#### American College of Radiology ACR Appropriateness Criteria<sup>®</sup> Right Upper Quadrant Pain

<u>Variant 1:</u>	Right upper qu	adrant pain.	Unknown etiology	. Initial Imaging.
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Procedure	Appropriateness Category	<b>Relative Radiation Level</b>	
US abdomen	Usually Appropriate	0	
CT abdomen with IV contrast	Usually Appropriate	♥♥♥	
Radiography abdomen	May Be Appropriate (Disagreement)	€€	
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	0	
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0	
CT abdomen without IV contrast	May Be Appropriate	♥♥♥	
Nuclear medicine scan gallbladder	Usually Not Appropriate	€€	
CT abdomen without and with IV contrast	Usually Not Appropriate	♥♥♥♥	

Variant 2:

Right upper quadrant pain. Suspected biliary disease. Initial imaging.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
US abdomen	Usually Appropriate	0
CT abdomen with IV contrast	May Be Appropriate	��€
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	0
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0
Nuclear medicine scan gallbladder	May Be Appropriate	€€
CT abdomen without IV contrast	May Be Appropriate	��€
CT abdomen without and with IV contrast	Usually Not Appropriate	€€€

Variant 3:

Right upper quadrant pain. No fever and no high white blood cell (WBC) count. Suspected biliary disease. Negative or equivocal ultrasound. Next imaging study.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	0
CT abdomen with IV contrast	Usually Appropriate	��€
MRI abdomen without IV contrast with MRCP	Usually Appropriate	0
Nuclear medicine scan gallbladder	May Be Appropriate	€€
CT abdomen without IV contrast	May Be Appropriate	��€
CT abdomen without and with IV contrast	Usually Not Appropriate	€€€

#### Variant 4:

Right upper quadrant pain. Fever, elevated WBC count. Suspected biliary disease. Negative or equivocal ultrasound. Next imaging study.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	0
CT abdomen with IV contrast	Usually Appropriate	♥♥♥
Nuclear medicine scan gallbladder	Usually Appropriate	€€
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0
CT abdomen without IV contrast	May Be Appropriate	♥♥♥
CT abdomen without and with IV contrast	Usually Not Appropriate	€€€€

<u>Variant 5:</u>

Right upper quadrant pain. Suspected acalculous cholecystitis. Negative or equivocal ultrasound. Next imaging study.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
Nuclear medicine scan gallbladder	Usually Appropriate	<b>\$</b>
CT abdomen with IV contrast	May Be Appropriate	€€
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	0
Image-guided biopsy liver	May Be Appropriate	Varies
MRI abdomen without IV contrast with MRCP	May Be Appropriate	0
CT abdomen without IV contrast	May Be Appropriate	€€
CT abdomen without and with IV contrast	Usually Not Appropriate	***

## **RIGHT UPPER QUADRANT PAIN**

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#### **Summary of Literature Review**

#### Introduction/Background

Acute right upper quadrant pain is one of the most common presenting symptom in hospital emergency departments, as well as outpatient settings. Although gallstone-related acute cholecystitis (AC) is a leading consideration in diagnosis, a myriad of extrabiliary sources including hepatic, pancreatic, gastroduodenal, and musculoskeletal should also be considered.

This review will focus on the diagnostic accuracy of imaging studies performed specifically to evaluate acute right upper quadrant pain, with biliary etiologies including AC and its complications being the most common. An additional consideration of extrabiliary sources such as acute pancreatitis, peptic ulcer disease, ascending cholangitis, liver abscess, hepatitis, and painful liver neoplasms remain a diagnostic consideration in the right clinical setting. Jaundice is an important clinical finding that suggests a different subset of conditions. Please refer to the ACR Appropriateness Criteria<sup>®</sup> topics on "Jaundice" [1] that pertains specifically to this clinical scenario. Additionally, other overlapping abdominal pain scenarios are covered in separate ACR Appropriateness Criteria<sup>®</sup> topics on "Acute Nonlocalized Abdominal Pain" [2], "Epigastric Pain" [3], "Acute Pancreatitis" [4], and "Suspected Small-Bowel Obstruction" [5].

Cholelithiasis is a common entity and AC is a common manifestation of gallstone disease afflicting more than 20 million people in the United States and is the leading cause of inpatient admissions for gastrointestinal disease [6]. AC can be life-threatening; therefore, timely diagnosis is essential for proper treatment. However, most patients with AC experience right upper quadrant abdominal pain, nausea, vomiting, anorexia, and fever [7].

Information derived only from clinical history, physical examination, and routine laboratory tests has not yielded acceptable likelihood ratios sufficient to predict the presence or absence of AC. Also, this information does not yield sufficient diagnostic certainty for making management decisions. Therefore, imaging studies play a major role in establishing a diagnosis of AC and assessing possible alternate diagnoses if AC is not present [8].

Unless otherwise stated, the ratings and recommendations for this document specifically relate to the adult nonpregnant patient.

#### Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

• There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

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The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through representation of such organizations on expert panels. Participation on the expert panel does not necessarily imply endorsement of the final document by individual contributors or their respective organization.

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• There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously where each procedure provides unique clinical information to effectively manage the patient's care).

## **Discussion of Procedures by Variant**

# Variant 1: Right upper quadrant pain. Unknown etiology. Initial Imaging.

In this clinical scenario, the patient presents with right upper quadrant pain and may have associated signs and symptoms. Although biliary disease is in the differential, it is not necessarily the leading consideration from the clinical presentation, and many other etiologies remain possible diagnostic considerations. Imaging methods for initial evaluation in patients in this clinical variant should be able to detect or exclude biliary disease and these other alternate diagnoses.

## **CT Abdomen**

CT scanners are the workhorse modality for the assessment of nonspecific abdominal pain. CT also has the advantage of assessment of complications related to AC, as well as diagnosis of extrabiliary sources of right upper quadrant pain. Unlike ultrasound (US), CT can also better visualize the gastrointestinal tract, including gastroduodenal abnormalities such as severe inflammation or perforation, colitis involving the hepatic flexure, and abnormalities of the adjacent osseous structures. Pancreatic masses and acute pancreatitis are similarly better evaluated. Contrast enhancement is an additional advantage that can aid in visualizing and characterizing enhancing hepatic, pancreatic, adrenal, and bowel lesions.

AC is the most common cause of right upper quadrant pain, and 95% of cases of AC have gallstones present. CT falls behind US in the detection of gallstones with a sensitivity of approximately 75% [7]. A 2018 study comparing abdominal US and CT showed "the sensitivity of CT for detecting AC was significantly greater than that of US: 85% versus 68% (P = .043), respectively; however, the negative predictive values of CT and US did not differ significantly: 90% versus 77% (P = .24-.26). Because there were no false-positives, the specificity and positive predictive values for both modalities were 100%." This study concluded CT was significantly more sensitive for diagnosing AC than US but stated CT and US are complementary and should be used if 1 study was negative and clinical suspicion remained high [9].

CT without intravenous (IV) contrast can detect some features and complications of AC, such as gallbladder wall thickening, pericholecystic inflammation, gas formation, and hemorrhage. However, some important features that add confidence to the diagnosis such as wall enhancement and adjacent liver parenchymal hyperemia, one of the earlier findings in AC, cannot be detected without IV contrast [7]. CT without and with IV contrast is not often viewed as helpful in assessing patients admitted with right upper quadrant abdominal pain because the noncontrast portion does not add value and little additional information is gained by the routine addition of a noncontrast phase to a contrast-enhanced phase in this clinical setting [10].

CT with IV contrast is a useful tool for the assessment of hepatic pathology such as liver abscess (including the ones <5 mm) and metastatic disease. Furthermore, dual-phase contrast-enhanced CT can detect hemorrhage including active extravasation from liver tumors such as adenomas or hepatocellular carcinomas with accurate identification of the bleeding source. Similarly, severe inflammation of the gastroduodenal region, as well as of the pancreas, can be well detected and characterized on contrast-enhanced CT. If the clinical question only pertains to the presence or absence of bowel perforation, noncontrast CT alone may be enough for the assessment.

## MRI Abdomen with MRCP

Abdominal MRI with MR cholangiopancreatography (MRCP) offers excellent soft tissue contrast, and visualization of the gallbladder, biliary tree, and structures outside of the biliary tree. The length of the examination and claustrophobia hinders this test as an initial modality for right upper quadrant pain. Patient motion artifact is another significant factor in claustrophobic, sick, and uncooperative patients. MRCP offers isolated visualization of the biliary tree and can assess for intraluminal biliary pathology including choledocholithiasis as a cause of biliary pain or an etiology for acute pancreatitis. Contrast-enhanced abdominal MRI can help characterize hepatic, pancreatic, adrenal, and renal lesions that are indeterminate on US and CT. MRI can be useful in cases in which findings on US and CT are equivocal. In such cases, MRI may better identify stones in the gallbladder neck or cystic duct, which are seen as filling defects on MRCP and T2-weighted images, and associated gallbladder wall abnormalities, including wall thickening and pericholecytic fluid [11]. MRCP provides excellent anatomic detail of the biliary tract and has a high sensitivity for detecting choledocholithiasis [12,13].

### Nuclear Medicine Scan Gallbladder

Tc-99m cholescintigraphy also has both high sensitivity and specificity (96% and 90%, respectively) for the diagnosis of AC but is limited in use in clinical practice because of several factors [14]. This modality is limited to visualization of the biliary tract, and therefore, alternative extrabiliary causes of right upper quadrant pain will not be detected. Although cholescintigraphy has a higher sensitivity and specificity for the evaluation of AC, US remains the initial test of choice detailed below in the US section [15-17]. The use of cholescintigraphy should be limited to patients with a high suspicion of AC and obstructive biliary disease in the presence of an equivocal US.

## **Radiography Abdomen**

Abdominal radiography is a commonly used first-line imaging modality for patients presenting with acute abdominal pain. Radiography has been shown to be of value for patients with suspected foreign body, bowel obstruction, and bowel perforation [18]. Several studies reported a high specificity of radiography in diagnosing small-bowel obstruction. However, it lacks the sensitivity and specificity of diagnosing other causes of abdominal pain [18-20]. A 2015 study showed that radiographs have lower sensitivity in detecting major abnormalities and supplemental imaging such as CT or US revealed major abnormalities in an additional 22% of patients whose radiographs were interpreted as normal [21]. Abdominal radiography has shown low utility in the diagnosis of common etiologies of abdominal pain, especially right upper quadrant pain including biliary and hepatic disease, acute pancreatitis, and peptic ulcer disease, and the findings can be noncontributory. Specifically, the inherent low soft tissue contrast of abdominal radiographs prevents diagnosis of typical right upper quadrant diseases including AC and hepatic pathologies. Gallstones, a common cause of biliary colic, are radiopaque in only 15% to 20% cases, and hence, the majority of the stones being radiolucent remain occult on radiography [22]. Several prospective studies [18,20,23] concluded that radiographs added only minimal value beyond clinical evaluation in the diagnostic workup of patients with acute abdominal pain. Few recent studies have analyzed the utility of abdominal radiographs for right upper quadrant pain specifically. Abdominal radiography has little utility as initial imaging for right upper quadrant abdominal pain with low sensitivity of 30% and has not been proven to be of value for expected other expected diagnoses, most importantly right upper quadrant pain [20,24].

# **US Abdomen**

US is the most useful modality for evaluation of right upper quadrant abdominal pain. It is very accurate in diagnosing or excluding gallstones, with a reported accuracy of 96% for the detection of gallstones [7], and helps differentiate cholelithiasis from gallbladder sludge, polyps, or masses.

AC is the most common cause of right upper quadrant abdominal pain. However, assessment of more than one-third of patients initially suspected of having AC will result in an alternative diagnosis [16].

US is the most useful first-line imaging modality in evaluating AC, with the additional advantage of identifying alternate diagnosis of hepatic disease. The reported sensitivity and specificity of US range from 50% to 100% and from 33% to 100%, respectively, with summary estimates of 81% and 83%, respectively [25]. A 2019 study showed US sensitivity and specificity were 61.8% and 98.4%, respectively; the sensitivity of US reached 85.2% and 90% in patients with AC/biliary colic and urolithiasis, respectively [26].

US is also the most useful imaging modality for the diagnosis of biliary colic, with an accuracy of 90% for demonstrating cholelithiasis, which may develop into AC if untreated in up to 20% of patients [27]. Furthermore, choledocholithiasis can lead to biliary obstruction and subsequent cholangitis or acute pancreatitis, and US has a sensitivity of up to 91% in detecting stones within the common bile duct [28].

Liver abscess and metastatic disease may also cause right upper quadrant pain. Similarly, symptomatic hepatic masses causing bleeding or hemoperitoneum may also be easily picked up on US.

US can also help identify renal pathology causing right upper quadrant pain with a sensitivity of 73% to 100% for the detection of hydronephrosis caused by renal obstruction with an overall improved sensitivity compared with radiography [27].

Adrenal pathology may also contribute to the list of causes of right upper quadrant pain. Adrenal hemorrhage can be easily identified as a mass without identifiable Doppler flow.

Ninety-five percent of patients with AC have gallstones, but the sensitivity of CT for the detection of these stones is only approximately 75%. Calcium-containing stones tend to be well seen; however, cholesterol stones may be isoattenuating or hypoattenuating compared with the attenuation of bile, making their detection difficult [29].

## Variant 2: Right upper quadrant pain. Suspected biliary disease. Initial imaging.

# CT Abdomen

Although it has not been advocated as a primary imaging examination for acute right upper quadrant pain, CT can confirm or refute the diagnosis of AC in equivocal cases based on US or scintigraphy, with a negative predictive value approaching 90% [30]. It is usually most appropriate to perform this examination after a US and/or cholescintigraphy. CT may reveal such complications as gangrene, gas formation, intraluminal hemorrhage, and perforation [15-17,30-35]. Furthermore, CT has been advocated as a useful modality in preoperative planning, with the absence of gallbladder wall enhancement or presence of a stone within the infundibulum associated with a higher rate of conversion from laparoscopic to open cholecystectomy. The CT findings in AC are similar to those encountered by US [7] with the exception of gallstones, which may not be detected by CT. Other potential findings include adjacent liver parenchymal hyperemia, which can only be assessed if IV contrast is administered. Abnormal gallbladder wall enhancement can be seen in more advanced cases, as well as if IV contrast is employed [7].

Of note, the sensitivity for the detection of gallstones on CT is only approximately 75% and is dependent on differing density of the stone relative to bile [7].

CT is usually preferred over MRI, largely because of its speed [30].

CT without IV contrast can detect some features and complications of AC, such as gallbladder wall thickening, pericholecystic inflammation, gas formation, and hemorrhage, although some important features, such as wall enhancement and adjacent liver parenchymal hyperemia, cannot be detected without IV contrast. Adjacent liver hyperemia is actually one of the earlier findings in AC and can be a very useful problem-solving tool [7].

CT without and with IV contrast is not often viewed as helpful in assessing patients admitted with right upper quadrant abdominal pain. Little additional information is gained by the routine addition of a noncontrast phase to a contrast-enhanced phase in this clinical setting, [10].

## MRI Abdomen with MRCP

The presence of AC can be further explored using abdominal MRI, which often includes the use of an IV gadolinium-based contrast agent in cases in which other imaging tests are equivocal [7]. Several studies have suggested that abdominal MRI is a reliable alternative and can be particularly helpful in the patient who is difficult to examine with US [36-38]. It can perform superiorly to US in cases of gallstones in the gallbladder neck, the cystic duct, or the common bile duct [7].

As with CT without IV contrast, noncontrast MRI will not be able to detect all the imaging features or potential complications of AC. However, noncontrast MRI with MRCP has excellent accuracy for the detection of biliary stone disease, and, therefore, a noncontrast MRI is generally preferred over a noncontrast CT.

## Nuclear Medicine Scan Gallbladder

Despite providing information limited to the hepatobiliary tract, cholescintigraphy has been advocated as a useful modality in this setting. Specifically, gallbladder nonvisualization with delayed imaging or morphine-augmented cholescintigraphy is highly accurate for evaluating the presence or absence of AC. One study states that gallbladder ejection fraction <30% may be useful in predicting the severity of cholecystitis and is associated with a higher complication rate in the setting of laparoscopic cholecystectomy [39]. However, although cholescintigraphy has a higher sensitivity and specificity for the evaluation of AC, US remains the initial test of choice for imaging patients with right upper quadrant pain for a variety of reasons, including shorter study time, morphologic evaluation, confirmation of the presence or absence of gallstones, evaluation of intrahepatic and extrahepatic bile ducts, and identification or exclusion of alternative diagnoses [15-17,40].

#### **US Abdomen**

US is the first choice of investigation for biliary symptoms or right upper quadrant abdominal pain. It is very accurate at diagnosing or excluding gallstones, with reported accuracy of 96% for the detection of gallstones [7], and may differentiate cholelithiasis from gallbladder sludge, polyps, or masses. The diagnosis of chronic cholecystitis is difficult on anatomic imaging. The gallbladder may appear contracted or distended, and pericholecystic fluid is usually absent.

An initial study from 1981 defined the sonographic Murphy sign as focal tenderness corresponding to a sonographically localized gallbladder, which, along with stones, sludge, and gallbladder wall thickening, allowed for differentiating AC from gallstones alone and chronic cholecystitis with gallstones [40]. Unfortunately, the

sonographic Murphy sign has a relatively low specificity for AC [41], and its absence is unreliable as a negative predictor of AC if the patient has received pain medication before imaging. Since that initial study, many subsequent studies have been conducted to assess the accuracy of US and cholescintigraphy. A meta-analysis by Shea et al [42] reviewed 22 studies evaluating cholescintigraphy and 5 studies evaluating US published between 1978 and 1990. The authors concluded that cholescintigraphy demonstrated the best sensitivity of 97% (95% confidence interval [CI], 96%-98%) and specificity of 90% (95% CI, 86%-95%) in detecting AC, whereas US had a sensitivity of 88% (95% CI, 74%-100%) and a specificity of 80% (95% CI, 62%-98%).

Other studies performed since then have shown similar findings. Although cholescintigraphy is recognized to have a higher sensitivity and specificity, US remains the initial imaging test of choice for imaging patients with suspected AC for a variety of reasons, including shorter study time, morphologic evaluation, confirmation of the presence or absence of gallstones, evaluation of intrahepatic and extrahepatic bile ducts, gallbladder wall edema, pericholecystic fluid, and identification or exclusion of alternative diagnoses [15-17,40].

However, the usefulness of US is limited in critically ill patients where gallbladder abnormalities are common in the absence of AC [22,43].

If complicated cholecystitis (emphysematous, hemorrhagic, gangrenous, or perforated, among others) is suspected, US remains the first choice of investigation for biliary symptoms or right upper quadrant abdominal pain. It is important to note, however, that some patients with complicated cholecystitis may present just like those with noncomplicated disease [7]. Depending on the complication, one may detect intraluminal hyperechoic blood products, intraluminal gas or gas in the gallbladder wall, intraluminal debris or membranes, or discontinuity of the gallbladder wall [7,30,44]. The gallbladder may appear contracted or distended, and pericholecystic fluid is variably present.

Although its sensitivity to some complications of cholecystitis is often limited, a normal appearance of the gallbladder, especially the wall, makes acute gallbladder pathology very unlikely. Thus, US remains the first imaging choice if complications of cholecystitis are suspected.

# Variant 3: Right upper quadrant pain. No fever and no high white blood cell (WBC) count. Suspected biliary disease. Negative or equivocal ultrasound. Next imaging study.

#### CT Abdomen

CT is not the first-line imaging test for suspected biliary causes of right upper quadrant abdominal pain. However, if US is negative for AC and there is no alternative diagnosis, CT, preferably with IV contrast, is the next preferred imaging examination for identifying those additional causes of right upper quadrant abdominal pain. When a diagnosis of AC is not prospectively suspected, CT may also be used to demonstrate AC in patients who have nonspecific abdominal pain. CT may also be valuable for further clarification of sonographic findings.

It is important to select the proper imaging protocol based on clinical information and other imaging. For example, evaluation for nephrolithiasis is best performed with a noncontrast-enhanced CT, whereas characterization of a liver lesion may be more accurate with a multiphasic CT or MRI, which may include precontrast and postcontrast images.

Detection of gallstones on CT with IV contrast depends on differing density of the stone relative to bile. Reported sensitivity for gallstone detection by CT is approximately 75%. Calcified gallstones are readily apparent. Cholesterol stones may also be seen as less dense than bile. Nitrogen gas may collect within degenerating gallstones, creating central fissures that may also be seen as different attenuation from bile [7].

The diagnosis of chronic cholecystitis is difficult to make at imaging. Chronic cholecystitis is associated with gallstones in 95% of cases and may result from a single or multiple recurrent episodes of AC. Chronic inflammation causes the gallbladder to become thickened and fibrotic. On CT, there may be absence of adjacent liver parenchymal hyperemia and pericholecystic inflammatory change, with nonvisualization of gallstones [7].

Noncontrast abdominal CT has very limited value in the assessment of suspected biliary sources of right upper quadrant abdominal pain. Unenhanced abdominal CT may or may not demonstrate cholelithiasis, depending on the density of the stones. Pericholecystic inflammatory fat stranding may be seen in AC. Evaluation of biliary ductal dilatation is limited.

CT without and with IV contrast is not often viewed as helpful in assessing patients admitted with right upper quadrant abdominal pain. Little additional information is gained by the routine addition of a noncontrast phase to a contrast-enhanced phase in this clinical setting [10].

## MRI Abdomen with MRCP

MRCP is excellent for the detection of cholelithiasis/choledocholithiasis, with reported sensitivity of 85% to 100%, specificity of 90%, and accuracy of 89% to 90% [7]. MRCP is superior to US in the evaluation of cystic duct and common bile duct calculi and calculi impacted in the gallbladder neck. Visualization of the common bile duct and even the cystic duct is a significant advantage of MRI over US in the evaluation of right upper quadrant pain [38].

MRI may also demonstrate findings to help distinguish acute from chronic cholecystitis. In chronic cholecystitis, gallbladder wall thickening related to chronic inflammation shows low signal intensity, as opposed to AC, which is associated with edema and T2 signal hyperintensity. Abdominal MRI with IV contrast may show perihepatic contrast enhancement in the setting of acute inflammation, which is helpful for differentiating AC from chronic cholecystitis [7].

Although contrast-enhanced examinations are preferred, MRI of the abdomen without IV contrast is also useful. It often provides improved characterization of incidental sonographic liver findings as compared to noncontrast CT. Standard T2-weighted MRI generally allows visualization of both normal caliber and dilated bile ducts. Noncontrast MRI with MRCP is very helpful in the follow-up of known hepatobiliary stone disease.

Abdominal MRI with, and sometimes without, IV contrast in combination with MRCP provides comprehensive evaluation of the hepatobiliary system. In addition to evaluating for cholelithiasis and choledocholithiasis, additional pathologies may be identified. Sources of biliary ductal dilatation, such as masses and lymph nodes, may be identified.

## Nuclear Medicine Scan Gallbladder

Low-grade, partial, or intermittent biliary obstruction may present with symptoms of recurrent right upper quadrant abdominal pain, mimicking chronic cholecystitis and numerous nonbiliary causes of abdominal pain. Nuclear medicine hepatobiliary imaging also aids in the diagnosis of partial biliary obstruction that is due to stones, biliary stricture, and sphincter of Oddi obstruction. Sphincter of Oddi evaluation with cholecystokinin cholescintigraphy does not carry the risk of pancreatitis, which may be seen with manometric evaluation. The use of cholecystokinin-augmented nuclear medicine hepatobiliary imaging in patients with pain of biliary origin is an acceptable practice under current Society of Gastrointestinal and Laparoendoscopic Surgeons clinical guidelines [45].

Nuclear medicine hepatobiliary imaging with calculation of the gallbladder ejection fraction after cholecystokinin infusion may be used to diagnose chronic gallbladder disease, partial biliary obstruction, and biliary dyskinesia as a cause of right upper quadrant pain. However, this test may be less useful in patients with atypical symptoms.

# Variant 4: Right upper quadrant pain. Fever, elevated WBC count. Suspected biliary disease. Negative or equivocal ultrasound. Next imaging study.

## **CT Abdomen**

Although it has not been advocated as a primary imaging examination for acute right upper quadrant pain, CT with IV contrast can confirm or refute the diagnosis of AC in equivocal cases based on US or scintigraphy, with a negative predictive value approaching 90% [30]. CT may reveal such complications as gangrene, gas formation, intraluminal hemorrhage, and perforation [15-17,30-35]. Furthermore, CT has been advocated as a useful modality in preoperative planning, with the absence of gallbladder wall enhancement or presence of a stone within the infundibulum associated with conversion from laparoscopic to open cholecystectomy. Prior knowledge of these imaging findings may help guide appropriate surgical approach [46].

Clinical conditions that can mimic AC, in terms of presentation with acute right upper quadrant pain, include chronic cholecystitis, peptic ulcer, pancreatitis, gastroenteritis, ascending cholangitis, and bowel obstruction, among others. However, AC is a fairly common disease that presents with right upper quadrant pain and is often the initial diagnosis to exclude. If US or scintigraphy are negative for AC and there is no alternative diagnosis, CT, preferably with IV contrast, is the next preferred imaging examination for identifying those disorders. When a diagnosis of AC is not prospectively suspected, CT may also be used to demonstrate AC in patients who have nonspecific abdominal pain.

The CT findings in AC are similar to those encountered by US [7] with the exception of gallstones, which may not be seen with CT. Other potential findings include adjacent liver parenchymal hyperemia, which cannot be detected without IV contrast. Abnormal gallbladder wall enhancement can be seen in more advanced cases [7].

CT without IV contrast can detect some features and complications of AC, such as gallbladder wall thickening, pericholecystic inflammation, gas formation, and hemorrhage, although some important features, such as wall enhancement and adjacent liver parenchymal hyperemia, cannot be detected without IV contrast. Adjacent liver hyperemia is actually one of the earlier findings in AC and can be a very useful problem-solving tool [7].

CT without and with IV contrast is not often viewed as helpful in assessing patients admitted with right upper quadrant abdominal pain. Little additional information is gained by the routine addition of a noncontrast phase to a contrast-enhanced phase in this clinical setting [10].

## MRI Abdomen with MRCP

The presence of AC can be further explored using abdominal MRI, which often includes the use of an IV gadolinium-based contrast agent, in cases in which other imaging tests are equivocal [7]. As with CT, MRI is not advocated as a primary imaging examination to evaluate acute right upper quadrant pain; however, several studies have suggested that abdominal MRI is a reliable alternative and can be particularly helpful in the patient who is difficult to examine with US [36-38]. Although factors such as longer acquisition times limit its use in the emergency setting, more consistent visualization of the extrahepatic biliary tree is an important advantage of its use [47,48].

MRI is considered the best modality for evaluating hepatic and biliary abnormalities that are not characterized by US. It can perform superiorly to US in cases of gallstones in the gallbladder neck, the cystic duct, or the common bile duct [7].

Few studies have examined the role of MRI in evaluating AC. MRI sensitivity estimates range from 50% to 91%, with specificity ranging from 79% to 89%. According to the meta-analysis by Kiewiet et al, the summary sensitivity is 85% (95% CI, 66%-95%) and the specificity is 81% (95% CI, 69%-90%) [25,38,47,48], similar to those of US. A study by Byott and Harris [49] advocated for the use of limited MRI (rapid acquisition half-Fourier acquisition single shot turbo spin echo [HASTE] coronal and axial sequences, without IV contrast) for evaluation of AC, especially in younger patients.

As with CT without IV contrast, noncontrast MRI will not be able to detect all the imaging features or potential complications of AC. However, noncontrast MRI with MRCP has excellent accuracy for visualization of normal and dilated bile ducts and the detection of stone disease compared to noncontrast CT. Standard T2-weighted imaging can better demonstrate gallbladder wall edema and pericholecystic fluid than noncontrast CT.

## Nuclear Medicine Scan Gallbladder

A 2012 meta-analysis by Kiewiet et al [25] included 40 studies evaluating cholescintigraphy and 26 studies evaluating US published between 1978 and 2010. This analysis confirmed the sensitivity and specificity values for AC noted by Shea et al [42], with respect to cholescintigraphy at 96% (95% CI, 94%-97%) and 90% (95% CI, 86%-93%), respectively. However, Kiewiet et al [25] reported a slightly lower sensitivity for US at 81% (95% CI, 75%-87%) and slightly higher specificity at 83% (95% CI, 74%-89%) compared with Shea's US findings. Similarly, direct comparisons of the diagnostic accuracy of US and cholescintigraphy performed in multiple studies have confirmed the superior accuracy of cholescintigraphy for AC. Despite providing information limited to the hepatobiliary tract, cholescintigraphy has been advocated as a useful diagnostic modality. In the setting of suspected AC, cholescintigraphy should be considered a first-line examination.

# Variant 5: Right upper quadrant pain. Suspected acalculous cholecystitis. Negative or equivocal ultrasound. Next imaging study.

# CT Abdomen

Patients with suspected acalculous cholecystitis are typically critically ill, and CT has a role in evaluating these patients [31]; however, as with US, the frequent prevalence of nonspecific abnormal imaging findings in the gallbladders of critically ill patients limit its diagnostic value. Nevertheless, when the gallbladder appears completely normal on CT, there is a low probability of any surgical finding in the gallbladder [50].

CT without IV contrast can detect some features and complications of acalculous cholecystitis, such as gallbladder wall thickening, pericholecystic inflammation, gas formation, and hemorrhage. However, some important features, such as wall enhancement and adjacent liver parenchymal hyperemia, cannot be detected on noncontrast CT and so IV contrast is preferred. Adjacent liver hyperemia is actually one of the earlier findings in acalculous cholecystitis and can be a very useful problem-solving tool [7].

CT without and with IV contrast is not often viewed as helpful in assessing patients admitted with right upper quadrant abdominal pain. Little additional information is gained by the routine addition of a noncontrast phase to a contrast-enhanced phase in this clinical setting [10].

## MRI Abdomen with MRCP

MRI has not been evaluated sufficiently in acalculous cholecystitis and is often impractical, given patient comorbidity. Therefore, its usefulness in the setting of suspected acalculous cholecystitis is limited. However, MRI may play a role in cases where other imaging tests are equivocal [7]. Several studies have suggested that abdominal MRI is a reliable alternative and can be particularly helpful in the patient who is difficult to examine with US [36-38]. MRI can be the next best imaging modality when acalculous cholecystitis is excluded, and MRI with MRCP is considered the best modality for evaluating hepatic and biliary abnormalities that are not characterized by US. It can perform superiorly to US in cases of gallstones in the gallbladder neck, the cystic duct, or the common bile duct [7].

## Nuclear Medicine Scan Gallbladder

Cholescintigraphy is a very sensitive diagnostic test because most cases of acalculous cholecystitis are associated with cystic duct obstruction, similar to the calculous form of the disease. Some cases of acalculous cholecystitis, however, are related to direct inflammation of the gallbladder, leading to false-negative studies when using cholescintigraphy [51]. It should also be noted that the specificity of cholescintigraphy may be limited in the critically ill patient where nonvisualization of the gallbladder may occur in the absence of inflammation despite preimaging cholecystokinin administration. However, cholescintigraphy remains the imaging examination of choice when acalculous cholecystitis is suspected.

## **Image-Guided Biopsy Liver**

Percutaneous cholecystostomy can be both diagnostic and therapeutic, and it is usually considered safe in hospitalized patients suspected of having acalculous cholecystitis [52,53]. Some of the diagnostic criteria by which a diagnosis of cholecystitis is made with percutaneous cholecystostomy include obstruction of the cystic duct in the clinical setting of suspected AC and improvement in symptoms of AC after placement of the cholecystostomy [54].

Following aspiration of the bile, gallbladder drainage catheter placement may be accomplished immediately, if indicated. This can frequently bridge patients to cholecystectomy at a subsequent time [55-57]. Definitive cholecystectomy is then sometimes performed [52]. It is more often used as a therapeutic option rather than solely for diagnosis.

#### Summary of Recommendations

- Variant 1: US abdomen or CT abdomen with IV contrast is usually appropriate for the initial imaging of right upper quadrant pain with an unknown etiology. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care). The panel did not agree on recommending radiography abdomen for patients in this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from this procedure. Imaging with this procedure is controversial but may be appropriate.
- Variant 2: US abdomen is usually appropriate for the initial evaluation for right upper quadrant pain with suspected biliary disease.
- Variant 3: MRI abdomen without and with IV contrast with MRCP or CT abdomen with IV contrast or MRI abdomen without IV contrast with MRCP is usually appropriate for right upper quadrant pain with no fever and no high white blood count with suspected biliary disease after a negative or equivocal US. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 4: MRI abdomen without and with IV contrast with MRCP or CT abdomen with IV contrast or nuclear medicine scan gallbladder is usually appropriate for right upper quadrant pain with fever, elevated WBC count with suspected biliary disease after a negative or equivocal US. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- Variant 5: Nuclear medicine scan gallbladder is usually appropriate for right upper quadrant pain with suspected acalculous cholecystitis after a negative or equivocal US.

#### **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <u>https://acsearch.acr.org/list</u>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Appropriateness Category Names and Definitions

#### **Relative Radiation Level Information**

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria<sup>®</sup> Radiation Dose Assessment Introduction document [58].

Relative Radiation Level Designations			
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
۲	<0.1 mSv	<0.03 mSv	
<b>*</b>	0.1-1 mSv	0.03-0.3 mSv	
€€	1-10 mSv	0.3-3 mSv	
€€€€	10-30 mSv	3-10 mSv	
€€€€	30-100 mSv	10-30 mSv	

\*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.