BMJ Best Practice

Cholelithiasis (Gallstones)

Straight to the point of care

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Summary

Gallstones (cholelithiasis) are highly prevalent, but most are asymptomatic. Cholelithiasis is the most common gastrointestinal condition to require hospitalization in developed countries.

Common risk factors include older age, a family history, female sex and pregnancy, obesity, rapid weight loss, and certain drugs.

Abdominal ultrasound provides effective diagnostic imaging.

Laparoscopic cholecystectomy is definitive treatment for symptomatic patients.

Complications such as cholecystitis, cholangitis, and pancreatitis develop in 3% of symptomatic patients annually.

Definition

Cholelithiasis is the presence of solid concretions (stones) in the gallbladder. Choledocholithiasis is the term used when gallstones have moved into the bile ducts. Symptoms occur if a stone obstructs the cystic, bile, or pancreatic duct.

Most gallstones in developed countries (>90%) consist of cholesterol.[1]

THEORY

Epidemiology

Cholelithiasis occurs in approximately 10% to 15% of adults in the US and Europe.[2]

The highest prevalence of cholelithiasis is in American Indian populations, followed by Northern Europeans.[2] [10] Prevalence rates are relatively low in Sub-Saharan Africa and Asia.[7] [11] [12]

Despite its high prevalence, cholelithiasis is generally asymptomatic in over 80% of people.[2] [13] Gallstone-related symptoms or complications, however, develop in 1% to 2% of previously asymptomatic individuals each year.[1] [2] [9] [14] [15] [16] [17] Once biliary colic has developed, over 50% of patients will go on to experience recurrent pain, while up to 3% per year develop complications (e.g., acute cholecystitis, cholangitis, acute pancreatitis).[2] [9] [18]

Risk factors

Strong

increasing age

The frequency of gallstones rises noticeably after the age of 40 years, peaking late in life.[2] [3] Age correlates positively with increased cholesterol secretion and saturation; however, the stone type found in older age tends to be pigment.[2]

female sex

Gallstones are 2-3 times more common in women than in men.[3] [4] [5] [6] [33] This may be due to increased cholesterol secretion into bile, induced by estrogen.[33]

Hispanic and American Indian ethnicity

The highest prevalence of gallstones is in people of Hispanic or American Indian ethnicity, reaching rates of over 50% among men and 70% among women ages >50 years, depending on the exact ethnic origin.[10] [34] [35]

family history of gallstones

There is an increased prevalence of gallstones in some families.[4] [5] Monozygotic twin studies show a higher concordance for gallstone disease than dizygotic twins.[5]

gene mutations

Genome-wide association studies have revealed a number of susceptibility genes for cholesterol gallstone disease: ABCG8 p.D19H (increasing cholesterol excretion); UGT1A1 in male carriers of the Gilbert syndrome variant rs6742078 (presumably the secreted bilirubin pigment functioning as the nucleating agent); SULT2A1, GCKR, and CYP7A1, which are all located in or near genes involved in cholesterol or bile acid metabolism; low frequency missense variants in SLC10A2, encoding the apical sodium-dependent ileal bile acid transporter; and TM4SF4, a gene implicated in liver regeneration and pancreatic development, although its role in gallstone disease is unclear.[6] [7] [36] [37]

elevated estrogen and progesterone levels

Increasing levels of estrogen heighten cholesterol saturation of bile, making women more prone to developing sludge and gallstones.[38] Higher levels of progesterone (e.g., in pregnancy) also cause gallbladder hypomotility, which further exacerbates gallstone formation.[7]

obesity, diabetes, and metabolic syndrome

Body mass index (BMI) >30, particularly abdominal or centripetal obesity, is a strong risk factor for gallstones.[1] [21] [39] [40] [41] Diabetes mellitus and insulin resistance, and the metabolic syndrome (consisting of abdominal obesity, hypertension, elevated fasting blood sugar levels, hypertriglyceridemia, and low high-density lipoprotein levels), also convey an increased risk of cholesterol gallstone formation and complicated disease when gallstones do occur.[1] [21] [26] [39] [42] [42] [43] The postulated mechanisms are elevated hepatic cholesterol secretion, depressed bile salt synthesis, increased pronucleating agents like mucin, and/or impaired gallbladder motility.[1] [19]

nonalcoholic fatty liver disease

A significant association exists between gallstone disease and nonalcoholic fatty liver disease (NAFLD); however, the underlying mechanism is unclear.[19] [44] [45] Although cholelithiasis and NAFLD conditions share common risk factors (obesity, insulin resistance, diabetes), evidence suggests that NAFLD is an independent risk factor for gallstone disease and for more severe gallstone disease.[19] [45]

prolonged fasting/rapid weight loss

Prolonged fasting causes gallbladder hypomotility and increases cholesterol excretion into bile.[46] The resulting overly saturated bile and bile stasis increase the risk for developing gallstones.

Patients undergoing weight loss surgery, already at risk for stone formation because of obesity, are at heightened risk of developing gallstones following the surgery, presumably because weight loss mobilizes excessive cholesterol into bile while bile acid secretion is decreased.[24] Weight loss surgery commonly causes formation of biliary sludge; most concretions disappear but some evolve into gallstones that persist.[47]

total parenteral nutrition (TPN)

TPN, frequently employed in clinical conditions with marked weight loss, causes gallbladder hypomotility and is strongly associated with the development of biliary sludge and gallstone disease.[23] The weight loss and gallbladder stasis increase the risk for cholesterol stone formation; pigment gallstones also form due to calcium bilirubinate sludge associated with TPN.[48]

use of octreotide

Octreotide, a somatostatin analog, impairs gallbladder and small intestinal motility, leading to gallbladder stasis, increased production of secondary bile acids, and cholesterol stone formation.[22] Short-term use of octreotide is not usually problematic, but the risk increases with the duration of treatment.[49]

use of glucagon-like peptide-1 (GLP-1) receptor agonists

GLP-1 receptor agonists are associated with an increased risk of bile duct and gallbladder disease.[50] [51]

use of ceftriaxone

Ceftriaxone has been associated with pigment stone development from the drug precipitating with calcium in bile.[25] [52]

terminal ileum disease or resection

Crohn disease commonly involves the terminal ileum; terminal ileum disease is associated with an increased risk of gallstones, in particular pigment stones.[7] [53] Excessive bile salts escape into the colon to increase the solubility of bilirubin pigment; more bilirubin pigment is absorbed and consequently more pigment returns to the liver. This results in excessive secretion of bile pigment and black pigment stones.[54] Cholesterol stones also form; bile acid malabsorption leads to a deficiency of cholesterol, such that the bile becomes overly saturated with cholesterol and stone formation.[55]

hemoglobinopathy

Sickle cell disease (SCD) and beta-thalassemia are hereditary hemolytic anemias, in which excessive breakdown of hemoglobin leads to a large output of bilirubin and consequent black pigment stone formation. Stones present at a young age, and often require cholecystectomy.[1] In SCD, sickling can cause bile duct ischemia. Cholecystectomy is often needed relatively early in life in patients with SCD due to confounding symptoms of abdominal pain associated with sickle cell crises, cholelithiasis, and sickle-cell intrahepatic cholestasis.[56]

cirrhosis

Gallstones are common in patients with liver cirrhosis, with a prevalence of 25% to 30% in this population.[57] This is likely related to abnormal pigment secretion, gallbladder hypomobility, and elevated estrogen levels in those with cirrhosis. Both cholesterol and black pigment stones occur, although black pigment stones are more common.[7] [58]

cystic fibrosis

Cystic fibrosis is a risk factor for gallstones due to bile acid malabsorption and hyperbilirubinemia.[54]

Weak

diet and lifestyle

The role of specific diets is not clear; diets high in refined carbohydrates and fat (cholesterol and triglycerides) and low in fiber are associated with gallstones.[39] [59] [60] Fruit and vegetable consumption, as part of a high-fiber diet, is correlated with a reduced risk of cholelithiasis.[61]

helicobacter pylori gallbladder infection

One meta-analysis found that infection of the gallbladder with *Helicobacter pylori* was associated with an increased risk of cholelithiasis and chronic cholecystitis (odds ratio 3.02).[62] However, subsequent research does not support this relationship.[63]

Etiology

Approximately 90% of gallstones in developed countries are composed of cholesterol.[1] [2] [4] [19] Cholesterol stones form in the gallbladder but can migrate into the common bile duct, occurring in about 10% to 15% of patients presenting for cholecystectomy.[20]

Some risk factors for cholesterol gallstones are modifiable, such as obesity, total parenteral nutrition, rapid weight reduction after weight loss surgery, and drugs (e.g., octreotide, ceftriaxone).[21] [22] [23] [24] [25] [26] Others, such as age, genetic factors, and female sex are not modifiable.[3] [4] [5] [6]

Approximately 15% of all gallstones are black pigment stones.[2] [7] [27] The pigment material consists of polymerized calcium bilirubinate. Patients with chronic hemolytic anemia, cirrhosis, cystic fibrosis, and ileal diseases are at highest risk of developing black pigment stones.[1] [2]

Brown pigment gallstones form de novo in bile ducts as a result of stasis and infection.[1] They typically consist of calcium bilirubinate, calcium salts of long-chain fatty acids, cholesterol, and mucin (glycoproteins primarily from bacterial biofilms). In developed countries, brown pigment stones usually arise following bacterial infection or from partial biliary obstruction, such as inflammatory strictures (e.g., primary biliary cirrhosis) or malignancy (e.g., cholangiocarcinoma).[1] [2] [7] In South East Asia, the major risk is chronic infectious cholangitis associated with biliary parasites such as *Clonorchis sinensis*, *Opisthorchis* species, and *Fasciola hepatica*.[1] [7]

Pathophysiology

Cholesterol cholelithiasis occurs as a result of three principal defects: bile supersaturated with cholesterol, accelerated nucleation, and gallbladder hypomotility such that this abnormal bile stagnates.

Cholesterol supersaturation of gallbladder bile occurs primarily when the liver secretes excessive amounts of cholesterol compared with its solubilizing agents (bile salts and lecithin). Precipitation of cholesterol microcrystals in the gallbladder then follows, initiated by the presence of nucleating agents (primarily biliary glycoproteins such as mucin). Impaired gallbladder contractility causes the cholesterol-rich bile to stagnate and be retained in the gallbladder. These microcrystals collect in a mucin scaffold and grow into overt gallstones.[19]

Symptoms and complications of cholelithiasis result when stones obstruct the cystic and/or bile ducts. Biliary pain occurs when a stone transiently obstructs the cystic duct. More persistent obstruction leads to acute cholecystitis.

Stones that pass into the biliary tract can cause obstruction at the ampulla of Vater, leading to reflux of pancreaticobiliary secretions back into the pancreatic duct, which can trigger activation of pancreatic enzymes, leading to acute biliary pancreatitis. Risk factors for acute biliary pancreatitis are multiple small stones (<5 mm), a dilated cystic duct, and normal gallbladder contractility.[28] [29] [30]

Mirizzi syndrome, an uncommon condition, occurs when a large gallstone becomes lodged in the neck of the gallbladder or in the cystic duct, compressing or causing inflammation of the common bile duct. The result is biliary obstruction and jaundice.[31]

If a gallstone erodes through the gallbladder wall, a cholecystoenteric fistula can develop, leading obstruction either in the duodenum (Bouveret syndrome) or more distally in an otherwise healthy small intestine, causing gallstone ileus.[32]

Classification

Types of stones in the biliary tract

Cholesterol gallstones

- Approximately 90% of gallstones in developed countries are composed of cholesterol.[1] [2] These form in the gallbladder.
- Risk factors include genetics and family history, obesity, metabolic syndrome, sudden weight reduction (e.g., following weight loss surgery), age, and female sex hormones.[3] [4] [5] [6]

Black pigment gallstones

- Around 15% of gallstones are black pigment stones, which consist of polymerized calcium bilirubinate.[1] [2] [7]
- Risk factors are age, chronic hemolytic anemia, cirrhosis, cystic fibrosis, and ileal disease.[1] [2]

Brown pigment stones (ductal stones)

- These stones form in the bile ducts as a result of stasis and infection.[1] They consist of unconjugated bilirubin and calcium salts of long-chain fatty acids.
- In developed countries, brown pigment stones usually arise following bacterial infection or from partial biliary obstruction, such as inflammatory strictures (e.g., primary biliary cirrhosis) or malignancy (e.g., cholangiocarcinoma).[1] [2] [7] In South East Asia, the major risk is chronic infectious cholangitis associated with biliary parasites such as *Clonorchis sinensis* , *Opisthorchis species* , and *Fasciola hepatica* .[1] [7]

Case history

Case history #1

A 46-year-old obese woman presents with a 6-hour history of moderate steady pain in the right upper quadrant (RUQ) that radiates through to her back. This pain began after eating dinner, gradually increased, and has remained constant over the last few hours. She has experienced previous episodes of similar pain for which she did not seek medical advice. Her vital signs are normal. The pertinent findings on physical exam are tenderness to palpation in the RUQ without guarding or rebound.

Other presentations

Biliary colic is characterized by steady, severe pain (intensity >5 on a scale of 1-10) in the RUQ of the abdomen lasting more than 15-30 minutes.[1] Simple biliary colic commonly requires an analgesic but should resolve within 5 hours.[8]

Acute cholecystitis presents with biliary pain lasting more than 5 hours, accompanied by inflammatory features such as fever, marked RUQ tenderness (Murphy's sign), and leukocytosis.[1] This can lead to sepsis.[9] See Acute cholecystitis .

Choledocholithiasis occurs when gallstones move into the bile ducts where they can cause obstruction. This results in biliary-type pain, often accompanied by cholestasis, which manifests as jaundice.

More sinister is acute cholangitis, a medical emergency, characterized by the Charcot triad of biliary pain, jaundice, and fever.[1] See Acute cholangitis .

Acute pancreatitis can occur when a stone that has passed distally to the ampulla then blocks the main pancreatic duct.[1] It presents with severe sudden-onset mid-epigastric or left upper quadrant abdominal pain (which often radiates into the back), nausea, and vomiting, accompanied by elevated pancreatic enzymes (lipase or amylase).[1] See Acute pancreatitis .

On rare occasions, a stone can perforate the gallbladder, leading to intestinal obstruction (gallstone ileus). Mirizzi syndrome is a rare complication in which the gallstone becomes impacted in the cystic duct or neck of the gallbladder, compressing the adjacent common hepatic duct, and resulting in biliary obstruction and jaundice.

Recommendations

Key Recommendations

Biliary pain, the most common symptom of cholelithiasis, results from either obstruction of the cystic duct or from obstruction and/or passage of a gallstone through the common bile duct. Biliary pain, cholecystitis, cholangitis, or pancreatitis develop annually in 1% to 2% of those with asymptomatic cholelithiasis.[1] [2] [9] [14] [15] [16] [17]

Features of cholecystitis, cholangitis, or pancreatitis may clinically overlap; therefore, accurate diagnostic imaging is critical. In addition to standard laboratory evaluation, the initial radiographic test of choice for symptomatic cholelithiasis is a transabdominal ultrasound.[71] [72] Subsequent imaging choice depends on the index of clinical suspicion for complications of cholelithiasis.

History

Typical biliary pain (biliary colic) occurs in the right upper quadrant or epigastric area, sometimes after the consumption of food, often around 1 hour after eating, particularly in the evening or at night time.[73] This constant pain increases in intensity and lasts for several hours. Pain of short duration (<30 minutes) is not biliary colic, while that of long duration (over 5 hours) suggests cholecystitis or another major complication.[1] Pain may be accompanied by nausea.[1]

Risk factors should be identified; these include a positive family history, obesity, diabetes, metabolic syndrome, use of certain drugs (e.g., octreotide, glucagon-like peptide-1 receptor agonists, ceftriaxone), terminal ileum disease, pregnancy, cirrhosis, and hemolytic anemia (e.g., sickle cell anemia or thalassemia).[4] [5] [21] [22] [50] [52] [53]

Physical exam

Physical exam is focused on identifying signs of any complications of cholelithiasis. Murphy's sign (inspiratory arrest when palpating the gallbladder fossa) is the most common abdominal exam feature in patients with symptomatic cholelithiasis.[1] It has a high sensitivity (97%) but poor specificity (48%) for acute cholecystitis.[74] Dyspepsia, heartburn, flatulence, and bloating are common, but are not characteristic for gallstone disease.[1] [2]

Fever suggests a complication such as acute cholecystitis. Jaundice is rare in simple acute cholecystitis, being more suggestive of a stone in the common duct, cholangitis, or pancreatitis.[31] [75]

Laboratory testing

Complete blood count and liver biochemistry are usually normal with an episode of simple biliary pain.

- An elevated white blood cell count suggests acute cholecystitis, cholangitis, or pancreatitis.[1] [31] See Acute cholecystitis and Acute cholangitis .
- Obstructive choledocholithiasis is commonly associated with deranged liver function tests; specifically, elevated alkaline phosphatase and elevated bilirubin.
- Brief biliary obstruction with subsequent stone passage causes an early, transient elevation in alanine aminotransferase before the alkaline phosphatase rises.[76]

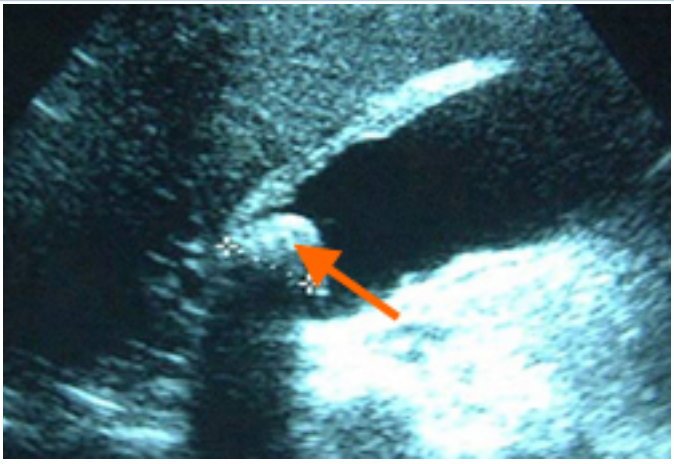
Patients who present with severe sudden-onset mid-epigastric or left upper quadrant abdominal pain (with or without radiation to the back) should have serum lipase levels taken to exclude pancreatitis.[1] See Acute pancreatitis .

- Serum lipase and amylase have similar sensitivity and specificity, but lipase levels remain elevated for longer (up to 14 days after symptom onset vs. 5 days for amylase), providing a higher likelihood of picking up the diagnosis in patients with a delayed presentation.[77] [78]

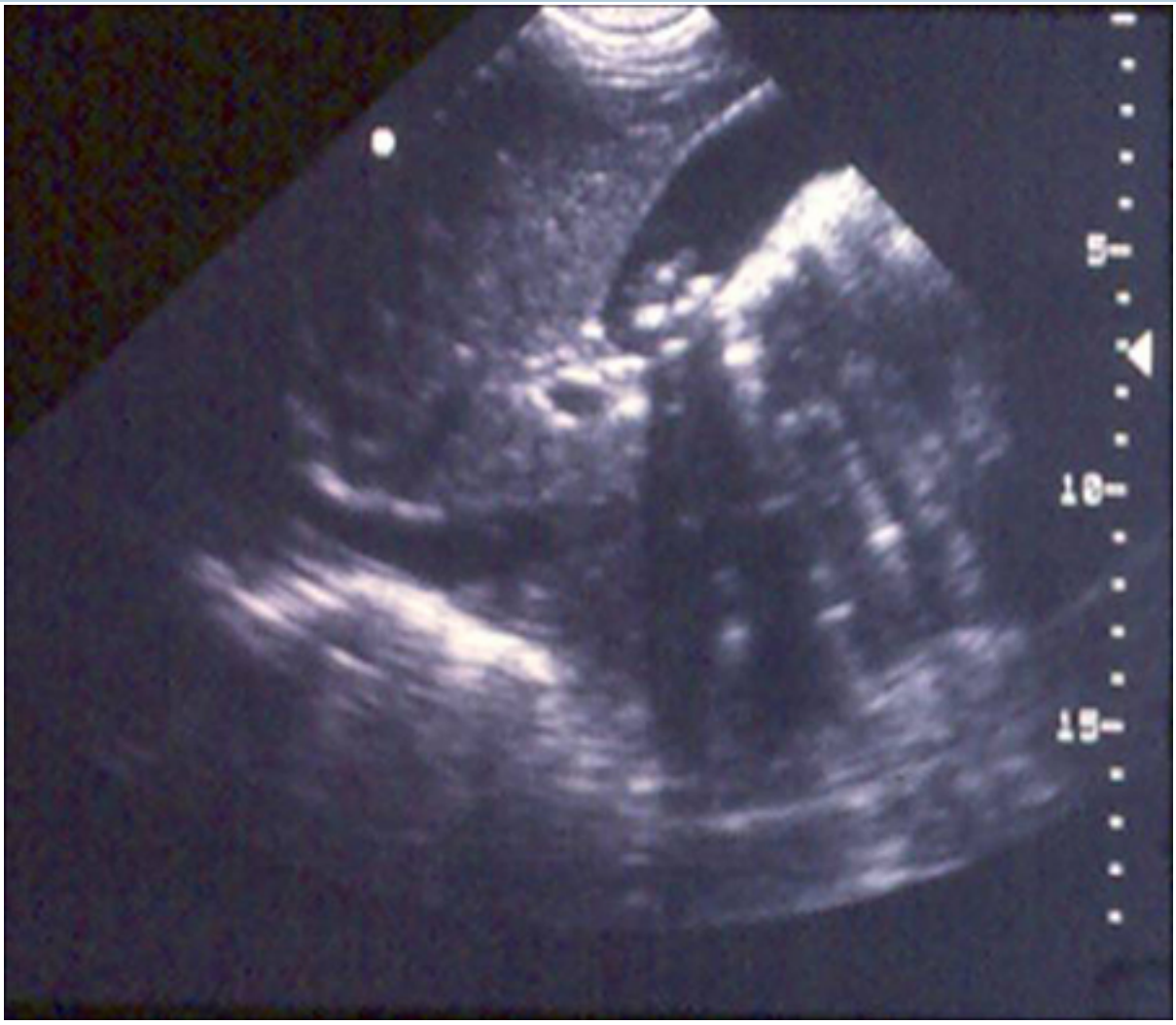
Abdominal ultrasound

The initial imaging test of choice in patients with suspected biliary pain is abdominal ultrasound to detect gallbladder stones or bile duct dilation caused by biliary obstruction.[1] [71] [72] [79] [80] If the history and exam, laboratory test results, and ultrasound findings are in agreement, no further imaging is needed.[81]

- If available, targeted point of care ultrasound (POCUS), performed at the bedside, can help to diagnose gallstones and expedite subsequent clinical decision making.[71] [72] [82] [83]
- Abdominal ultrasound, however, has low sensitivity for choledocholithiasis, despite being accurate in identifying any associated bile duct dilation.[84] [85]
- For acute calculous cholecystitis, abdominal ultrasound has high sensitivity for detecting stones, as well as distension of the gallbladder lumen, plus any inflammatory features, gallbladder wall thickening, pericholecystic fluid, and/or a positive radiologic Murphy's sign.[84]



Ultrasound of acute cholecystitis and presence of gallstones: the arrow points to a gallstone in the fundus of the gallbladder with its echogenic shadow below
Courtesy of Charles Bellows and W. Scott Helton; used with permission



Gallbladder ultrasound demonstrating cholelithiasis with characteristic shadowing
Courtesy of Kuojen Tsao; used with permission

Subsequent imaging

Further imaging may be required based on the clinical characteristics and associated index of clinical suspicion for complications.

- If choledocholithiasis is suspected (e.g., dilated bile ducts or abnormal liver biochemistry), magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound scan (EUS) is warranted.[75] [84]
- MRCP has a sensitivity of 95% and specificity of 97% for the detection of bile duct stones.[75] [86] However, it has a reduced sensitivity (65%) for the detection of small (<5 mm) biliary stones.[86] [87]
- EUS is similarly accurate for the detection of bile duct stones, especially in patients who are unable to undergo an MRCP (e.g., those with implanted devices). Depending on local expertise, EUS may be more accurate than MRCP, and can be useful for detecting patients at low to moderate risk of bile duct stones (negative imaging but positive symptoms and/or blood tests) who would benefit from a subsequent endoscopic retrograde cholangiopancreatography (ERCP).[1] [20] [88] [89] [90] [91] [92] [93] [94] [95]
- If initial imaging is negative but clinical features and/or blood tests are suggestive of choledocholithiasis and the patient is at high risk of complications (e.g., acute cholangitis, acute pancreatitis), ERCP is recommended. ERCP can be both diagnostic and therapeutic, enabling removal of any obstructing stones to provide biliary drainage.[94] [Evidence B]

- An unremarkable abdominal ultrasound in the presence of biliary pain may warrant an abdominal computed tomography scan to evaluate for alternative diagnoses (e.g., acute cholangitis or gallstone pancreatitis) and to identify potential complications of acute cholecystitis (e.g., emphysema of the gallbladder wall, abscess formation, perforation).[1] [79] [95]

History and exam

Key diagnostic factors

right upper quadrant (RUQ) or epigastric pain (lasting >30 minutes) (common)

Typical biliary pain occurs in the RUQ or epigastric area, sometimes after the consumption of food. This constant pain typically increases in intensity and lasts for several hours (biliary colic).[1] Pain of short duration (<30 minutes) is not biliary colic, while that of long duration (over 5 hours) suggests cholecystitis or another major complication.[1] Pain may be accompanied by nausea and sometimes vomiting.[1]

Dyspepsia, heartburn, flatulence, and bloating are common, but these features are not characteristic for gallstone disease.[1] [2]

Other diagnostic factors

postprandial pain (common)

Onset of pain may be after a meal, often around 1 hour after eating, particularly at night time.[73]

RUQ or epigastric tenderness (common)

Murphy's sign (inspiratory arrest when palpating the gallbladder fossa) has a high sensitivity (97%) but poor specificity (48%) for acute cholecystitis.[74] Murphy's sign is more suggestive of cholecystitis.[1]

nausea (uncommon)

Nausea may be present but more often accompanies pain from acute cholecystitis.[1]

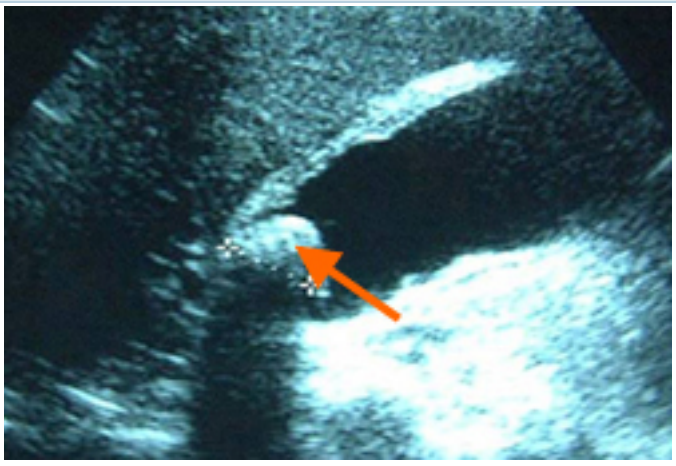
jaundice (uncommon)

Jaundice develops primarily in patients with choledocholithiasis, and is characteristic of cholangitis.[31] [75] Jaundice is uncommon in simple acute cholecystitis, except for Mirizzi syndrome (a rare complication in which a gallstone becomes impacted in the cystic duct or neck of the gallbladder, causing compression or inflammation of the common bile duct or common hepatic duct, resulting in obstruction and jaundice).[31]

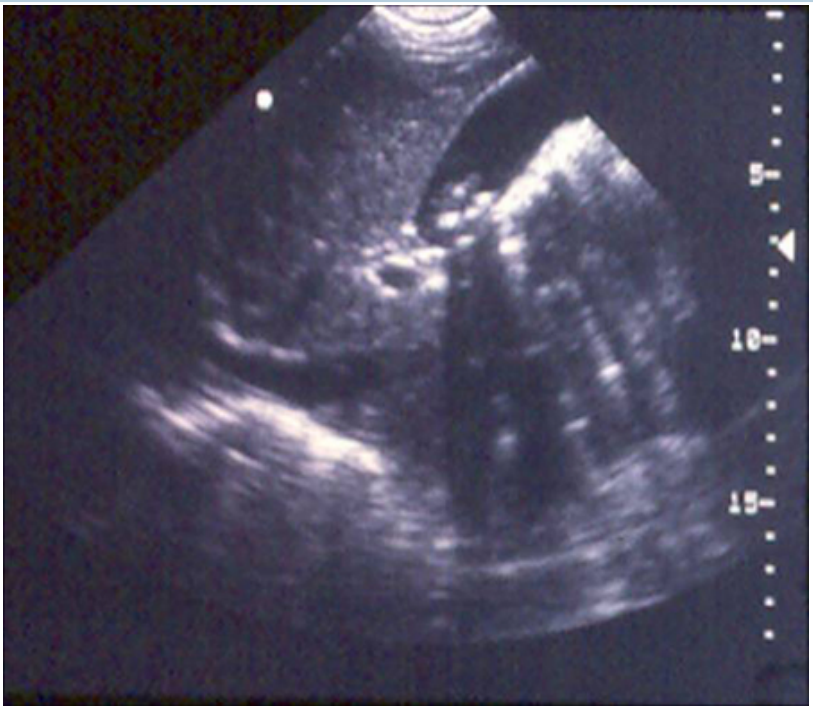
Tests

1st test to order

Test	Result
abdominal ultrasound Abdominal ultrasound is the initial imaging test of choice used to detect gallbladder stones or bile duct dilation caused by biliary obstruction.[1] [71] [72] [79] [80] If the history and exam, laboratory test results, and ultrasound findings are in agreement, no further imaging is needed.[81] If available, targeted point of care ultrasound (POCUS), performed at the bedside, can help to diagnose gallstones and expedite subsequent clinical decision making.[71] [72] [82] Abdominal ultrasound, however, has low sensitivity for choledocholithiasis, despite being accurate in identifying any associated bile duct dilation.[84] [85] For acute calculous cholecystitis, abdominal ultrasound has high sensitivity for detecting stones, as well as distension of the gallbladder lumen, plus any inflammatory features, gallbladder wall thickening, pericholecystic fluid, and/or a positive radiologic Murphy's sign.[84]	cholelithiasis: stones in the gallbladder choledocholithiasis: stones in the bile duct with or without bile duct dilation



Ultrasound of acute cholecystitis and presence of gallstones: the arrow points to a gallstone in the fundus of the gallbladder with its echogenic shadow below
Courtesy of Charles Bellows and W. Scott Helton; used with permission

Test	Result
 *Gallbladder ultrasound demonstrating cholelithiasis with characteristic shadowing* *Courtesy of Kuojen Tsao; used with permission*	
serum liver function tests For biliary pain, with or without jaundice. Elevated alkaline phosphatase suggests obstruction of the cystic or bile duct. Passage of a common bile duct stone may be revealed by a transiently elevated alanine aminotransferase, even before the rise in alkaline phosphatase.[76]	uncomplicated cholelithiasis: normal choledocholithiasis: elevated alkaline phosphatase, elevated bilirubin
CBC For biliary pain, with or without fever	normal in simple (uncomplicated) biliary colic elevated WBCs suggest inflammation from a complication of cholelithiasis (acute cholecystitis, cholangitis, or pancreatitis)[1] [31]
serum lipase or amylase For severe sudden-onset mid-epigastric or left upper quadrant abdominal pain, with or without radiation to the back, to exclude pancreatitis. Serum lipase is the preferred test; lipase levels remain elevated for longer (up to 14 days after symptom onset vs. 5 days for amylase), providing a higher likelihood of picking up a diagnosis of acute pancreatitis in patients with a delayed presentation.[77] [78]	usually normal in uncomplicated cholelithiasis elevated (>3 times upper limit of normal) in acute pancreatitis

Other tests to consider

Test	Result
magnetic resonance cholangiopancreatography (MRCP) For suspected choledocholithiasis that is not confirmed by abdominal ultrasound. MRCP has a sensitivity of 95% and specificity of 97% for the detection of bile duct stones.[75] [86] However, it has a reduced sensitivity (65%) for the detection of small (<5 mm) biliary stones.[86] [87]	stones in gallbladder or bile duct
endoscopic ultrasound scan (EUS) For suspected choledocholithiasis (e.g., positive symptoms ± blood tests) but negative abdominal ultrasound. Can be used to evaluate patients who are unable to undergo an MRCP (e.g., those with implanted devices). Depending on local expertise, EUS may be more accurate than MRCP, and can be useful for detecting patients at low to moderate risk of bile duct stones (negative ultrasound imaging but positive symptoms and/or blood tests) who would benefit from a subsequent endoscopic retrograde cholangiopancreatography.[1] [20] [88] [89] [90] [91] [92] [93] [94] [95] EUS is not suitable for patients who have had gastrointestinal bypass procedures.[20]	stones in gallbladder or bile duct
endoscopic retrograde cholangiopancreatography (ERCP) If initial imaging is negative but clinical features and/or blood tests are suggestive of choledocholithiasis and the patient is at high risk of complications (e.g., acute cholangitis, acute pancreatitis), ERCP is recommended. ERCP can be both diagnostic and therapeutic, enabling removal of any obstructing stones to provide biliary drainage.[94] [Evidence B]	stones in gallbladder or bile duct
abdominal CT scan If abdominal ultrasound is unremarkable, CT abdomen with intravenous contrast can be used to investigate alternate diagnoses such as suspected acute (ascending) cholangitis or gallstone pancreatitis, and to identify potential complications of acute cholecystitis (e.g., emphysema of the gallbladder wall, abscess formation, perforation).[1] [79] [95]	may be normal or show stones in the gallbladder, and possibly in the bile or pancreatic ducts may show acute (ascending) cholangitis: bile duct dilation with choledocholithiasis may show acute pancreatitis: diffuse or segmental enlargement of the pancreas

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Acalculous cholecystitis	• Positive Murphy's sign (tenderness suddenly becomes worse during deep inspiration and produces inspiratory arrest). In the intensive care unit setting, findings are often subtle.	• Abdominal ultrasound: no gallstones; may produce Murphy's sign. • Hepatobiliary iminodiacetic acid (HIDA) scan: gallbladder nonvisualization.
Nonbiliary acute pancreatitis	• History is helpful in identifying alcohol use, possible offending drugs, or recent biliary tract endoscopy/surgery.	• Triglycerides: elevated; usually >1000 mg/dL (can be lower in fasting patients). • Lipase: elevated for up to 14 days after symptom onset. • Calcium: elevated; checking ionized calcium is useful. • IgG4: for autoimmune pancreatitis. • Magnetic resonance cholangiopancreatography/ abdominal ultrasound: normal bile ducts.
Peptic ulcer disease (PUD)	• May have ulcer risk factors: *Helicobacter pylori* infection, nonsteroidal anti-inflammatory drug (NSAID) use, smoking, increased age, or positive family history of PUD. Presents with burning or gnawing pain in the upper abdomen, particularly with food consumption and often improved with antacids.	• Esophagogastroduodenoscopy: peptic ulcer. • *H pylori* breath/stool antigen test: may be positive if *H pylori* causative.
Gallbladder cancer	• Can present with painless jaundice and/or weight loss, although often presents late with upper abdominal pain.	• CT abdomen: may reveal intrahepatic mass lesion, dilated intrahepatic ducts, and/or localized lymphadenopathy.
Gallbladder polyps	• Often found incidentally on imaging for other conditions.	• Abdominal ultrasound: polypoidal lesion.
Sphincter of Oddi dysfunction (SOD)	• Postcholecystectomy biliary pain.	• Endoscopic retrograde cholangiopancreatography with biliary manometry: lack of sludge or retained stones; should only be undertaken in those with abdominal pain after cholecystectomy who have significant laboratory or

Condition	Differentiating signs / symptoms	Differentiating tests
		imaging abnormalities (type I or type II SOD).[96]

Recommendations

Key Recommendations

Asymptomatic cholelithiasis

Patients who have cholelithiasis with no symptoms do not usually require treatment; in most people, the risk of surgical complications outweighs the risk of leaving the gallstones untreated.[1] [16] [31] Annual follow-up of asymptomatic patients is recommended.[31]

Prophylactic cholecystectomy in asymptomatic individuals might be considered if there is high risk of gallbladder carcinoma (e.g., gallstones >3 cm, multiple gallstones, or a partially calcified "porcelain" gallbladder), or when the risk of gallstone formation and its complications are high (e.g., in those with sickle cell disease).[27] [2] [31] Prophylactic cholecystectomy is not routinely recommended for obese patients undergoing weight loss surgery. Rather, cholecystectomy should be reserved for obese patients who become symptomatic following surgery.[1] [98]

Symptomatic cholelithiasis

Give patients adequate analgesia for biliary colic.[99] Refer to local guidelines for choice of suitable analgesic and dose. Nonsteroidal anti-inflammatory drugs (NSAIDs) may benefit patients with biliary colic but must be used with caution particularly in patients with a likelihood of early surgery, due to increased risk of gastrointestinal bleeding.[1] [100]

Laparoscopic cholecystectomy is the procedure of choice for symptomatic cholelithiasis and should be performed as soon as possible; prompt surgical treatment decreases surgical morbidity, operating time, and duration of hospital stay.[1] [72] [101] [102] [103]

Clinical decision tools have identified patient attributes in those with uncomplicated symptomatic gallstone disease that are associated with the most benefit from cholecystectomy:[104]

- a high baseline pain score
- pain radiating through to the back
- a positive response to simple analgesia
- nausea
- absence of a history of heartburn
- no previous abdominal surgery
- advanced age.

Most patients with symptomatic cholelithiasis should be considered for laparoscopic cholecystectomy, unless they are unable to tolerate general anesthesia or have a serious cardiopulmonary disease or other comorbidity that makes surgery unsuitable.[102]

Appropriate supportive care for patients undergoing surgery includes nothing by mouth, intravenous fluids, and analgesia.[99] [105]

Despite similarities in mortality and complications between laparoscopic and open cholecystectomy, laparoscopic surgery is associated with reduced length of hospital stay and shorter recovery time, and so is preferred.[1] [97] [101] In pregnant patients, laparoscopic cholecystectomy is preferred and ideally carried out in the second trimester.[72] [106]

Open laparotomy is indicated (occasionally, in practice) if:[31] [72] [102] [107]

- laparoscopy is technically difficult (e.g., it is difficult to establish pneumoperitoneum, key anatomy is not clear, or there is concern for possible iatrogenic injury)
- there is inflammation, adhesions, intra-abdominal fat, or bleeding/untreated coagulopathy that call for an open procedure
- gallbladder cancer is suspected.

Patients with uncomplicated gallstone pancreatitis should undergo laparoscopic cholecystectomy during the same admission (ideally within 48 hours).[20]

Choledocholithiasis

Documented common bile duct stones warrant removal because they may cause serious obstructive complications such as acute cholangitis, hepatic abscess, or pancreatitis.[31] [97] [108] [109] A combination of biliary pain, gallbladder stones, a dilated common bile duct (>6 mm) on ultrasonography, and abnormal liver biochemistry (particularly an elevated bilirubin >68 micromoles/L or >4 g/dL) or pancreatic enzyme elevation suggests that a stone may have migrated into the common bile duct.[1]

If your patient is symptomatic with biliary colic, give adequate analgesia.[99] Refer to local guidelines for choice of suitable analgesic and dose.

Endoscopic retrograde cholangiopancreatography (ERCP)

ERCP with biliary sphincterotomy and stone extraction is the treatment of choice to avoid complications from choledocholithiasis.[20] [97] [109] [Evidence B]

- In about 10% to 15% of patients, sphincterotomy with standard extraction techniques is not successful, usually due to the stone being large (>1.5 cm), impacted, or located proximal to a stricture.[110] These patients require lithotripsy (fragmentation), papillary balloon dilation, and long-term biliary stenting.[20] [75] [109] [110] [111]

Following endoscopic stone extraction, definitive treatment with cholecystectomy reduces the risk of recurrent biliary events, in particular cholangitis or pancreatitis.[1] [112]

- For most patients with simultaneous gallbladder and bile duct stones, early laparoscopic cholecystectomy should generally follow ERCP and stone extraction as soon as any anesthetic or surgical issues are resolved (within 24-72 hours).[1] [20] [113]
- One Cochrane review compared the benefits and harms of this two-stage procedure with the "laparoscopic-endoscopic rendezvous", which combines the two techniques in a single-stage operation. There was insufficient evidence to determine the effects of the laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy techniques in people undergoing laparoscopic cholecystectomy in terms of mortality and morbidity.[114] Although no firm conclusions could be drawn, the single stage procedure may have longer operating times but reduce the overall length of hospital stay.[20] [114]

Laparoscopic common bile duct exploration

Laparoscopic common bile duct exploration, although technically difficult, is as effective for stone clearance as ERCP performed prior to or after cholecystectomy, and has demonstrated similar rates of mortality and morbidity.[115] [116] [117] [Evidence B]

- For patients at an intermediate risk of a common bile duct stone (abnormal liver biochemistry with more modest bilirubin elevations; biliary pancreatitis; and age >55 years), initial cholecystectomy with intraoperative cholangiography and common bile duct exploration may shorten hospitalization without increasing complications.[75] [97] [118]
- Laparoscopic common bile duct exploration should also be considered in patients with surgically altered anatomy (e.g., gastric surgery) or failed ERCP.[119]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute		(summary)
symptomatic cholelithiasis		
	1st	**cholecystectomy**
	plus	**supportive care**
choledocholithiasis with or without symptoms		
	1st	**endoscopic retrograde cholangiopancreatography (ERCP)**
	plus	**supportive care**
	consider	**lithotripsy, papillary balloon dilation, or long-term biliary stenting**
	2nd	**laparoscopic common bile duct exploration**
	plus	**supportive care**

Ongoing		(summary)
asymptomatic cholelithiasis		
	1st	**observation**

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: see disclaimer

Acute

symptomatic cholelithiasis

1st **cholecystectomy**

» Laparoscopic cholecystectomy is the procedure of choice for symptomatic cholelithiasis and should be performed as soon as possible; prompt surgical treatment decreases surgical morbidity, operating time, and duration of hospital stay.[1] [72] [101] [102] [103]

» Clinical decision tools have identified patient attributes in those with uncomplicated symptomatic gallstone disease that are associated with the most benefit from cholecystectomy: a high baseline pain score, pain radiating through to the back, a positive response to simple analgesia, nausea, absence of a history of heartburn, no previous abdominal surgery, and advanced age.[104]

» Most patients with symptomatic cholelithiasis should be considered for laparoscopic cholecystectomy, unless they are unable to tolerate general anesthesia or have a serious cardiopulmonary disease or other comorbidity that makes surgery unsuitable.[102]

» Despite similarities in mortality and complications between laparoscopic and open cholecystectomy, laparoscopic surgery is associated with reduced length of hospital stay and shorter recovery time, and so is preferred.[1] [97] [101]

» In pregnant patients, laparoscopic cholecystectomy is preferred and ideally carried out in the second trimester.[72] [106]

» Open laparotomy is indicated (occasionally, in practice) if laparoscopy is technically difficult (e.g., it is difficult to establish pneumoperitoneum, key anatomy is not clear, or there is concern for possible iatrogenic injury), if there is inflammation, adhesions, intra-abdominal fat, or bleeding/untreated coagulopathy, or if gallbladder cancer is suspected.[31] [72] [102] [107]

Acute

		» Patients are usually consented to the initial laparoscopic approach and conversion to an open procedure may be required. » Patients with uncomplicated gallstone pancreatitis should undergo laparoscopic cholecystectomy during the same admission (ideally within 48 hours).[20]
	plus	**supportive care** Treatment recommended for ALL patients in selected patient group » Give patients adequate analgesia for biliary colic.[99] Appropriate supportive care for patients undergoing surgery also includes nothing by mouth and intravenous fluids.[105] » Nonsteroidal anti-inflammatory drugs (NSAIDs) may benefit patients with biliary colic but must be used with caution particularly in patients with a likelihood of early surgery, due to increased risk of gastrointestinal bleeding.[1] [100]
choledocholithiasis with or without symptoms		
	1st	**endoscopic retrograde cholangiopancreatography (ERCP)** » Documented common bile duct stones warrant removal because they may cause serious obstructive complications such as acute cholangitis, hepatic abscess, or pancreatitis.[31] [97] [108] [109] A combination of biliary pain, gallbladder stones, a dilated common bile duct (>6 mm) on ultrasonography, and abnormal liver biochemistry (particularly an elevated bilirubin >68 micromoles/L or >4 g/dL) or pancreatic enzyme elevation suggests that a stone may have migrated into the common bile duct.[1] » Choledocholithiasis is best detected through endoscopic ultrasound or magnetic resonance cholangiopancreatography.[75] » ERCP with biliary sphincterotomy and stone extraction is the treatment of choice to avoid complications from choledocholithiasis.[20] [97] [109] [Evidence B] In about 10% to 15% of patients, sphincterotomy with standard extraction techniques is not successful and usually due to the stone being large (>1.5 cm), impacted, or located proximal to a stricture.[110] These patients require lithotripsy (fragmentation), papillary balloon dilation, and long-term biliary stenting.[20] [75] [109] [110] [111]

Acute

» Following endoscopic stone extraction, definitive treatment with cholecystectomy reduces the risk of recurrent biliary events, in particular cholangitis or pancreatitis.[1] [112] For most patients with simultaneous gallbladder and bile duct stones, early laparoscopic cholecystectomy should generally follow ERCP and stone extraction as soon as any anesthetic or surgical issues are resolved (within 24-72 hours).[1] [20] [113] One Cochrane review compared the benefits and harms of this two-stage procedure with the "laparoscopic-endoscopic rendezvous", which combines the two techniques in a single-stage operation. There was insufficient evidence to determine the effects of the laparoscopic-endoscopic rendezvous versus preoperative endoscopic sphincterotomy techniques in people undergoing laparoscopic cholecystectomy in terms of mortality and morbidity.[114] Although no firm conclusions could be drawn, the single stage procedure may have longer operating times but reduce the overall length of hospital stay.[20] [114]

plus **supportive care**

Treatment recommended for ALL patients in selected patient group

» If your patient is symptomatic with biliary colic, give adequate analgesia.[99] Appropriate supportive care for patients undergoing surgery also includes nothing by mouth and intravenous fluids.[105]

» Nonsteroidal anti-inflammatory drugs (NSAIDs) may benefit patients with biliary colic but must be used with caution particularly in patients with a likelihood of early surgery, due to increased risk of gastrointestinal bleeding.[1] [100]

consider **lithotripsy, papillary balloon dilation, or long-term biliary stenting**

Treatment recommended for SOME patients in selected patient group

» ERCP may require various lithotripsy modalities, papillary balloon dilation, and long-term biliary stenting.[20] [109] [110] [111]

2nd **laparoscopic common bile duct exploration**

» Laparoscopic common bile duct exploration, although technically difficult, is as effective for stone clearance as ERCP performed prior to or after cholecystectomy and has demonstrated similar rates of mortality and morbidity.[115] [116] [117] [Evidence B]

Acute

» For patients at an intermediate risk of a common bile duct stone (abnormal liver biochemistry with more modest bilirubin elevations; biliary pancreatitis; and age >55 years), initial cholecystectomy with intraoperative cholangiography and common bile duct exploration may shorten hospitalization without increasing complications.[75] [97] [118]

» Laparoscopic common bile duct exploration should also be considered in patients with surgically altered anatomy (e.g., gastric surgery) or failed ERCP.[119]

plus **supportive care**

Treatment recommended for ALL patients in selected patient group

» If your patient is symptomatic with biliary colic, give adequate analgesia.[99] Appropriate supportive care for patients undergoing surgery also includes nothing by mouth and intravenous fluids.[105]

» Nonsteroidal anti-inflammatory drugs (NSAIDs) may benefit patients with biliary colic but must be used with caution particularly in patients with a likelihood of early surgery, due to increased risk of gastrointestinal bleeding.[1] [100]

Ongoing

asymptomatic cholelithiasis

1st **observation**

» Patients who have cholelithiasis with no symptoms do not usually require treatment; in most people, the risk of surgical complications outweighs the risk of leaving the gallstones untreated.[1] [16] [31] Annual follow-up of asymptomatic patients is recommended.[31]

» Prophylactic cholecystectomy in asymptomatic individuals might be considered if there is high risk of gallbladder carcinoma (e.g., gallstones >3 cm, multiple gallstones, or a partially calcified "porcelain" gallbladder), or when the risk of gallstone formation and its complications are high (e.g., in those with sickle cell disease).[27] [2] [31] Prophylactic cholecystectomy is generally not routinely recommended for obese patients undergoing weight loss surgery. Rather, cholecystectomy should be reserved for obese patients who become symptomatic following surgery.[1] [98]

Primary prevention

Although the evidence for a preventative effect is weak, lifestyle modification remains the cornerstone of primary prevention of gallstones. Preventative lifestyle modifications recommended in practice include a diet high in fiber, protein, calcium, and vitamin C and low in saturated fat, and maintenance of a healthy body weight, combined with moderate physical activity.[1] [2] [7] [27] [61] [64] [65] [66] [67]

Preventative medical therapy with ursodiol, which lowers cholesterol saturation in bile, can be used to reduce the short-term risk of stone formation in obese individuals undergoing rapid weight loss through dietary caloric restriction or weight loss surgery.[68] In those undergoing surgery, ursodiol has only been shown to be effective when used preoperatively.[68] In this setting, ursodiol should only be used until the patient's weight has stabilized, as the evidence for its efficacy is limited.[1] [69] Ursodiol has limited value for dissolving established gallstones and is not recommended for any other patient groups.[70]

Patient discussions

Patients with asymptomatic gallbladder stones, found incidentally, should be reassured that they do not need treatment unless they develop symptoms (provided the gallbladder and biliary tree were normal on investigation).[80]

Patients should be advised to avoid food and drink that triggers their symptoms until they have their gallbladder or gallstones removed, but they can resume normal diet after surgery/intervention for stones.[80] If eating or drinking triggers existing symptoms, or causes new symptoms to develop after removal of the gallbladder or gallstones, patients should seek further medical advice.[80] In practice, if patients develop abdominal pain, fever, nausea and/or vomiting, anorexia, or changes in mental status after surgery, they should also consult their doctor.

Patient information is available from the following resource. [NIDDK: gallstones]

Monitoring

Monitoring

Patients who experience therapy-related complications require follow-up with their physicians. Annual follow-up of asymptomatic patients is recommended.[31]

There are no recommended secondary preventive measures.[1]

Complications

Complications	Timeframe	Likelihood
endoscopic retrograde cholangiopancreatography (ERCP)-associated pancreatitis	**short term**	**medium**
Pancreatitis following ERCP is the most common complication of the procedure, occurring in 3.5% of patients.[123] It is associated with female sex, age <65 years, a longer biliary cannulation time, and precut-sphincterotomy.[124] It is usually managed with analgesia, intravenous hydration, and nutritional support. Indomethacin rectal suppository, given immediately after the ERCP, can help prevent this complication.[97] [123] [125]		
iatrogenic bile duct injuries	**short term**	**low**
Bile duct injury is defined as any damage to the bile duct, including leakage of bile, iatrogenic bile duct injury, and biliary strictures. Bile leak occurs in 0.5% to 1.5% of patients undergoing laparoscopic cholecystectomy, and is associated with significant morbidity and higher 1-2 year mortality compared with patients who have uncomplicated surgery.[1] [135] [136] Bile duct injuries occur in 0.4% to 1.5% of patients undergoing cholecystectomy and are due to direct surgical trauma or from partial/complete transection of the bile duct due to clips or ligation.[136] In the short term (acute or the perioperative state), bile duct injuries can lead to bleeding or perforation and biliary obstruction. More long term, bile duct strictures can develop. Biliary strictures are generally preventable. Diagnosis is with laboratory tests (elevated white cell count, bilirubin, liver enzymes) and imaging (contrast computed tomography or magnetic resonance cholangiopancreatography), and patients can develop persistent pain, fever, nausea, and vomiting post cholecystectomy.[1] Risk factors for bile duct injury are Mirizzi syndrome, impacted cystic duct stones, and abnormal anatomy.[1] If detected intraoperatively, primary surgical repair can be performed; otherwise bile duct injuries are usually managed with endoscopic transpapillary biliary stent insertion, unless there has been complete transection.[1] If there is a concomitant biloma (a collection of bile outside of the biliary tree), percutaneous drainage may also be necessary and antibiotics should be started immediately.[136]		
post-sphincterotomy bleeding	**short term**	**low**
The frequency of bleeding as a complication of ERCP with sphincterotomy and stone extraction varies from 1% to 48% depending on what definition is applied, such as the magnitude of bleeding (limited vs. life-threatening), and if it occurred during the procedure.[137] Risk factors for post-sphincterotomy bleeding include a stone impaction at the ampulla, bleeding during initial sphincterotomy, cholangitis prior to ERCP, deranged coagulation, and recent hemodialysis.[138] [139] This complication is commonly recognized at the time of the procedure and can be treated with endoscopic hemostatic techniques, such as injection of epinephrine.[138]		
Bouveret syndrome	**long term**	**low**
If a gallstone erodes through the gallbladder wall, a cholecystoenteric fistula can develop and lead to gastric outlet obstruction, known as Bouveret syndrome. This usually presents with nausea, vomiting, and abdominal pain, although it can present with symptoms of upper gastrointestinal bleeding, such as hematemesis or melena.[133] Diagnosis is made on abdominal x-ray demonstrating gastrointestinal tract obstruction, ultrasound, or computed tomography or magnetic resonance imaging.[133] Treatment to relieve the obstruction commonly entails endoscopic extraction of the stone with placement of a temporary biliary stent, or surgery with common bile duct exploration to close the fistula. Cholecystectomy is usually then warranted to prevent stone recurrence.[133] [134]		

Complications	Timeframe	Likelihood
gallstone ileus	**long term**	**low**
If a stone erodes through the gallbladder wall and creates a cholecystoenteric fistula, the stone can then pass into, and lead to obstruction of, the narrowest segment of healthy bowel, often the terminal ileum.[32] This presents with symptoms of bowel obstruction (nausea, vomiting, crampy abdominal pain, distension).[32] Computed tomography is the most accurate imaging modality to confirm the diagnosis; treatment is usually with surgery.[32]		
cholecystitis	**variable**	**low**
Acute cholecystitis occurs when obstruction of the cystic duct leads to gallbladder inflammation. Patients usually have intense, steady right upper quadrant pain (sometimes radiating to the back, right shoulder, or chest), a positive Murphy's sign, fever, nausea, vomiting, and leukocytosis.[1] Diagnosis can be made on abdominal ultrasound (demonstrating gallbladder stones, with either a sonographic Murphy's sign or thickened gallbladder).[1] Computed tomography (CT) can accurately demonstrate gallbladder distention and thickening, as well as complications such as fistulae, gallbladder wall emphysema, and perforation.[1] Cholescintigraphy (hepatobiliary iminodiacetic acid [HIDA] scan) demonstrating absence of gallbladder filling is over 90% accurate, although false positives can occur in fasting and intensive care unit patients.[1] [126] [127] HIDA scans are only performed if ultrasound and CT are not diagnostic, as the lack of gallstone visualization and ionizing radiation make this test less favorable.[1] Treatment involves intravenous hydration, antibiotics, analgesia as needed, and early cholecystectomy. Evidence suggests that early cholecystectomy is associated with shorter hospital stay and fewer recurrent symptoms.[128] Patients unsuitable for surgery can be managed with percutaneous cholecystostomy tube placement.[1]		
acute cholangitis	**variable**	**low**
Acute cholangitis occurs when there is complete obstruction of the bile duct resulting in cholestasis and infected bile. The classic presentation is biliary pain, jaundice, and fever (Charcot triad).[1] Hypotension and altered mental status may also be present (Reynolds pentad). Leukocytosis and abnormal liver function tests are typical.[1] Bacterial cholangitis should be considered a medical emergency. Treatment involves intravenous hydration, broad-spectrum antibiotics, analgesia, and biliary decompression within 24-48 hours.[1] The preferred method of biliary decompression is ERCP with sphincterotomy and stone extraction.[129] Biliary stent placement without stone removal, percutaneous drainage, or surgical common bile duct exploration are alternative options if endoscopic decompression fails or if there are contraindications to endoscopic procedures, such as coagulopathy.[1] [31] [130] If ERCP fails, endoscopic ultrasound-guided biliary drainage, percutaneous drainage, or surgical common bile duct exploration may become necessary.[131]		
acute biliary pancreatitis	**variable**	**low**
Occurs when there is pancreatic outflow obstruction or reflux of bile into the pancreatic duct. Patients usually present with severe epigastric abdominal pain with or without radiation into the back, nausea and vomiting, and elevated pancreatic enzymes.[1] Diagnosis is confirmed on ultrasound, which demonstrates common bile duct dilation, although it is less accurate for detecting gallstones.[1] Treatment involves aggressive intravenous hydration, analgesia, and consideration of ERCP with sphincterotomy and stone extraction within 72 hours of admission (for severe acute pancreatitis with evidence of biliary obstruction and/or cholangitis).[20] [31] [132] Mild acute pancreatitis requires only fluids and supportive care.		

FOLLOW UP

Complications	Timeframe	Likelihood
Cholecystectomy should be offered before discharge from the hospital.		
Mirizzi syndrome	**variable**	**low**
Mirizzi syndrome is when a large gallstone becomes lodged in the cystic duct and compresses or causes inflammation of the common hepatic duct, resulting in biliary obstruction and jaundice.[31] It is an uncommon complication of cholelithiasis, occurring in 0.18% to 0.35% of patients with cholecystectomy in the US.[31] There are several subtypes of the syndrome, classified by the amount of involved duct and presence/absence of a fistula.[31] Mirizzi syndrome is typically treated with laparoscopic cholecystectomy, although the open procedure is preferred for certain subtypes.[1] [31]		

Prognosis

The outlook for patients with symptomatic cholelithiasis managed by cholecystectomy is favorable. The same holds for patients with choledocholithiasis who undergo endoscopic retrograde cholangiopancreatography with biliary sphincterotomy and stone extraction, followed later by cholecystectomy.

Recurrent choledochal problems

Recurrent bile duct stones occur in 5% to 20% of patients after endoscopic sphincterotomy.[1] Risk factors for recurrent choledochal problems include: pre-existing patient factors (e.g., bile composition and biliary anatomy); factors related to the sphincterotomy (sphincter ablation and papillary stenosis); bile duct dilatation to >13 mm; multiple common bile duct stones; and brown pigment stones.[75] [120] [121] [122]

Diagnostic guidelines

International

ACR appropriateness criteria: right upper quadrant pain [79]

Published by: American College of Radiology **Last published:** 2022

ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis [20]

Published by: American Society for Gastrointestinal Endoscopy **Last published:** 2019

2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis [72]

Published by: World Society of Emergency Surgery **Last published:** 2020

Updated guideline on the management of common bile duct stones (CBDS) [97]

Published by: British Society of Gastroenterology (UK) **Last published:** 2017

Evidence-based clinical practice guidelines for cholelithiasis [31]

Published by: Japanese Society of Gastroenterology **Last published:** 2017

EASL clinical practice guidelines on the prevention, diagnosis and treatment of gallstones [1]

Published by: European Association for the Study of the Liver **Last published:** 2016

Treatment guidelines

International

SAGES guidelines for the clinical application of laparoscopic biliary tract surgery [102]

Published by: Society of American Gastrointestinal and Endoscopic Surgeons **Last published:** 2010

Updated guideline on the management of common bile duct stones (CBDS) [97]

Published by: British Society of Gastroenterology **Last published:** 2017

Evidence-based clinical practice guidelines for cholelithiasis [31]

Published by: Japanese Society of Gastroenterology **Last published:** 2017

EASL clinical practice guidelines on the prevention, diagnosis and treatment of gallstones [1]

Published by: European Association for the Study of the Liver **Last published:** 2016

Online resources

1. NIDDK: gallstones *(external link)*

EVIDENCE TABLES

Evidence tables

How does early routine endoscopic retrograde cholangiopancreatography (ERCP) compare with early conservative management in people with acute gallstone pancreatitis?

This table is a summary of the analysis reported in a Cochrane Clinical Answer that focuses on the above important clinical question.

Cochrane Clinical Answers

View the full source Cochrane Clinical Answer

Evidence B *

Confidence in the evidence is moderate or low to moderate where GRADE has been performed and there may be no difference in effectiveness between the intervention and comparison for key outcomes.

Population: Adults with clinical signs/symptoms suggestive of acute gallstone pancreatitis or confirmed acute gallstone pancreatitis #

Intervention: ERCP combined with conservative management (within 72 hours of admission)

Comparison: Early conservative management (within 30 days of admission)

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
All-cause mortality during hospitalization up to 3 months	No statistically significant difference #	Low
Local complications defined by the Atlanta Classification at 10 days to 3 months	No statistically significant difference #	Moderate
Systemic complications defined by the Atlanta Classification at 10 days to 3 months	No statistically significant difference #	Moderate
ERCP-related complication: post-ERCP bleeding (time period unclear)	No statistically significant difference	GRADE assessment not performed for this outcome
ERCP-related complications other than bleeding (time period unclear)	See note #	GRADE assessment not performed for this outcome
ERCP-related mortality	-	The reviewers did not assess this outcome

Note

- The Cochrane review which underpins this Cochrane Clinical Answer (CCA) states that the timing of ERCP (urgent <24 hours versus early <72 hours) should depend on the level of suspicion, the condition of the patient, and response to initial conservative management
- The CCA also mentioned a possible benefit of early routine ERCP for patients with biliary obstruction (see the underlying Cochrane review for more details and subgroup analysis).

The CCA is for unselected patients with gallstone pancreatitis. However, it includes subgroup analyses selecting patients with concurrent cholangitis which found some benefit for early routine ERCP with reduced mortality, local complications, and systemic complications compared with conservative management. The reviewers did not perform a GRADE assessment (see CCA for more details and subgroup analysis).

Results reported narratively (see the CCA for more details).

EVIDENCE TABLES

In adults with bile duct stones, how does surgical treatment compare with endoscopic treatment for improving outcomes?

This table is a summary of the analysis reported in a Cochrane Clinical Answer that focuses on the above important clinical question.

Cochrane Clinical Answers

View the full source Cochrane Clinical Answer

Evidence B * Confidence in the evidence is moderate or low to moderate where GRADE has been performed and there may be no difference in effectiveness between the intervention and comparison for key outcomes.

Population: Adults with common bile duct stones

Intervention: Laparoscopic cholecystectomy plus laparoscopic common bile duct exploration (LC plus LCBDE)

Comparison: Endoscopic retrograde cholangiopancreatography (ERCP) plus LC

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
LC plus LCBDE versus preoperative ERCP plus LC		
Mortality at 30 days	No statistically significant difference	Moderate
Total morbidity (time point unclear)	No statistically significant difference	Moderate
Retained stones (time point unclear)	No statistically significant difference	Moderate
Failure of procedure (time point unclear)	No statistically significant difference	Moderate
Conversion to open surgery (time point unclear)	No statistically significant difference	Moderate
Quality of life (time point unclear)	No statistically significant difference #	GRADE assessment not performed for this outcome #
Hospital stay	Unknown #	GRADE assessment not performed for this outcome
LC plus LCBDE versus LC plus postoperative ERCP		
Mortality (time point unclear)	Unknown #	GRADE assessment not performed for this outcome

Outcome	Effectiveness (BMJ rating)†	Confidence in evidence (GRADE)‡
Total morbidity (time point unclear)	No statistically significant difference	Moderate
Retained stones after primary intervention (time point unclear)	Favors intervention	Moderate
Failure of procedure (time point unclear)	No statistically significant difference	Moderate
Conversion to open surgery (time point unclear)	No statistically significant difference	Moderate
Hospital stay	Unknown #	GRADE assessment not performed for this outcome
Quality of life	-	None of the studies identified by the review assessed this outcome

Note

Results reported narratively (see the Cochrane Clinical Answer for more details).

The Cochrane reviewers did not perform a GRADE assessment but the single RCT providing evidence for this outcome was at low risk of bias for all domains.

No meta-analysis was done for this outcome and the results from five RCTs were reported narratively. Two showed a shorter stay with LC + LCBDE compared with preoperative ERCP + LC; the other three found no statistically significant difference between groups.

* Evidence levels

The Evidence level is an internal rating applied by BMJ Best Practice. See the EBM Toolkit for details.

Confidence in evidence

A - High or moderate to high

B - Moderate or low to moderate

C - Very low or low

† Effectiveness (BMJ rating)

Based on statistical significance, which demonstrates that the results are unlikely to be due to chance, but which does not necessarily translate to a clinical significance.

‡ Grade certainty ratings

High	The authors are very confident that the true effect is similar to the estimated effect.
Moderate	The authors are moderately confident that the true effect is likely to be close to the estimated effect.
Low	The authors have limited confidence in the effect estimate and the true effect may be substantially different.
Very Low	The authors have very little confidence in the effect estimate and the true effect is likely to be substantially different.

BMJ Best Practice EBM Toolkit: What is GRADE?

Key articles

- European Association for the Study of the Liver (EASL). EASL clinical practice guidelines on the prevention, diagnosis and treatment of gallstones. J Hepatol. 2016 Jul;65(1):146-81. Full text Abstract
- ASGE Standards of Practice Committee; Buxbaum JL, Abbas Fehmi SM, Sultan S, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc. 2019 Jun;89(6):1075-105;e15. Full text Abstract
- Tazuma S, Unno M, Igarashi Y, et al. Evidence-based clinical practice guidelines for cholelithiasis 2016. J Gastroenterol. 2017 Mar;52(3):276-300. Full text Abstract

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Images

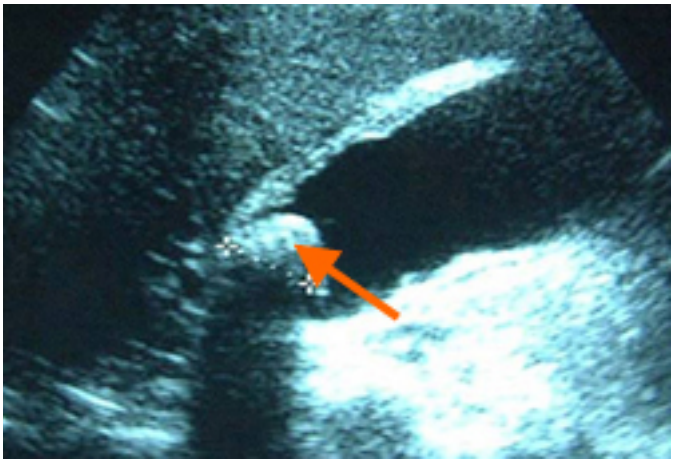

Figure 1: Ultrasound of acute cholecystitis and presence of gallstones: the arrow points to a gallstone in the fundus of the gallbladder with its echogenic shadow below

Courtesy of Charles Bellows and W. Scott Helton; used with permission

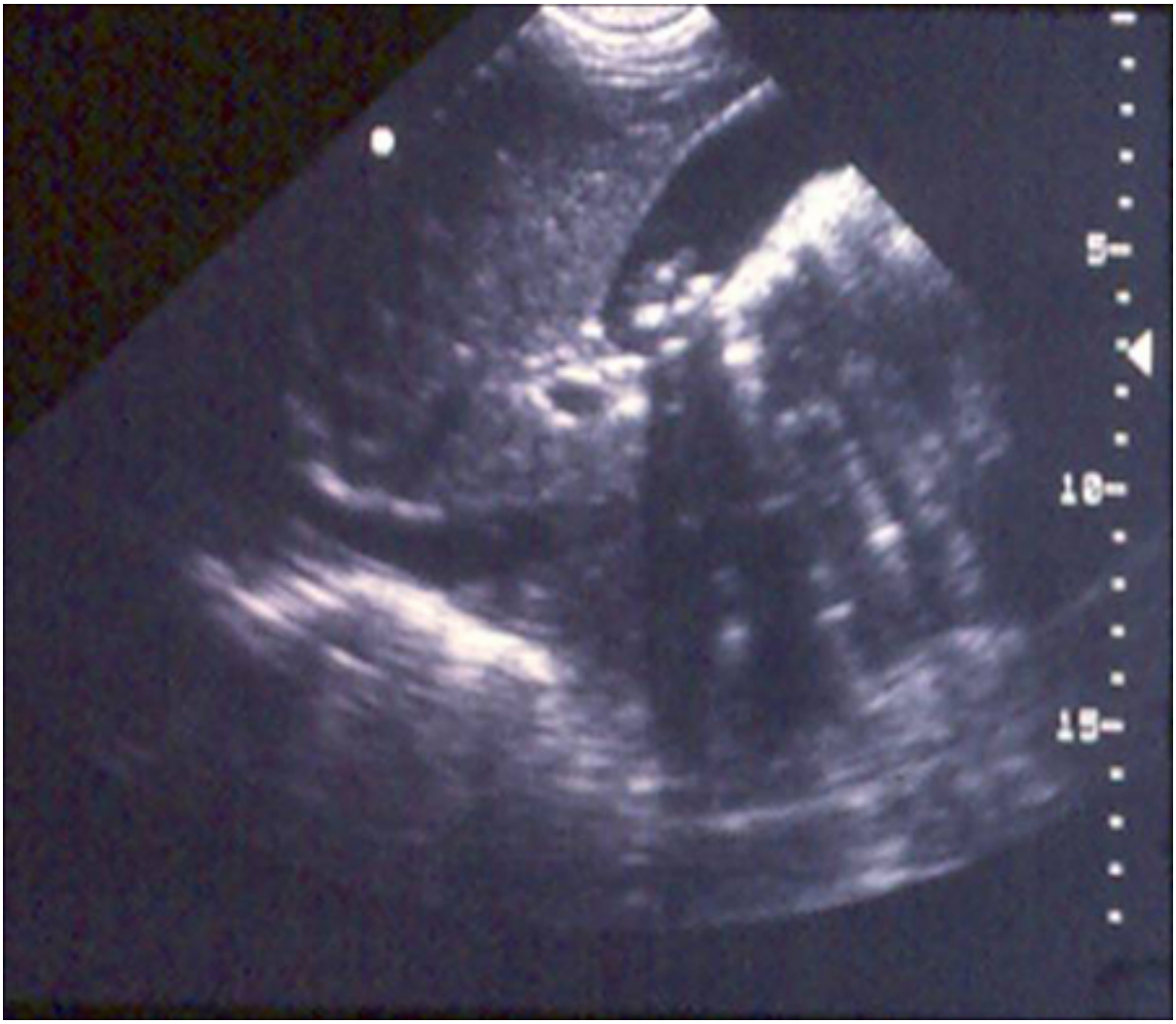

Figure 2: Gallbladder ultrasound demonstrating cholelithiasis with characteristic shadowing

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Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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This approach is in line with the guidance of the International Bureau of Weights and Measures Service.

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