

**American College of Radiology
ACR Appropriateness Criteria®
Jaundice**

Variant: 1 Jaundice. No known predisposing conditions. Initial imaging.

| Procedure | Appropriateness Category | Relative Radiation Level |
|--|--------------------------|--------------------------|
| US abdomen | Usually Appropriate | ○ |
| MRI abdomen without and with IV contrast with MRCP | Usually Appropriate | ○ |
| CT abdomen with IV contrast | Usually Appropriate | ⦿⦿⦿ |
| MRI abdomen without IV contrast with MRCP | May Be Appropriate | ○ |
| US abdomen endoscopic | Usually Not Appropriate | ○ |
| ERCP | Usually Not Appropriate | ⦿⦿⦿ |
| CT abdomen without IV contrast | Usually Not Appropriate | ⦿⦿⦿ |
| CT abdomen without and with IV contrast | Usually Not Appropriate | ⦿⦿⦿⦿ |

Variant: 2 Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

| Procedure | Appropriateness Category | Relative Radiation Level |
|--|--------------------------|--------------------------|
| US abdomen | Usually Appropriate | ○ |
| MRI abdomen without and with IV contrast with MRCP | Usually Appropriate | ○ |
| MRI abdomen without IV contrast with MRCP | Usually Appropriate | ○ |
| CT abdomen with IV contrast | Usually Appropriate | ⦿⦿⦿ |
| US abdomen endoscopic | May Be Appropriate | ○ |
| ERCP | May Be Appropriate | ⦿⦿⦿ |
| CT abdomen without IV contrast | Usually Not Appropriate | ⦿⦿⦿ |
| CT abdomen without and with IV contrast | Usually Not Appropriate | ⦿⦿⦿⦿ |

Variant: 3 Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

| Procedure | Appropriateness Category | Relative Radiation Level |
|--|-----------------------------------|--------------------------|
| US abdomen | Usually Appropriate | ○ |
| MRI abdomen without and with IV contrast with MRCP | Usually Appropriate | ○ |
| CT abdomen with IV contrast | Usually Appropriate | ⦿⦿⦿ |
| MRI abdomen without IV contrast with MRCP | May Be Appropriate (Disagreement) | ○ |
| US abdomen endoscopic | Usually Not Appropriate | ○ |
| ERCP | Usually Not Appropriate | ⦿⦿⦿ |
| CT abdomen without IV contrast | Usually Not Appropriate | ⦿⦿⦿ |
| CT abdomen without and with IV contrast | Usually Not Appropriate | ⦿⦿⦿⦿ |

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Summary of Literature Review

Introduction/Background

Jaundice (hyperbilirubinemia) results from the accumulation of bilirubin (a byproduct of heme metabolism) in body tissues and can be caused by a variety of clinical disorders, including bilirubin overproduction, impaired bilirubin conjugation, biliary obstruction, and hepatic inflammation [1-3]. In the initial presentation of an adult patient with jaundice, traditional descriptions to help identify those with potential malignant etiologies categorize the patient regarding whether or not there is the presence of "pain." However, because patient descriptions of pain are subjective, in clinical practice and in most published papers, jaundice is not classified into categories based on pain [4-6]. Recognizing the movement away from categorizing etiologies of jaundice in terms of pain, this ACR Appropriateness Criteria focuses instead on all categories of jaundice by using a combination of the clinical findings, presentation, and laboratory values to separate the variants. In the initial presentation of jaundice, the patient's presentation or condition may be complicated by acute infections, such as cholangitis (eg, right upper quadrant pain, fever, jaundice) or cholecystitis; acute inflammatory conditions, such as pancreatitis or acute hepatitis; or fulminant hepatic failure or cirrhosis. Causes may also include hemolysis, intrahepatic or inherited biliary disorders, medication toxicity, choledocholithiasis, sepsis or low perfusion states, and tumor- or malignancy-related causes of biliary obstruction. In the United States, the most common causes of all types of jaundice fall into the following four categories: (1) hepatitis, (2) alcoholic liver disease, (3) blockage of the common bile duct (CBD) by a gallstone or tumor, and (4) toxic reaction to a drug or medicinal herb [7].

The most common etiology of jaundice internationally varies by geography, type of hospital, and demographics. There are few studies published to date exploring the relative incidence of jaundice, with two widely cited studies from Europe (Bjornsson et al [8] and Whitehead et al [9], respectively) showing malignancy as the most common etiology of severe jaundice, with a study from Vietnam describing cirrhosis as the most common etiology of all comers with jaundice.

The next most common etiologies of severe jaundice were sepsis/shock (22%, 27/121), cirrhosis (21%, 25/121), CBD stones [10] (13%, 16/121), drugs (0.5%, 7/121), autoimmune hepatitis (0.2%, 2/121), and viral hepatitis (0.2%, 2/121) [9]. A study from the United States cites sepsis as the most common etiology of new-onset jaundice (22% of the study population), with decompensation of pre-existing chronic liver disease as the next most common cause (20.5%), followed by alcoholic hepatitis (16%), gallstone disease (14%), Gilbert syndrome (5.6%), malignancy (6.2%), and hemolysis (2.5%) [11]. Reasons for these widely conflicting results as to the dominant cause of jaundice include geographical disparities, tertiary referral versus community hospital settings, study design (whether severe or mild jaundice was studied), inpatient versus outpatient setting, ethnicity, socioeconomic status, and other demographic features of the study population.

Clinically, differentiating between the various potential etiologies of jaundice requires a detailed history, targeted physical examination, and pertinent laboratory studies (eg, a hepatic profile,

conjugated versus unconjugated bilirubinemia, complete blood count, etc), the results of which allow the physician to categorize the type of jaundice [12]. Broadly, jaundice can be clinically categorized in many ways; however, a commonly used distinction based on laboratory findings is to differentiate unconjugated (nonobstructive) hyperbilirubinemia (ie, hepatitis/sepsis, alcoholic liver disease, drug-induced liver disease) and conjugated (obstructive) hyperbilirubinemia (CBD obstruction, commonly by stones or tumor). There is a paucity of rigorous evidence directly comparing the following primary imaging methods used in evaluating the jaundiced patient: abdominal ultrasound (US), CT, MR cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic US [13].

Special Imaging Considerations

Radiography

Radiographs rarely provide any information on the site or the cause of obstruction and have a limited role in the evaluation of the jaundiced patient. Occasionally, radiographs may be useful as they are expeditiously obtained, and can quickly assess for the presence of calcified gallstones in the gallbladder or CBD [14], find calcific deposits in the pancreas (in the setting of chronic pancreatitis), and evaluate for the presence of an indwelling biliary or pancreatic stent.

Discussion of Procedures by Variant

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

The most common causes of all types of jaundice are: (1) hepatitis/sepsis, (2) alcoholic liver disease, (3) blockage of the CBD by a stone or tumor, and (4) toxic reaction to a drug or medicinal herb [7]. Of these common etiologies, imaging is most useful in the setting of suspected underlying cirrhosis or CBD obstruction, as it can demonstrate either the morphologic redistribution of the liver in cirrhosis and/or depict findings of portal hypertension, and, in CBD obstruction, depict dilation of the bile ducts and potentially identify the reason for the obstruction. Imaging can also be a useful tool to help exclude active biliary obstruction and the presence of cirrhosis in a patient presenting with an unclear cause of jaundice.

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

A. US Abdomen

An abdominal US focuses on generating images of the upper abdominal structures (eg, the liver, gallbladder, CBD, and the portions of the pancreas not obscured by overlying bowel gas). In the initial presentation of jaundice, abdominal US can detect both cirrhosis and the presence of dilated intrahepatic/extrahepatic bile ducts. For detection of cirrhosis, US shows an overall sensitivity of 65% to 95%, with a positive predictive value of 98% [15-19]. The most accurate finding on US in liver cirrhosis is a nodular surface, which is more sensitive on the undersurface of the liver than the superior surface (86% versus 53%) [15]. Similarly, US is accurate for the depiction of biliary obstruction, with a wide range of reported sensitivities (32%–100%) and specificities (71%–97%) [20-25]. However, the cause of the biliary obstruction is not always clear on US. For example, biliary ductal calculi are not detected with the same sensitivity as gallbladder calculi [26,27], with reported sensitivities for CBD stone detection on US [21,22,28] ranging from 22.5% to 75% [26,27] because the subhepatic common duct may not be visible because of overlaying bowel gas. Sensitivity of detection can be increased between 70% to 86% by combining tissue harmonic imaging with the findings of elevated bilirubin, patient >55 years of age, and the finding of CBD dilatation between 6 to 10 mm [26,29]. The presence of multiple small (<5 mm) gallstones in the gallbladder creates a

4-fold risk for migration of these stones into the CBD [30]. As there is a low prevalence (5%–10%) of choledocholithiasis in patients with symptomatic cholelithiasis, a normal CBD caliber on US has a 95% to 96% negative predictive value [22,31]. US is recommended by many organizations, including the American College of Gastroenterology, as the initial diagnostic test of choice in patients with suspected obstruction of the common duct [32].

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

B. CT Abdomen

CT is a noninvasive modality that acquires images rapidly. Contrast-enhanced CT is typically used to image patients with jaundice because there is limited evidence of the utility of noncontrast CT in detecting the cause of jaundice. Contrast-enhanced CT is very sensitive (74%–96%) and specific (90%–94%) for detecting biliary obstruction [33]. Multidetector CT (MDCT) can determine the site and the cause of biliary obstruction more accurately than US [34–36]. After the advent of MDCT in the late 1990s, which allowed for improved spatial resolution (as low as 0.6-mm slice thickness) and isotropic reconstructions in multiple planes, several articles showed that MDCT sensitivity for the presence of biliary obstruction improved to >90% [37–39]. In patients with acute biliary obstruction and suspected complicating conditions, such as cholangitis, cholecystitis, or pancreatitis, a postintravenous contrast-enhanced abdominal CT study is useful in defining the level of obstruction, likely cause, and coexistent complications [40,41]. It is unlikely that a CT without and with intravenous (IV) contrast examination is necessary for the evaluation (as opposed to a single-phase postcontrast CT scan), as the morphology alone of a stone or mass on a single-phase postcontrast examination is typically enough to suggest the best diagnosis (ie, it is not necessary to prove enhancement or lack thereof in an area with classic morphologic imaging features suggestive of a stone or, alternatively, a mass). CT can be used to detect partially or completely calcified biliary calculi but is insensitive for detecting bilirubinate or cholesterol calculi [33,38]. Many gallstones are not radiopaque (available estimates in the older radiology literature suggest that up to 80% of gallstones are noncalcified) [27,42]. Older studies comparing older technology CT and US from the 1990s demonstrate that CT has a sensitivity between 39% to 75% for detection of gallstones compared with US [43]. However, isotropic data routinely obtained with current multislice technology can be reconstructed using narrow collimation and smaller reconstruction intervals, which allow for better visualization of the calculi [33,38].

For the accuracy of cirrhosis detection, a study comparing CT, MRI, and US (compared with explant livers resected for hepatocellular carcinoma at the time of transplant), found that CT had an accuracy of 67%, MRI an accuracy of 70.3%, and US an accuracy of 64% [44]. A more recent study from 2016 showed that use of surface nodularity quantification on CT was highly accurate (area under the receiver operating characteristic curve of 0.929) in differentiating cirrhotic from noncirrhotic liver [45].

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

C. MRI Abdomen

MRI is an advanced noninvasive imaging technique that uses powerful magnets to obtain high-contrast images of the abdomen; it is more time consuming (typically requiring image acquisitions of 30 minutes) than either CT or US but offers improved contrast resolution over CT and US. MRI can accurately demonstrate both the site and cause of biliary obstruction [34,46]. MRI can be performed with a variety of specific sequences, one of which is a heavily T2-weighted fluid-sensitive 3-D sequence, acquired over 3 to 5 minutes in the coronal plane using respiratory triggering or diaphragmatic gating, which is called MRCP [47]. This sequence uses the intrinsic

differential T2 contrast between the fluid in the biliary tree (very high T2 relaxation time) and the remaining organs (much lower T2 relaxation time) to generate a cholangiogram without requiring contrast injection. Source images from a 3-D MRCP sequence have been shown to be useful in depicting the 3-D anatomy of the biliary and pancreatic ducts [48,49].

For detection of ductal calculi, MRI (with or without MRCP sequences) is more sensitive than CT or US [26,34,50-53]. IV contrast administration with MRCP is not necessary in the evaluation of patients with suspected CBD stones; however, IV contrast improves the sensitivity of MRCP for the detection of peribiliary enhancement (a finding in cholangitis, which can complicate an obstructing CBD stone) and improves the confidence in the diagnosis and staging of unsuspected pancreaticobiliary tumors [54-56]. For diagnosis of CBD stones, MRCP (without IV contrast) has a reported sensitivity ranging from 77% to 88%, specificity between 50% to 72%, accuracy of 83%, positive predictive value between 87% to 90%, and negative predictive value between 27% to 72%, as compared to the gold standard of ERCP [57,58]. However, MRCP has diminishing sensitivity with decreasing stone sizes of <4 mm [58-60]. The reasons for the low specificity of MRCP for tiny CBD stones are multifactorial. One such factor is that there is an increased likelihood for spontaneous stone passage when stones are <4 mm in size; therefore, the stone may be present for the MRCP but have passed by the time of the ERCP. Similarly, the sensitivity of MRCP may be affected by stones in the gallbladder that pass into the CBD between the MRCP and the ERCP [60]. Additionally, studies that compare MRCP to ERCP use ERCP as the gold standard, which intrinsically biases the results toward ERCP. In patients with previous gastroenteric anastomoses, MRCP is accurate in evaluating the extrahepatic biliary ductal system with superior accuracy compared to ERCP or EUS that is due to technical difficulties in being able to advance the endoscope into the biliopancreatic limb. MRCP is less morbid than ERCP imaging; however, ERCP imaging offers the potential for intervention (CBD stone extraction or biopsy of an obstructing lesion).

MRCP is more sensitive than US for determining the cause of biliary obstruction when dilated bile ducts are seen on US [61]. In patients with suspected sclerosing cholangitis or biliary stricture, MRCP is the preferred imaging modality, avoiding the possibility of suppurative cholangitis that may be induced by endoscopic catheter manipulation of an obstructed biliary system [53]. MRCP findings may guide directed approaches, such as ERCP, with brushing, percutaneous transhepatic biliary stenting, or reconstructive surgery [34,51-53,62,63].

For the accuracy of detection of cirrhosis, a study comparing CT, MRI, and US (compared with explant livers resected for hepatocellular carcinoma at the time of transplant), found that CT had an accuracy of 67%, MRI an accuracy of 70.3%, and US an accuracy of 64% [44]. See the ACR Appropriateness Criteria[®] topic on "Chronic Liver Disease" [64].

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

D. ERCP

ERCP is an invasive procedure that is typically performed by gastroenterologists or general surgeons in an interventional suite or operating room under general anesthesia and requires advancing an endoscope into the duodenum, with cannulation of the ampulla and injection of contrast into the CBD with fluoroscopic images obtained to image the biliary tree. ERCP may be performed with a concomitant sphincterotomy, biopsy, or stent deployment (CBD or pancreatic). ERCP is the most commonly performed invasive diagnostic and therapeutic biliary procedure. Because of significant advances in cross-sectional imaging, in particular the advent of MRCP, ERCP

currently has more of a therapeutic role [65-67].

ERCP is not useful in the setting of jaundice caused by suspected hepatitis/sepsis, alcoholic liver disease, or in the case of medical drug toxicity. In the setting of suspected biliary obstruction, particularly if there is high concern for CBD stones or malignant obstruction, ERCP may be performed as the initial diagnostic and therapeutic imaging modality [68]. ERCP is very sensitive for detecting biliary ductal calculi [26,53]. However, as an interventional procedure, ERCP has risk of between 4% (111 of 2,769) up to 5.2% (872 of 16,855) of major complications (pancreatitis, cholangitis, hemorrhage, and perforation), with a 0.4% (11 of 2,769) mortality risk [69,70]. These factors need to be weighed against the potential benefits of ERCP [53,68,71,72]. The main indication for ERCP remains management of CBD stones, which can be cleared via balloon sweep of the duct in 80% to 95% of cases [71,73]. In stones >15 mm in size, ERCP alone is often not successful in removing the stone, and other advanced endoscopic techniques are needed [74,75].

Variant 1: Jaundice. No known predisposing conditions. Initial imaging.

E. US Abdomen Endoscopic

EUS is an invasive procedure that is typically performed by gastroenterologists or general surgeons in an interventional suite or operating room under general anesthesia and requires advancing an endoscope equipped with an US probe into the duodenum, with sonographic images obtained of the pancreaticobiliary tree. EUS may be performed with a concomitant fine-needle aspiration (FNA) or biopsy. EUS offers high-resolution sonographic imaging of the head of the pancreas/distal CBD, and as such can be used to detect small distal biliary ductal calculi, can locally stage pancreatic or periampullary neoplasms, and can guide FNA or biopsy [76-80]. EUS is limited by its narrow field of view and therefore cannot detect pathology outside of its imaging field of view (ie, cannot see pathology beyond the region to which the sonographic probe is physically adjacent) [81,82]. Complications from EUS have been reported in up to 6.3% of patients (most commonly postprocedural pancreatitis) [83]. The sensitivity, specificity, and accuracies of EUS with FNA biopsy for solid pancreatic tumor are 90.8%, 96.5%, and 91%, respectively [79,84,85].

There is a very limited role for EUS in the initial evaluation of a jaundiced patient. There are some studies from the gastroenterology literature that report high success of EUS in detection of tiny CBD stones that are <4 mm; however, generally, if the patient has a cholestatic presentation with a dilated CBD, the CBD will be presumptively swept at the time of ERCP without using an EUS to confirm this diagnosis [86].

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

Obstructive jaundice (conjugated hyperbilirubinemia) is jaundice resulting from obstruction to the flow of bile from the liver to the duodenum. The differential diagnosis of jaundice that is due to biliary obstruction in adults includes intrinsic and extrinsic tumors, choledocholithiasis, primary sclerosing cholangitis, parasitic infections, lymphoma, AIDS cholangiopathy, acute and chronic pancreatitis, and strictures after invasive procedures [12,32]. The panel concurs with multiple other society recommendations [32,86-89], that the usual initial imaging evaluation of a patient presenting with conjugated hyperbilirubinemia will include a right upper quadrant US. US will be able to confirm an obstructive process (dilatation of the intrahepatic or extrahepatic biliary tree) and may be able to localize the site of the obstruction (CBD, gallbladder, biliary bifurcation, pancreatic head) and show whether it is likely benign (choledocholithiasis, cholecystitis) or malignant (Klatskin tumor, pancreatic head mass, hepatic mass, etc), thus pointing to the best next

test (or intervention) for further workup.

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

A. US Abdomen

US is a noninvasive imaging technique that effectively evaluates obstructive jaundice [89,90]. For that reason, it is the most common first-line imaging modality used when obstructive jaundice is suspected clinically [32]. US is used to determine the presence of obstructive jaundice by depicting dilated bile ducts, with reported sensitivities ranging from 32% to 100% and specificities of 71% to 97% [20-25]. The cause of the obstruction (benign or malignant) is less often definitively seen on US, particularly in the distal CBD, with reported sensitivity for detection of a distal CBD stone ranging from 22.5% to 75% [20-22]. False-negative US studies are typically due either to the inability to visualize the extrahepatic biliary tree (often from interposed bowel gas or large body habitus) or to the absence of biliary dilation in the presence of acute obstruction. US is less accurate than either CT or MRCP for determining the site and the cause of obstruction [20,22,34-36,76].

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

B. MRI Abdomen

MRI is an advanced noninvasive imaging technique that uses powerful magnets to obtain high-contrast images of the abdomen; it is more time consuming (typically requiring imaging acquisitions of 30 minutes) than either CT or US but offers improved contrast resolution over other modalities. MRI can accurately demonstrate both the site and cause of biliary obstruction [34,46]. MRI can be performed with a variety of specific sequences, one of which is a heavily T2-weighted fluid-sensitive 3-D sequence, which is acquired over a 3- to 5-minute period in the coronal plane using respiratory triggering or diaphragmatic gating, also called MRCP [47]. Source images from a 3-D MRCP sequence have been shown to be useful in depicting the 3-D anatomy of the biliary and pancreatic ducts [48,49]. For detection of ductal calculi, MRI (with or without MRCP sequences) is more sensitive than CT or US [26,34,50-52]. For diagnosis of CBD stones, MRCP has a reported sensitivity ranging from 77% to 88%, specificity between 50% to 72%, accuracy of 83%, positive predictive value between 87% to 90%, and negative predictive value between 27% to 72%, as compared to the gold standard of ERCP [57,58]. MRCP is less morbid than ERCP imaging; however, ERCP imaging offers the potential for intervention (CBD stone extraction or biopsy of an obstructing lesion).

MRI offers similar sensitivity and specificity to CT imaging for the presurgical evaluation and staging of pancreatic adenocarcinoma [54]. Both MRI and CT are superior to ERCP and EUS for the staging of pancreaticobiliary malignancies (including cholangiocarcinomas and pancreatic head/body/tail malignancies), as MRI and CT enable cross-sectional imaging of all the organs of the upper abdomen and can detect vascular encasement and metastatic disease, whereas ERCP is limited to imaging of the biliary ductal system only, and EUS is limited to evaluation of regions within its small field of view [91-93]. MRI performed with diffusion sequences and gadoxetate disodium is more sensitive than CT for the detection of liver metastases from pancreaticobiliary malignancies [94-96]. The use of MRCP may decrease the number of ERCP examinations obtained prior to elective cholecystectomy (if no CBD stone is seen at the time of MRCP and there is no clinical suspicion for biliary obstruction, then surgeons may choose to proceed directly to cholecystectomy) [26,61]. MRCP is valuable in the clinical situation of failed ERCP [26,53], in

patients who are too sick to undergo ERCP [97], and in patients with hilar biliary obstructions that are due to ductal tumor or periductal compression [51,52,63,98-101]. MRCP offers additive value over US in pregnant patients with suspected pancreaticobiliary disease and is more sensitive than US for determining the cause of biliary obstruction when dilated bile ducts are seen on US [61].

If the bilirubin is elevated and there is a dilated CBD on US, there is controversy in the literature as to the best test for workup, MRCP or ERCP [102,103]. MRCP is noninvasive and highly accurate in diagnosing causes of mechanical CBD obstruction, whereas ERCP is invasive with a 4% to 5% morbidity risk and a 0.4% mortality risk, is slightly more accurate than MRCP (for choledocholithiasis) and is able to offer the benefit of therapeutic intervention [69,70]. Decisions for the next step of imaging in this scenario should be based on the suspicion for and the patient's clinical status. In the clinical scenario of an elevated bilirubin and the absence of CBD dilatation on US, the American College of Gastroenterology recommends additional laboratory testing, with consideration for eventual liver biopsy [32] without recommendations for additional imaging beyond US. However, given the wide variety of tumors that are known to cause jaundice and the known limitations of both laboratory values (eg, CEA, CA 19-9, CA 125, etc) and US in detecting hepatic metastases, biliary strictures/masses and pancreatic pathology, it is prudent to evaluate the jaundiced patient with or without a nondilated biliary tree with either MDCT or MRI/MRCP to exclude pathology in these areas [104,105].

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

C. CT Abdomen

CT is a rapidly obtained (scans typically take <1 minute to acquire) noninvasive imaging technique and is useful in the workup of suspected biliary obstruction. Most studies evaluate contrast-enhanced CT (using an iodinated nonionic contrast agent); however, there is limited data on the utility of noncontrast CT for biliary obstruction. Contrast-enhanced CT is more sensitive (74%–96%) and specific (90%–94%) than US for detecting biliary obstruction [33]. Additionally, MDCT can determine the site and the cause of biliary obstruction more accurately than US [34-36].

After the advent of MDCT in the late 1990s, which allowed for improved spatial resolution as low as 0.6-mm slice thickness and isotropic reconstructions in multiple planes, several articles showed that MDCT sensitivity for the presence of biliary obstruction improved to >90% [37-39]. MDCT of 64-slice and higher using minimum-intensity projection and multiplanar reconstructions has excellent spatial resolution and accuracy for staging of biliary malignancies and helps differentiate benign from malignant strictures [37,106-109].

When there is clinical suspicion for a malignant biliary obstruction, CT is highly accurate both for diagnosis and for staging of pancreatic or biliary malignancy (with accuracies for staging ranging from 80.5%–97%) [37,39,106,110-112]. Reported sensitivity, specificity, and accuracy of MDCT for the diagnosis of malignant strictures is 95%, 93.35%, and 88.5%, respectively [37]. CT cholangiopancreatography generated by slab volume imaging with minimum-intensity projections and curved planar reformations may be useful for preintervention planning [33,106]. MDCT is accurate in depicting local tumor extension and potential resectability [52,106,107], with Vargas et al [112] finding negative predictive values of 87% (20/23 patients) for determining local resectability of pancreatic carcinoma. Important information in pancreaticobiliary tumor staging includes tumoral involvement of the biliary confluence, encasement of the superior mesenteric and portal vein, peripancreatic tumor extension, regional adenopathy, and hepatic metastases [113].

MRI (with or without MRCP) is highly accurate for tumor detection and staging. For example, accuracy rates for MRI with MRCP and MDCT are similar: 90.7% versus 85.1% for bilateral secondary biliary confluence involvement and 87% for both in detecting intrapancreatic CBD involvement in bile duct malignancies [52,54]. Biphasic CT of the abdomen with pancreatic and portal venous phase imaging through the liver, biliary tree, and pancreas is the standard protocol for diagnosis and staging of suspected pancreaticobiliary malignancies. See also the ACR Appropriateness Criteria[®] topic on "[Staging of Pancreatic Ductal Adenocarcinoma](#)" [114]. Ongoing challenges in all imaging modalities involved in staging malignancies, including MDCT, are the limited sensitivity in detecting micrometastatic disease to the liver and small peritoneal implants [112].

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

D. ERCP

ERCP is an invasive procedure that is typically performed by gastroenterologists or general surgeons in an interventional suite or operating room under general anesthesia and requires advancing an endoscope into the duodenum, with cannulation of the ampulla and injection of contrast into the CBD with fluoroscopic images obtained to image the biliary tree. ERCP may be performed with a concomitant sphincterotomy, biopsy, or stent deployment (CBD or pancreatic). ERCP is the most commonly performed invasive diagnostic and therapeutic biliary procedure. Because of significant advances in cross-sectional imaging, in particular the advent of MRCP, ERCP currently has an almost exclusively therapeutic role [65-67].

In the setting of suspected biliary obstruction, particularly if there is high concern for CBD stones or malignant obstruction, ERCP may be performed as the initial diagnostic and therapeutic imaging modality [68]. ERCP is very sensitive for detecting biliary ductal calculi [26,53]. However, as an interventional procedure, ERCP has a risk of between 4% (111 of 2,769) to 5.2% (872 of 16,855) for major complications (pancreatitis, cholangitis, hemorrhage, and perforation), with a 0.4% (11 of 2,769) mortality risk [69,70]. These factors need to be weighed against the potential benefits of ERCP [53,68,71,72].

The main indication for ERCP remains management of CBD stones, which can be cleared in 80% to 95% of cases with a balloon sweep of the CBD [71,73]. Therapeutic endoscopic intervention, including sphincterotomy, can remove the CBD stone and may be curative when done prior to cholecystectomy (keeping in mind that up to 5% of patients may be recurrent primary CBD stone formers), but it has associated morbidity of up to 10% because of the risk of iatrogenic pancreatitis [53,72]. ERCP is limited in the evaluation of patients with previous gastroenteric anastomoses, as it is technically difficult to advance the endoscope into the biliopancreatic limb of the anastomosis. ERCP also remains the standard procedure for stent placement in cases of obstructive jaundice. When deployed for distal CBD strictures, stenting via ERCP is successful in more than 90% of cases [115]. For diagnostic yield from ERCP-guided FNA of biopsies of solid pancreatic neoplasms, ERCP demonstrated sensitivity between 57.1% (for pancreatic body/tail neoplasms) and 82.4% (for pancreatic head neoplasms) [116].

In patients with suspected sclerosing cholangitis or biliary stricture, ERCP should be performed with caution, as suppurative cholangitis may be induced by endoscopic catheter manipulation of an obstructed biliary system [53]. MRCP findings may guide directed approaches, such as ERCP, with brushing, percutaneous transhepatic biliary stenting, or reconstructive surgery [34,51-

[53,62,63](#)].

Studies from the gastroenterology literature show that ERCP has equivalent or greater sensitivity for tumor detection (provided the tumor is in the pancreatic head/duodenum or CBD), with superior sensitivity particularly for ampullary carcinoma, but it does not provide staging information for operability [\[76\]](#). Tissue diagnosis can be obtained by endoscopically directed brushing or guided US with FNA [\[71,76,78,117,118\]](#); however, results of brush cytology for biliary strictures from pancreatic malignancies are inferior (46% sensitive) relative to biliary malignancies (68%) [\[119\]](#). In patients with suspected malignant biliary obstruction and negative or equivocal CT or MRI examinations, ERCP with EUS may provide an imaging and cytologic diagnosis (FNA) [\[78,120\]](#).

As an interventional procedure, ERCP has risk of between 4% (111 of 2,769) to 5.2% (872 of 16,855) for major complications (pancreatitis, cholangitis, hemorrhage, and perforation), with a 0.4% (11 of 2,769) mortality risk [\[69,70\]](#). These factors need to be weighed against the potential benefits of ERCP [\[53,68,71,72\]](#). The main indication for ERCP remains management of CBD stones, which can be cleared in 80% to 95% of cases [\[71,73\]](#). ERCP also remains the standard procedure for stent placement in cases of obstructive jaundice. When deployed for distal CBD strictures, stenting via ERCP is successful in more than 90% of cases [\[115\]](#). For diagnostic yield from ERCP-guided FNA of biopsies of solid pancreatic neoplasms, ERCP demonstrated sensitivity between 57.1% (for pancreatic body/tail neoplasms) and 82.4% (for pancreatic head neoplasms) [\[116\]](#).

Endoscopic or percutaneous transhepatic biliary drainage is appropriate for patients who are not candidates for surgery and may even be useful in operative candidates for whom there is a delay to definitive surgical resection. Standard ERCP is sufficient in 90% to 95% of patients who require biliary decompression. Factors that contribute to ERCP failure include gastric outlet or duodenal obstruction that is due to tumor invasion, or altered anatomy from diverticula or prior surgery. Percutaneous transhepatic cholangiography as well as EUS-guided biliary drainage are both effective for biliary decompression [\[117\]](#).

Variant 2: Jaundice. Suspected mechanical obstruction based on initial imaging, clinical condition, or laboratory values.

E. US Abdomen Endoscopic

EUS is an invasive procedure that is typically performed by gastroenterologists or general surgeons in an interventional suite or operating room under general anesthesia and requires advancing an endoscope equipped with an US probe into the duodenum, with sonographic images obtained of the pancreaticobiliary tree. EUS may be performed with a concomitant FNA or biopsy. EUS offers high-resolution sonographic imaging of the head of the pancreas/distal CBD, and as such can be used to detect small distal biliary ductal calculi, can locally stage pancreatic or periampullary neoplasms, and can guide FNA or biopsy [\[76-80\]](#). EUS is limited by its narrow field of view and therefore cannot detect pathology outside of its imaging field of view (ie, cannot see pathology beyond the region to which the sonographic probe is physically adjacent) [\[81,82\]](#). Complications from EUS have been reported in up to 6.3% of patients (most commonly postprocedural pancreatitis) [\[83\]](#). The sensitivity, specificity, and accuracies of EUS with FNA biopsy for solid pancreatic tumor are 90.8%, 96.5%, and 91%, respectively [\[79,84,85\]](#).

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

Patients with unconjugated hyperbilirubinemia (nonobstructive) jaundice most commonly have diffuse hepatocellular disease (eg, cirrhosis, hepatitis), inability of the liver to handle a bilirubin load (eg, hemolytic anemia), or a bilirubin metabolism deficiency (eg, Gilbert disease [1], Crigler-Najjar syndrome, etc). Differentiating between these nonobstructive etiologies of jaundice is typically done through analysis of characteristic history and physical examination findings, as well as diagnostic laboratory profiles. If imaging is performed in these settings, it will confirm the absence of a mechanical obstruction and may point to an alternate etiology for the elevated bilirubin levels (eg, features of liver cirrhosis) [32]. Therefore, the largest role of imaging in unconjugated hyperbilirubinemia is in excluding other potential diagnoses.

This variant title is broad in order to give the clinician the most lenience in possible reasons for reaching this point in the diagnostic workup. One of the heavily debated portions of this variant title is the inclusion of patients with suspected medical, metabolic, or functional etiology of jaundice "based on initial imaging." For the purposes of this section, it is assumed that the initial imaging was not a diagnostic US of the liver (it could be an echocardiogram with incomplete imaging of the liver, a chest CT that captured a portion of the liver, or point-of-care US imaging for a diagnostic pleurocentesis, etc). If a diagnostic US of the liver were already performed, it would make little sense to repeat the US.

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

A. US Abdomen

In the initial setting of jaundice with a laboratory and clinical picture suggestive of a lack of biliary obstruction, US is usually performed as the initial evaluation [32]. US can confirm the absence of a mechanical obstruction, with specificities ranging between 71% to 97% [20-25]. US images may suggest an alternate etiology for the elevated bilirubin (such as cirrhosis), with US having an overall sensitivity of 65% to 95%, with a positive predictive value of 98% for the detection of cirrhosis [15-19]. The most accurate finding on sonography in liver cirrhosis is a nodular surface, which is more sensitive on the undersurface of the liver than the superior surface (86% versus 53%) [15]. If the US is negative, the American College of Gastroenterology recommends additional laboratory testing assessing for liver failure, ultimately suggesting a liver biopsy [32].

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

B. MRI Abdomen

MRI with MRCP may be of additional value in the setting of a negative US and clinical workup inconclusive for the etiology of the bilirubin elevation, particularly if there is concern for potential primary sclerosing cholangitis or primary biliary cirrhosis [32,105]. Proceeding directly to liver biopsy may run the risk of a false-negative biopsy, as the early disease process is patchy in the initial stages of primary sclerosing cholangitis or primary biliary cirrhosis; these diseases are nonglobal in their initial manifestations. Therefore, MRCP may help better detect pathology in these situations [121-123]. MRI may be useful when there is questionable hepatic parenchymal disease based on laboratory findings, as these modalities may show changes of early fibrosis (particularly if MR elastography is used), cirrhosis, or general hepatic inflammation [124]. Although there are not many data comparing contrast-enhanced MRI with noncontrast MRI in the setting of a nonobstructive jaundice, there are data showing that contrast administration improves the sensitivity for the detection of acute cholangitis and the detection of primary sclerosing cholangitis [125,126].

Although less sensitive than contrast-enhanced MRI, a noncontrast MRI (including MRCP) may be of use for this variant, as there are imaging findings seen on both C+ MRCP and C- MRCP. For example, both studies are useful in the assessment of subtle regions of peripheral biliary dilatation within the liver (seen in early manifestations of primary sclerosing cholangitis), in the detection of hepatolithiasis (which can occur secondary to surgical reconstructions and in the setting of recurrent pyogenic cholangitis), volume redistribution of the liver/inferior surface nodularity (seen in cirrhosis from varying underlying etiologies), detection of regions of peripheral fibrosis or other morphologic/signal abnormalities that can be associated with jaundice, and in unsuspected intra- or extrahepatic biliary strictures (from surgery or infectious etiologies) [127].

If there is concern for a previously unsuspected underlying hepatocellular disease, MRI shows a moderately high accuracy in detection of cirrhosis; a study comparing CT, MRI, and US (compared with explant livers resected for hepatocellular carcinoma at the time of transplant) found that CT had an accuracy of 67%, MRI an accuracy of 70.3%, and US an accuracy of 64% [44] for the detection of underlying cirrhosis. MRI is not very sensitive or specific for the diagnosis of acute hepatitis; however, several studies have found a significant relationship between the apparent diffusion coefficient and inflammation scores (ie, livers in the setting of acute hepatitis may have high signal on high b-value diffusion-weighted images) [128,129]. When imaging does not yield a cause for jaundice (ie, there is no biliary obstruction and no parenchymal process to explain jaundice), liver dysfunction or an infiltrative process must be excluded, and liver biopsy will be the most effective next step in diagnosis [12,32].

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

C. CT Abdomen

MDCT may be useful in the setting of nonobstructive jaundice when there is questionable hepatic parenchymal disease based on laboratory findings, as these modalities may show changes of early fibrosis, cirrhosis, or general hepatic inflammation [124]. When imaging does not yield a cause for jaundice (ie, there is no biliary obstruction and no parenchymal process to explain jaundice), liver dysfunction or an infiltrative process must be excluded, and liver biopsy will be the most effective next step in diagnosis [12,32].

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

D. ERCP

There is limited to no role for ERCP in the setting of nonobstructive jaundice.

Variant 3: Jaundice. Suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. No suspected mechanical obstruction.

E. US Abdomen Endoscopic

There is limited to no role for EUS in the setting of nonobstructive jaundice.

Summary of Recommendations

- **Variant 1:** US abdomen, CT abdomen with IV contrast, or MRI abdomen without and with IV contrast with MRCP is usually appropriate for the initial imaging of jaundice with no known

predisposing conditions. These procedures are equivalent alternatives.

- **Variant 2:** CT abdomen with IV contrast, MRI abdomen without and with IV contrast with MRCP, MRI abdomen without IV contrast with MRCP, or US abdomen is usually appropriate for jaundice when initial imaging is suggestive of mechanical obstruction based on initial imaging, clinical condition, or laboratory values. These procedures are equivalent alternatives.
- **Variant 3:** MRI abdomen without and with IV contrast with MRCP, CT abdomen with IV contrast, or US abdomen is usually appropriate for jaundice when mechanical obstruction is not suspected in the setting of suspected medical, metabolic, or functional etiologies based on initial imaging, clinical condition, or laboratory values. These procedures are equivalent alternatives.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. 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, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Appropriateness Category Names and Definitions

| 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. |

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® [Radiation Dose Assessment Introduction](#) document [130].

| Relative Radiation Level Designations | | |
|---|--|--|
| Relative Radiation Level* | Adult Effective Dose Estimate Range | Pediatric Effective Dose Estimate Range |
| ○ | 0 mSv | 0 mSv |
| ☢ | <0.1 mSv | <0.03 mSv |
| ☢ ☢ | 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.

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