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	O
CT abdomen with IV contrast	Usually Appropriate	☢☢☢
MRI abdomen without and with IV contrast with MRCP	Usually Appropriate	O
MRI abdomen without IV contrast with MRCP	May Be Appropriate	O
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢
CT abdomen without IV contrast	Usually Not Appropriate	☢☢☢
ERCP	Usually Not Appropriate	☢☢☢
US abdomen endoscopic	Usually Not Appropriate	O

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

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

JAUNDICE

Expert Panel on Gastrointestinal Imaging: Nicole M. Hindman, MD[a]; Hina Arif-Tiwari, MD[b]; Ihab R. Kamel, MD, PhD[c]; Waddah B. Al-Refaie, MD[d]; Twyla B. Bartel, DO, MBA[e]; Brooks D. Cash, MD[f]; Victoria Chernyak, MD, MS[g]; Alan Goldstein, MD[h]; Joseph R. Grajo, MD[i]; Jeanne M. Horowitz, MD[j]; Aya Kamaya, MD[k]; Michelle M. McNamara, MD[l]; Kristin K. Porter, MD, PhD[m]; Pavan K. Srivastava, MD[n]; Atif Zaheer, MD[o]; Laura R. Carucci, MD.[p]

Summary of Literature Review

Background/Introduction

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

[a]New York University Medical Center, New York, New York. [b]University of Arizona, Banner University Medical Center, Tucson, Arizona. [c]Panel Chair, Johns Hopkins University School of Medicine, Baltimore, Maryland. [d]Georgetown University Hospital, Washington, District of Columbia; American College of Surgeons. [e]Global Advanced Imaging, PLLC, Little Rock, Arkansas. [f]University of Texas McGovern Medical School, Houston, Texas; American Gastroenterological Association. [g]Montefiore Medical Center, Bronx, New York. [h]UMass Medical School, Worcester, Massachusetts. [i]University of Florida College of Medicine, Gainesville, Florida. [j]Northwestern University, Chicago, Illinois. [k]Stanford University Medical Center, Stanford, California. [l]University of Alabama Medical Center, Birmingham, Alabama. [m]University of Alabama Medical Center, Birmingham, Alabama. [n]University of Illinois College of Medicine, Chicago, Illinois; American College of Physicians. [o]Johns Hopkins Hospital, Baltimore, Maryland. [p]Specialty Chair, Virginia Commonwealth University Medical Center, Richmond, Virginia.

Reprint requests to: publications@acr.org

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.

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].

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].

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].

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].

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.

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 to 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].

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].

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].

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].

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.

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].

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].

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].

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

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 go to www.acr.org/ac.

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**
O	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".		

References

1. Friedman LS. Chapter 16: Liver, Biliary Tract, & Pancreas Disorders. In: Papadakis MA, McPhee SJ, Rabow MW, eds. *Current Medical Diagnosis & Treatment 2017*. 56 ed. New York, NY: McGraw-Hill Education; 2017.
2. Reisman Y, Gips CH, Lavelle SM, Wilson JH. Clinical presentation of (subclinical) jaundice--the Euricterus project in The Netherlands. United Dutch Hospitals and Euricterus Project Management Group. Hepatogastroenterology 1996;43:1190-5.
3. Saini S. Imaging of the hepatobiliary tract. N Engl J Med 1997;336:1889-94.
4. Greig JD, Krukowski ZH, Matheson NA. Surgical morbidity and mortality in one hundred and twenty-nine patients with obstructive jaundice. Br J Surg 1988;75:216-9.
5. Hollands MJ, Little JM. Obstructive jaundice in chronic pancreatitis. HPB Surg 1989;1:263-70.
6. Kalser MH, Barkin J, MacIntyre JM. Pancreatic cancer. Assessment of prognosis by clinical presentation. Cancer 1985;56:397-402.
7. Herrine SK. Merck Manual. Professional Version. Jaundice. Available at: http://www.merckmanuals.com/professional/hepatic-and-biliary-disorders/approach-to-the-patient-with-liver-disease/jaundice. Accessed November 30, 2018.
8. Bjornsson E, Ismael S, Nejdet S, Kilander A. Severe jaundice in Sweden in the new millennium: causes, investigations, treatment and prognosis. Scand J Gastroenterol 2003;38:86-94.
9. Whitehead MW, Hainsworth I, Kingham JG. The causes of obvious jaundice in South West Wales: perceptions versus reality. Gut 2001;48:409-13.
10. Hung LN, Le Huong NT, Thuy An NT. Jaundice in Adult in-Patients at a Tertiary General Hospital. Journal of Biosciences and Medicines 2015;03:1-11.
11. Vuppalanchi R, Liangpunsakul S, Chalasani N. Etiology of new-onset jaundice: how often is it caused by idiosyncratic drug-induced liver injury in the United States? Am J Gastroenterol 2007;102:558-62; quiz 693.
12. Wolkoff AW. The Hyperbilirubinemias. In: Kasper DL, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine, 19e*. 19 ed. New York, NY: McGraw-Hill Education; 2015.
13. Manning A, Frazee R, Abernathy S, et al. Protocol-Driven Management of Suspected Common Duct Stones. J Am Coll Surg 2017;224:645-49.
14. Feld R, Kurtz AB, Zeman RK. Imaging the gallbladder: a historical perspective. AJR Am J Roentgenol 1991;156:737-40.
15. Colli A, Fraquelli M, Andreoletti M, Marino B, Zuccoli E, Conte D. Severe liver fibrosis or cirrhosis: accuracy of US for detection--analysis of 300 cases. Radiology 2003;227:89-94.
16. Hartman PC, Oosterveld BJ, Thijssen JM, Rosenbusch GJ, van den Berg J. Detection and differentiation of diffuse liver disease by quantitative echography. A retrospective assessment. Invest Radiol 1993;28:1-6.

17. Layer G, Zuna I, Lorenz A, et al. Computerized ultrasound B-scan texture analysis of experimental diffuse parenchymal liver disease: correlation with histopathology and tissue composition. J Clin Ultrasound 1991;19:193-201.
18. Soresi M, Giannitrapani L, Cervello M, Licata A, Montalto G. Non invasive tools for the diagnosis of liver cirrhosis. World J Gastroenterol 2014;20:18131-50.
19. Vigano M, Visentin S, Aghemo A, Rumi MG, Ronchi G. US features of liver surface nodularity as a predictor of severe fibrosis in chronic hepatitis C. Radiology 2005;234:641; author reply 41.
20. Pasanen PA, Partanen KP, Pikkarainen PH, Alhava EM, Janatuinen EK, Pirinen AE. A comparison of ultrasound, computed tomography and endoscopic retrograde cholangiopancreatography in the differential diagnosis of benign and malignant jaundice and cholestasis. Eur J Surg 1993;159:23-9.
21. Laing FC, Jeffrey RB, Wing VW. Improved visualization of choledocholithiasis by sonography. AJR Am J Roentgenol 1984;143:949-52.
22. Liu TH, Consorti ET, Kawashima A, et al. Patient evaluation and management with selective use of magnetic resonance cholangiography and endoscopic retrograde cholangiopancreatography before laparoscopic cholecystectomy. Ann Surg 2001;234:33-40.
23. Mitchell SE, Clark RA. A comparison of computed tomography and sonography in choledocholithiasis. AJR Am J Roentgenol 1984;142:729-33.
24. Wermke W, Schulz HJ. [Sonographic diagnosis of bile duct calculi. Results of a prospective study of 222 cases of choledocholithiasis]. Ultraschall Med 1987;8:116-20.
25. Gurusamy KS, Giljaca V, Takwoingi Y, et al. Ultrasound versus liver function tests for diagnosis of common bile duct stones. Cochrane Database Syst Rev 2015:CD011548.
26. Williams EJ, Green J, Beckingham I, Parks R, Martin D, Lombard M. Guidelines on the management of common bile duct stones (CBDS). Gut 2008;57:1004-21.
27. Bortoff GA, Chen MY, Ott DJ, Wolfman NT, Routh WD. Gallbladder stones: imaging and intervention. Radiographics 2000;20:751-66.
28. Pasanen P, Partanen K, Pikkarainen P, Alhava E, Pirinen A, Janatuinen E. Ultrasonography, CT, and ERCP in the diagnosis of choledochal stones. Acta Radiol 1992;33:53-6.
29. Ripolles T, Ramirez-Fuentes C, Martinez-Perez MJ, Delgado F, Blanc E, Lopez A. Tissue harmonic sonography in the diagnosis of common bile duct stones: a comparison with endoscopic retrograde cholangiography. J Clin Ultrasound 2009;37:501-6.
30. Costi R, Sarli L, Caruso G, et al. Preoperative ultrasonographic assessment of the number and size of gallbladder stones: is it a useful predictor of asymptomatic choledochal lithiasis? J Ultrasound Med 2002;21:971-6.
31. Yang MH, Chen TH, Wang SE, et al. Biochemical predictors for absence of common bile duct stones in patients undergoing laparoscopic cholecystectomy. Surg Endosc 2008;22:1620-4.
32. Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. Am J Gastroenterol 2017;112:18-35.
33. Anderson SW, Lucey BC, Varghese JC, Soto JA. Accuracy of MDCT in the diagnosis of choledocholithiasis. AJR Am J Roentgenol 2006;187:174-80.
34. Maurea S, Caleo O, Mollica C, et al. Comparative diagnostic evaluation with MR cholangiopancreatography, ultrasonography and CT in patients with pancreatobiliary disease. Radiol Med 2009;114:390-402.
35. Pickuth D. Radiologic diagnosis of common bile duct stones. Abdom Imaging 2000;25:618-21.
36. Varghese JC, Liddell RP, Farrell MA, Murray FE, Osborne H, Lee MJ. The diagnostic accuracy of magnetic resonance cholangiopancreatography and ultrasound compared with direct cholangiography in the detection of choledocholithiasis. Clin Radiol 1999;54:604-14.
37. Tongdee T, Amornvittayachan O, Tongdee R. Accuracy of multidetector computed tomography cholangiography in evaluation of cause of biliary tract obstruction. J Med Assoc Thai 2010;93:566-73.
38. Tseng CW, Chen CC, Chen TS, Chang FY, Lin HC, Lee SD. Can computed tomography with coronal reconstruction improve the diagnosis of choledocholithiasis? J Gastroenterol Hepatol 2008;23:1586-9.
39. Mathew RP, Moorkath A, Basti RS, Suresh HB. Value and Accuracy of Multidetector Computed Tomography in Obstructive Jaundice. Pol J Radiol 2016;81:303-9.
40. Petrescu I, Bratu AM, Petrescu S, Popa BV, Cristian D, Burcos T. CT vs. MRCP in choledocholithiasis jaundice. J Med Life 2015;8:226-31.

41. Wyatt SH, Fishman EK. Biliary tract obstruction. The role of spiral CT in detection and definition of disease. Clin Imaging 1997;21:27-34.
42. Zeman RK. Cholelithiasis and cholecystitis. In: Gore RM, Levine MS, Laufer I, eds. *Textbook of gastrointestinal radiology*. Philadelphia: W.B. Saunders Co.; 1994:1636-74.
43. Benarroch-Gampel J, Boyd CA, Sheffield KM, Townsend CM, Jr., Riall TS. Overuse of CT in patients with complicated gallstone disease. J Am Coll Surg 2011;213:524-30.
44. Kudo M, Zheng RQ, Kim SR, et al. Diagnostic accuracy of imaging for liver cirrhosis compared to histologically proven liver cirrhosis. A multicenter collaborative study. Intervirology 2008;51 Suppl 1:17-26.
45. Smith AD, Branch CR, Zand K, et al. Liver Surface Nodularity Quantification from Routine CT Images as a Biomarker for Detection and Evaluation of Cirrhosis. Radiology 2016;280:771-81.
46. Munir K, Bari V, Yaqoob J, Khan DB, Usman MU. The role of magnetic resonance cholangiopancreatography (MRCP) in obstructive jaundice. J Pak Med Assoc 2004;54:128-32.
47. Yoon JH, Lee SM, Kang HJ, et al. Clinical Feasibility of 3-Dimensional Magnetic Resonance Cholangiopancreatography Using Compressed Sensing: Comparison of Image Quality and Diagnostic Performance. Invest Radiol 2017;52:612-19.
48. Kang SK, Heacock L, Doshi AM, Ream JR, Sun J, Babb JS. Comparative performance of non-contrast MRI with HASTE vs. contrast-enhanced MRI/3D-MRCP for possible choledocholithiasis in hospitalized patients. Abdom Radiol (NY) 2017;42:1650-58.
49. Sun N, Xu Q, Liu X, Liu W, Wang J. Comparison of preoperative evaluation of malignant low-level biliary obstruction using plain magnetic resonance and coronal liver acquisition with volume acceleration technique alone and in combination. Eur J Med Res 2015;20:92.
50. Aube C, Delorme B, Yzet T, et al. MR cholangiopancreatography versus endoscopic sonography in suspected common bile duct lithiasis: a prospective, comparative study. AJR Am J Roentgenol 2005;184:55-62.
51. Choi JY, Lee JM, Lee JY, et al. Navigator-triggered isotropic three-dimensional magnetic resonance cholangiopancreatography in the diagnosis of malignant biliary obstructions: comparison with direct cholangiography. J Magn Reson Imaging 2008;27:94-101.
52. Park HS, Lee JM, Choi JY, et al. Preoperative evaluation of bile duct cancer: MRI combined with MR cholangiopancreatography versus MDCT with direct cholangiography. AJR Am J Roentgenol 2008;190:396-405.
53. Hekimoglu K, Ustundag Y, Dusak A, et al. MRCP vs. ERCP in the evaluation of biliary pathologies: review of current literature. J Dig Dis 2008;9:162-9.
54. Chen FM, Ni JM, Zhang ZY, Zhang L, Li B, Jiang CJ. Presurgical Evaluation of Pancreatic Cancer: A Comprehensive Imaging Comparison of CT Versus MRI. AJR Am J Roentgenol 2016;206:526-35.
55. Joo I, Lee JM. Imaging bile duct tumors: pathologic concepts, classification, and early tumor detection. Abdom Imaging 2013;38:1334-50.
56. Tirkes T, Menias CO, Sandrasegaran K. MR imaging techniques for pancreas. Radiol Clin North Am 2012;50:379-93.
57. Kolodziejczyk E, Jurkiewicz E, Pertkiewicz J, et al. MRCP Versus ERCP in the Evaluation of Chronic Pancreatitis in Children: Which Is the Better Choice? Pancreas 2016;45:1115-9.
58. Scaffidi MG, Luigiano C, Consolo P, et al. Magnetic resonance cholangio-pancreatography versus endoscopic retrograde cholangio-pancreatography in the diagnosis of common bile duct stones: a prospective comparative study. Minerva Med 2009;100:341-8.
59. Kondo S, Isayama H, Akahane M, et al. Detection of common bile duct stones: comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. Eur J Radiol 2005;54:271-5.
60. Reid J, Dolan R, Patel M, Fleming R, Young D, Hair A. Size of common bile duct stones on MRCP predicts likelihood of positive findings at ERCP. Surgeon 2017;15:119-22.
61. Oto A, Ernst R, Ghulmiyyah L, Hughes D, Saade G, Chaljub G. The role of MR cholangiopancreatography in the evaluation of pregnant patients with acute pancreaticobiliary disease. Br J Radiol 2009;82:279-85.
62. Kim TU, Kim S, Lee JW, et al. Ampulla of Vater: comprehensive anatomy, MR imaging of pathologic conditions, and correlation with endoscopy. Eur J Radiol 2008;66:48-64.

63. Masselli G, Manfredi R, Vecchioli A, Gualdi G. MR imaging and MR cholangiopancreatography in the preoperative evaluation of hilar cholangiocarcinoma: correlation with surgical and pathologic findings. Eur Radiol 2008;18:2213-21.
64. Horowitz JM, Kamel IR, Arif-Tiwari H, et al. ACR Appropriateness Criteria® Chronic Liver Disease. J Am Coll Radiol 2017;14:S391-S405.
65. Carr-Locke DL. Overview of the role of ERCP in the management of diseases of the biliary tract and the pancreas. Gastrointest Endosc 2002;56:S157-60.
66. Lim JH. Cholangiocarcinoma: morphologic classification according to growth pattern and imaging findings. AJR Am J Roentgenol 2003;181:819-27.
67. Lomanto D, Pavone P, Laghi A, et al. Magnetic resonance-cholangiopancreatography in the diagnosis of biliopancreatic diseases. Am J Surg 1997;174:33-8.
68. Baron TH, Petersen BT, Mergener K, et al. Quality indicators for endoscopic retrograde cholangiopancreatography. Am J Gastroenterol 2006;101:892-7.
69. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol 2007;102:1781-8.
70. Loperfido S, Angelini G, Benedetti G, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointest Endosc 1998;48:1-10.
71. Aronson N, Flamm CR, Mark D, et al. Endoscopic retrograde cholangiopancreatography. Evid Rep Technol Assess (Summ) 2002:1-8.
72. Costamagna G, Familiari P, Marchese M, Tringali A. Endoscopic biliopancreatic investigations and therapy. Best Pract Res Clin Gastroenterol 2008;22:865-81.
73. Caddy GR, Tham TC. Gallstone disease: Symptoms, diagnosis and endoscopic management of common bile duct stones. Best Pract Res Clin Gastroenterol 2006;20:1085-101.
74. Gopinathan PM, Pichan G, Sharma VM. Role of dehydration in heat stress-induced variations in mental performance. Arch Environ Health 1988;43:15-7.
75. Lauri A, Horton RC, Davidson BR, Burroughs AK, Dooley JS. Endoscopic extraction of bile duct stones: management related to stone size. Gut 1993;34:1718-21.
76. Chen WX, Xie QG, Zhang WF, et al. Multiple imaging techniques in the diagnosis of ampullary carcinoma. Hepatobiliary Pancreat Dis Int 2008;7:649-53.
77. Krishna NB, LaBundy JL, Saripalli S, Safdar R, Agarwal B. Diagnostic value of EUS-FNA in patients suspected of having pancreatic cancer with a focal lesion on CT scan/MRI but without obstructive jaundice. Pancreas 2009;38:625-30.
78. Krishna NB, Mehra M, Reddy AV, Agarwal B. EUS/EUS-FNA for suspected pancreatic cancer: influence of chronic pancreatitis and clinical presentation with or without obstructive jaundice on performance characteristics. Gastrointest Endosc 2009;70:70-9.
79. Ross WA, Wasan SM, Evans DB, et al. Combined EUS with FNA and ERCP for the evaluation of patients with obstructive jaundice from presumed pancreatic malignancy. Gastrointest Endosc 2008;68:461-6.
80. Sharaiha RZ, Kumta NA, Desai AP, et al. Endoscopic ultrasound-guided biliary drainage versus percutaneous transhepatic biliary drainage: predictors of successful outcome in patients who fail endoscopic retrograde cholangiopancreatography. Surg Endosc 2016;30:5500-05.
81. Kamata K, Kitano M, Omoto S, et al. New endoscopic ultrasonography techniques for pancreaticobiliary diseases. Ultrasonography 2016;35:169-79.
82. Polkowski M, Larghi A, Weynand B, et al. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. Endoscopy 2012;44:190-206.
83. Eloubeidi MA, Chen VK, Eltoum IA, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy of patients with suspected pancreatic cancer: diagnostic accuracy and acute and 30-day complications. Am J Gastroenterol 2003;98:2663-8.
84. Banafea O, Mghanga FP, Zhao J, Zhao R, Zhu L. Endoscopic ultrasonography with fine-needle aspiration for histological diagnosis of solid pancreatic masses: a meta-analysis of diagnostic accuracy studies. BMC Gastroenterol 2016;16:108.
85. Chang KJ, Nguyen P, Erickson RA, Durbin TE, Katz KD. The clinical utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointest Endosc 1997;45:387-93.

86. Maple JT, Ben-Menachem T, Anderson MA, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc 2010;71:1-9.
87. Winger J, Michelfelder A. Diagnostic approach to the patient with jaundice. Prim Care 2011;38:469-82; viii.
88. European Association for the Study of the L. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol 2009;51:237-67.
89. Fargo MV, Grogan SP, Saguil A. Evaluation of Jaundice in Adults. Am Fam Physician 2017;95:164-68.
90. Molvar C, Glaenzer B. Choledocholithiasis: Evaluation, Treatment, and Outcomes. Semin Intervent Radiol 2016;33:268-76.
91. Bao PQ, Johnson JC, Lindsey EH, et al. Endoscopic ultrasound and computed tomography predictors of pancreatic cancer resectability. J Gastrointest Surg 2008;12:10-6; discussion 16.
92. Tamm EP, Balachandran A, Bhosale PR, et al. Imaging of pancreatic adenocarcinoma: update on staging/resectability. Radiol Clin North Am 2012;50:407-28.
93. Vukobrat-Bijedic Z, Husic-Selimovic A, Bijedic N, et al. Sensitivity of EUS and ERCP Endoscopic Procedures in the Detection of Pancreatic Cancer During Preoperative Staging Correlated with CT and CT Angiography Imaging Methods. Acta Inform Med 2014;22:160-3.
94. Ito T, Sugiura T, Okamura Y, et al. The diagnostic advantage of EOB-MR imaging over CT in the detection of liver metastasis in patients with potentially resectable pancreatic cancer. Pancreatology 2017;17:451-56.
95. Karaosmanoglu AD, Onur MR, Ozmen MN, Akata D, Karcaaltincaba M. Magnetic Resonance Imaging of Liver Metastasis. Semin Ultrasound CT MR 2016;37:533-48.
96. Niekel MC, Bipat S, Stoker J. Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment. Radiology 2010;257:674-84.
97. Rosch T, Meining A, Fruhmorgen S, et al. A prospective comparison of the diagnostic accuracy of ERCP, MRCP, CT, and EUS in biliary strictures. Gastrointest Endosc 2002;55:870-6.
98. Lee DH, Lee JM, Kim KW, et al. MR imaging findings of early bile duct cancer. J Magn Reson Imaging 2008;28:1466-75.
99. Ryoo I, Lee JM, Chung YE, et al. Gadobutrol-enhanced, three-dimensional, dynamic MR imaging with MR cholangiography for the preoperative evaluation of bile duct cancer. Invest Radiol 2010;45:217-24.
100. Yu SA, Zhang C, Zhang JM, et al. Preoperative assessment of hilar cholangiocarcinoma: combination of cholangiography and CT angiography. Hepatobiliary Pancreat Dis Int 2010;9:186-91.
101. Di Cesare E, Puglielli E, Michelini O, et al. Malignant obstructive jaundice: comparison of MRCP and ERCP in the evaluation of distal lesions. Radiol Med 2003;105:445-53.
102. Adam V, Bhat M, Martel M, et al. Comparison Costs of ERCP and MRCP in Patients with Suspected Biliary Obstruction Based on a Randomized Trial. Value Health 2015;18:767-73.
103. Meagher S, Yusoff I, Kennedy W, Martel M, Adam V, Barkun A. The roles of magnetic resonance and endoscopic retrograde cholangiopancreatography (MRCP and ERCP) in the diagnosis of patients with suspected sclerosing cholangitis: a cost-effectiveness analysis. Endoscopy 2007;39:222-8.
104. Liu L, Xu HX, Wang WQ, et al. Serum CA125 is a novel predictive marker for pancreatic cancer metastasis and correlates with the metastasis-associated burden. Oncotarget 2016;7:5943-56.
105. Wernecke K, Rummeny E, Bongartz G, et al. Detection of hepatic masses in patients with carcinoma: comparative sensitivities of sonography, CT, and MR imaging. AJR Am J Roentgenol 1991;157:731-9.
106. Bang BW, Jeong S, Lee DH, Kim CH, Cho SG, Jeon YS. Curved planar reformatted images of MDCT for differentiation of biliary stent occlusion in patients with malignant biliary obstruction. AJR Am J Roentgenol 2010;194:1509-14.
107. Choi YH, Lee JM, Lee JY, et al. Biliary malignancy: value of arterial, pancreatic, and hepatic phase imaging with multidetector-row computed tomography. J Comput Assist Tomogr 2008;32:362-8.
108. Furukawa H, Ikuma H, Asakura-Yokoe K, Uesaka K. Preoperative staging of biliary carcinoma using 18F-fluorodeoxyglucose PET: prospective comparison with PET+CT, MDCT and histopathology. Eur Radiol 2008;18:2841-7.
109. Seo H, Lee JM, Kim IH, et al. Evaluation of the gross type and longitudinal extent of extrahepatic cholangiocarcinomas on contrast-enhanced multidetector row computed tomography. J Comput Assist Tomogr 2009;33:376-82.

110. Ni Q, Wang H, Zhang Y, et al. MDCT assessment of resectability in hilar cholangiocarcinoma. Abdom Radiol (NY) 2017;42:851-60.
111. Pietryga JA, Morgan DE. Imaging preoperatively for pancreatic adenocarcinoma. J Gastrointest Oncol 2015;6:343-57.
112. Vargas R, Nino-Murcia M, Trueblood W, Jeffrey RB, Jr. MDCT in Pancreatic adenocarcinoma: prediction of vascular invasion and resectability using a multiphasic technique with curved planar reformations. AJR Am J Roentgenol 2004;182:419-25.
113. Choi JY, Kim MJ, Lee JM, et al. Hilar cholangiocarcinoma: role of preoperative imaging with sonography, MDCT, MRI, and direct cholangiography. AJR Am J Roentgenol 2008;191:1448-57.
114. Qayyum A, Tamm EP, Kamel IR, et al. ACR Appropriateness Criteria(R) Staging of Pancreatic Ductal Adenocarcinoma. J Am Coll Radiol 2017;14:S560-S69.
115. Raijman I. Biliary and pancreatic stents. Gastrointest Endosc Clin N Am 2003;13:561-92, vii-viii.
116. Malak M, Masuda D, Ogura T, et al. Yield of endoscopic ultrasound-guided fine needle aspiration and endoscopic retrograde cholangiopancreatography for solid pancreatic neoplasms. Scand J Gastroenterol 2016;51:360-7.
117. Maranki J, Hernandez AJ, Arslan B, et al. Interventional endoscopic ultrasound-guided cholangiography: long-term experience of an emerging alternative to percutaneous transhepatic cholangiography. Endoscopy 2009;41:532-8.
118. Sai JK, Suyama M, Kubokawa Y, Watanabe S, Maehara T. Early detection of extrahepatic bile-duct carcinomas in the nonicteric stage by using MRCP followed by EUS. Gastrointest Endosc 2009;70:29-36.
119. Gress TM. Molecular diagnosis of pancreatobiliary malignancies in brush cytologies of biliary strictures. Gut 2004;53:1727-9.
120. Saifuku Y, Yamagata M, Koike T, et al. Endoscopic ultrasonography can diagnose distal biliary strictures without a mass on computed tomography. World J Gastroenterol 2010;16:237-44.
121. Burak KW, Angulo P, Lindor KD. Is there a role for liver biopsy in primary sclerosing cholangitis? Am J Gastroenterol 2003;98:1155-8.
122. Olsson R, Hagerstrand I, Broome U, et al. Sampling variability of percutaneous liver biopsy in primary sclerosing cholangitis. J Clin Pathol 1995;48:933-5.
123. Steele IL, Levy C, Lindor KD. Primary sclerosing cholangitis--approach to diagnosis. MedGenMed 2007;9:20.
124. Zhang X, Gao X, Liu BJ, et al. Effective staging of fibrosis by the selected texture features of liver: Which one is better, CT or MR imaging? Comput Med Imaging Graph 2015;46 Pt 2:227-36.
125. Elsayes KM, Oliveira EP, Narra VR, et al. MR and MRCP in the evaluation of primary sclerosing cholangitis: current applications and imaging findings. J Comput Assist Tomogr 2006;30:398-404.
126. Dave M, Elmunzer BJ, Dwamena BA, Higgins PD. Primary sclerosing cholangitis: meta-analysis of diagnostic performance of MR cholangiopancreatography. Radiology 2010;256:387-96.
127. Bali MA, Pezzullo M, Pace E, Morone M. Benign biliary diseases. Eur J Radiol 2017;93:217-28.
128. Girometti R, Furlan A, Esposito G, et al. Relevance of b-values in evaluating liver fibrosis: a study in healthy and cirrhotic subjects using two single-shot spin-echo echo-planar diffusion-weighted sequences. J Magn Reson Imaging 2008;28:411-9.
129. Lewin M, Poujol-Robert A, Boelle PY, et al. Diffusion-weighted magnetic resonance imaging for the assessment of fibrosis in chronic hepatitis C. Hepatology 2007;46:658-65.
130. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf. Accessed November 30, 2018.