Choledocholithiasis: Clinical manifestations, diagnosis, and management

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Literature review current through: **Sep 2023.**
This topic last updated: **Feb 28, 2023.**

INTRODUCTION

Choledocholithiasis refers to the presence of gallstones within the common bile duct. This topic will review the clinical manifestations and diagnosis of choledocholithiasis. The treatment of choledocholithiasis, as well as the epidemiology and the general management of patients with gallstones, are discussed separately:

- (See "Endoscopic management of bile duct stones".)
- (See "Gallstones: Epidemiology, risk factors and prevention".)
- (See "Approach to the management of gallstones".)
- (See "Overview of gallstone disease in adults".)
- (See "Overview of nonsurgical management of gallbladder stones".)

EPIDEMIOLOGY

According to the National Health and Nutrition Examination Survey (NHANES III), over 20 million Americans are estimated to have gallbladder disease (defined as the presence of gallstones on transabdominal ultrasound or a history of cholecystectomy) [1,2]. Cholelithiasis and cholecystitis are responsible for over 1.4 million annual emergency department visits in the United States [3]. Approximately 10 to 15 percent of individuals with gallstones will develop symptomatic gallstone disease over the course of a decade [4]. It has been estimated that 5 to

20 percent of patients have choledocholithiasis at the time of cholecystectomy, with the incidence increasing with age [5-11]. Of those with symptomatic gallstones, 10 percent will also have choledocholithiasis and this number increases to 15 percent when patients are presenting with acute cholecystitis [12].

ETIOLOGY

Primary choledocholithiasis (ie, formation of stones within the common bile duct) typically occurs in the setting of bile stasis (eg, patients with cystic fibrosis), resulting in a higher propensity for intraductal stone formation. Older adults with large bile ducts and periampullary diverticular are also at elevated risk for the formation of primary bile duct stones. Patients with recurrent or persistent infection involving the biliary system frequently form bile duct stones, a phenomenon seen most commonly in populations from East Asia. Other causes include ischemia due to hepatic artery injury, which may occur post-liver transplant. The causes of primary choledocholithiasis often affect the biliary tract diffusely, so patients may have both extrahepatic and intrahepatic biliary stones. Intrahepatic stones may be complicated by recurrent pyogenic cholangitis. (See "Recurrent pyogenic cholangitis".)

Secondary choledocholithiasis results from the passage of gallstones from the gallbladder into the common bile duct. In Western countries, most cases of choledocholithiasis are secondary to gallbladder stones.

CLINICAL MANIFESTATIONS

Patients with choledocholithiasis typically present with biliary-type pain and laboratory testing that reveals a cholestatic pattern of liver test abnormalities (ie, elevated bilirubin and alkaline phosphatase). Patients with uncomplicated choledocholithiasis are typically afebrile and have a normal complete blood count and pancreatic enzyme levels. Occasionally, patients are asymptomatic. In such patients, the diagnosis may be suspected because of abnormal liver blood tests, abnormalities seen on imaging studies obtained for unrelated reasons, or when an intraoperative cholangiogram obtained during cholecystectomy suggests the presence of a common bile duct (CBD) stone. (See "Approach to the patient with abnormal liver biochemical and function tests", section on 'Patterns of liver test abnormalities'.)

Complications of choledocholithiasis include acute pancreatitis and acute cholangitis. Patients with acute pancreatitis typically have elevated serum pancreatic enzyme levels, and patients with acute cholangitis are often febrile with a leukocytosis. Rarely, patients with long-standing biliary obstruction develop secondary biliary cirrhosis. (See 'Complicated choledocholithiasis' below.)

Uncomplicated choledocholithiasis

Symptoms — Most patients with choledocholithiasis are symptomatic, although occasional patients are asymptomatic. Symptoms associated with choledocholithiasis include right upper quadrant or epigastric pain, nausea, and vomiting. The pain is often more prolonged than is seen with typical biliary colic (which typically resolves within six hours). (See "Overview of gallstone disease in adults", section on 'Biliary colic'.)

The pain from choledocholithiasis resolves when the stone either passes spontaneously or is removed. Some patients have intermittent pain due to transient blockage of the CBD. Transient blockage occurs when there is retention and floating of stones or debris within the bile duct, a phenomenon referred to as a "ball-valve" effect.

Physical examination — On physical examination, patients with choledocholithiasis often have right upper quadrant or epigastric tenderness. Patients may also appear jaundiced. Courvoisier's sign (a palpable gallbladder on physical examination) may be seen when gallbladder dilation develops because of an obstruction of the CBD. It is more often associated with malignant CBD obstruction, but has been reported with choledocholithiasis [13].

Laboratory tests — Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations are typically elevated early in the course of biliary obstruction, sometimes dramatically. Later, liver tests are typically elevated in a cholestatic pattern, with increases in serum bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase (GGT) exceeding the elevations in serum ALT and AST. (See "Approach to the patient with abnormal liver biochemical and function tests", section on 'Patterns of liver test abnormalities'.)

Since liver tests may be elevated due to a wide variety of etiologies, the positive predictive value of elevated liver tests is poor [11,14,15]. On the other hand, the negative predictive value of normal liver tests is high. Thus, normal liver tests play a greater role in excluding choledocholithiasis than elevated liver tests play in diagnosing stones.

Improving liver blood tests combined with symptom resolution suggests that a patient with choledocholithiasis has spontaneously passed the gallstone, although it can occur if a stone ball-valves up into the duct and does not exclude the possibility of more than one stone in the bile duct.

Complicated choledocholithiasis — The two major complications associated with choledocholithiasis are pancreatitis and acute cholangitis.

Acute pancreatitis — In addition to the findings associated with uncomplicated choledocholithiasis, patients with biliary pancreatitis typically present with nausea, vomiting, abdominal pain, elevations in serum amylase and lipase (by definition greater than three times the upper limit of normal), and/or imaging findings suggestive of acute pancreatitis. (See "Clinical manifestations and diagnosis of acute pancreatitis", section on 'Clinical features'.)

Acute cholangitis — Patients with acute cholangitis may present with Charcot's triad (fever, right upper quadrant pain, and jaundice) and leukocytosis. In severe cases, bacteremia and sepsis may additionally lead to hypotension and altered mental status (Reynolds' pentad). Cholangitis contributes to nearly 2400 deaths per year in the United States [3]. (See "Acute cholangitis: Clinical manifestations, diagnosis, and management", section on 'Clinical manifestations'.)

Long-standing biliary obstruction from various causes, including CBD stones, may result in liver disease that may progress to cirrhosis, a phenomenon referred to as secondary biliary cirrhosis [1,5]. Although rare in the setting of bile duct stones, secondary biliary cirrhosis may eventually result in the same cirrhosis-related complications that occur with other etiologies. Relief of biliary obstruction has been shown to result in regression of liver fibrosis in patients with secondary biliary cirrhosis in the setting of chronic pancreatitis and choledochal cysts [6,7]. It is likely, but not known, whether stone removal results in similar improvement in liver disease in patients with choledocholithiasis-induced secondary biliary cirrhosis.

DIFFERENTIAL DIAGNOSIS

Patients with uncomplicated gallstone disease, acute cholecystitis, sphincter of Oddi dysfunction, or functional gallbladder disorder may all present with biliary colic, and patients with liver disease, hematologic disorders, or biliary obstruction from any cause may present with jaundice (table 1). Choledocholithiasis can typically be differentiated from these other entities based on the patient's history, laboratory tests, and abdominal imaging.

Patients with choledocholithiasis typically present acutely with sudden onset of pain that may be stuttering and progress to prolonged episodes of pain. On the other hand, the episodes of pain in patients with uncomplicated gallstone disease, sphincter of Oddi dysfunction, or functional gallbladder disorder typically last less than six hours and often occur intermittently. In addition, patients with uncomplicated gallstone disease or functional gallbladder disorder should have normal laboratory tests and imaging (though patients with sphincter of Oddi dysfunction may have bile duct dilation and elevations in the alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase that normalize between attacks). Endoscopic ultrasound or magnetic resonance cholangiopancreatography may be required to identify choledocholithiasis. (See "Overview of gallstone disease in adults" and "Functional gallbladder disorder in adults".)

Like patients with choledocholithiasis, patients with acute cholecystitis may have prolonged episodes of pain that start suddenly. However, patients with acute cholecystitis generally do not have significantly elevated (greater than three times the upper limit of normal) bilirubin or alkaline phosphatase levels unless there is a secondary process causing cholestasis. In addition, abdominal imaging in acute cholecystitis typically reveals a normal CBD, gallbladder wall thickening, and a sonographic Murphy's sign. (See "Acute calculous cholecystitis: Clinical features and diagnosis".)

There are numerous causes of jaundice in addition to choledocholithiasis (table 1). Choledocholithiasis is differentiated from these other conditions by the presence of biliary-type pain and sometimes by a dilated CBD on abdominal imaging. (See "Diagnostic approach to the adult with jaundice or asymptomatic hyperbilirubinemia", section on 'Terminology'.)

INITIAL DIAGNOSTIC EVALUATION

Patients suspected of having choledocholithiasis are diagnosed with a combination of laboratory tests and imaging studies. The first imaging study obtained is typically a transabdominal ultrasound. Additional testing may include magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS). Endoscopic retrograde cholangiopancreatography (ERCP) is reserved for therapeutic purposes after determining a very high probability of common bile duct (CBD) stones, or cholangitis, and/or other diagnostic procedures have confirmed the presence of choledocholithiasis. ERCP carries a high risk of complications including pancreatitis, hemorrhage, or perforation from sphincterotomy, and other adverse events. The aim of the diagnostic evaluation is to confirm or exclude the presence of CBD stones using the least invasive, most accurate, and most cost-effective imaging modality [16]. The specific approach is determined by the level of clinical suspicion, availability of imaging modalities, and patient factors (eg, contraindications to a particular test) (algorithm 1). Our approach is consistent with the 2019 guideline by the American Society for Gastrointestinal Endoscopy (ASGE) [17].

Whom to suspect — Patients are often suspected of having choledocholithiasis when they present with right upper quadrant pain with elevated liver enzymes in a primarily cholestatic pattern (compared with the AST and ALT, there is disproportionate elevation of the alkaline phosphatase, gamma-glutamyl transferase, and bilirubin). (See 'Assess risk of choledocholithiasis' below.)

Initial evaluation — In a patient suspected of having choledocholithiasis based on the history, physical examination, and laboratory testing, we start by obtaining a transabdominal ultrasound. (See 'Transabdominal ultrasound' below.)

Laboratory findings — If not already done, we also obtain a complete blood count to look for leukocytosis (which may suggest acute cholangitis has developed), liver tests, and pancreatic enzyme levels to evaluate for concurrent pancreatitis. (See "Management of acute pancreatitis", section on 'Management of underlying predisposing conditions'.)

Transabdominal ultrasound — The initial imaging study of choice in patients with suspected CBD stones is a transabdominal ultrasound of the right upper quadrant. Transabdominal ultrasound can evaluate for cholelithiasis, choledocholithiasis, and CBD dilation. It is readily available, noninvasive, permits bedside evaluation, and provides a low-cost means of evaluating the CBD for stones.

The sensitivity of transabdominal ultrasound for choledocholithiasis ranges from 20 to 90 percent [17]. In a meta-analysis of five studies, the pooled sensitivity of ultrasound for detecting a CBD stone was 73 percent, with a specificity of 91 percent [18]. Transabdominal ultrasound has poor sensitivity for stones in the distal CBD because the distal CBD is often obscured by bowel gas in the imaging field [19-21]. Occasionally, a definite CBD stone (one that casts a shadow) can be imaged by transabdominal ultrasound (image 1).

A dilated CBD on transabdominal ultrasound is suggestive of, but not specific for, choledocholithiasis [9,11,14]. A cutoff of 6 mm is often used to classify a duct as being dilated, however, this may change with advancing age or with a history of cholecystectomy [17]. However, using a cutoff of 6 mm may miss CBD stones [22]. One study of 870 patients undergoing cholecystectomy found that stones were often detected in patients whose ducts would have been classified as "nondilated" using the 6 mm cutoff [23]. In addition, the probability of a stone in the CBD increased with increasing CBD diameter:

- 0 to 4 mm: 3.9 percent
- 4.1 to 6 mm: 9.4 percent
- 6.1 to 8 mm: 28 percent
- 8.1 to 10 mm: 32 percent

- >10 mm: 50 percent

Conversely, because the diameter of the CBD increases with age, older adults may have a normal duct with a diameter that is >6 mm. Following cholecystectomy, the CBD may dilate to 10 mm. (See 'Prior cholecystectomy' below.)

Assess risk of choledocholithiasis — Results of laboratory tests and transabdominal ultrasound are used to stratify a patient as high risk, intermediate risk, or low risk for having choledocholithiasis. Subsequent management varies depending on the patient's level of risk of choledocholithiasis (algorithm 1) [17]. (See 'Subsequent evaluation and management' below.)

- High risk – Patients with any one of the following are considered at high risk for a CBD stone and have an estimated probability of having a CBD stone of >50 percent:
  - The presence of a CBD stone on transabdominal ultrasound or cross-sectional imaging.
  - Acute cholangitis.
  - A serum bilirubin greater than 4 mg/dL (68 micromol/L) **and** a dilated CBD on ultrasound (more than 6 mm in a patient with a gallbladder in situ and more than 8 mm in those that have had a cholecystectomy).
- Intermediate risk – Patients with any one of the following are considered to be at intermediate risk with an estimated 10 to 50 percent probability of having a CBD stone:
  - Abnormal liver biochemical tests.
  - Age >55.
  - Dilated CBD on ultrasound or cross-sectional imaging.
- Low risk
  - No predictors present.

These risk criteria have been proposed by the ASGE in their 2019 guidelines on the role of endoscopy in the evaluation and management of choledocholithiasis. They differ from the 2010 ASGE guidelines where either a serum bilirubin >4 mg/dL (68 micromol/L) **or** a dilated CBD on ultrasound >6 mm in a patient with a gallbladder in situ were considered high-risk predictors [17]. In a very large cohort of 2724 patients using a more restrictive high-risk criteria that required both a serum bilirubin >4 mg/dL **and** bile duct dilation, this improved the specificity of finding a CBD stone at the time of ERCP from 74 to 94 percent [24]. (See 'Subsequent evaluation and management' below.)

SUBSEQUENT EVALUATION AND MANAGEMENT

High risk of common bile duct stone

Choice of treatment — In patients with acute cholangitis, and in patients with both ongoing evidence of biliary obstruction and acute pancreatitis, preoperative endoscopic retrograde cholangiopancreatography (ERCP) with stone removal is indicated; if ERCP is unsuccessful, endoscopic ultrasound-guided rendezvous may facilitate access for ERCP [25]. If endoscopic drainage is not feasible due to altered anatomy or other reasons, the patient may undergo percutaneous biliary drainage (algorithm 1). (See 'Concomitant acute pancreatitis' below.)

For all other patients at high risk for having common bile duct (CBD) stones, options include ERCP with stone removal followed by elective cholecystectomy or cholecystectomy with intraoperative ERCP or CBD exploration/postoperative ERCP [26]. For most patients, the choice of treatment depends on available expertise and patient preference.

In the United States at least, the use of ERCP is rising and the use of surgical CBD exploration is declining [27,28]. Outcomes for laparoscopic versus endoscopic treatment have been compared in randomized trials and observational studies [29-35]. A 2018 network meta-analysis aimed to determine the optimal approach for the treatment of gallstone disease with choledocholithiasis, comparing preoperative ERCP plus laparoscopic cholecystectomy, laparoscopic cholecystectomy with laparoscopic CBD exploration, laparoscopic cholecystectomy plus intraoperative ERCP, and laparoscopic cholecystectomy plus postoperative ERCP [36]. Twenty trials with 2489 patients were included. Same-session laparoscopic cholecystectomy with intraoperative ERCP was the most successful, safest, and had the shortest length of hospital stay. However, intraoperative ERCP may not be feasible at some centers. Although laparoscopic cholecystectomy plus laparoscopic CBD exploration had the shortest operative time, least total cost, and lowest acute pancreatitis rate, it had a higher risk of biliary leak. It should be noted that some of the intraoperative ERCP studies used a rendezvous technique where a transcystic guidewire was passed laparoscopically across the major papilla, which would then facilitate atraumatic biliary ERCP cannulation, potentially explaining higher rates of success compared with preoperative and postoperative ERCP. However, this technique is not universal among centers. (See "Surgical common bile duct exploration".)

Preoperative ERCP and elective cholecystectomy — ERCP can diagnose and remove CBD stones (image 2). The sensitivity of ERCP for choledocholithiasis is estimated to be 80 to 93 percent, with a specificity of 99 to 100 percent [37,38]. However, ERCP is invasive, requires technical expertise, and is associated with complications such as pancreatitis, bleeding, and perforation. Endoscopic techniques for CBD stone clearance include sphincterotomy and/or balloon dilation of the ampulla followed by stone extraction using baskets and extraction balloons as well as mechanical lithotripsy. These techniques are discussed in detail separately. (See "Endoscopic management of bile duct stones".)

Laparoscopic cholecystectomy with intraoperative CBD exploration or postoperative ERCP — Intraoperative CBD exploration is performed selectively, based on surgeon preference and local expertise. Laparoscopic cholecystectomy with concomitant bile duct exploration has the advantage of being a single-stage procedure that both removes the gallbladder and clears the CBD. The disadvantages are that it requires greater technical expertise and equipment and takes a longer operative time than laparoscopic cholecystectomy alone.

If CBD exploration or ERCP is not performed intraoperatively, ERCP can be performed postoperatively. A potential disadvantage of this approach is the need for a second anesthesia and reoperation for duct clearance if ERCP fails. However, this is rare in centers with significant ERCP experience. (See "Surgical common bile duct exploration".)

Intermediate risk of CBD stone — Intermediate-risk patients have an estimated 10 to 50 percent probability of having a CBD stone. Such patients require additional evaluation (magnetic resonance cholangiopancreatography [MRCP] or endoscopic ultrasound [EUS]) to rule out choledocholithiasis prior to direct ERCP, given the risks associated with the procedure [17]. Alternatively, such patients may also proceed directly to laparoscopic cholecystectomy with intraoperative cholangiography. CBD stones identified on intraoperative cholangiogram can be removed by laparoscopic CBD exploration (in centers with the requisite expertise) or by intraoperative or postoperative ERCP. The choice is based on local endoscopic and surgical expertise.

Additional imaging (MRCP or EUS) — Patients at intermediate risk may be considered for cholecystectomy with intraoperative cholangiography or additional imaging to confirm the presence of a CBD stone prior to an ERCP. MRCP is often the preferred imaging modality for CBD stones in patients at intermediate risk (image 3) [39,40]. Deciding which test should be performed depends on various factors such as ease of availability, cost, patient-related factors, and the suspicion for a small stone (table 2). If an ERCP can be performed at the same setting as the EUS, performing EUS may facilitate therapy by ERCP, especially if the clinical suspicion for a CBD stone is high (image 4). A meta-analysis from 2017 showed that the pooled sensitivity of EUS was higher than MRCP. The pooled sensitivity and specificity of EUS was 97 percent and 90 percent, respectively, and for MRCP was 87 percent and 92 percent, respectively [41]. The lower sensitivity of MRCP may be due to difficulty detecting small stones [<6 mm, (image 5)] [42]. (See 'Intermediate risk of CBD stone' above.)

CBD stone visualized — If the MRCP or EUS is positive for a CBD stone, patients should undergo either preoperative ERCP and elective cholecystectomy or laparoscopic cholecystectomy with intraoperative ERCP, CBD exploration, or postoperative ERCP. (See 'Laparoscopic cholecystectomy with intraoperative CBD exploration or postoperative ERCP' above.)

CBD stone not visualized — If the MRCP is negative for a CBD stone, but the suspicion for a CBD stone remains moderate to high (eg, in a patient whose laboratory tests are not improving), EUS is an appropriate next step. In many centers, the endoscopist performing the EUS can perform an ERCP during the same session if a stone is found.

In all other patients with an MRCP that is negative for a CBD stone, an elective cholecystectomy (provided gallstones or biliary sludge were demonstrated on preoperative imaging) can be performed.

Laparoscopic cholecystectomy with intraoperative imaging — Laparoscopic cholecystectomy with intraoperative cholangiography or intraoperative ultrasonography is an alternative strategy in patients at intermediate risk for a CBD stone. The decision regarding intraoperative cholangiography or intraoperative ultrasonography depends upon availability and surgical expertise [43].

- **Intraoperative cholangiography** – Intraoperative cholangiography has an estimated sensitivity of 59 to 100 percent for diagnosing choledocholithiasis, with a specificity of 93 to 100 percent [38,44-46]. However, it may be technically unfeasible in patients with a severely inflamed gallbladder or with a tiny or inflamed cystic duct. Laparoscopic exploration of the CBD for removal of intraductal stones is technically challenging, highly operator-dependent, and is not routinely performed by many surgeons [47]. (See "Laparoscopic cholecystectomy", section on 'Evaluation for choledocholithiasis' and "Surgical common bile duct exploration", section on 'Intraoperative cholangiography'.)

- **Intraoperative ultrasonography** – During laparoscopy, an ultrasound probe is inserted into the peritoneal cavity though a 10-mm trochar and is used to scan the bile ducts. The reported sensitivity and specificity are over 90 percent in experienced hands, and it has been suggested that the routine use of intraoperative ultrasound followed by selective intraoperative cholangiography leads to the accurate diagnosis of choledocholithiasis while reducing the need for intraoperative cholangiography [48]. The use of intraoperative ultrasound may also decrease the rate of bile duct injury [49]. However, it is associated with a longer learning curve, equipment costs, and is not as widely available [44].

Subsequent management is based on results of intraoperative imaging:

- If intraoperative imaging is positive, patients can undergo laparoscopic CBD exploration (in centers with the requisite expertise) or intraoperative or postoperative ERCP. (See 'Laparoscopic cholecystectomy with intraoperative CBD exploration or postoperative ERCP' above.)

- If intraoperative imaging is negative for a CBD stone, the patient can proceed to elective cholecystectomy.

Low risk of CBD stone — Low-risk patients are estimated to have a <10 percent probability of having a CBD stone [17]. (See 'Assess risk of choledocholithiasis' above.)

Gallstones/sludge on imaging — If gallstones or sludge are present within the gallbladder on transabdominal ultrasound and the patient is a good surgical candidate, the patient should proceed to cholecystectomy without imaging of the CBD preoperatively or intraoperatively. Alternative therapies, such as medical gallstone dissolution, may be considered for patients who are not surgical candidates. (See "Overview of nonsurgical management of gallbladder stones", section on 'Oral bile acid dissolution therapy'.)

Without gallstones/sludge — In the absence of gallstones on imaging, alternative explanations for the patient's pain should be sought. (See "Evaluation of the adult with abdominal pain", section on 'Right upper quadrant pain'.)

Special circumstances

Concomitant acute pancreatitis — Patients with both acute pancreatitis and acute cholangitis should undergo urgent (<24 hours) ERCP [17]. (See "Management of acute pancreatitis", section on 'Gallstone pancreatitis'.)

In patients with gallstone pancreatitis and persistent obstruction **without** cholangitis, urgent ERCP (within 24 hours) is not indicated. In such patients, therapeutic ERCP can be performed either before the cholecystectomy, if there is a strong suspicion of a stone in the bile duct, or if confirmed by other imaging. ERCP can also be considered in patients who will be discharged from the hospital before cholecystectomy, which is typically due to necrotizing pancreatitis. However, ERCP in the presence of sterile necrotizing pancreatitis may introduce risk of early infection of the necrosis, which can be highly morbid [50]

In patients with acute pancreatitis but equivocal evidence of bile duct stones (eg, improving liver enzyme tests and/or improvement or resolution of pain), MRCP or EUS followed by ERCP only if the EUS/MRCP reveals a CBD stone is an attractive option because it can detect CBD stones but is not associated with pancreatitis.

Issues related to ERCP in patients with acute biliary pancreatitis are discussed elsewhere. (See "Management of acute pancreatitis", section on 'Endoscopic retrograde cholangiopancreatography'.)

Prior cholecystectomy — Choledocholithiasis will sometimes be suspected in a patient who has previously undergone cholecystectomy. Choledocholithiasis can occur in this setting if a gallstone escapes from the gallbladder during cholecystectomy, stones were within the CBD but clinically silent and unrecognized at the time of the cholecystectomy, or if there is de novo stone formation within the CBD. (See "Laparoscopic cholecystectomy", section on 'Postcholecystectomy syndrome'.)

Following cholecystectomy, the CBD may dilate to 10 mm or more, especially in older adult patients. In such patients, transabdominal ultrasound is less helpful because a dilated CBD seen on ultrasound may be the result of a CBD stone, or it may be the result of the cholecystectomy. One approach to patients who have undergone a prior cholecystectomy and who present with biliary-type pain and liver test abnormalities, but in whom there is uncertainty following a transabdominal ultrasound as to the presence of a bile duct stone, is to proceed with an MRCP or EUS to confirm the presence of a stone. If a stone is absent, it is important to consider alternative etiologies including sphincter of Oddi dysfunction. (See 'Differential diagnosis' above.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Cholecystitis and other gallbladder disorders" and "Society guideline links: Gallstones" and "Society guideline links: Biliary infection and obstruction".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5^{th} to 6^{th} grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10^{th} to 12^{th} grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: ERCP (endoscopic retrograde cholangiopancreatography) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Epidemiology** – Choledocholithiasis refers to the presence of gallstones within the common bile duct. It has been estimated that 5 to 20 percent of patients with gallstones will have choledocholithiasis at the time of cholecystectomy, with the incidence increasing with age. (See 'Epidemiology' above.)

- **Clinical manifestations** – Most patients with choledocholithiasis are symptomatic, although occasional patients are asymptomatic. Symptoms associated with choledocholithiasis include right upper quadrant or epigastric pain, nausea, and vomiting. The pain is often more prolonged than is seen with typical biliary colic (which typically resolves within six hours). On physical examination, patients with choledocholithiasis often have right upper quadrant or epigastric tenderness. Patients may also appear jaundiced. (See 'Symptoms' above and 'Physical examination' above.)

- **Laboratory findings** – Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are typically elevated early in the course of biliary obstruction. Later, liver tests are typically elevated in a cholestatic pattern, with elevations in serum bilirubin, alkaline phosphatase, and gamma-glutamyl transpeptidase being more pronounced than those in ALT and AST. (See 'Laboratory tests' above.)

- **Complications** – Complications of choledocholithiasis include acute pancreatitis and acute cholangitis. Patients with acute pancreatitis typically have elevated serum pancreatic enzyme levels, and patients with acute cholangitis are often febrile with leukocytosis. (See 'Complicated choledocholithiasis' above.)

- **Initial evaluation and assessment of risk of choledocholithiasis** – Patients suspected of having choledocholithiasis are diagnosed with a combination of laboratory tests and imaging studies. The first imaging study obtained is typically a transabdominal ultrasound.

The results of laboratory testing and transabdominal ultrasound are then used to stratify a patient as high risk, intermediate risk, or low risk for having choledocholithiasis (algorithm 1). (See 'Initial diagnostic evaluation' above.)

- High risk – Patients with any one of the following are considered at high risk for a common bile duct (CBD) stone and have an estimated probability of having a CBD stone of >50 percent:
  - The presence of a CBD stone on transabdominal ultrasound or cross-sectional imaging.
  - Acute cholangitis.
  - A serum bilirubin greater than 4 mg/dL (68 micromol/L) **and** a dilated CBD on ultrasound (more than 6 mm in a patient with a gallbladder in situ and more than 8 mm in those that have had a cholecystectomy).
- Intermediate risk – Patients with any one of the following are considered to be at intermediate risk with an estimated 10 to 50 percent probability of having a CBD stone:
  - Abnormal liver biochemical tests.
  - Age >55.
  - Dilated CBD on ultrasound or cross-sectional imaging.
- Low risk
  - No predictors present.

- **Additional evaluation based on risk of choledocholithiasis**
  - Patients at high risk for having common bile duct stones and with an intact gallbladder generally proceed to endoscopic retrograde cholangiopancreatography (ERCP) with stone removal, followed by elective cholecystectomy, or they undergo cholecystectomy with intraoperative cholangiography, followed by intraoperative or postoperative ERCP; where expertise is available, laparoscopic common bile duct exploration can be performed. Precholecystectomy ERCP followed by cholecystectomy is appropriate in patients with acute cholangitis, in those with ongoing evidence of biliary obstruction and acute pancreatitis. (See 'High risk of common bile duct stone' above.)
  - Patients at intermediate risk either undergo preoperative endoscopic ultrasound or magnetic resonance cholangiopancreatography, or they proceed to laparoscopic cholecystectomy with intraoperative cholangiography or ultrasonography. Subsequent management choices are as above. (See 'Intermediate risk of CBD stone' above.)

- Patients at low risk can proceed directly to cholecystectomy without additional testing, provided gallstones or sludge were seen on preoperative imaging. (See 'Low risk of CBD stone' above.)

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Topic 13922 Version 39.0

GRAPHICS

Classification of jaundice according to type of bile pigment and mechanism

Unconjugated hyperbilirubinemia
Increased bilirubin production*
Extravascular hemolysis
Extravasation of blood into tissues
Intravascular hemolysis
Dyserythropoiesis
Wilson disease
Impaired hepatic bilirubin uptake
Heart failure
Portosystemic shunts
Some patients with Gilbert syndrome
Certain drugs¶ – Rifampin, probenecid, flavaspadic acid, bunamiodyl
Impaired bilirubin conjugation
Crigler-Najjar syndrome types I and II
Gilbert syndrome
Neonates
Hyperthyroidism
Ethinyl estradiol
Liver diseases – Chronic hepatitis, advanced cirrhosis

Conjugated hyperbilirubinemia
Defect of canalicular organic anion transport
Dubin-Johnson syndrome
Defect of sinusoidal reuptake of conjugated bilirubin
Rotor syndrome

Conjugated hyperbilirubinemia (continued)
Extrahepatic cholestasis (biliary obstruction)
Choledocholithiasis
Intrinsic and extrinsic tumors (eg, cholangiocarcinoma, pancreatic cancer)
Primary sclerosing cholangitis
AIDS cholangiopathy
Acute and chronic pancreatitis
Strictures after invasive procedures
Certain parasitic infections (eg, *Ascaris lumbricoides*, liver flukes)
Intrahepatic cholestasis
Viral hepatitis
Alcohol-associated hepatitis
Non-alcohol-associated steatohepatitis
Chronic hepatitis
Primary biliary cholangitis
Drugs and toxins (eg, alkylated steroids, chlorpromazine, herbal medications [eg, Jamaican bush tea], arsenic)
Sepsis and hypoperfusion states
Infiltrative diseases (eg, amyloidosis, lymphoma, sarcoidosis, tuberculosis)
Total parenteral nutrition
Postoperative cholestasis
Following organ transplantation
Hepatic crisis in sickle cell disease
Pregnancy

	End-stage liver disease

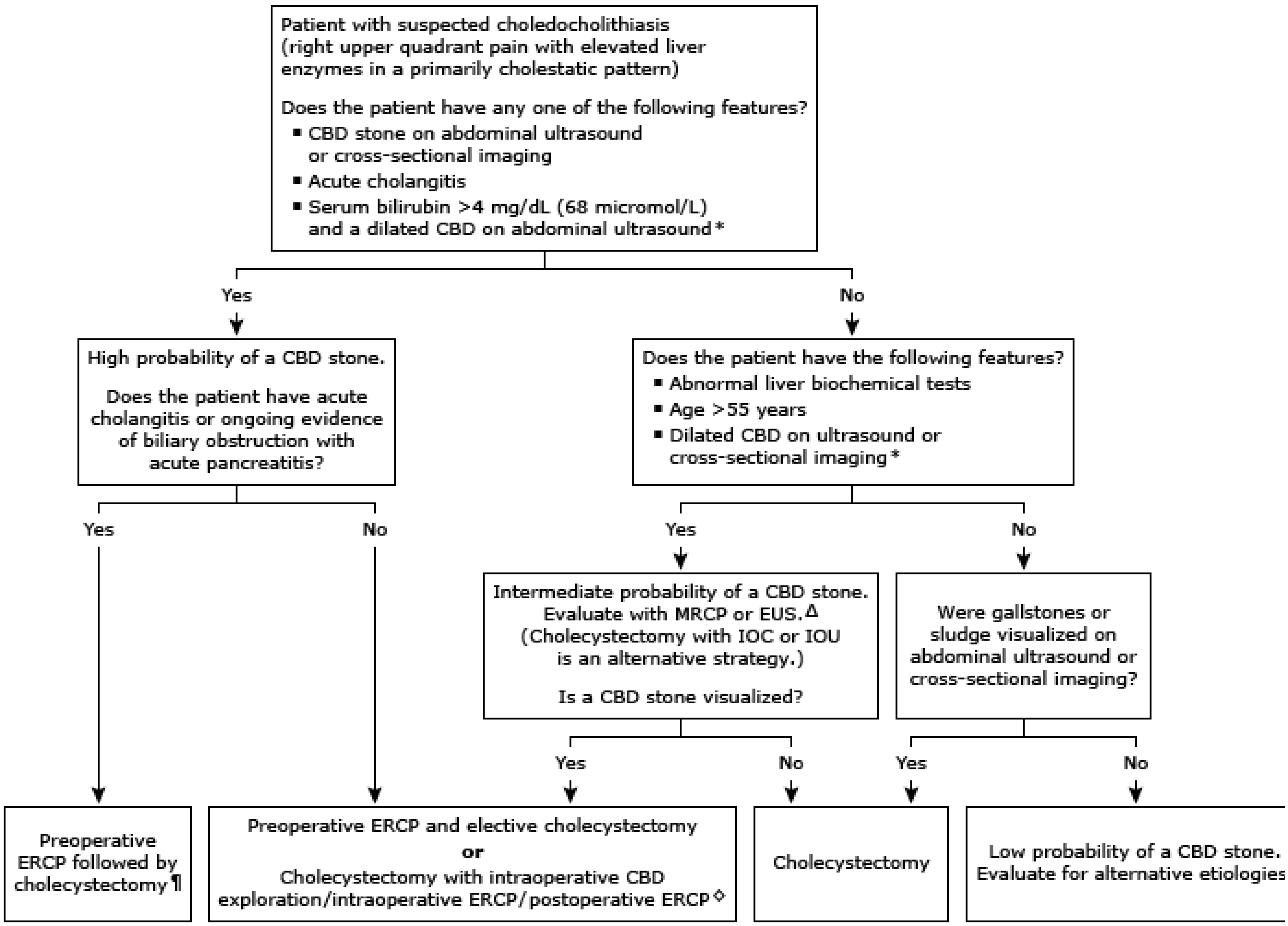
AIDS: acquired immunodeficiency syndrome.

* Serum bilirubin concentration is usually less than 4 mg/dL (68 mmol/L) in the absence of underlying liver disease.

¶ The hyperbilirubinemia induced by drugs usually resolves within 48 hours after the drug is discontinued.

Graphic 55607 Version 13.0

Suggested approach for the evaluation and management of suspected choledocholithiasis[1]



CBD: common bile duct; ERCP: endoscopic retrograde cholangiopancreatogram; EUS: endoscopic ultrasound; IOC: intraoperative cholangiogram; IOU: intraoperative ultrasonography; MRCP: magnetic resonance cholangiopancreatogram.

* A common bile duct measuring more than 6 mm in a patient with a gallbladder in situ and more than 8 mm in those that have had a cholecystectomy.

¶ Refer to UpToDate content on surgical common bile duct exploration and acute pancreatitis.

Δ If no stone is visualized on MRCP but suspicion for a CBD stone remains moderate to high (eg, in a patient whose laboratory tests are not improving), EUS is an appropriate next step.

◊ Decision is based on available expertise.

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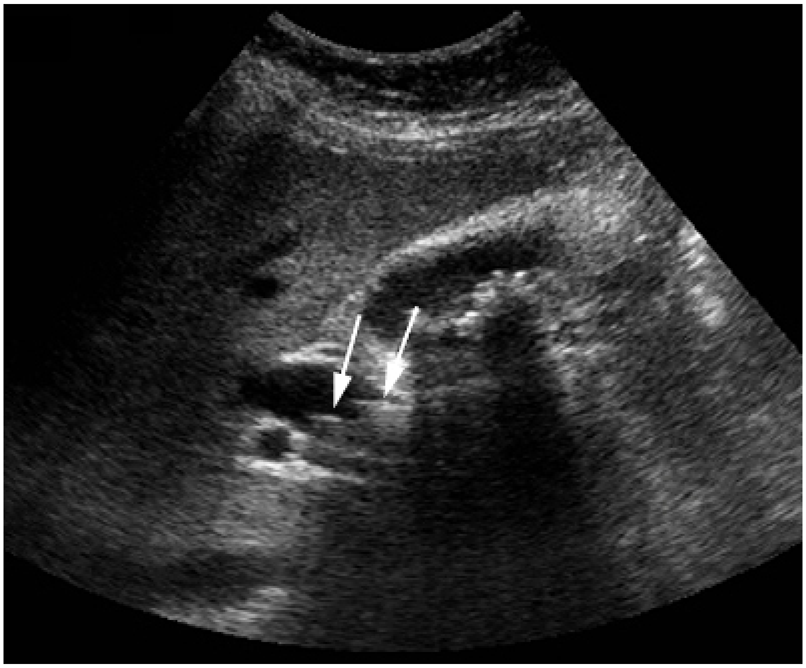
Graphic 66945 Version 4.0

Transabdominal ultrasound showing common bile duct stones

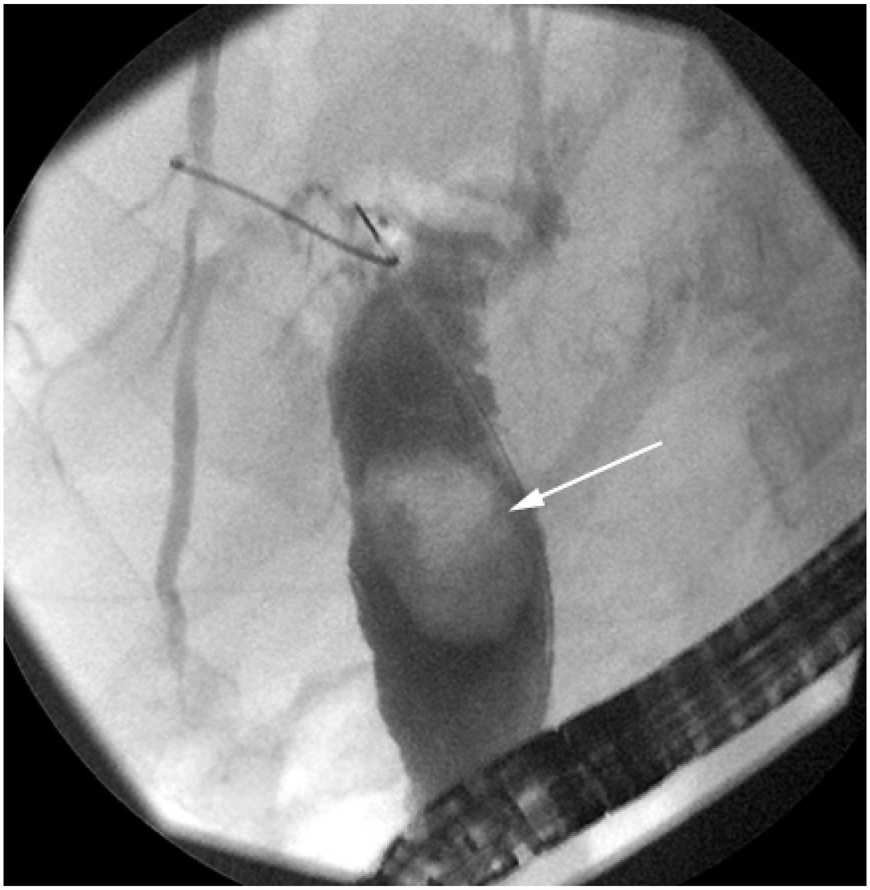


A transverse ultrasound in the region of the porta hepatis shows multiple shadowing stones (arrows) within a dilated distal common bile duct.

Courtesy of ML Freeman, MD.

Graphic 62309 Version 5.0

Common bile duct stone on endoscopic retrograde cholangiopancreatography (ERCP)

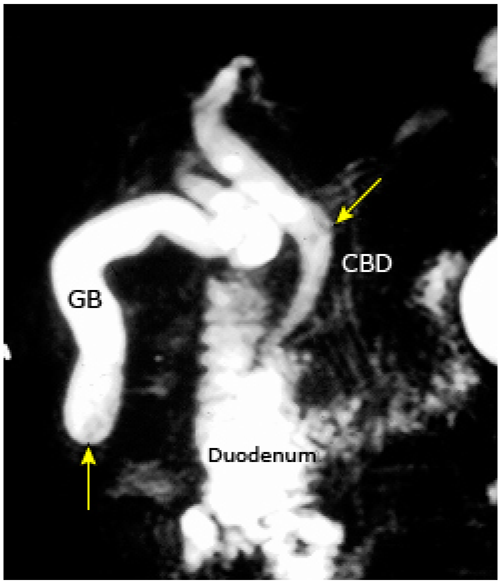


Cholangiogram showing large (2 cm) common bile duct stone (arrow).

Courtesy of Martin L. Freeman, MD.

Graphic 59987 Version 5.0

Common bile duct stones



Magnetic resonance cholangiopancreatography study, obtained in a 60-year-old woman with recurrent right upper quadrant pain and an unremarkable ultrasound examination, shows small stones (arrows) in the GB and the CBD.

CBD: common bile duct; GB: gallbladder.

Courtesy of Jonathan Kruskal, MD.

Graphic 80729 Version 3.0

Advantages and disadvantages associated with MRCP and EUS for the evaluation of choledocholithiasis

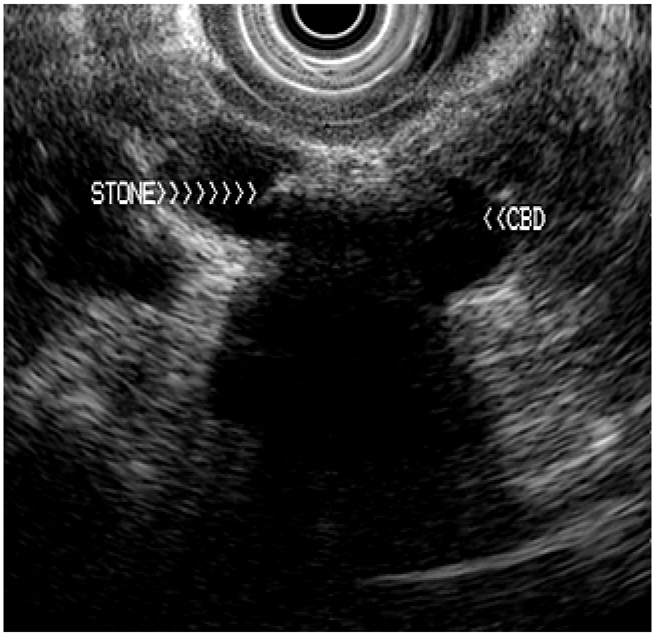
MRCP
Advantages
Noninvasive
Intravenous contrast usually given but not required
Established technique, widely available
Disadvantages
Time consuming
Contraindications such as cardiac pacemaker/defibrillator, intracranial metal clips
False-positive studies (eg, intraductal artifacts such as air or blood, image reconstruction artifacts, motion artifacts)
False-negative studies (eg, stones in dilated CBD or stones <5 mm in the distal duct may not be visualized well)
EUS
Advantages
Very high resolution (0.1 mm) compared with MRCP (1.5 mm)
Dynamic imaging allowing manipulation and magnification of image for better visualization
ERCP can potentially be performed in the same setting for stone removal
Can be performed at the bedside in critically ill patients
Disadvantages
More invasive than MRCP
Need for sedation
Risks associated with sedation (eg, cardiopulmonary compromise) and endoscopy (eg, bleeding and perforation)
Limited availability of equipment and trained endosonographers
Not possible or limited role in altered anatomy (eg, pyloric stenosis, Roux-en-Y bypass)

CBD: common bile duct; ERCP: endoscopic retrograde cholangiopancreatography; EUS: endoscopic ultrasound; MRCP: magnetic endoscopic retrograde cholangiopancreatography.

Courtesy of ML Freeman, MD.

Graphic 73388 Version 1.0

Choledocholithiasis seen on endoscopic ultrasound

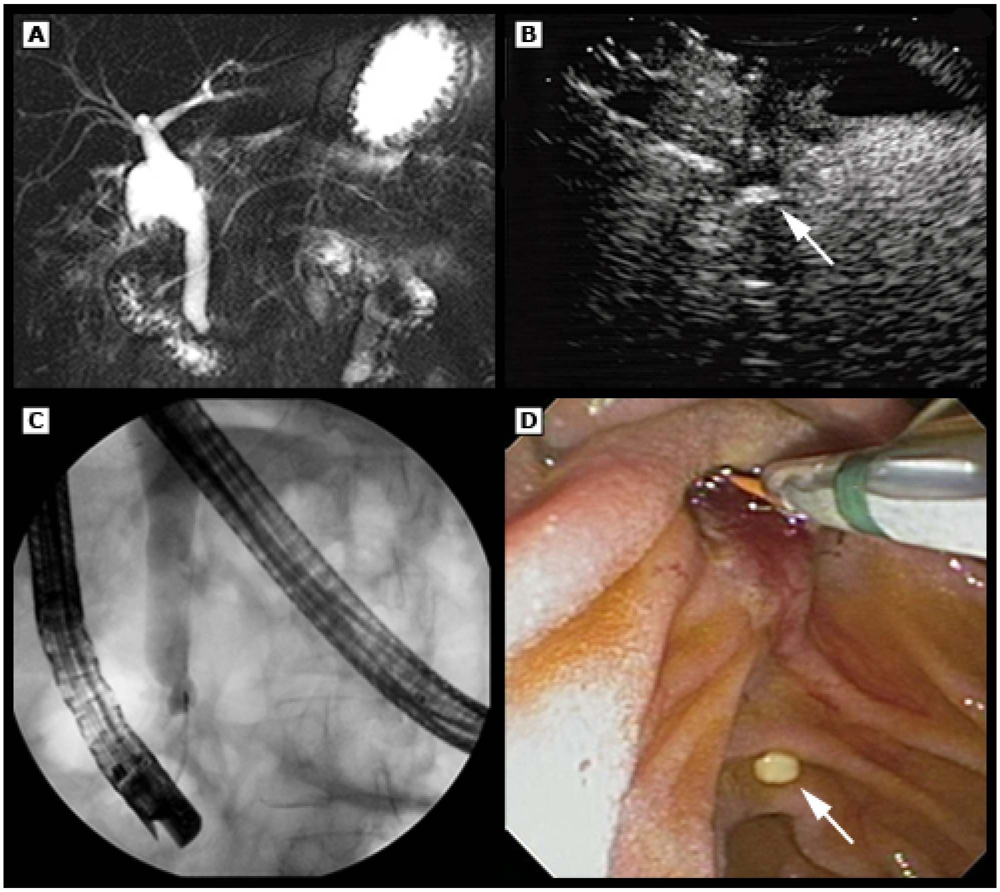


Endosonographic image of a gallstone in the common bile duct.

Courtesy of Gavin C Harewood, MD and Mauritis J Wiersema, MD.

Graphic 64622 Version 3.0

Comparison of MRCP/ERCP and EUS for the detection of common bile duct stones



Small bile duct stone missed by magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP), but shown by endoscopic ultrasound (EUS). This demonstrates the superior sensitivity of EUS for small bile duct stones. A) MRCP showing dilated bile duct with no apparent stone, incidental pancreas divisum. B) EUS in same patient showing very small bile duct stone (<5 mm) (arrow). C) ERCP in same patient showing dilated common bile duct without apparent stone. D) Endoscopic view of extracted stone after biliary sphincterotomy (arrow).

Courtesy of ML Freeman, MD.

Graphic 60410 Version 3.0

Contributor Disclosures

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Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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