques, analogous to those used widely to manage urinary stones, or by intracorporeal methods under endoscopic guidance.

Extracorporeal shock wave lithotripsy (ESWL) involves stone fragmentation using shock waves directed by fluoroscopy or ultrasonography. Complete stone clearance can be achieved in up to 90% of patients in an average of 1.5 sessions. Reported complications include subcutaneous and biliary bleeding, arrhythmias, and discomfort. Electrohydraulic lithotripsy (EHL) uses a direct choledochoscope with a mother-baby scope technique to generate intraductal shock waves to fragment the stones. Successful duct clearance can be achieved in 90% of cases, with a 9% risk of pancreatitis/cholangitis and a 1% bile leak rate. Finally, laser lithotripsy uses laser light and a mother-baby scope technique to generate a shock wave at the stone surface. Effective fragmentation can be achieved in 92% of cases, with the majority requiring only one session. Reported complications, including biliary bleeding and cholangitis, occur in 7% of cases using this technique. Laser lithotripsy and EHL require two skilled endoscopists, and all require specialized equipment, limiting their universal availability.

**Summary**

Choledocholithiasis is a common problem. Risk stratification and diagnosis rely on the clinical presentation, serum chemistry, and imaging techniques. Multiple imaging modalities are available to visualize stones in the CBD, with varying success rates and applications. Noninvasive imaging modalities have largely supplanted cholangiography for diagnosis due to their high sensitivity and specificity without the risk of complications associated with cannulation of the CBD. Treatment options for choledocholithiasis include surgical, endoscopic, and percutaneous techniques; the choice of duct clearance strategy depends on available resources, expertise, and patient factors [see Figure 8].

**Gallstone Pancreatitis**

**Pathophysiology**

Acute pancreatitis refers to acute inflammation of the pancreas. In the case of gallstone pancreatitis, this is a result of transient obstruction of the pancreatic ductal system by the passage of stones or sludge through the biliary system. The result is intra-acinar cell activation of digestive enzymes leading to local inflammation as well as systemic inflammation mediated by inflammatory cytokines. Gallstones account for 35 to 60% of cases of acute pancreatitis. Mild cases of pancreatitis are characterized by interstitial edema of the pancreas and peripancreatic inflammation and fluid. Severe, or necrotizing, pancreatitis is associated with devitalization of pancreatic tissue, necrosis of the pancreas (acinar cells, islet cells, and/or ductal cells), and variable amounts of pancreatic hemorrhage. Infection of necrotic fatty tissues of the pancreas or surrounding retroperitoneal structures may occur.

**Diagnosis**

Diagnosis and clinical manifestations of acute pancreatitis are covered elsewhere. Attributing the etiology of pancreatitis to gallstones can be challenging. Acute pancreatitis in the presence of gallstones and elevated liver enzymes, especially in the absence of another common etiologic agent, such as alcohol, is suggestive of a biliary etiology. Although liver function may be normal in some patients (15 to 20%) and visualization of the gallbladder and biliary duct system can be challenging in acute pancreatitis due to bowel distention and local inflammation, the presence of elevated liver enzymes and gallstones is 95 to 98% sensitive and 100% specific in diagnosing a biliary etiology of pancreatitis.

**Management Controversies in Gallstone Pancreatitis**

**Endoscopic Retrograde Cholangiopancreatography**

As gallstone pancreatitis results from passage of stones or sludge through the biliary system, biliary obstruction and the need for ERCP must be considered. Pancreatitis is recognized as one of the most common complications of ERCP, but ERCP has proven to be safe in the setting of acute pancreatitis without significant worsening of pancreatitis following the procedure. However, most biliary obstructions in gallstone pancreatitis are transient, calling into question not only the necessity but also the timing of ERCP in this disease.

Recent meta-analyses have concluded that early ERCP (within 72 hours of diagnosis) does not result in improvement in overall complications or mortality in patients with mild or severe pancreatitis and no evidence of cholangitis. Local and pancreatic complications are similarly not reduced by performing early ERCP for patients with mild or severe pancreatitis. However, patients with clinical or biochemical evidence of biliary obstruction and/or cholangitis should undergo ERCP as these patients benefit from decreased systemic and local complications as well as improved mortality (RR 0.2).

**Timing of Operation**

Gallstone pancreatitis is an indication for cholecystectomy; however, the timing of operation must be carefully considered as the potential risk of operative complications due to local inflammation and the risk of recurrent pancreatitis while waiting for interval cholecystectomy must be weighed. It is now accepted practice that laparoscopic cholecystectomy should be performed during the index admission for patients with mild biliary pancreatitis as there is no increase in operative complications, conversion rates, or mortality. Interval cholecystectomy, even as soon as 2 weeks after discharge, is associated with a risk of recurrent biliary complications, including recurrent pancreatitis, biliary colic, and cholecystitis, as high as 30%. The timing of surgery in patients with severe gallstone pancreatitis can be difficult to determine and must be evaluated on a case-by-case basis. Substantial periampullary inflammation and fluid collections may make surgery technically challenging in this patient population. It is advisable to allow these fluid collections to mature or regress prior to surgical intervention. In the event that they do require definitive surgical drainage, it can be done concurrently with cholecystectomy but should occur at least 6 weeks from the onset of pancreatitis in most cases. Furthermore, the patient’s overall condition may not allow for surgery during...

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Figure 8  Treatment algorithm for suspected choledocholithiasis.56 CBD = common bile duct; CBDE = common bile duct exploration; ERCP = endoscopic retrograde cholangiopancreatography; EUS = endoscopic ultrasonography; IOC = intraoperative cholangiography; MRCP = magnetic resonance cholangiopancreatography.

the index admission. Severe gallstone pancreatitis can result in serious systemic illness, organ failure, and prolonged intensive care unit (ICU) admission, which may leave patients significantly debilitated. In cases of severe gallstone pancreatitis, interval cholecystectomy is acceptable and, when combined with endoscopic sphincterotomy, is associated with very low rates of recurrence prior to interval cholecystectomy.77,78

Mirizzi Syndrome and Cholecystobiliary Fistula

**Classification**

Mirizzi syndrome is a chronic complication of gallstone disease with an incidence of 1 to 2% in patients with gallstones. Mirizzi syndrome is more common in females and those with long-standing gallstones (> 30 years). This syndrome occurs when an impacted gallstone in the gallbladder infundibulum causes external compression on the biliary system (typically the CBD), leading to biliary obstruction. Chronically, this may lead to pressure ulceration, erosion, and, subsequently, cholecystobiliary (cholecystocholedochal or cholecystohepatic) fistula. Cholecystobiliary fistula is rare but represents the more severe spectrum of the same disease process as Mirizzi syndrome. Chronic inflammation commonly leads to either obliteration or shortening of the cystic duct. The presentation of Mirizzi syndrome may be acute or chronic. Hyperbilirubinemia is the most common finding. In the acute setting, the patient may present with jaundice, acute cholecystitis, acute cholangitis, or acute pancreatitis. In the chronic setting, there is typically a history of vague pain accompanied by episodic jaundice.79
Several classifications of Mirizzi syndrome have been proposed, but the two most commonly used are those of McSherry and colleagues and Csendes and colleagues. In McSherry and colleagues' classification, compression of the duct and cholecystobiliary fistula is classified as type I and type II, respectively. Csendes and colleagues' classification also classifies extrinsic compression of the duct as type I but divides cholecystobiliary fistula into three different classes based on severity: type II lesions involve erosion of the CBD wall up to one third of its circumference, type III lesions involve erosion of the CBD wall up to two thirds of its circumference; and type IV lesions imply complete destruction of the CBD wall. Type I lesions account for 11 to 45% of cases, whereas Csendes type IV lesions rarely occur (approximately 6% of cases).

IMAGING

As only 54% of patients presenting with Mirizzi syndrome have clinical symptoms, preoperative imaging plays an important role in identifying patients with the syndrome. Furthermore, preoperative diagnosis of Mirizzi syndrome is essential whenever possible due to a high number of bile duct injuries occurring in cases where the pathology was not recognized preoperatively. Ultrasonography may be helpful in making or confirming the diagnosis of Mirizzi syndrome. Typical findings include a shrunken and contracted gallbladder, an impacted gallstone in the gallbladder neck–cystic duct junction, and dilated intrahepatic bile ducts and CBD proximal to the stone with normal ducts distal to the impacted stone. Although these findings are classic, they are visualized only in a minority of patients presenting with the syndrome. MRCP is a high-resolution imaging tool that can help delineate the often complex biliary anatomy in these patients [see Figure 9]. CT shows similar findings and offers little advantage over ultrasonography in diagnosis other than excluding malignancy in cases where there is diagnostic uncertainty.

ERCP is an important tool in the diagnosis of Mirizzi syndrome and in evaluating the presence of a cholecystobiliary fistula; it should be performed preoperatively in all patients with confirmed or suspected Mirizzi syndrome. Preoperative imaging aids in operative planning may impact the planned procedure and can provide an anatomic roadmap for the surgeon of what to expect in the operating room. In patients with jaundice, ERCP also permits decompression of the biliary tree, and in some cases, stone retrieval may be possible. In patients where ERCP is not possible, or in cases of technical failure, PTC is also effective in demonstrating the relevant anatomy. Increasingly, MRCP is being used in the workup and diagnosis of Mirizzi syndrome but lacks the interventional capabilities of ERCP.

TREATMENT

Surgery for gallstone disease in the presence of Mirizzi syndrome can be challenging due to inflammation and fibrosis in the areas as well as the distorted anatomy. The use of laparoscopy remains controversial, with many surgeons favoring an open surgical approach. Attempts at laparoscopic surgery carry an estimated conversion rate of more than 40%. In a recent systematic review by Antoniou and colleagues, the most common reasons for conversion include adhesions in the Calot triangle (41%), uncertain or abnormal biliary anatomy (32%), and unsuccessful stone retrieval (14%). When the diagnosis of Mirizzi syndrome is identified preoperatively, conversion rates are significantly lower (26% versus 55%), reinforcing the importance of preoperative diagnosis. Complication rates from laparoscopic and open surgery appear to be similar, with an overall complication rate of 16% and significant rates of bile duct injury (4%), residual stone (4%), and postoperative bile leak (2.4%).

The surgical approach requires incision of the gallbladder fundus and removal of the impacted stone prior to beginning the cholecystectomy. Many experts advocate partial cholecystectomy for type I lesions to avoid dissection in the area of inflamed and potentially distorted triangle of Calot. In type II lesions, bilioenteric bypass is typically required following gallbladder removal to deal with the cholecystobiliary fistula. Bile duct exploration may be required. Other techniques of dealing with the CBD fistula have been suggested, such as primary repair when possible, drainage of the fistula with a T tube, or choledochoplasty.

Gallstone Ileus

Gallstone ileus accounts for 1 to 3% of mechanical small bowel obstructions and occurs most commonly in elderly patients (mean age 65 to 75) and women (3 to 16:1). The estimated mortality of this uncommon problem remains high at 15 to 18%; however, this is mostly accounted for by the advanced age of and multiple comorbidities in these patients.

Figure 9 Magnetic resonance cholangiopancreatogram showing a large gallstone causing Mirizzi syndrome.
complete) due to an impacted gallstone in the small bowel. The gallstone enters the intestines via a cholecystoenteric fistula typically involving the duodenum but may involve the stomach, colon, or small bowel. Cholecystoenteric fistula typically results after an episode of acute cholecystitis, leading to inflammation and adhesions that allow erosion of the gallstone into the bowel. Small stones (< 2.5 cm) typically pass through the bowel without ill effects. Stones larger than 2.5 cm have the potential to cause gallstone ileus, with the most common sites of obstruction being the terminal ileum and ileocecal valve. Rarely, gastric outlet obstruction can occur as a result of large stones eroding into the stomach through a cholecystogastric fistula.

**DIAGNOSIS**

Signs and symptoms of gallstone ileus may be nonspecific and usually are those consistent with small bowel obstruction. Patients may present with a prolonged clinical course (several days) and may describe episodic pain and obstructive symptoms secondary to “tumbling” of the stone and intermittent obstruction. Due to the nonspecific nature of symptoms in gallstone ileus, only 20 to 50% of patients have a correct preoperative diagnosis. Classic imaging findings on a plain x-ray are known as the Rigler triad and include bowel obstruction, a gallstone visualized in the intestines, and pneumobilia [see Figure 10]. However, the complete triad is seen in less than 35% of plain films belonging to patients presenting with the condition. CT is the diagnostic test of choice for gallstone ileus, with a sensitivity of more than 90%. CT evidence of gallstone ileus includes visible gallstone at the transition point of a partial or complete bowel obstruction, pneumobilia, and inflammation in the area of the cholecystoenteric fistula.

**TREATMENT**

The primary goal of treatment in gallstone ileus is to relieve the acute intestinal obstruction. Enterolitotomy is performed by creating an enterotomy proximal to the stone to allow for its removal and relief of the obstruction [see Figure 11]. The entire small bowel should be examined to ensure that no other stones are present. Consideration may be given to performing the procedure laparoscopically in highly selected patients deemed reasonable candidates (they can tolerate pneumoperitoneum; the bowel is minimally distended) and the surgeon has adequate laparoscopic skills and comfort running the bowel and performing and closing an enterotomy. Given the age and comorbidity of most patients presenting with this condition, adding operative time and complexity to the procedure must be considered carefully.

Whether or not the cholecystoenteric fistula should be addressed at the time of surgery for gallstone ileus is an important question. Performing cholecystectomy and addressing the enteric fistula in the presence of acute inflammation are likely to be a very challenging procedure fraught with the risk of complications. In their review of more than 1,000 cases of gallstone ileus, Reisner and Cohen found that addressing only the obstruction with enterolitotomy had a significantly lower mortality compared with a combined procedure that involved closure of the cholecystoenteric fistula. Furthermore, the incidence of gallstone complications following enterolitotomy was low; recurrence of gallstone ileus occurred in less than 5% of patients, and only 10% of patients went on to require cholecystectomy for biliary symptoms. As such, simple enterolitotomy is the procedure of choice for gallstone ileus. Only in rare patients should a combined procedure be considered. These include intraoperative findings of a very severely inflamed gallbladder or gangrenous cholecystitis.

**Acute Acalculous Cholecystitis**

Acute acalculous cholecystitis is characterized by acute inflammation of the gallbladder in the absence of gallstones and represents about 10% of cases of acute cholecystitis. Acute acalculous cholecystitis typically occurs in patients who are critically ill; inflammation of the gallbladder is presumed to be secondary to a combination of biliary stasis and ischemia. The most common risk factor associated with acalculous cholecystitis is critical illness requiring ICU admission; an estimated 0.2 to 0.4% of ICU patients develop
Acalculous cholecystitis. Other risk factors include trauma, recent surgery (especially cardiac or gastrointestinal), sepsis, burn victims, total parenteral nutrition (TPN), and prolonged fasting. A number of infectious agents have been linked to acalculous cholecystitis, including brucellosis, leptospirosis, tuberculosis, salmonellosis, cholera, Q fever, disseminated candidiasis, cytomegalovirus, and Epstein-Barr virus. Acalculous cholecystitis in outpatients may be related to risk factors such as HIV, posttransplantation immunosuppression, congestive heart failure, diabetes mellitus, and various vasculitides. In rare circumstances, biliary obstruction due to ascariasis or Echinococcus infection, ampullary stenosis, or hemobilia may predispose to acalculous cholecystitis. Patient demographics differ from those associated with calculous acute cholecystitis; acalculous cholecystitis occurs more commonly in men (ratio 2 to 3:1) and in older patients.

In contrast to calculous cholecystitis, acute acalculous cholecystitis is associated with a high mortality. The estimated mortality is 21 to 30%, but this high incidence is mostly related to the underlying critical illness, with sepsis from acalculous cholecystitis being a contributing factor. Complications of acalculous cholecystitis are common, including gangrene (50%), perforation (10%), and gallbladder empyema. Overall, approximately 40% of critically ill patients with acalculous cholecystitis have a gallbladder-related complication, and these patients have an increased mortality. Outpatients who present with acalculous cholecystitis (typically those patients with diabetes, vascular disease, etc.) represent a different patient population altogether. With timely diagnosis and prompt cholecystectomy, these patients have a very good prognosis and mortality is rare.

CLINICAL PRESENTATION

The diagnosis of acalculous cholecystitis can be challenging. Signs and symptoms can be nonspecific and include abdominal pain, fever, leukocytosis, abnormal liver enzymes, and sepsis. In critically ill patients, these nonspecific signs and symptoms are confounded by the concomitant illness and the fact that patients are frequently intubated, sedated, and unable to provide a description of symptoms. Delays in the diagnosis of acalculous cholecystitis may account for some of the high incidence of gallbladder gangrene associated with this condition. A high index of suspicion must be maintained in any critically ill patient with unexplained sepsis or clinical deterioration.

IMAGING

Ultrasound findings of acalculous cholecystitis include a thickened gallbladder wall, pericholecystic fluid or edema,
a distended gallbladder, and, less commonly, intramural or intraluminal gas. Ultrasonography has the advantage of being portable, allowing for rapid bedside evaluation of critically ill patients. Despite being highly specific (> 90%), the sensitivity of ultrasonography is generally low, with estimates ranging from 20 to 50%. The benefit of ultrasonography therefore may lie in identifying those patients with normal findings in whom acalculous cholecystitis can effectively be ruled out.\(^9\) If acute acalculous cholecystitis is suspected, percutaneous aspiration of the gallbladder contents can decompress the gallbladder and provide fluid for cell count, Gram stain, and bacteriology.

CT can be helpful in the diagnosis of acalculous cholecystitis, but the sensitivity and specificity are similar to those for ultrasonography. CT has the added disadvantages of requiring patient transport and involves radiation and contrast exposure. As such, the main value of CT lies in patients with diagnostic uncertainty or those for whom alternate intra-abdominal sources of sepsis are being considered.\(^9\)\(^9\)

Cholescintigraphy (HIDA scanning) has better sensitivity (67 to 100%) than ultrasonography or CT. The specificity is estimated to be high as well. False positives may occur and are usually due to severe bile stasis that accompanies critical illness, prolonged fasting, and/or TPN use. Such significant bile stasis prevents uptake of the radioactive tracer, resulting in a falsely positive test. Performing HIDA scanning requires not only patient transport but also anywhere from 1 to 6 hours to complete the evaluation. In the critically ill patient population, this is a serious limitation of the test. In outpatients who present with acalculous cholecystitis, HIDA scanning is a good diagnostic test.\(^9\)\(^0\)

Finally, the use of laparoscopy has been described in the diagnosis of acalculous cholecystitis. In patients who can tolerate pneumoperitoneum, bedside laparoscopy can be performed in the ICU and provides a high degree of diagnostic accuracy. Given the equipment requirements of diagnostic laparoscopy and the generally very fragile state of patients with acalculous cholecystitis, alternative means of diagnosis are generally preferred.\(^9\)\(^0\)\(^2\) In the event of positive findings, further intervention, such as laparoscopic choledochotomy or laparoscopic cholecystostomy tube placement (if the patient can tolerate surgery), is best carried out in the operating room.

**TREATMENT**

In patients who are fit to undergo surgery (including those who present with outpatient acalculous cholecystitis), laparoscopic cholecystectomy is the treatment of choice. However, the majority of patients with acalculous cholecystitis present excessively high surgical risks due to their underlying illness, recent trauma, etc. As such, alternative measures of management are usually undertaken. Given the high incidence of gallbladder-related complications, such as gangrene and perforation, as well as the difficulty of evaluating evolution of the disease in this fragile population, early cholecystostomy is recommended. A cholecystostomy tube can be placed at the bedside under ultrasound guidance, and the majority of patients improve following tube placement. If the patient fails to improve within 24 hours, displacement of the cholecystostomy tube, frank gangrene of the gallbladder, or free perforation should be suspected.

A contrast radiograph through the tube can provide useful information. In patients with suspected gangrene, especially in the presence of free extravasation of contrast, cholecystostomy is not sufficient treatment, and cholecystectomy, despite the high risks, is required to control sepsis. In those who do not improve following tube placement, the diagnosis should be reconsidered, especially if the contrast study shows good positioning of the tube, no leak, and good drainage. After successful drainage, the cholecystostomy tube should be left in place for 3 weeks to allow for a mature track to form, especially if the tube was placed into the gallbladder transperitoneally. When access to the gallbladder is obtained through the liver, the tube can be removed once the patient has recovered. In most critically ill patients, in the absence of gallstones, no further treatment is required. This is in contrast to patients who have cholecystostomy tubes placed for calculous cholecystitis. The latter group have a high risk of recurrent symptoms and should have their gallbladders removed if they are fit for surgery once they have recovered from critical illness.\(^9\)\(^0\)

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