Ultrasonographic Evaluation of Right Upper Quadrant Pain in Emergency Departments

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KEYWORDS

• Right upper quadrant pain • Gallstones • Acute cholecystitis
• Ultrasound • Gallbladder disease

Acute right upper quadrant (RUQ) pain is a common reason that patients present to hospital emergency departments. The differential diagnosis is broad and most commonly encompasses disorders of the gallbladder, biliary tract, liver, subphrenic spaces, and gastrointestinal and genitourinary tracts (**Box 1**). Since the signs and symptoms of these disorders are often nonspecific and may frequently overlap, imaging is pivotal for prompt patient management.

DIFFERENTIAL DIAGNOSIS

In the emergency department setting, the primary diagnosis to be established or excluded for a patient presenting with RUQ pain is acute cholecystitis.[1–3] Acute cholecystitis, or acute inflammation of gallbladder, may develop if there is persistent cystic duct or gallbladder neck obstruction lasting more than 6 hours. In addition to pain, patients also often develop nausea, vomiting, chills, and fever. RUQ tenderness and guarding are common with acute cholecystitis. As many as 20% of patients may have mild hyperbilirubinemia,[4] and if there is common bile duct obstruction, levels greater than 4 mg per 100 ml may occur. Leukocytosis and elevations of alkaline phosphatase, aminotransferase (transaminase), and amylase may occur.

Approximately 95% of cases of cholecystitis are because of gallstones. Gallstone disease is one of the most common medical problems leading to surgical intervention. In the United States, gallstone disease is the most common inpatient diagnosis among gastrointestinal and liver diseases.[5] The annual expenditure of $5.8 billion for gallstone treatment is exceeded only by that of gastroesophageal reflux disease.[6] Mean prevalence rates of 10% to 15% in adult Europeans and 3% to 5% in African and Asian populations have been reported.[7] In the United States, the prevalence rates range from 5% among non-Hispanic black men to 27% among Mexican-American women.[8] In American Indians, gallstone disease is epidemic and found in 73% of adult female Pima Indians.[9] In women, factors that predispose to gallstones are increased weight, increased age, and increased parity. In men, increased age also predisposes to gallstones.[10] More than 80% of gallstone carriers are unaware of their gallbladder disease.[7,11] About 1% to 2% of patients develop complications per year and often need surgery.[12] In North America, 75% of gallstones are cholesterol stones, the rest are pigment

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Box 1
Common causes of RUQ pain

Biliary: cholelithiasis, cholecystitis, cholangitis

Hepatic: abscess, hepatitis, mass, Budd-Chiari syndrome

Pancreas: pancreatitis, pancreatic cancer

Renal: nephrolithiasis, pyelonephritis

Stomach: gastritis, peptic ulcer

Bowel: appendicitis, colitis, diverticulitis, enteritis, intussusception

Pulmonary: pneumonia, embolus

Others: costochondritis, herpes zoster, myocardial infarction

stones.[13] Pigment stones are common in patients who have hemolytic disorders, such as sickle cell disease, biliary tract infection, or cirrhosis.

DIAGNOSTIC WORKUP OF RUQ PAIN

Nonimaging Tests

Although a careful history taking and physical examination can often provide important clues to the diagnosis of RUQ pain, the signs and symptoms of the many conditions listed in **Box 1** overlap greatly. Therefore, a number of laboratory tests are relatively routine. Liver function tests are helpful because certain abnormalities can strongly suggest hepatobiliary disease, and the pattern of abnormality on these tests can point toward liver parenchymal processes or biliary processes. Renal, pancreatic, and cardiac abnormalities can be identified in many cases by obtaining a urinalysis, serum amylase and lipase levels, and an electrocardiograph, respectively.

An evidence-based diagnosis of acute cholecystitis was studied in a meta-analysis published in 2003,[14] which showed that no clinical or laboratory finding had a high or low enough likelihood ratio to predict the presence or absence of acute cholecystitis. This study further supported the evidence that imaging studies are essential for establishing or excluding the diagnosis of acute cholecystitis and for the establishment or exclusion of alternate diagnoses, if acute cholecystitis is not present.

Imaging Tests

A wide variety of imaging techniques exist to evaluate patients with RUQ pain. These techniques include chest and abdominal radiography, luminal studies of the gastrointestinal tract, ultrasonography (US), biliary scintigraphy, computed tomography (CT), and magnetic resonance (MRI).

The American College of Radiology revised the appropriateness criteria for imaging tests for evaluating patients presenting with RUQ pain in 2010.[15] A rating scale of 1 (usually not appropriate) to 9 (usually appropriate) is used to denote relative appropriateness of imaging tests that are used for evaluating patients presenting with RUQ pain. In addition to RUQ pain, if a patient has clinical findings of fever, elevated white blood cell count, and a positive clinically elicited Murphy sign, then the primary imaging test recommended with the highest rating of 9 is US. Abdominal CT (preferably with contrast), cholescintigraphy, and abdominal MRI with or without contrast each have a rating of 6 and should be performed only if sonographic findings are inconclusive or require additional problem solving. Even if the patient presents with RUQ pain without fever, elevated white blood cell count, or Murphy sign, the imaging test of choice with a rating of 9 remains US. CT, cholescintigraphy, and MRI, each with a rating of 6, are recommended only if sonographic findings are inconclusive or require additional problem solving. Abdominal US has been rated 9 in most variants of clinical presentation of patients with RUQ pain, except in acalculous cholecystitis in which it is rated 8. Even in that setting for acalculous cholecystitis, the other imaging modalities are rated only 6 or less.

Some of the reasons for which US is the preferred imaging test in patients with RUQ pain include better availability, lack of ionizing radiation, better morphologic evaluation of the gallbladder for complications, confirmation of the presence or absence of gallstones, evaluation of intrahepatic and extrahepatic bile ducts, and identification or exclusion of alternative diagnoses.[1,16–18] The positive predictive value of sonography in identifying patients who would benefit from cholecystectomy is 99%.[19]

When sonographic evaluation is nonconclusive for acute cholecystitis, scintigraphy is often the next imaging test of choice. Cholescintigraphy has been reported to have similar accuracy for the diagnosis of acute cholecystitis.[20] Several investigations have directly compared the accuracy of cholescintigraphy and US for the diagnosis of acute cholecystitis.[21] These studies have shown an overall sensitivity and specificity of 86% to 97% and 73% to 100%, respectively, for cholescintigraphy and 81% to 100% and 60% to 100%, respectively, for US.[22–25] However, scintigraphy is incapable of diagnosing nonbiliary conditions and up to two-thirds of patients seen in the

emergency department with suspected cholecystitis do not have cholecystitis. In addition, the longer time required to perform scintigraphy (up to 4 hours to separate acute from chronic cholecystitis) is a limitation. This time can, however, be diminished by half, with the use of intravenous morphine. If the sonogram is confusing or inconclusive, scintigraphy should be considered as a powerful problem solver, provided it would potentially change patient management.[25]

Abdominal CT can be valuable when US results shows a complex process centered over the gallbladder, and the differential diagnosis includes both complicated cholecystitis and gallbladder cancer. Abdominal CT is also needed in some cases to distinguish emphysematous cholecystitis from porcelain gallbladder (see later). In addition, when sonography shows a normal stone-free gallbladder and no other explanation for the patient's pain, then CT can be very helpful to survey the entire abdomen to identify alternative diagnoses. MRI/magnetic resonance cholangiopancreatography examination is generally obtained to better characterize masses in the liver or other solid organs identified on US or to search for possible obstructive process in the extrahepatic biliary tree. This technique is especially applicable when the US examination was technically challenging to perform because of the patient's body habitus or when extensive bowel gas compromises the sonographic examination.

NORMAL GALLBLADDER

The normal gallbladder is a fluid-filled ovoid structure with a thin, smooth echogenic wall (**Fig. 1**). The gallbladder is located inferior to the interlobar fissure between the left and right hepatic lobes. Anatomically, the gallbladder is divided into the neck, body, and fundus. The neck of the gallbladder generally lies closest to the liver hilum. Folds in the gallbladder commonly occur at the neck and fundus. The spiral valves of Heister are small folds in the cystic duct or gallbladder neck; they can appear as tiny protuberances in the cystic duct and should not be confused for stones or polyps (**Fig. 2**). The fundus is variable in position and can be located anywhere from the diaphragm to the iliac crest.

The gallbladder wall normally has a thickness less than 3 mm in a fasted patient. The wall can appear thickened if the gallbladder is contracted, but even in the contracted state, the wall thickness usually does not exceed 3 mm (**Fig. 3**). The transverse (short axis) diameter of the gallbladder should be shorter than 4 cm. The gallbladder length is more variable and less useful diagnostically, but a reasonable upper limit of normal length is 8 to 10 cm.

TECHNIQUE

Ideally, patients should fast for 6 to 8 hours for a gallbladder sonogram to ensure adequate gallbladder distension and to reduce upper abdominal bowel gas. Fasting prevents contraction of the gallbladder and allows for better detection of stones and better evaluation of the wall. However, fasting may not be always feasible in a patient presenting to the emergency department with acute RUQ pain, and a recent meal is not a contraindication to sonography in this situation.

A midfrequency (3–5 MHz) sector transducer is typically used to scan the gallbladder and right upper abdomen. In unusually thin patients, higher-frequency linear or curved arrays can be used to obtain higher-resolution images. In unusually

Fig. 1. Normal gallbladder. Longitudinal view shows an oval-shaped gallbladder with a thin wall measuring 7.1 × 2.6 cm.

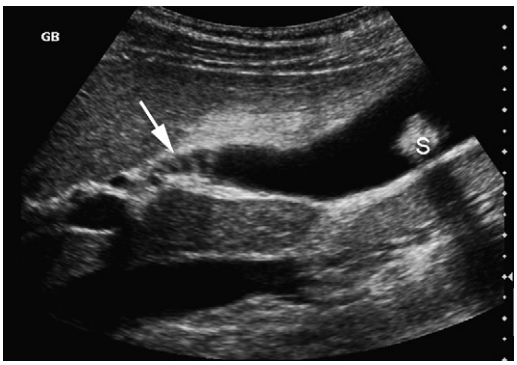

Fig. 2. Valves of Heister. Longitudinal view of the gallbladder neck shows small closely spaced folds at the origin of the cystic duct (*arrow*). A stone (S) is also present in the body of the gallbladder.

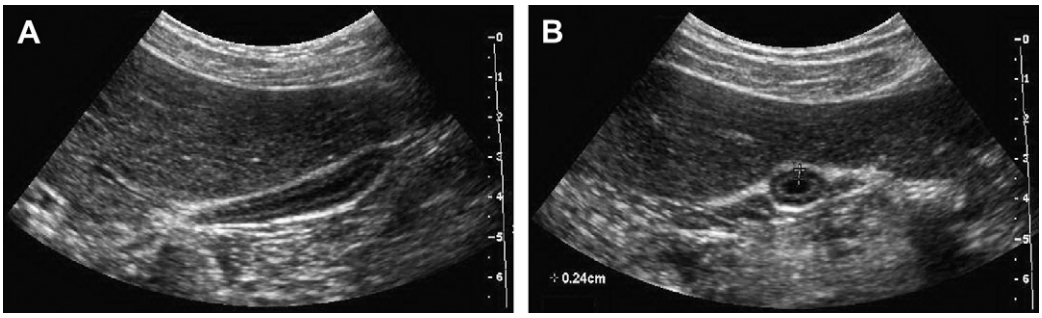

Fig. 3. Contracted gallbladder. (*A*) Longitudinal view shows a very narrow lumen measuring approximately 5 mm. Note the apparent wall thickening. (*B*) Transverse view shows that despite the appearance of wall thickening, the wall is within normal limits measuring only 2.4 mm.

obese patients, lower-frequency phased-array transducers may be necessary. Harmonic imaging and real-time compounding are helpful for both eliminating artifactual echoes and accentuating real echoes from the gallbladder, especially in obese patients.

The gallbladder is usually best seen from a subcostal approach with the patient in a left lateral decubitus or left posterior oblique position during deep inspiration. If the gallbladder is unusually high, an intercostal window may be necessary. Imaging should be performed with the patient in prone and upright positions to help visualize stones that might otherwise be hidden in the gallbladder neck and to assess for mobility of any detected stones. Careful attention should be paid to both the neck and fundus of the gallbladder because stones can sometimes hide in these locations.

Acute Cholecystitis

In most patients, acute cholecystitis occurs because of persistent obstruction of the cystic duct or gallbladder neck by an impacted stone. If the obstructing process is not removed or if the inflammation of gallbladder continues, necrosis and perforation of the gallbladder wall may occur, eventually leading to peritonitis and sepsis. Sonographic findings that favor a diagnosis of acute cholecystitis include (1) gallstones, (2) gallbladder enlargement, (3) gallbladder wall thickening, (4) impacted stone in the gallbladder neck or cystic duct, (5) pericholecystic fluid, and (6) focal tenderness directly over the gallbladder (positive sonographic Murphy sign). A combination of these signs in the appropriate clinical setting is important because any of these individual signs in isolation is nonspecific. For instance, gallstones are generally required to make the diagnosis of cholecystitis, but most patients with stones detected on sonography do not have cholecystitis. However, the combination of gallstones and a positive sonographic Murphy sign has a positive predictive value of 92% and a negative predictive value of 95%.[19] Additional sonographic findings in more advanced acute cholecystitis include (1) sloughed mucosal membranes, (2) wall disruption, (3) wall ulceration, and (4) focal bulge of the wall.

Gallstones

Approximately 95% of patients with acute cholecystitis have gallstones. So, detection of stones is an extremely important aspect for the evaluation of acute cholecystitis. Sonography has a sensitivity of greater than 95% for detecting stones. This test is more sensitive than any other test, and therefore, sonography has assumed the primary role in the evaluation of suspected acute cholecystitis. In addition, the negative predictive value of sonography for gallstones is greater than 97%, so sonography is very accurate in excluding cholecystitis by showing a stone-free gallbladder.

The typical sonographic appearance of a gallstone is a mobile, echogenic, shadowing structure in the lumen of the gallbladder (**Fig. 4**). Shadowing and mobility are important because they help distinguish stones from masses and tumefactive sludge. Shadowing is primarily related to stone size and not to stone composition. For shadow production, the ultrasound beam should intercept the center of the stone and the stone should absorb a critical portion of the sound pulse, which is rarely a problem when stones are large in relation to the beam width. With small stones, however, adjusting the focal zone of the beam to correspond to the depth of the stone is critical. Using a higher-frequency transducer (**Fig. 5**) and inactivating the compound imaging feature (**Fig. 6**) also improve the chances of demonstrating shadowing with small stones. If shadowing is not

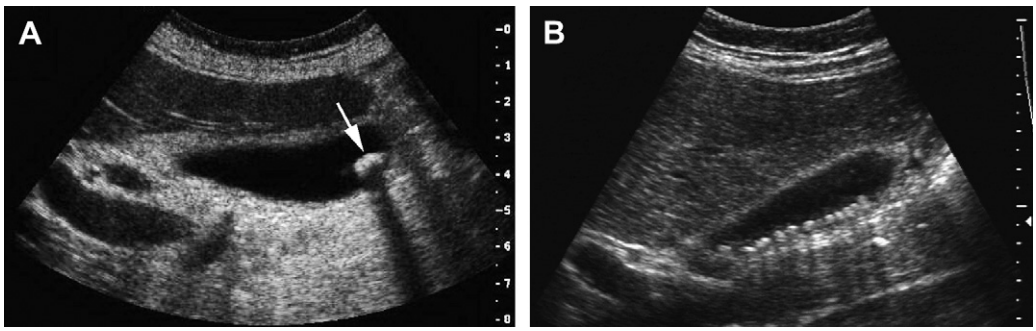

Fig. 4. Typical gallstones in 2 different patients. (*A*) Longitudinal view shows a typical gallstone (*arrow*) with a strong acoustic shadow. (*B*) Longitudinal view shows multiple smaller stones with weak acoustic shadows.

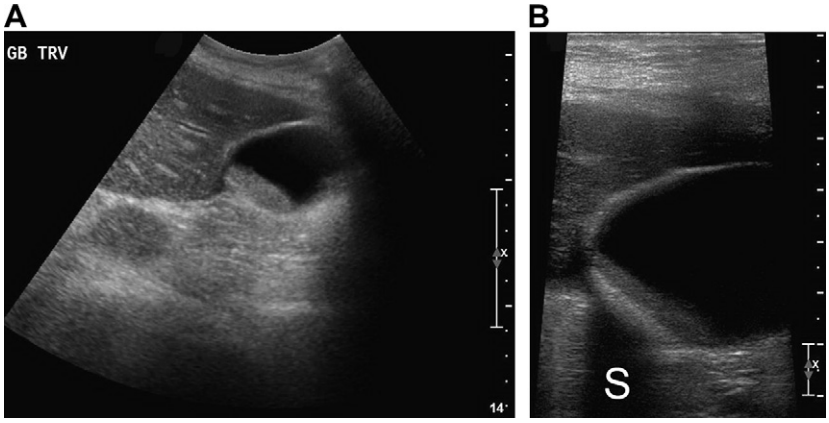

Fig. 5. Effect of transmit frequency on shadowing. (*A*) Transverse view obtained with a 5-MHz curved array probe shows echogenic nonshadowing material in the dependent portion of the gallbladder. (*B*) Similar view with a 9-MHz linear array probe shows shadowing. The presence of shadowing changes the diagnosis from sludge to a combination of sludge and small stones (S).

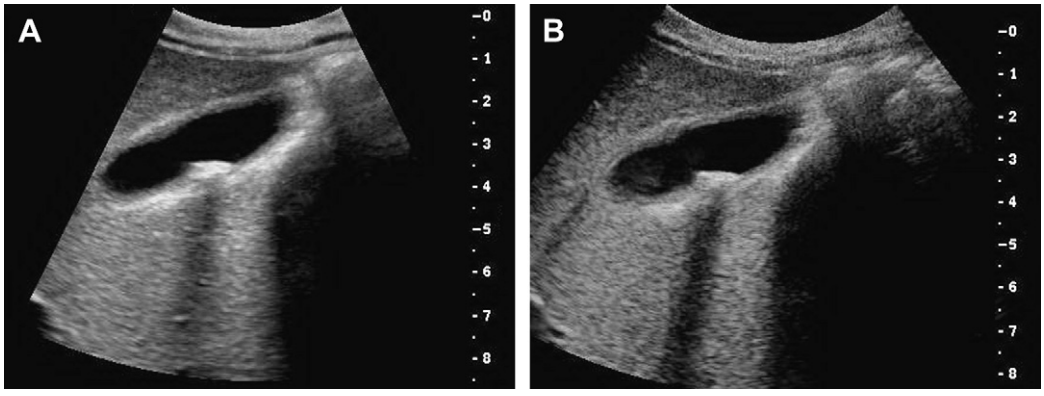

Fig. 6. Effect of real-time compounding on shadowing. (*A*) Longitudinal view obtained with active compounding shows stones with a faint shadow. (*B*) Similar view with inactive compounding shows a much stronger shadow.

detected despite all these adjustments, the differential includes gallstones and tumefactive sludge. Small, mobile, nonshadowing, intraluminal structures are generally gallstones. Tumefactive sludge generally forms larger masslike aggregates (**Fig. 7**). Occasionally, a follow-up sonogram is helpful to distinguish between these 2 possibilities. Polyps and other masses may also simulate small nonshadowing stones, but unlike stones, they are not mobile and are not necessarily in the dependent portion of the gallbladder (**Fig. 8**).

When gallstones are seen, it is important to determine if they are mobile when changing the patient's position: turning the patient to the left or right or to a prone or upright position may cause the gallstone to move to a dependent position (**Fig. 9**). Occasionally, if gallstones are numerous, they may not appear to be mobile because there may not be enough room to move. In some cases, it is possible to identify the impacted stone that is causing the obstruction in the gallbladder neck (**Fig. 10**). However, it is not unusual to see mobile nonobstructing stones in the lumen without visualization of the obstructing stone in the cystic duct.

Occasionally, when the gallbladder is filled with a large stone or an aggregate of multiple stones, it produces a wall-echo-shadow complex (**Fig. 11**). The presence of this complex often indicates a contracted and diseased gallbladder that is unable to perform its primary function of storing bile, but it is rarely seen with acute cholecystitis. This sign comprises 3 arc-shaped lines.[26] The gallbladder wall appears as a central hypoechoic line. Deep to this line, an echogenic line arises from the stones. Deeper to this echogenic line is the intense dark acoustic shadowing. Also seen is an echogenic line representing pericholecystic fat at the interface of the gallbladder wall and liver.

When the specific gravity of bile is unusually high and exceeds the specific gravity of stones, the stones may float. This lower specific gravity indicates that the floating stones are composed of cholesterol. These floating stones are most frequently seen after intravenous injection of iodinated contrast when there has been vicarious excretion of contrast into the gallbladder. The presence of floating stones has no particular association with acute cholecystitis.

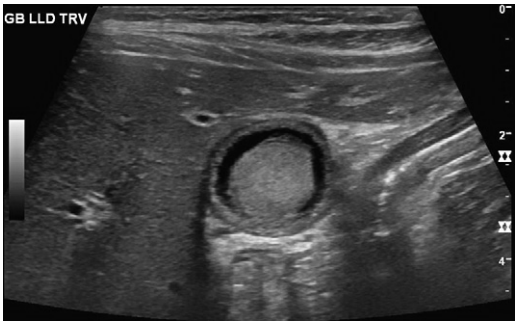

Fig. 7. Tumefactive sludge. Transverse view shows a round nonshadowing structure in the gallbladder lumen. Doppler views showed no detectable internal vascularity.

Fig. 8. Polyps. Longitudinal view shows 3 adjacent echogenic lesions on the nondependent wall of the gallbladder (*arrows*). None of these structures were mobile.

Gallbladder Wall Thickening

Gallbladder wall thickening greater than or equal to 3 mm is present in many patients with acute cholecystitis (**Fig. 12**). The positive predictive value of the combination of gallstones and wall thickening (in a population of patients with a prevalence of cholecystitis of 62%) is 94%. The negative predictive value of this combination is 98%.[19]

It is important to realize that in most cases of acute cholecystitis, the wall thickening is not severe. It is also important to remember that there are many other causes of wall thickening, which are listed in **Box 2**. The gallbladder wall is particularly prone to edema and can become visibly thickened because of a large variety of causes other than cholecystitis. Therefore, conditions causing systemic edema, such as heart failure, renal failure, and hypoproteinemia, are very common causes of gallbladder wall thickening. Adjacent inflammatory processes such as hepatitis and pancreatitis are also relatively common. Conditions that effect venous outflow from the liver and gallbladder, such as cirrhosis, portal hypertension, and portal vein thrombosis, are also causes of gallbladder wall thickening. One common misconception is that ascites is a cause of gallbladder wall thickening. It is true that ascites and wall thickening frequently coexist, but there is no cause-and-effect relationship. The nonbiliary

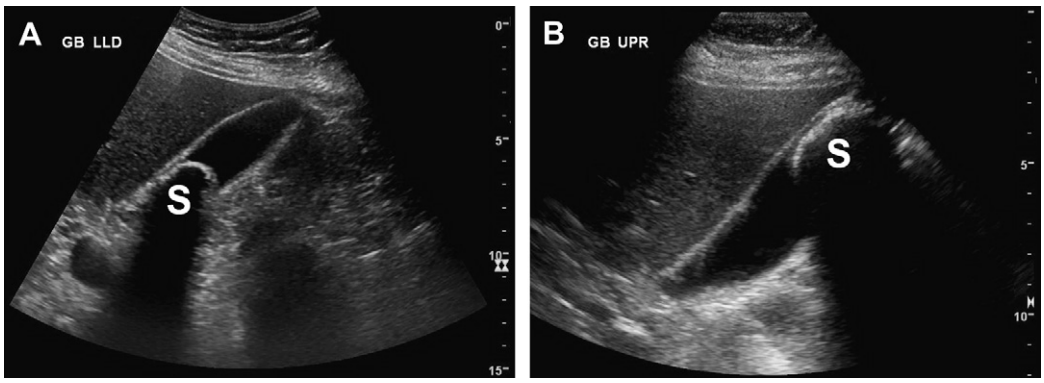

Fig. 9. Gallstone mobility. (*A*) Longitudinal view of the gallbladder with the patient in a left lateral decubitus shows a large stone (S) in the gallbladder neck. (*B*) Similar view with the patient in an upright position shows that the stone (S) has moved into the fundus, thus excluding the possibility of stone impaction.

causes of wall thickening typically produce the most markedly thickened walls that one will encounter and walls that are thicker than typically seen with acute cholecystitis. Therefore, a thick gallbladder wall in the absence of stones, gallbladder enlargement, or a positive Murphy sign should certainly not be equated with cholecystitis, and a careful survey for sonographic signs of heart failure, cirrhosis, pancreatitis, or other nonbiliary causes of wall thickening should be performed (**Fig. 13**). Patients with asymptomatic nonimpacted gallstones and wall edema from nonbiliary causes can be a diagnostic challenge sonographically. In the proper clinical setting, scintigraphy can be very helpful in further evaluating this type of patient.

Adenomyomatosis is another cause of gallbladder wall thickening that can potentially be confused with acute cholecystitis. The focal and segmental forms of adenomyomatosis rarely simulate cholecystitis, but the diffuse form can occasionally pose diagnostic problems. In most cases, the clinical history is very helpful because adenomyomatosis is largely asymptomatic. Useful sonographic signs are intramural comet tail artifacts that arise from crystals within Rokitansky-Aschoff sinuses, as well as a lack of gallbladder enlargement and a negative Murphy sign (**Fig. 14**).[27] Although rarely needed, an MRI can sometimes identify Rokitansky-Aschoff sinuses that are sonographically occult and assist in the diagnosis of adenomyomatosis.

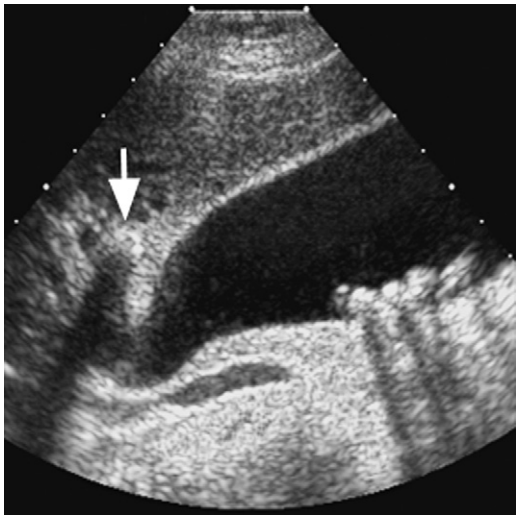

Fig. 10. Acute cholecystitis with an impacted stone. Longitudinal view of the gallbladder shows several stones in the lumen. An additional stone that was originally overlooked is impacted at the junction of the neck and the cystic duct (*arrow*). (*Data from* Middleton W, Kurtz A. Ultrasound: the requisites. 2nd edition. Philadelphia: Mosby; 2004. p. 37.)

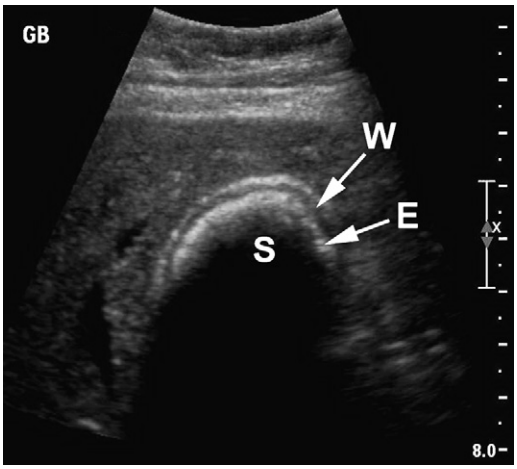

Fig. 11. Wall-echo-shadow complex in a gallbladder completely filled with stones. Transverse view of the gallbladder shows the hypoechoic wall (W), the echogenic reflection from the stones (E), and the shadow (S).

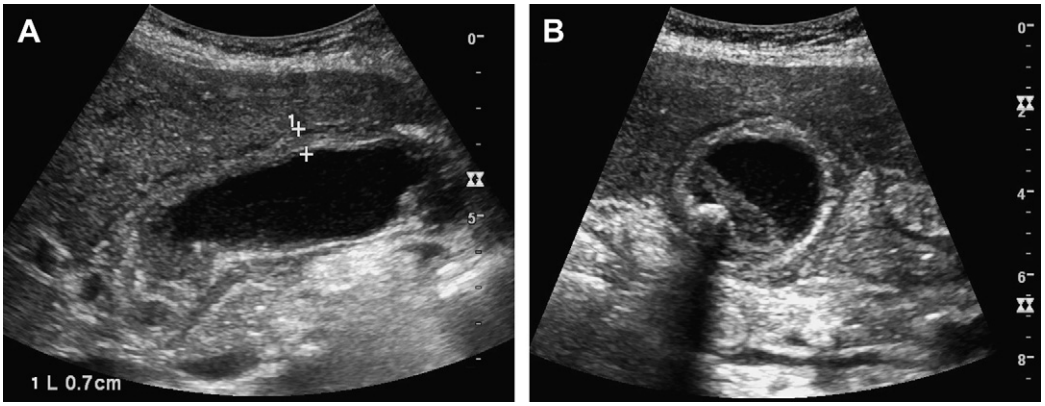

Fig. 12. Acute cholecystitis with gallbladder wall thickening. (*A*) Longitudinal view of the gallbladder shows a thickened wall measuring 7 mm. (*B*) Transverse view also shows a thick wall in addition to a stone and sludge.

It has been reported that the sensitivity and specificity of diagnosing acute cholecystitis can be improved with color and power Doppler US evaluation of the gallbladder wall.[28] However, in most situations, Doppler evaluation is not necessary and adds little to the diagnosis.

Gallbladder Enlargement

Gallbladder enlargement is an additional sign of acute cholecystitis. In the appropriate clinical setting, an enlarged gallbladder should raise suspicion of acute cholecystitis, and a careful search for additional signs should be performed (Fig. 15). However, like most signs of cholecystitis, gallbladder enlargement by itself is neither highly sensitive nor highly specific. As mentioned earlier, a normal gallbladder generally has a width less than 4 cm and a length less than 8 to 10 cm. The width is a more important dimension because of the normal variation in gallbladder length. A long thin gallbladder is much less worrisome than a short wide gallbladder.

Box 2
Differential diagnosis of thickened gallbladder wall

- Physiology
  - Contraction of the gallbladder because of the recent consumption of a fatty meal
- Gallbladder disease
  - Acute cholecystitis
  - Acute acalculous cholecystitis
  - Adenomyosis
  - Gallbladder cancer
- Nongallbladder disease
  - Cirrhosis/portal hypertension
  - Portal vein thrombosis
  - Pancreatitis
  - Acute hepatitis
  - Hypoproteinemia
  - Congestive cardiac failure
  - Renal failure

Data from Chong W, Shah M. Sonography of right upper quadrant pain. Ultrasound Clin 2008;3(1):122.

Pericholecystic Fluid

Pericholecystic fluid is present in less than 20% of patients with acute cholecystitis. It is seen as a focal fluid collection adjacent to the gallbladder wall (Fig. 16). Pericholecystic fluid can appear anywhere around the circumference of the gallbladder but is most often adjacent to the fundus. Recognizing this fluid is important because it generally indicates a more advanced case of cholecystitis. Pericholecystic fluid should be differentiated from gallbladder wall edema, which is more concentric. Pericholecystic fluid should also be distinguished from pericholecystic ascites, which is less masslike and conforms to the shape of the gallbladder and adjacent structures.

Sonographic Murphy Sign

The sonographic Murphy sign refers to localized tenderness directly over the gallbladder. This sign is considered positive when pressure applied with transducer elicits tenderness only over the gallbladder or when maximal tenderness is located over the gallbladder. As mentioned earlier, a combination of gallstones and a positive sonographic Murphy sign has a positive predictive value of 92%.[19] A negative sonographic Murphy sign is less helpful. Causes of a false-negative

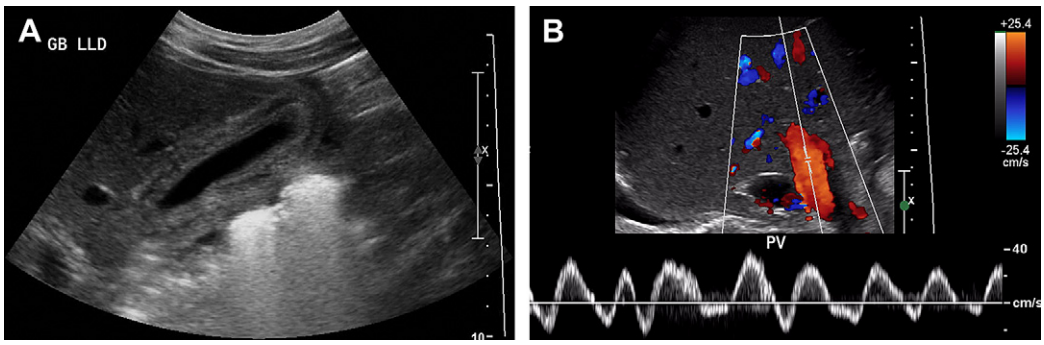

Fig. 13. Heart failure with gallbladder wall thickening. (*A*) Longitudinal view of the gallbladder shows diffuse concentric wall thickening, but no stones, and a somewhat contracted lumen. (*B*) Pulsed Doppler waveform from the portal vein shows abnormal pulsatility consistent with congestive heart failure and passive hepatic congestion.

Murphy sign include patient nonresponsiveness, pain medication, diabetic patient, or inability to press directly on the gallbladder because of large ascites or deeply positioned gallbladder either deep to liver or ribs. A very important cause of a negative Murphy sign is gallbladder wall necrosis, which leads to denervation of the gallbladder wall by gangrenous changes.

Acalculous Cholecystitis

Acute acalculous cholecystitis accounts for approximately 5% of all cases of acute cholecystitis and occurs most commonly in patients in intensive care units. Predisposing factors include trauma, mechanical ventilation, hyperalimentation, postoperative state, diabetes mellitus, vascular insufficiency, prolonged fasting, burns, and postpartum state. These conditions tend to increase the risk for gallbladder ischemia. Patients with suspected acalculous cholecystitis are challenging to assess clinically, and an increased morbidity and mortality rate are partly because of the difficulty and delay in making the diagnosis. The sonographic features of enlargement and wall thickening that are useful in other populations of patients are also signs of acalculous cholecystitis (**Fig. 17**). However, these features frequently exist in patients in the intensive care unit without intrinsic gallbladder disease. Therefore, the sonographic evaluation of these patients is also difficult. Scintigraphy can be a helpful adjunct to sonography, but false-positives are common and limit its usefulness. As a result, guided cholecystostomy tube placement is often performed to decompress the gallbladder if there is a high index of clinical suspicion and the gallbladder is distended on US results.[29]

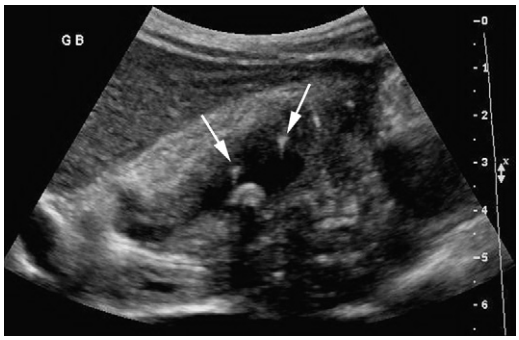

Fig. 14. Adenomyomatosis with gallbladder wall thickening. Longitudinal view of the gallbladder shows a thick wall, a gallstone, and several intramural reflectors with comet tail artifacts (*arrows*).

Gangrenous Cholecystitis

Increased intraluminal pressure in the gallbladder from acute cholecystitis may produce gallbladder wall ischemia and ultimately necrosis, resulting in gangrenous cholecystitis. Gangrenous cholecystitis complicates 2% to 38% of cases.[30] The sonographic Murphy sign may be negative in a large number of these patients, probably because of denervation of the gallbladder wall by gangrenous changes.[31] Progression of gangrenous cholecystitis can lead to perforation of gallbladder, resulting in peritonitis and sepsis, leading to higher morbidity and mortality. Findings on US that are of concern for gangrenous cholecystitis include mucosal ulcerations, sloughed membranes, focal bulge/disrupted wall, and lack of Murphy sign, despite other convincing signs of acute cholecystitis (**Fig. 18**).

Emphysematous Cholecystitis

Emphysematous cholecystitis is a rare condition that is associated with the presence of gas-forming bacteria in the wall of the gallbladder.

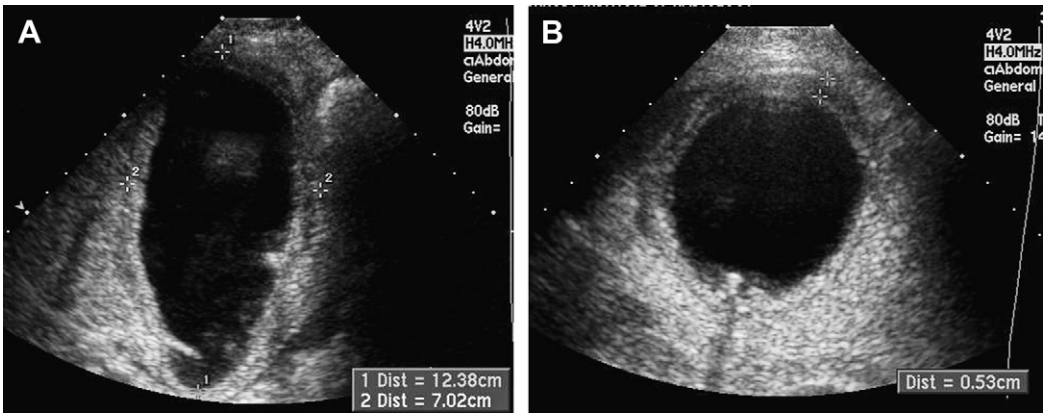

Fig. 15. Acute cholecystitis with gallbladder enlargement. (*A*) Longitudinal view shows an enlarged gallbladder measuring 12.3 × 7.0 cm. (*B*) Transverse view shows a thick wall measuring 5.3 mm and a small stone. (*Data from* Middleton W. General and vascular ultrasound: case review series. Philadelphia: Mosby; 2007. p. 47.)

About 40% of the patients are diabetic. Gallbladder stones are often absent. In these patients, it is thought that cystic artery occlusion caused by inflammation from acute cholecystitis or small vessel atherosclerosis leads to gallbladder wall ischemia, which further leads to overgrowth of gas-producing bacteria. The Clostridia bacteria are most frequently isolated in these instances, with *Clostridium welchii* being the most common.[32] Escherichia coli is isolated with the second most frequency. The mortality rate for acute emphysematous cholecystitis is 15% to 20% (compared to 1.4% for uncomplicated acute cholecystitis), primarily because of a 5-fold increased incidence of gallbladder wall gangrene and perforation.[33] Hence, emphysematous cholecystitis is a surgical emergency requiring prompt diagnosis and treatment. Definitive treatment is cholecystectomy, but percutaneous cholecystostomy is often used as a temporizing procedure in critically ill patients.

Sonographically, gas in the gallbladder wall appears as a nondependent hyperechoic focus with dirty shadowing or ring-down/comet tail artifact (**Fig. 19**).[34] Associated gas in the lumen may move with changes in the patient's position. Care must be taken to distinguish air in the gallbladder wall from a gallbladder packed with stones or calcification in the gallbladder wall (porcelain gallbladder) because both might appear echogenic with posterior acoustic attenuation. Typically, air produces dirty shadowing, whereas calcification and stones produce clean shadowing. However, there can be an overlap in their sonographic appearance, and in difficult cases, abdominal

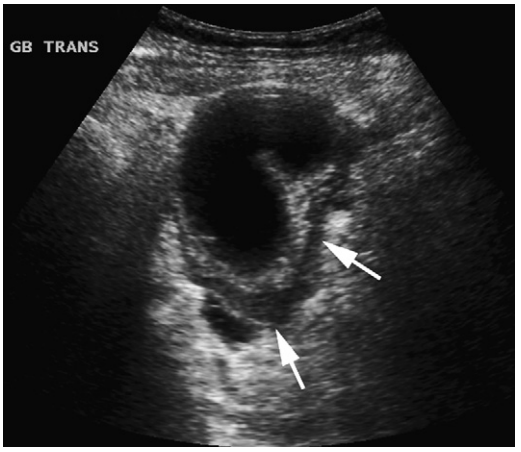

Fig. 16. Acute cholecystitis with pericholecystic fluid. Transverse view shows a slightly folded gallbladder with a localized collection of adjacent fluid (*arrows*).

Fig. 17. Acalculous cholecystitis. Longitudinal view shows an enlarged gallbladder measuring 11.6 × 5.1 cm and mild gallbladder wall thickening. No stones were identified.

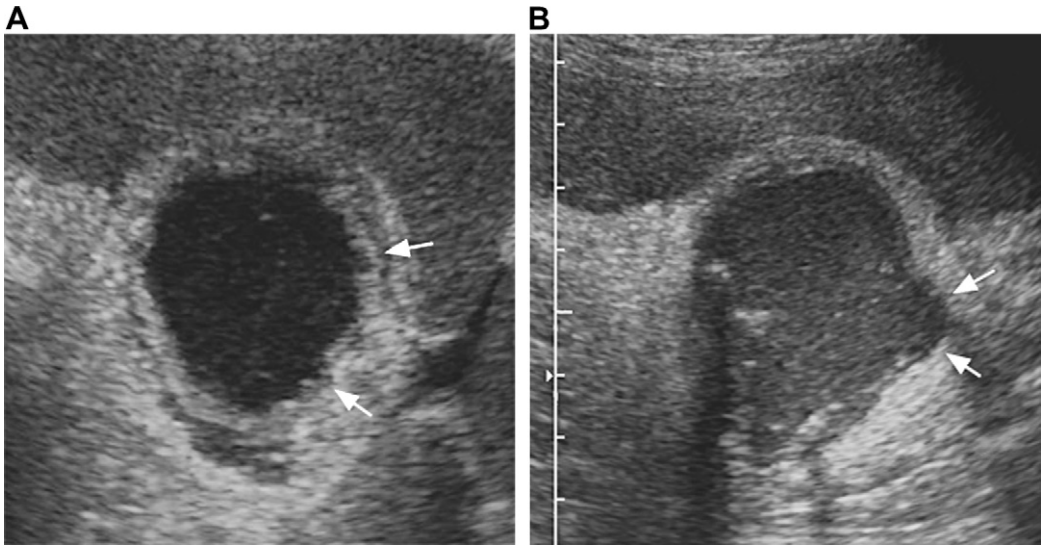

Fig. 18. Gangrenous cholecystitis. (*A*) Magnified transverse view of the gallbladder shows a thick wall with several focal areas of mucosal ulceration (*arrows*). (*B*) Magnified transverse view of the gallbladder in another patient shows a focal bulge in the wall (*arrows*). (*Data from* Middleton W, Kurtz A. Ultrasound: the requisites. 2nd edition. Philadelphia: Mosby; 2004. p. 38.)

radiography and/or CT[35] can allow for definitive distinction between mural gas and calcification. Extensive intramural gas in the gallbladder may mimic the gas-filled bowel and make visualization of the gallbladder impossible. Hence, CT should also be considered in patients with acute RUQ pain in whom the gallbladder is not definitely identified at sonography. Isolated air in the gallbladder lumen can result after recent instrumentation of the biliary tree, such as endoscopic retrograde cholangiopancreatography, placement of biliary stents, or biliary enteric anastomosis, and should not be confused with emphysematous cholecystitis. If iatrogenic causes are excluded, gas in the gallbladder lumen may also indicate a cholecystoenteric fistula.

Gallbladder Perforation

Gallbladder perforation is a serious complication of acute cholecystitis with a mortality rate of

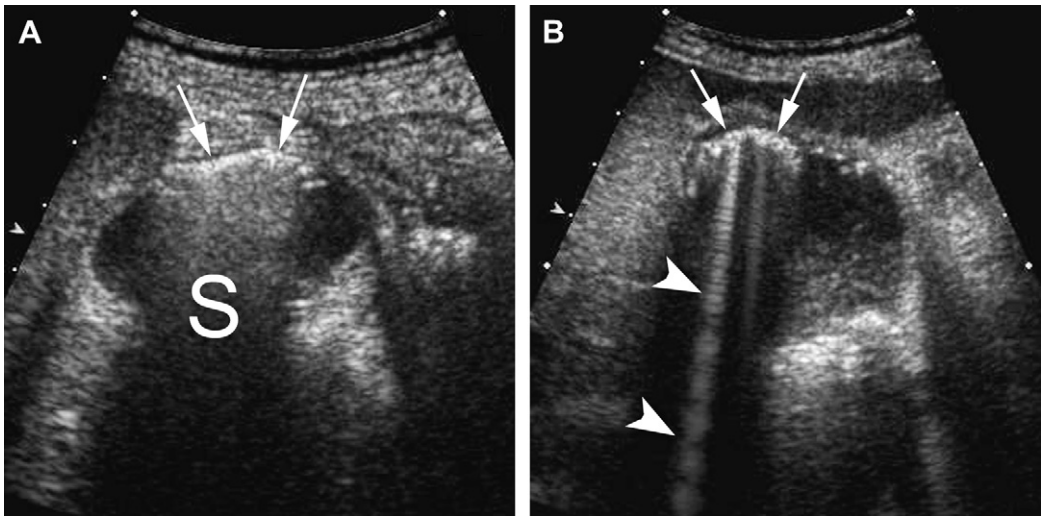

Fig. 19. Emphysematous cholecystitis. (*A*) Transverse view shows very bright reflectors in the nondependent portion of the gallbladder (*arrows*) and an associated dirty shadow (S). (*B*) Transverse view shows similar nondependent bright reflectors (*arrows*) and associated ring-down artifact (*arrowheads*).

12% to 16%. This condition occurs in less than 10% of cases of acute cholecystitis. Early detection reduces morbidity and mortality. Predisposing factors for gallbladder perforation include infections, malignancy, steroid therapy, diabetes mellitus, and atherosclerotic heart disease.[36] Niemeier[37] has classified gallbladder perforations into 3 categories: acute, subacute, and chronic. Acute perforation has the worst prognosis because it often results in generalized peritonitis. Subacute perforation is generally contained and often presents with a pericholecystic abscess. Chronic perforation often presents with an internal cholecystic fistula to the duodenum or common bile duct. Most perforations are subacute, accounting for 60% of all cases. Chronic perforations account for 30%, and acute perforations account for 10% of cases. The most common site of perforation is the fundus because it is the most distal part with regard to blood supply. Elderly patients are more susceptible to gallbladder perforation. The incidence of perforation is known to increase 4-fold, with a delay in surgery of more than 2 days from the onset of abdominal symptoms.[38] It may often be difficult to clinically differentiate gallbladder perforation from uncomplicated cholecystitis because the bile leak from a ruptured gallbladder might be contained in the extraperitoneal gallbladder fossa and hence might not produce symptoms of peritonitis immediately.

On sonographic examination, presence of focal bulge, discontinuity, focal intramural fluid collection involving the wall of gallbladder, or a complex pericholecystic fluid collection should raise concern for gallbladder perforation. Visualization of a defect in the gallbladder, also known as hole sign, is a definitive sign of gallbladder perforation (**Fig. 20**).[39] Often, distension of the gallbladder and edema of its walls may be the earliest signs of impending perforation[40]

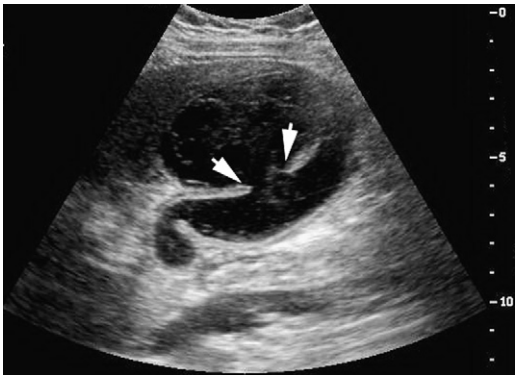

Fig. 20. Gallbladder perforation. Longitudinal view shows a hole in the wall of the gallbladder (*arrows*) with extravasation of luminal contents into the pericholecystic region.

SUMMARY

Sonography is the primary imaging modality for the evaluation of RUQ pain. This technique is more effective at diagnosing and evaluating gallstones than any other imaging test. Cholescintigraphy is a valuable test of gallbladder function that is very useful in the evaluation of suspected acute cholecystitis when US is confusing or indeterminate. CT is not a primary modality in the evaluation of RUQ pain but is very useful in further evaluating complicated cholecystitis and gallbladder neoplasms. An understanding of sonographic findings of complications of acute cholecystitis and possible alternative diagnoses aids in prompt diagnosis and appropriate management of patients with RUQ pain.

REFERENCES

1. Hanbidge AE, Buckler PM, O'Malley ME, et al. From the RSNA refresher courses: imaging evaluation for acute pain in the RUQ. Radiographics 2004;24(4):1117–35.
2. Popkharitov AI. Laparoscopic cholecystectomy for acute cholecystitis. Langenbecks Arch Surg 2008; 393(6):935–41.
3. Khan MN, Nordon I, Ghauri AS, et al. Urgent cholecystectomy for acute cholecystitis in a district general hospital—is it feasible? Ann R Coll Surg Engl 2009;91(1):30–4.
4. Gadacz TR. Cholelithiasis and cholecystitis. In: Zuidema GD, editor. Shackelford's surgery of the alimentary tract. 3rd edition. Philadelphia: W.B. Saunders Co; 1991. p. 174–85.
5. Russo MW, Wei JT, Thiny MT, et al. Digestive and liver diseases statistics, 2004. Gastroenterology 2004;126:1448–53.
6. Sandler RS, Everhart JE, Donowitz M, et al. The burden of selected digestive diseases in the United States. Gastroenterology 2002;122:1500–11.
7. Attili AF, Carulli N, Roda E, et al. Epidemiology of gallstone disease in Italy: prevalence data of the Multicenter Italian Study on Cholelithiasis (M.I.COL.). Am J Epidemiol 1995;141:158–65.
8. Everhart JE, Khare M, Hill M, et al. Prevalence and ethnic differences in gallbladder disease in the United States. Gastroenterology 1999;117:632–9.
9. Everhart JE, Yeh F, Lee ET, et al. Prevalence of gallbladder disease in American Indian populations: findings from the Strong Heart Study. Hepatology 2002;35:1507–12.
10. Hopper KD, Landis JR, Meilstrup JW, et al. The prevalence of asymptomatic gallstones in the general population. Invest Radiol 1991;26:939–45.

11. Heaton KW, Braddon FE, Mountford RA, et al. Symptomatic and silent gallstones in the community. Gut 1991;32:316–20.
12. Friedman GD, Raviola CA, Fireman B. Prognosis of gallstones with mild or no symptoms: 25 years of follow-up in a health maintenance organization. J Clin Epidemiol 1989;42:127–36.
13. Lee SP, Kuver R. Gallstones. In: Yamada T, editor. Textbook of gastroenterology. 2nd edition. Philadelphia: J.B. Lippincott Co; 1995. p. 2187–212.
14. Trowbridge RL, Rutkowski NK, Shojania KG. Does this patient have acute cholecystitis? JAMA 2003; 289(1):80–6.
15. American College of Radiology appropriateness criteria: RUQ Pain. American College of Radiology. 2010. Available at: http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonGastrointestinalImaging/RightUpperQuadrantPainDoc13.aspx. Accessed August 19, 2010.
16. Bennett GL, Balthazar EJ. Ultrasound and CT evaluation of emergent gallbladder pathology. Radiol Clin North Am 2003;41(6):1203–16.
17. Smith EA, Dillman JR, Elsayes KM, et al. Cross-sectional imaging of acute and chronic gallbladder inflammatory disease. AJR Am J Roentgenol 2009; 192(1):188–96.
18. Laing FC, Federle MP, Jeffrey RB, et al. Ultrasonic evaluation of patients with acute RUQ pain. Radiology 1981;140(2):449–55.
19. Ralls PW, Colletti PM, Lapin SA, et al. Real time sonography in suspected acute cholecystitis: prospective evaluation of primary and secondary signs. Radiology 1985;155:767–71.
20. Weissmann HS, Frank MS, Bernstein LH, et al. Rapid and accurate diagnosis of acute cholecystitis with 99m Tc-IDA cholescintigraphy. AJR Am J Roentgenol 1979;132:523–8.
21. Ziessman HA. Acute cholecystitis, biliary obstruction, and biliary leakage. Semin Nucl Med 2003;33: 279–96.
22. Shuman WP, Mack LA, Rudd TG, et al. Evaluation of acute RUQ pain: sonography and 99mTcPIPIDA cholescintigraphy. AJR Am J Roentgenol 1982;139: 61–4.
23. Ralls PW, Colletti PM, Halls JM, et al. Prospective evaluation of 99mTc-IDA cholescintigraphy and gray-scale ultrasound in the diagnosis of acute cholecystitis. Radiology 1982;144:369–71.
24. Worthen NJ, Uszler JM, Funamura JL. Cholecystitis: prospective evaluation of sonography and 99mTc-HIDA cholescintigraphy. AJR 1981;137:973–8.
25. Freitas JE, Mirkes S, Fink-Bennett DM, et al. Suspected acute cholecystitis—comparison of hepatobiliary scintigraphy and ultrasonography. Clin Nucl Med 1982;7:364–7.
26. MacDonald FR, et al. The WES triad—a specific sonographic sign of stones in the contracted gallbladder. Gastrointest Radiol 1981;6:39–41.
27. Raghavendra BN, Subramanyam BR, Balthazar EJ, et al. Sonography of adenomyomatosis of the gallbladder: radiologic-pathologic correlation. Radiology 1983;146:747–52.
28. Soyer P, Brouland JP, Boudiaf M, et al. Color velocity imaging and power Doppler sonography of the gallbladder wall: a new look at sonographic diagnosis of acute cholecystitis. AJR Am J Roentgenol 1998;171: 183–8.
29. Barie PS, Eachempati SR. Acute acalculous cholecystitis. Gastroenterol Clin North Am 2010;39(2): 343–57.
30. Jeffrey RB, Laing FC, Wong W, et al. Gangrenous cholecystitis: diagnosis by ultrasound. Radiology 1983;148:219–21.
31. Simeone JF, Brink JA, Mueller PR, et al. The sonographic diagnosis of acute gangrenous cholecystitis: importance of the Murphy sign. AJR Am J Roentgenol 1989;152(2):289–90.
32. Garcia-Sancho Tellez L, Rodriquez,-Montes JA, Fernandez de Lis S, et al. Acute emphysematous cholecystitis. Report of twenty cases. Hepatogastroenterology 1999;46:2144–214.
33. Mentzer RM Jr, Golden GT, Chandler JG, et al. A comparative appraisal of emphysematous cholecystitis. Am J Surg 1975;129:10–5.
34. Bloom RA, Libson E, Lebensart PD, et al. The ultrasound spectrum of emphysematous cholecystitis. J Clin Ultrasound 1989;17:251–6.
35. Grayson DE, Abbott RM, Levy AD, et al. Emphysematous infections of the abdomen and pelvis: a pictorial review. Radiographics 2002;22:543–61.
36. Derici H, Kara C, Bozdag AD, et al. Diagnosis and treatment of gallbladder perforation. World J Gastroenterol 2006;12:7832–6.
37. Niemeier OW. Acute free perforation of the gallbladder. Ann Surg 1934;99:922–4.
38. Harland C, Mayberry JF, Toghill PJ. Type 1 free perforation of the gallbladder. J R Soc Med 1985;78:725–8.
39. Sood BP, Kalra N, Gupta S, et al. Role of sonography in the diagnosis of gallbladder perforation. J Clin Ultrasound 2002;30:270–4.
40. Soiva M, Pamilo M, Päivänsalo M, et al. Ultrasonography in acute gallbladder perforation. Acta Radiol 1988;29:41–4.