Imaging, 22 (2013), 51415473

GASTROINTESTINAL IMAGING

Imaging of the jaundiced adult

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Summary

- There are many techniques for imaging the jaundiced patient; the rationale for investigation depends on the history, examination and biochemistry.
- Transabdominal ultrasound is the initial technique of choice; it will differentiate between obstructive and non-obstructive causes in the majority of cases and can demonstrate the cause of obstruction in some cases.
- Multislice CT and MRI, in particular magnetic resonance cholangiopancreatography, are excellent problem-solving tools that can accurately show the level and determine the cause of obstruction.
- Endoscopic ultrasound (EUS) is increasingly being used to assess patients with suspected biliary tract obstruction, in particular when there is a suspicion of a small obstructing lesion such as ampullary tumours not demonstrable on cross-sectional imaging. This technique has an important role in the assessment of focal pancreatic and biliary lesions with the added benefit of obtaining biopsy for tissue diagnosis.
- Advances in cross-sectional imaging and EUS have placed endoscopic retrograde cholangiopancreatography and percutaneous transhepatic cholangiography in mainly therapeutic roles.

doi: 10.1259/imaging/51415473

Cite this article as: Rudralingam V, Sukumar SA. Imaging of the jaundiced adult. Imaging 2013;22:51415473.

Abstract. *Jaundice is a clinical finding that is a frequent cause of referral for imaging. Based on the clinical history, physical examination and blood biochemistry alone, it is often impossible to accurately distinguish between an obstructive and a non-obstructive cause of jaundice, thus radiological evaluation is essential. The primary aim of radiology is to assess whether the cause is obstructive and to determine the cause of obstruction when present. This paper aims to discuss the range of imaging modalities available and highlights the strengths of each modality. We present a rational imaging strategy to evaluate the jaundiced adult.*

Jaundice manifests as yellow discolouration of the skin, mucous membranes and sclerae. It is due to a rise in serum bilirubin and is usually detected at serum bilirubin levels of approximately 40 μmol l^{-1}.

This symptom is a frequent cause of referral for imaging. Therefore it is essential to have a clear understanding of the underlying metabolic pathway in order to utilise imaging appropriately to make a correct diagnosis.

Causes of jaundice can be classified as pre-hepatic, hepatic and post-hepatic. Bilirubin is derived as a breakdown product of haem molecules. In the pre-hepatic phase there is increased non-water-soluble (unconjugated) bilirubin in the blood bound to plasma albumin. This is taken up by the liver hepatocytes, where there is glucuronide conjugation of the bilirubin to form a water-soluble (conjugated) bilirubin. In the post-hepatic phase, the water-soluble bilirubin is passed into the gut *via* the bile ducts, where some is excreted in the stool and the remainder is metabolised, reabsorbed and passed out in the urine as urobilinogen. The important finding of bilirubin in the urine indicates the presence of conjugated bilirubinaemia.

Blood biochemistry is useful in establishing the presence of abnormal liver function tests and evaluating the bilirubin level. Although it is said to be possible to try and establish whether a patient presenting with jaundice has a pre-hepatic, hepatic or post-hepatic abnormality from the type of bilirubin elevation in the blood, in the majority of patients there is a mixed picture with elevation of both conjugated and unconjugated bilirubin.

By assessing these biochemical parameters, the potential cause of jaundice can fall into one of two categories:

1. Obstructive (usually post-hepatic), where the drainage of bile is impeded.
2. Non-obstructive (pre-hepatic and hepatic), where there is excessive haemolysis or disturbance in hepatic parenchymal function.

The clinical approach to investigating the jaundiced patient is based on two main biochemical factors. If

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bilirubin is absent in the urine, the reasons are due to a non-obstructive cause and radiological imaging has a limited role. If present in the urine, then the cause is likely to be owing to obstruction of the excretion of bile from the normal route and radiological imaging plays a crucial role in the evaluation.

The second factor depends on the liver function tests. In a jaundiced patient with normal liver biochemistry the causes are likely to be pre-hepatic and imaging is not routinely indicated. If the liver function tests are abnormal, radiological imaging is appropriate to evaluate the liver parenchyma and bile ducts.

Based on clinical history, physical examination and blood biochemistry alone, it is often impossible to accurately distinguish between an obstructive and a non-obstructive cause of jaundice, thus radiological evaluation is essential. The primary aims of radiology are to assess whether the cause of jaundice is obstructive and to determine the cause of obstruction when present.

The role of the different imaging modalities will be addressed below. It is best practice to perform the imaging with a degree of urgency, as this will help to accurately triage the patients from the initial point of referral into the appropriate medical or surgical treatment pathway.

Imaging in this situation is based upon two pathways:

- Cross-sectional imaging to depict the anatomical appearance of the biliary system to evaluate the level and image the cause of the obstruction, or the functional assessment of the lack of drainage of bile, which is best appreciated on nuclear scintigraphy or cholangiography, although the latter also depicts the anatomy and sometimes the cause of obstruction.
- Transabdominal ultrasound (TAUS), CT and MR scanning offer a non-invasive, safe, timely and cost-effective pathway of investigating these patients.

While the presence of dilatation of the bile ducts in radiology is suggestive of obstruction, there are three basic caveats or pitfalls to remember:

- There may be obstruction without dilatation seen early in the course of disease. Extrahepatic bile duct dilatation precedes intrahepatic duct dilatation by up to 4 or 5 days and intrahepatic duct dilatation may not be apparent in the early stages [1, 2]. This picture may also occur with intermittent impaction of calculi or reduced pliability of the liver.
- Dilatation without obstruction can be seen in patients with a choledochal cyst (type 1 Todani's classification) or in patients in whom a stone has been passed. A dilated duct may take 30–50 days to revert to normal calibre [3]. In repeated obstruction the duct may not return to a normal calibre.
- Dysmotility syndromes may also cause dilatation without obstruction [4]. It is not uncommon to see a persistently dilated duct in the elderly patient, particularly with a history of previous cholecystectomy (Figures 1 and 2).

Non-biliary mimics of obstruction [4] such as portal vein thrombosis or periportal oedema (Figure 1a,b) could be mistaken for dilated bile ducts (Figure 2a).

Cross-sectional imaging

Ultrasound

TAUS of the abdomen is universally established as the most useful first-line imaging study in the jaundiced adult [5, 6]. It has been accepted as a dynamic, non-invasive and inexpensive method without the use of ionising radiation and is thus considered safe. It provides an excellent evaluation of liver parenchyma and assessment of the presence or absence of bile duct dilatation.

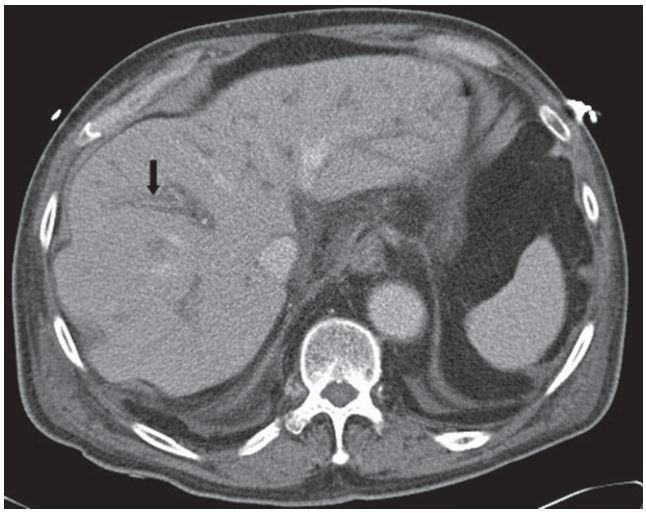
Technical advances in the scanners have greatly improved image quality. The cystic nature of both the gallbladder and the bile ducts, particularly when dilated, provides an inherently high contrast resolution compared with the adjacent tissues that is easy to detect. Tissue harmonic imaging is a further useful feature that improves contrast and leads to improved visualisation of the bile duct lumen and wall [2, 7–9].

Unfortunately there is some limitation of the visualisation of the extrahepatic duct system on TAUS. In 30–50% of patients, bowel gas can obscure the duct or the body habitus and adjacent abdominal structures can render the imaging of the distal common bile duct (CBD) difficult [2, 7–9]. Changing the patient position and choosing a different sonographic window are simple manoeuvres that can help to improve visualisation of the distal duct.

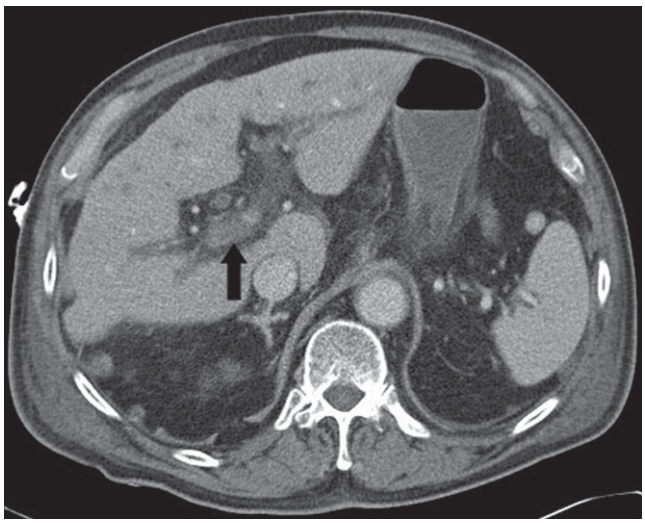
The appearance of dilated intrahepatic ducts is of tubular structures with a branching or stellate pattern adjacent to the vessels in the portal triads (Figure 3a). Colour Doppler is a useful tool to distinguish adjacent vessels from ducts (Figure 3b). Left lobe ducts often appear more prominent and dilate at an earlier stage than the right hepatic ducts [10]. The right and left hepatic ducts, which are the first-order branches of the common hepatic duct, are routinely seen on sonography and it is not uncommon to visualise normal second-order branches [10] with modern scanners. The detection of the more peripheral intrahepatic ducts is said to be a sensitive indicator with >95% accuracy in the diagnosis of bile duct obstruction [7]. False positive diagnoses are rarely seen [10]. The sensitivity of ultrasound in defining the level of obstruction and cause can be wide, ranging from 27% to 95% [7, 10–12] and 23% to 88% [7, 10, 11], respectively, and depends on operator skill as well as the differences in patient population [1].

In many clinical settings, TAUS along with the combination of history, examination and blood biochemistry is sufficient to distinguish between jaundice owing to obstructive or non-obstructive causes. In patients with obstruction, the baseline TAUS will often dictate the need for further imaging and guide the type of intervention required (surgery or endoscopic intervention). In some patients where there is diagnostic doubt, or a tumour has been detected, a CT scan is performed for further assessment and staging.

If there is a strong history for calculi, however, with no evidence of ductal stones on ultrasound or an obstruction is not identified, then further imaging with MR cholangiopancreatography (MRCP) is more appropriate (Figure 4a–c). Endoscopic ultrasound (EUS) has increasingly been used for further evaluation if there



(a)



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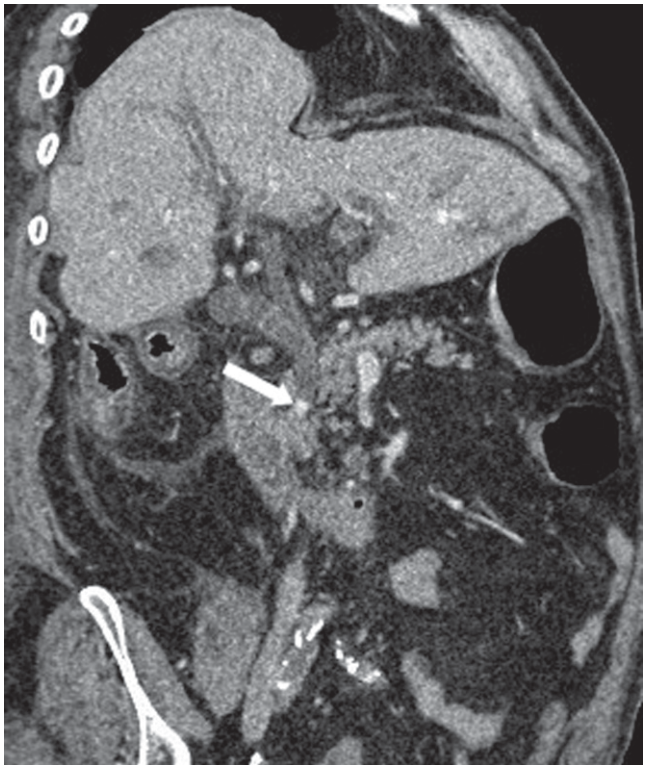


(c)

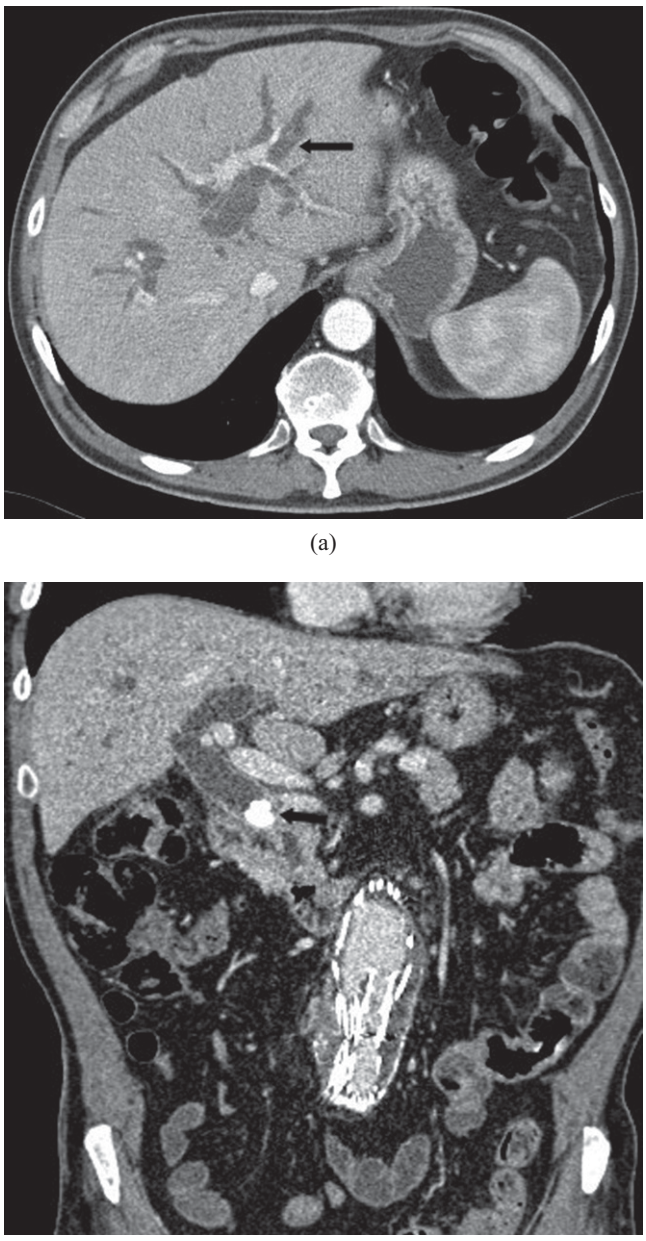
Figure 1. Axial CT images through the abdomen in a 50-year-old acutely unwell man with acute cholangitis. (a) Periportal oedema: note the periportal low density is ill-defined and circumferential (black arrow) which helps in differentiation from dilated intrahepatic ducts (see Figure 6a). (b) Thrombosis of the right branch of portal vein (black arrow). (c) Coronal reconstruction shows an obstructing calcified 5 mm gallstone (white arrow) in the ampulla with upstream dilatation of the common bile duct. The patient underwent emergency endoscopic retrograde cholangiopancreatography sphincterotomy and bile duct stent insertion.

remains a high index of suspicion with normal cross-sectional imaging (see Figure 7b).

In addition to the assessment of the gallbladder and bile duct system, ultrasound has an important role in the evaluation of the liver parenchyma and characterisation of focal liver lesions. In recent years, ultrasound contrast agents have been increasingly used to assess focal liver lesions. The new-generation intravenous microbubble contrast agents and optimised software in modern scanners has transformed the ability of ultrasound to characterise focal liver abnormalities and improve detection rate of metastasis [13]. The contrast agents are easy to use and well tolerated by patients. The limitations of this technique are primarily cost and the time involved in performing the injection and scan. If a liver biopsy is required the ultrasound-guided approach is a safe and reliable method of obtaining tissue.

CT

CT scans are increasingly obtained as the first-line imaging modality in a broad range of symptoms that may be related to the biliary tract with or without biochemical derangement. CT of the abdomen is complementary to ultrasound in evaluating the jaundiced patient but has the drawback of a significant radiation dose to the patient. In addition, rapid infusion of intravenous iodinated contrast is required to provide adequate



(a)

(b)

Figure 2. Axial CT abdomen (a) and coronal reconstruction (b) in a 75-year-old man with a history of abdominal pain and jaundice. (a) Black arrow points to dilated intrahepatic ducts. (b) Coronal CT shows large 1.2 cm obstructing calcified gallstone in the suprapancreatic portion of the common bile duct. Previous endovascular repair of abdominal aortic aneurysm noted.

opacification of the blood vessels and liver parenchyma as the enhancement pattern of the liver parenchyma allows good visualisation of the intrahepatic biliary ducts (Figure 2a). The drawback is that this increases both the cost and the risk of adverse reactions for the patient [14].

For patients with an underlying malignancy, CT scan will provide important information regarding the local resectability of disease and distant metastatic disease in one single study.

The choice of technique and phase of scanning is important in making a correct diagnosis on abdominal CT. The scans can be acquired in different phases of contrast enhancement to best demonstrate different types of pathology depending on the clinical question. The different timing of contrast-enhanced study includes arterial dominant, portal venous phase and delayed phase study.

Although CT scanning is not the imaging technique of choice for patients with suspected bile duct stones, the pre-contrast scan is the most useful phase for demonstrating bile duct stones (Figure 5). This scan can demonstrate other salient findings such as pancreatic calcification and is useful for planning the post-contrast scans. For the evaluation of other causes of obstruction, the post-intravenous scans are essential.

CT scanning has been found to have a sensitivity of 96–100% [7, 15, 16], which is higher than ultrasound, in the detection of obstruction. Several studies have shown CT to be as effective as ultrasound in determining the calibre of the intrahepatic and extrahepatic ducts and better than ultrasound in the delineation of the CBD along its length [7]. With the latest multidetector CT scanners normal peripheral bile ducts can be seen on post-contrast images [17].

The level of obstruction can be identified on CT scans in almost all of the cases [7, 16] but with the cause identified in only approximately 70% [7, 15] of the literature. In our experience, the combination of increasing speed of acquisition and spatial resolution with modern multidetector CT (MDCT) scans will continue to improve diagnostic accuracy.

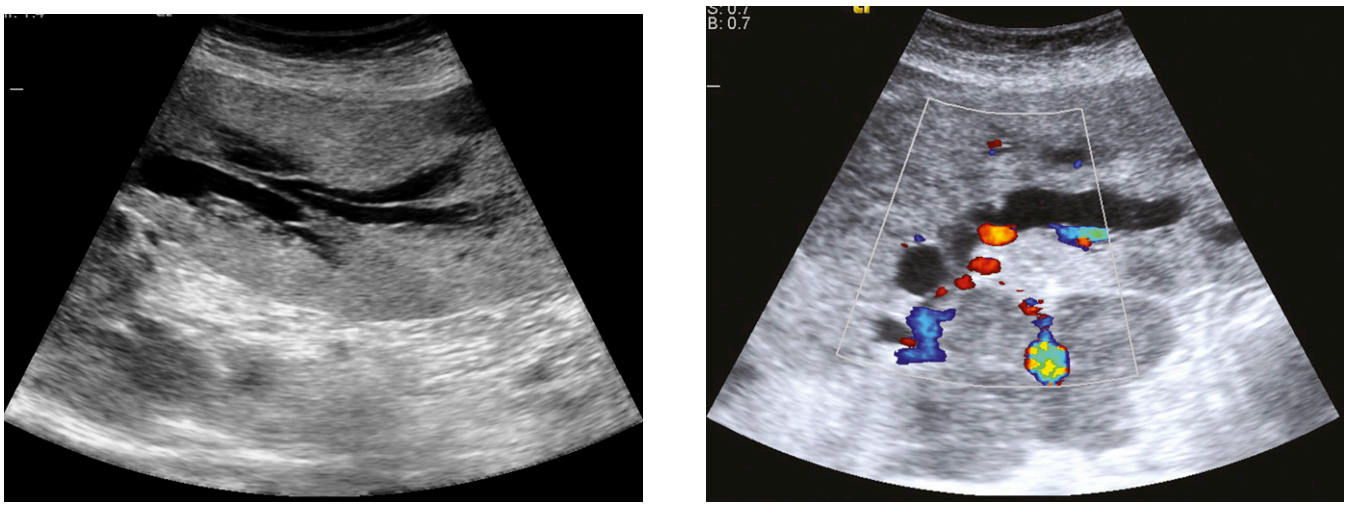
The ability to acquire thin slices in a single breath-hold with MDCT allows for overlapping reconstructions, removing significant image degradation. This will allow for better evaluation of subtle lesions and also provides high-resolution multiplanar reconstructions that can demonstrate the anatomy and visualise abnormalities in three-dimensional (3D) images and oblique planes [1].

MR scanning

MRI provides a comprehensive evaluation of the liver parenchyma, biliary system and vasculature. With superior inherent soft-tissue characterisation compared with CT, MRI has traditionally been reserved to problem solve equivocal findings on CT. However, MRI and MRCP are now routinely being used as the primary imaging modalities of the hepatobiliary system. They have the added advantage that these techniques can be performed in one sitting.

MRI has proven to be an excellent non-invasive and accurate imaging technique without the use of ionising radiation and in many cases without the need for intravenous contrast administration. It is relatively operator independent with negligible morbidity. The most commonly used intravenous contrast is a gadolinium chelate, which has good patient safety and tolerability [18, 19]. Patients with a past history of allergic reaction to iodinated contrast are better imaged with MR scanning.

Recently, a strong association has been made in the literature between the gadolinium-based contrast agent and the development of nephrogenic systemic fibrosis (NSF), a multisystemic fibrosing disorder in patients with acute renal failure and end-stage renal failure on dialysis [20]. If contrast is absolutely necessary, in addition



(a) (b)

Figure 3. (a,b) Ultrasound scan images through the liver in a female patient with jaundice showing dilated intrahepatic ducts. Colour Doppler can help distinguish dilated duct from adjacent vessel (b). This was secondary to a carcinoma in the head of the pancreas.

to closely monitoring renal function, only the smallest possible dose should be used.

The main limitations of MR scanning are predominantly owing to the difficulty in scanning certain groups of patients, for example those with claustrophobia or patients with pacemakers, but also the limited ability to offer therapeutic intervention.

MRCP has been shown to have an overall 96–100% accuracy for the level of obstruction and 90% accuracy for the cause of obstruction [1, 21] (Figure 7). Comparisons have mostly been made with direct cholangiography, usually endoscopic retrograde cholangiopancreatography (ERCP) in cases of biliary obstruction, particularly in stone disease but also for the evaluation of malignant obstruction [22, 23]. A combination of T_1 and T_2 weighted gradient echo axial heavily T_2 weighted thin section scans in coronal and coronal oblique planes together with thick slab cholangiographic T_2 weighted images to delineate anatomy are obtained for MRCP [23]. The thin section scans will provide information of the biliary anatomy and demonstrate any luminal abnormalities such as ductal stones (Figures 4c and 6b).

MRCP consistently demonstrates biliary ducts above a stricture that can be difficult to assess with ERCP and is therefore a useful adjunct and guide to management with ERCP [22, 24, 25] (Figure 8). This is particularly so in patients with biliary enteric reconstructions with gastrojejunostomy or obstructive lesions of the oesophagus and the stomach. MRCP can accurately determine the level of bile duct obstruction and can help to determine the intervention options, for example percutaneous transhepatic cholangiography (PTC) with antegrade stenting or a retrograde approach with ERCP (Figure 6b,c) [26].

Some drawbacks are that, in comparison with direct cholangiography, MRCP does not display functional information and has a lower resolution and therefore may miss small ampullary lesions or mild strictures. Signal averaging in the reconstruction can average out the different signal intensity changes from small calculi that may be obscured [1].

A good combination of sequences that will adequately evaluate most parenchymal abnormalities in the liver include gradient echo T_1 weighted, fast spin echo (FSE)/turbo spin echo (TSE) T_2 weighted and dynamic post-contrast T_1 weighted sequences.

Contrast-enhanced MR of the liver using hepatocyte-specific agents such as gadoxetic acid disodium (Primovist) is excreted in the bile ducts and will be useful in providing dynamic enhanced images of the liver parenchyma and subsequently a delayed functional MRCP images at the time of excretion in bile [7, 19]. Potential uses include the evaluation of focal liver lesions in cirrhotic patients (Figure 11a–d), choledochal cyst and assessment of bile leaks in post-cholecystectomy patients.

Endoscopic ultrasound

EUS combines two established diagnostic techniques and makes it possible to directly evaluate the layers of the wall of the gastrointestinal tract as well as the adjacent surrounding structures [27]. EUS is useful in suspected cases of bile duct obstruction, particularly when no apparent cause is demonstrated on cross-sectional imaging. By placing the endoscope in the stomach and duodenum, this allows for direct visualisation of the pancreas, bile and pancreatic duct. The close proximity of the probe allows for the detection of subtle abnormalities including tiny gravel-like stones or small ampullary lesions. EUS can precisely localise, characterise and stage focal lesions, in particular focal pancreatic lesions. This technique also offers EUS-guided fine-needle aspiration (FNA) and core biopsy in biliary strictures and focal lesions with very little risk. If required, patients can proceed to have an ERCP in the same session after EUS.

With ampullary lesions, demonstrating the extent of disease with EUS is vital to determine management either with endocopic resection in disease confined to the mucosae or with Whipple's procedure (Figure 7a).

EUS has a trend towards higher sensitivity than MRCP in the detection of bile duct stones; this is mainly in the

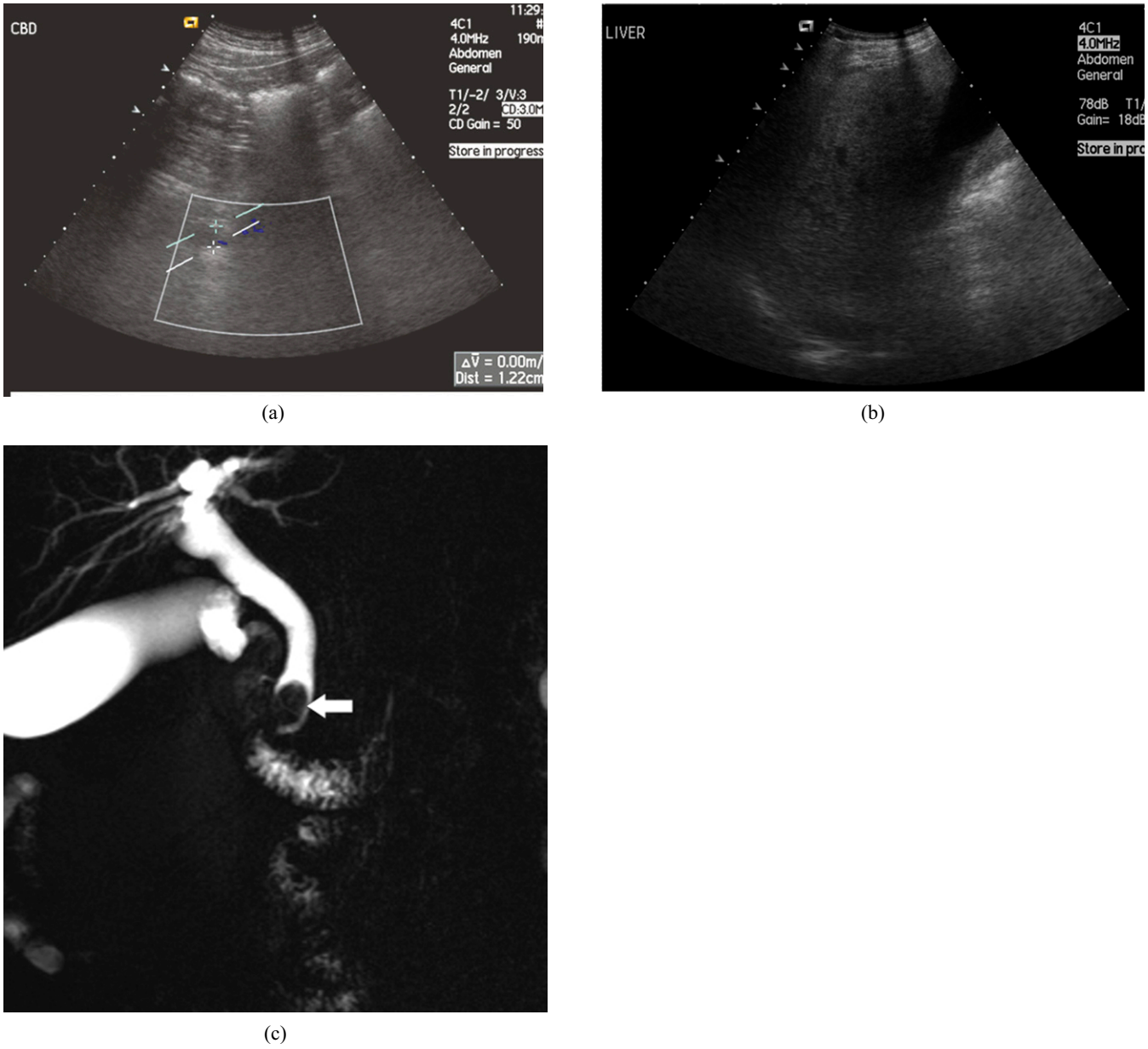


Figure 4. A 50-year-old overweight man presented with abdominal pain and abnormal liver function tests. Ultrasound of abdomen-limited assessment was carried out. Fatty infiltration of the liver (a) and a dilated common bile duct (CBD) were detected. Poor view of distal CBD (b). (c) Coronal maximum intensity projection image shows obstructing stone in the lower CBD (white arrow). Patient underwent endoscopic retrograde cholangiopancreatography and sphincterotomy.

detection of small stones with minimal bile duct dilatation (Figure 7b) [28]. There is evidence that EUS is at least as accurate as ERCP in the diagnosis of common bile duct stones with an overall sensitivity of 88% [29]. EUS also has the ability to detect gallstones, sludge and crystals in the gallbladder in symptomatic patients with normal transabdominal ultrasound.

EUS can effectively evaluate the bile duct and offers staging possibilities. In contrast, ERCP can delineate the biliary anatomy but only infer the extent of bile duct involvement. In addition, with ERCP the tumour itself is not visible and there is significant associated morbidity. Assessment of the mid and lower portion of the common bile duct is straightforward but is slightly limited with hilar strictures owing to the limited field of view [28]. There is a role for intraductal ultrasonography (IDUS) in the evaluation of patients with obstruction but no obvious lesion on conventional EUS. This modality can also be used in the evaluation of cholangiocarcinoma. However, availability and expertise is limited.

Functional imaging

Scintigraphy

This still has some value in the detection of bile duct obstruction, particularly early in the disease, but this is not a sensitive modality for assessing the level or cause of obstruction. It is limited by the fact that in patients with

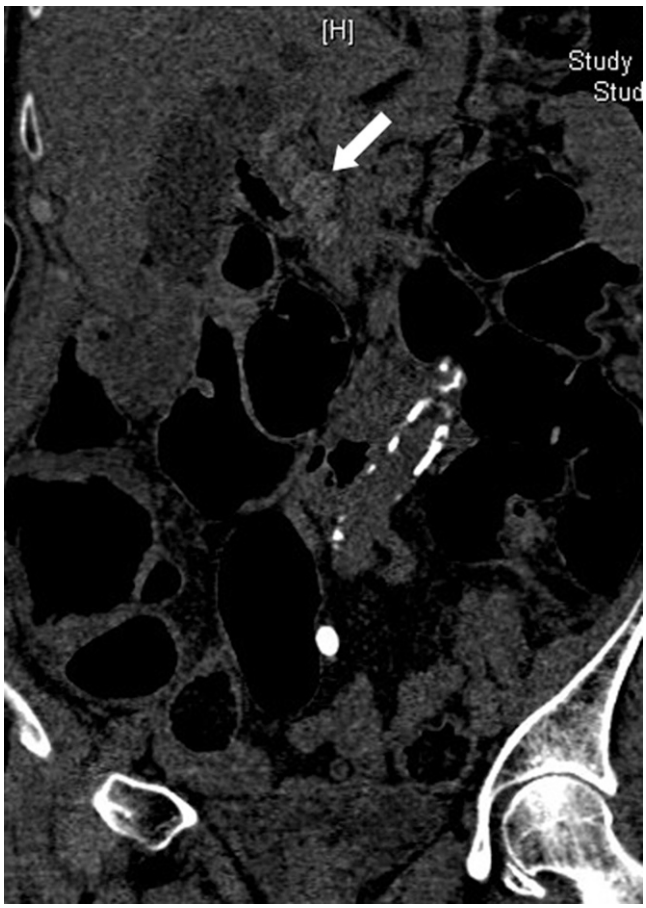


Figure 5. A 60-year-old woman underwent a CT pneumocolon and incidentally detected multiple calcified gallstones in the common bile duct shown on this coronal CT scan image (white arrow). Note the gallstones are best seen on the unenhanced scan.

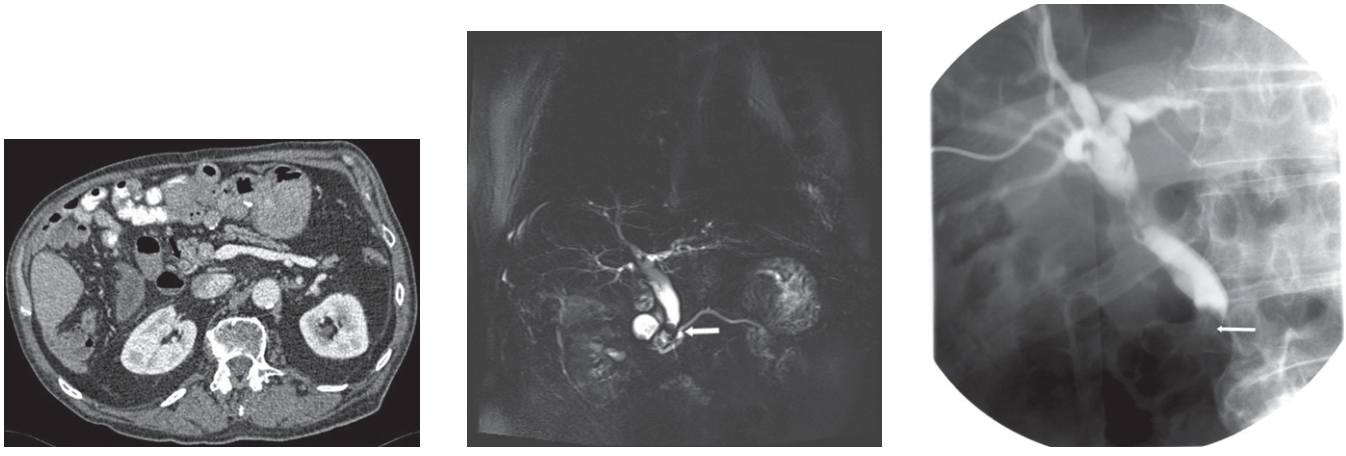
high bilirubin levels or marked hepatocellular disease, adequate tracer is not eliminated in the biliary system. The tracer used, $^{99}Tc^{m}$ hydroxyiminodiacetic acid, is excreted in the bile and can be most useful in the imaging of a dilated duct without obstruction and shows delayed elimination into the bowel. In these cases, which are predominantly used pre-operatively in mapping choledochal cysts, scintigraphy now appears largely redundant and is being replaced by MRCP [30] or CT, which has a markedly higher resolution.

CT cholangiography

In this technique a slow intravenous infusion of meglumine iotroxate is given, which is excreted in the bile and shows up the contrast-filled biliary system well on CT. It still has a limited role in the patient with an obstructed system. It has a higher sensitivity for intraduct calculi (92%) [31] than plain CT; however, contrast safety is a concern and the technique is limited by the fact that the excretion of contrast into the bile is not effective at bilirubin levels above 50 μmol l^{-1}. The role of this examination is now being superseded by MR cholangiography in most cases, excluding the very small <2 mm duct stones [31]. CT cholangiography may also be useful in pre-operative mapping for some types of choledochal cysts to show communication with the biliary tree.

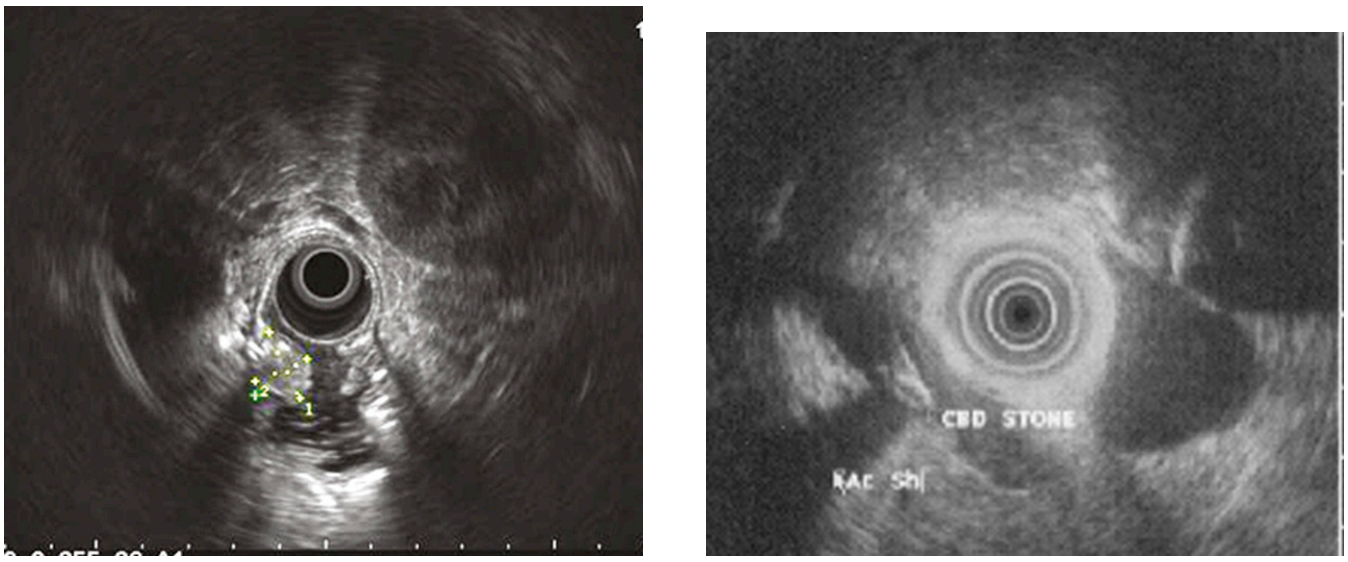
Direct cholangiography

Direct cholangiography remains the gold standard in depicting subtle changes within the bile ducts, evaluating and treating suspected bile duct injuries (Figure 9) and the detection of small common duct calculi. If opacification of the biliary system is obtained, cholangiography is said to have almost 100% sensitivity in the detection of obstruction [1]. ERCP is more often performed than PTC. Both are invasive investigations which are significantly operator dependent, with a relatively high morbidity of 1–7% for ERCP [21] and 3–5% for PTC [7, 15]. ERCP has



(a) (b) (c)

Figure 6. A 75-year-old man with previous history of gastric surgery for peptic ulcer disease presenting with deranged liver function test. Black arrow on axial post-contrast CT scan (a) shows filling defect in the lower common bile duct compatible with a possible obstructing gallstone. Note subtle heterogeneous density at this site on post-contrast scan. Subsequent thin slice coronal magnetic resonance cholangiopancreatography image (b) confirms signal void consistent with a stone in the lower common bile duct (CBD) (white arrow) with upstream dilatation of the CBD and intrahepatic ducts. Because of previous gastrojejunostomy, the patient underwent a percutaneous transhepatic cholangiography to remove the bile duct stone. The white arrow points to filling defect consistent with the stone in the lower CBD (c).



(a) (b)

Figure 7. Two different patients with jaundice and no definitive diagnosis on cross-sectional imaging with CT. Image (a) shows a polypoidal lesion within the ampulla consistent with a biopsy-proven adenoma (courtesy of Dr J Ramesh, consultant gastroenterologist, University Hospital of South Manchester NHS Foundation Trust). Image (b) demonstrates a small distal common bile duct stone with characteristic posterior acoustic enhancement (courtesy of Dr VY Kaushik, consultant gasteroenterologist, Royal Blackburn Hospital).

an unsuccessful cannulation rate of 3–10% [21, 32, 33]. ERCP has a sensitivity of 90–96% and specificity of 98% in detecting CBD stones [34, 35], although it has been recently suggested that MRCP demonstrates intrahepatic stones better than ERCP [36]. Use in mapping of the duct system pre-operatively for choledochal cysts can be suboptimal if the duct size is large with contrast being diluted, and studies suggest that MRCP imaging is as good as cholangiography in these cases [30]. PTC gives excellent imaging with a success rate of up to 99% [1, 37] although this is dependent on the presence of biliary dilatation. Direct cholangiography does not demonstrate abnormalities extrinsic to the duct lumen.

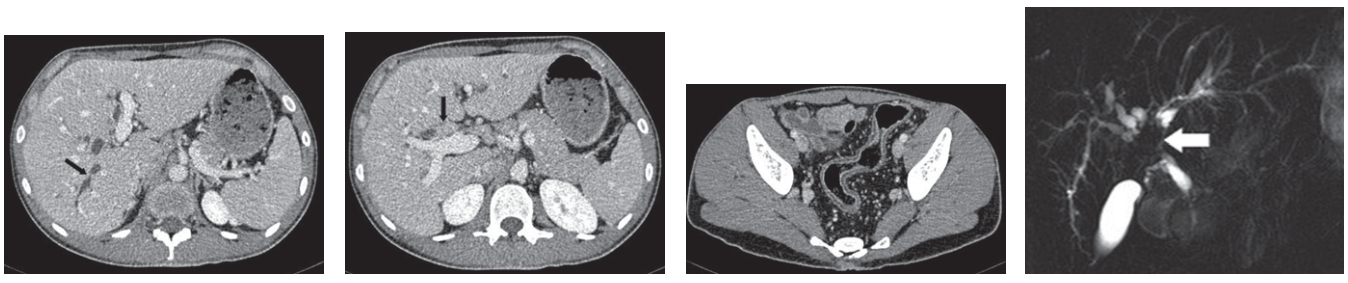
The most significant advantage of both ERCP and PTC is primarily in a therapeutic role. These techniques permit stent insertion across strictures and the ability to extract stones, which will alleviate symptoms including jaundice. In addition, tissue for diagnosis can be obtained from biopsy or brushings with ERCP. ERCP is usually the favoured technique with PTC being reserved for management of patients in whom ERCP has failed or may not be possible (*e.g.* previous bilioenteric anastomosis).

Pathological processes causing jaundice

Once the presence of obstruction has been detected, accurate evaluation of the level of obstruction is important in defining the cause and in planning treatment. Various disease processes are associated with different levels of obstruction and in a clinical setting this classification is more relevant for arriving at the correct diagnosis [1].

The level of obstruction can be divided into four broad categories:

1. intrahepatic
2. porta hepatis
3. suprapancreatic
4. pancreatic.



(a) (b) (c) (d)

Figure 8. Axial CT images in a 35-year-old patient with longstanding ulcerative colitis with new onset of jaundice. Note intrahepatic bile duct strictures with pre-stenotic dilatation on axial CT (a). Dominant bile duct stricture (black arrow) with significant irregular concentric mass-like thickening (b).This was confirmed to represent a cholangiocarcinoma on recent surgery. The large bowel shows features of longtstanding colitis (c). Magnetic resonance cholangiopancreatography image shows the "beaded/pruned tree" appearance of the intra- and extrahepatic ducts owing to multiple, short segment strictures (white arrow) (d). Note the dominant stricture noted in the liver hilum corresponding to the CT abnormality.

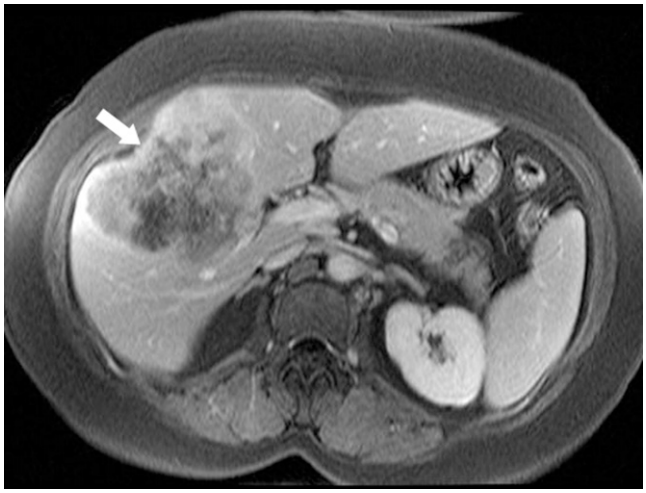


Figure 9. Axial T_1 post-contrast scan through the liver in an 80-year-old woman. This is a biopsy-proven mass-forming cholangiocarcinoma. Note heterogeneous enhancement and focal retraction of the liver capsule (white arrow).

Obstruction at the intrahepatic level may be due to space-occupying diseases of the liver or primary sclerosing cholangitis (PSC). At the porta hepatis level, PSC and malignancies such as cholangiocarcinoma, metastases and invasive gallbladder carcinoma are the most relevant causes. At the suprapancreatic bile duct level, iatrogenic causes, mostly post-cholecystectomy, pancreatitis and malignancies such as cholangiocarcinoma, metastatic nodes and pancreatic carcinoma, are important. Impacted stones in the cystic duct can cause obstruction at this level, termed Mirrizzi's syndrome.

At the pancreatic and ampullary level, calculi are the most common cause of obstruction [10, 38] although neoplasms and pancreatitis can also cause obstruction. Malignancies at this level include pancreatic carcinoma, which is the most likely finding, and other less common entities such as an ampullary carcinoma are important [1, 39].

General principles of differentiating benign from malignant strictures apply to all the imaging modalities. Benign bile duct strictures can usually be differentiated on cross-sectional imaging techniques as these strictures are more likely to have a smooth tapering appearance than malignant strictures, which generally have an irregular outline with an abrupt change in calibre often with an associated mass [14].

Intrahepatic pathologies

Primary sclerosing cholangitis

PSC may show no features of note on cross-sectional imaging in the early stages of disease and the diagnosis is often based on clinical, biochemical and hepatic histological findings. As the disease progresses, there is progressive bile duct wall thickening and development of multifocal strictures and dilatations affecting both small and large bile ducts (Figure 8a–d). These changes can be detected on ultrasound, 3D reconstructed images on MDCT scans [40] and MRI. Although early subtle changes are not seen well on MRCP, this non-invasive alternative is considered the best initial approach to diagnose PSC, with

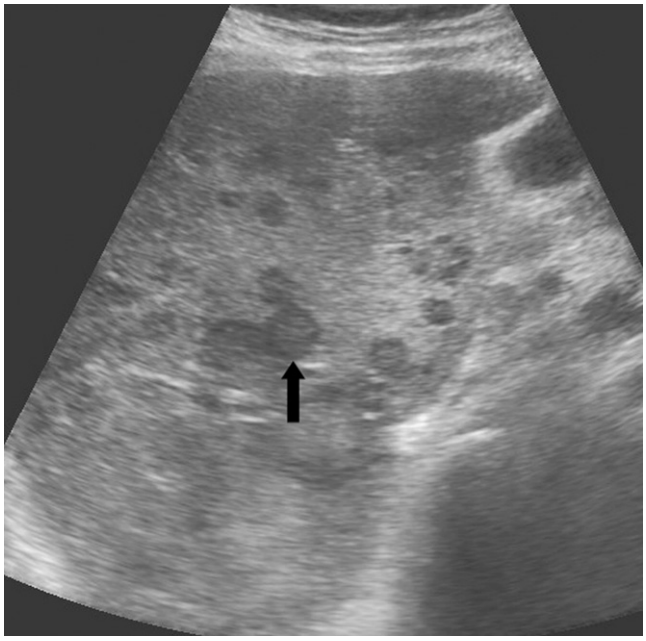


Figure 10. Ultrasound showing multiple liver metastasis with a target-like appearance (black arrow) in a patient with a known primary colonic cancer.

the precaution that in the presence of cirrhosis and duct distortion this can lead to false positive and false negative diagnoses [24] (Figure 10). The term "beaded or pruned tree" appearance commonly used in MRCP refers to the findings of multifocal dilated and strictured appearance of the bile ducts (Figure 8d). On CT and MRI, there can be hyperaemia on post-contrast scans in the involved segmental bile duct wall and liver parenchyma and also segmental atrophy. There is often enlarged periportal and porta caval lymph nodes which are not necessarily a sign of malignancy. Eventually cirrhotic changes and features of portal hypertension develop and can be identified on ultrasound and CT [10, 41]. The complication of cholangiocarcinoma is raised by the appearance of a new dominant stricture (particularly if there is proximal bile duct dilatation) or a liver mass. One of the problems in making the diagnosis of cholangiocarcinoma complicating PSC is that with both contrast-enhanced CT and contrast-enhanced MR, a focally thickened, enhancing bile duct wall can be detected. In such cases it is impossible to distinguish between benign changes and a small cholangiocarcinoma on imaging grounds alone (Figure 8b,d). EUS along with ERCP and brushing the bile duct wall for cytological analysis may be helpful.

Acquired immunodeficiency syndrome (AIDS)-related cholangiopathy is an important condition that should not be overlooked in the immunocompromised patient. Patients can present with a cholestatic pattern of abnormal liver function tests. Often the only finding is non-specific bile duct wall thickening and minor biliary dilatation. Recognising this entity is important to avoid unnecessary intervention.

Neoplastic disease

Jaundice is usually a late feature in hepatocellular carcinoma (HCC). This is usually related to compression of the bile duct by tumour or direct extension into the bile

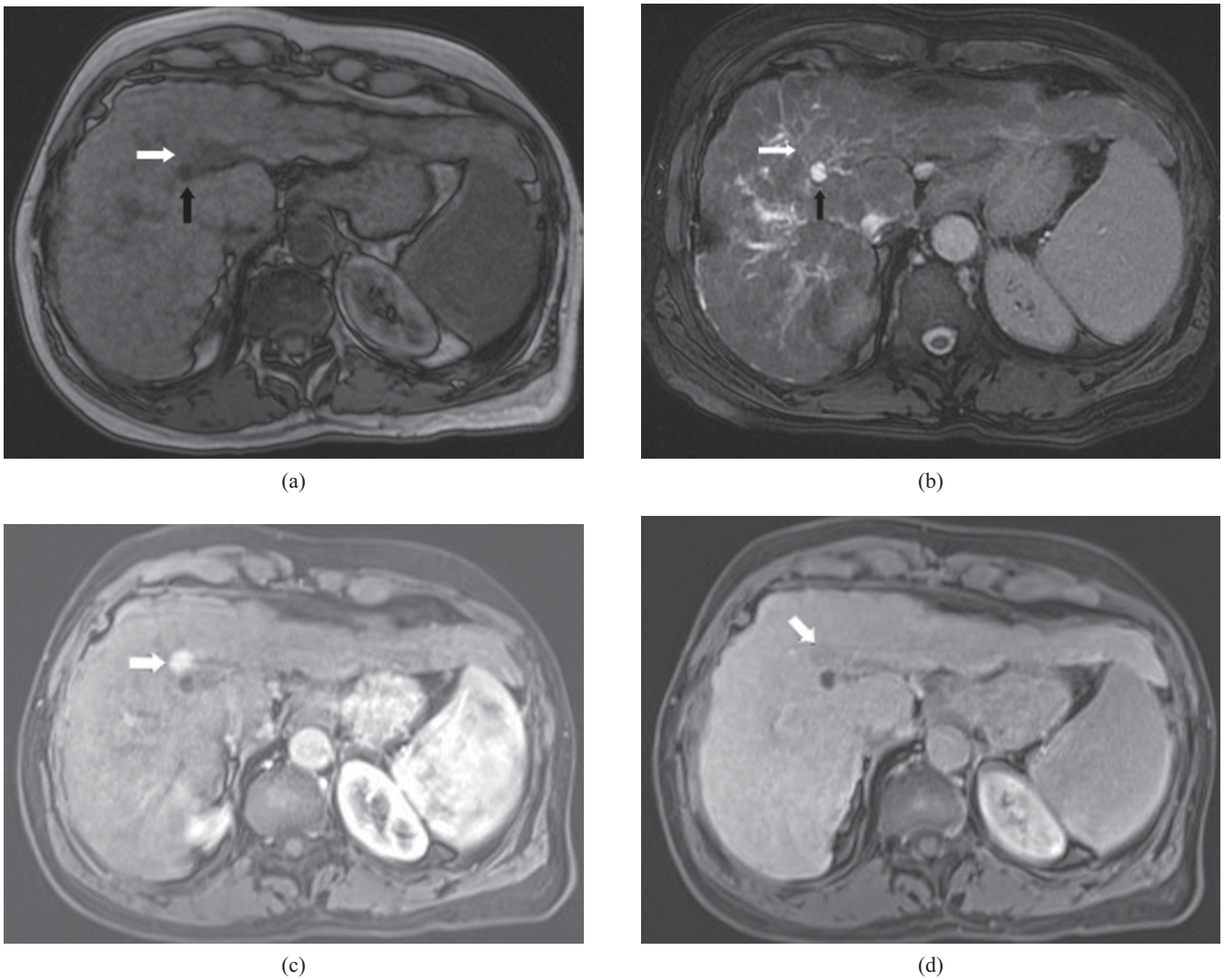


Figure 11. A 60-year-old man with hepatic cirrhosis secondary to viral hepatitis. MR images show established cirrhotic liver. Black arrows point to a simple cyst with simple fluid signal (axial T_1 weighted image (a) hypointense and (b) hyperintense on T_2 weighted image). White arrow points to hepatoma. This lesion is (a) mildly hypointense on T_1 and (b) mildly hyperintense on T_2 weighted images. Following dynamic post-contrast images with intravenous Primavist, the lesion shows arterial enhancement (c) and washes out on the delayed phase scan (d). The patient underwent radiofrequency ablation.

ducts [37]. In the majority of the cases excluding the fibrolamellar variant, the presence of underlying chronic liver disease is a major contributory factor. The features of HCC are very variable and non-specific on TAUS, with either a solitary lesion or multifocal lesions. The mass is commonly hypoechoic when small but more complex with mixed low and hyperechoic regions when larger [37].

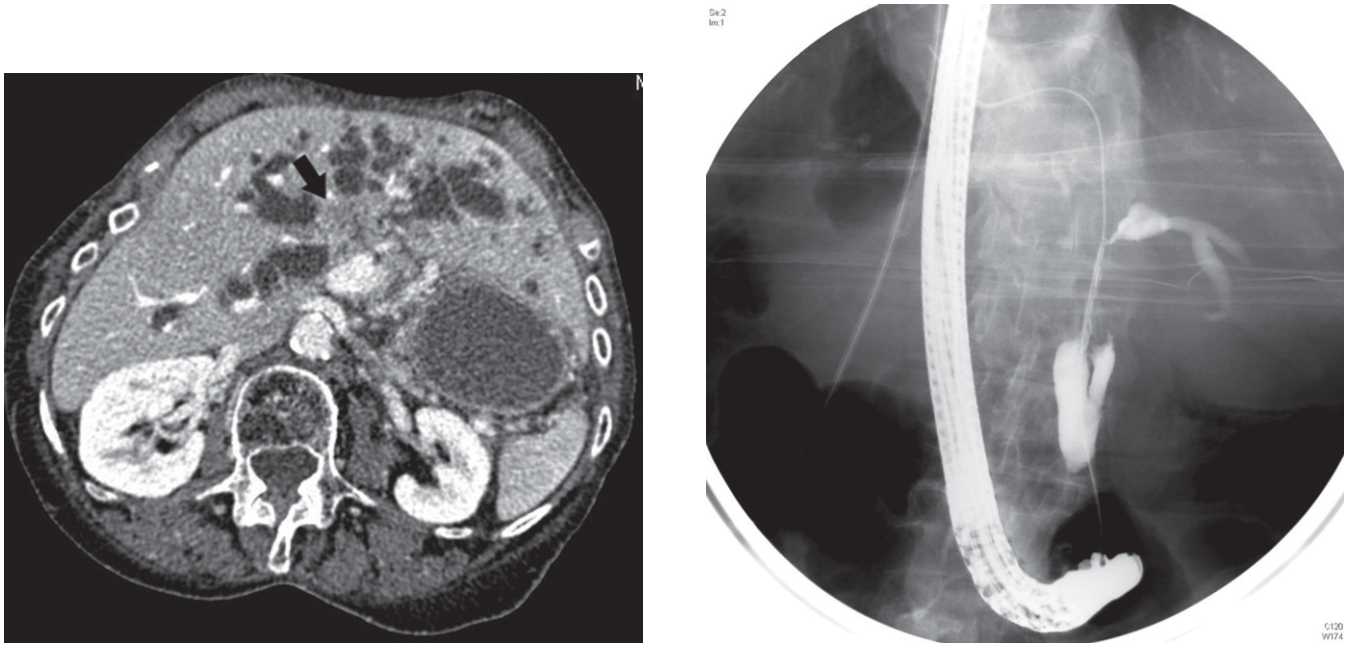
CT is more useful in the diagnosis and, in particular, the staging of HCC and aids in treatment mapping. HCC shows variable density. On the plain scan, there may be low-density regions representing internal fat or hyperdense components reflecting internal haemorrhage. The enhancement pattern is equally variable. There is a propensity towards venous invasion and the tumour thrombus can also be seen to enhance in a similar manner to the underlying lesion.

HCC on MRI also has a variety of signal patterns depending on size and histological type but as with CT there is often increased enhancement seen on the arterial phase and appearing more hypointense in the portal venous examination.

Cholangiocarcinoma is the most common tumour of the bile ducts but can be difficult to detect at any level on ultrasound. The morphological types are classified as mass forming (commonly intrahepatic and poorly differentiated); periductal infiltrating (the usually hilar lesions that are well differentiated); and intraductal (the least common, usually papillary type) [4].

Intrahepatic mass-forming cholangiocarcinoma are less common than hilar lesions [10, 39, 42]. The appearance of intrahepatic cholangiocarcinoma on CT can be very non-specific with a variable enhancement pattern, often more frequently seen on portal venous phase scanning than on arterial phase scanning [39]. The enhancement commences predominantly peripherally with filling in to the centre of the lesion and often retention of contrast on delayed scans [39]. Atrophy of liver parenchyma with retraction of the overlying liver capsule at presentation sometimes helps differentiate this lesion from other causes on CT [39] (Figure 9).

MR has been suggested as a better evaluation tool than CT for cholangiocarcinoma [24]; however, like CT, it does



(a) (b)

Figure 12. Axial CT (a) in a 82-year-old woman with painless jaundice. CT shows Klatskin-type cholangiocarcinoma at the confluence of the right and left hepatic duct (black arrow). The patient underwent palliative endoscopic retrograde cholangiopancreatography (ERCP) (b). Note ERCP is unable to show extraluminal extent of disease but provides palliative treatment.

not appear to show specific features for intrahepatic lesions, which are usually low signal on T_1 and slightly higher signal than liver on T_2 weighted images. As on CT, enhancement on delayed images and atrophy of adjacent liver parenchyma can help identify this lesion [39] (Figure 13).

Metastatic disease involving a large volume of the parenchyma or causing areas of obstruction to the biliary system occasionally presents with jaundice and this is assessed well on ultrasound with a sensitivity of approximately 80% in the detection of metastases [13]. Metastases have variable appearances on ultrasound but the most frequent finding is of variable sized rounded hypoechoic lesions with a peripheral ring of increased echogenicity described as a "bull's eye or target" lesion (Figure 10) [35, 43].

Real-time imaging with contrast ultrasound is useful to show the malignant behaviour of liver lesions. Recognising a chaotic pattern of arterial enhancement and washout in the portal or delayed phase assessment, which refers to the loss of enhancement compared with the background liver, is a typical phenomenon of malignant lesions including HCC, cholangiocarcinoma and metastasis [44].

On MR, using liver-specific contrast agents, such as hepatocyte selective agents, which are not taken up by abnormal metastatic lesions, can aid in the diagnosis of metastases. HCC can show variable enhancement with this contrast agent [13] for instance, well-differentiated HCC may show ill-defined retention of contrast on the delayed scans. Reticuloendothelial specific agents which are not usually taken up by either metastases or HCC can be used but the time of examination and lack of availability makes the routine use of this impractical [13, 18] and is probably best reserved for selective cases where the diagnosis is highly probable but has not been established.

Porta hepatis and suprapancreatic duct abnormalities

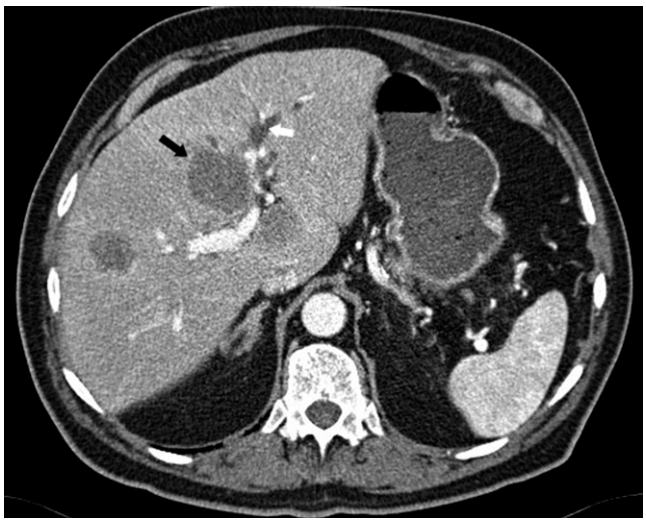
Neoplastic lesions

Cholangiocarcinoma is most common at the hilar level, termed a Klatskin tumour [10, 39, 42]. Classically, the Klatskin tumour manifests as segmental dilatation and non-union of the right and left main ducts at the porta hepatis (Figure 12a,b). On TAUS occasionally a hyperechoic soft-tissue mass is identified, as with the intrahepatic tumour [39]. Often the only sign of this tumour on TAUS is duct dilatation proximal to the tumour (*i.e.* intrahepatic for hilar and both intrahepatic and extrahepatic in distal cholangiocarcinoma). The malignant enhancement pattern of these mass-forming lesions can be assessed with contrast ultrasound [13].

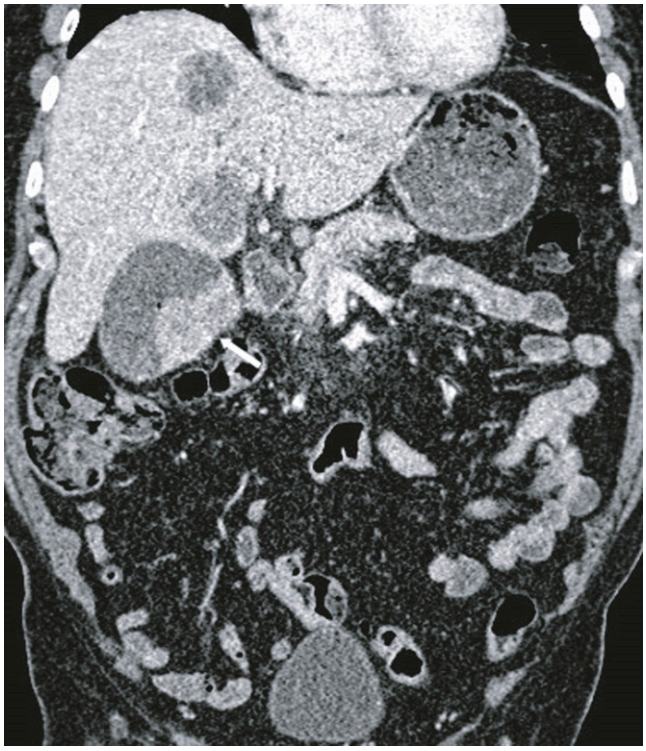
On CT scanning, cholangiocarcinoma at this level may show a small mass, as with the intrahepatic cholangiocarcinoma, or enhancing or thickened bile duct walls in periductal tumours. Often only a stricture is seen. Using the MDCT scan protocols with thin sections, intraductal soft-tissue components or solid enhancing ducts may be more readily detected (Figure 14) in the intraductal type. Small distal CBD carcinomas can be difficult to evaluate on any imaging modality. In these circumstances, EUS is useful to further assess these subtle abnormalities.

Contrast-enhanced MRI may better demonstrate the extent of the tumour, particularly on the delayed post-contrast images. MRI provides excellent depiction of the ductal and vascular anatomy which influences both surgical management and non-surgical methods of providing biliary drainage.

Rarely carcinoma of the gallbladder can cause obstructive jaundice predominantly owing to local invasion or metastases (Figure 13a,b). Ultrasound is the first-line



(a)



(b)

Figure 13. Axial and coronal scans through the upper abdomen in a patient with painless jaundice. (a,b) Dilated intrahepatic ducts (white arrow) secondary to metastasis (black arrow) from a primary gallbladder carcinoma.

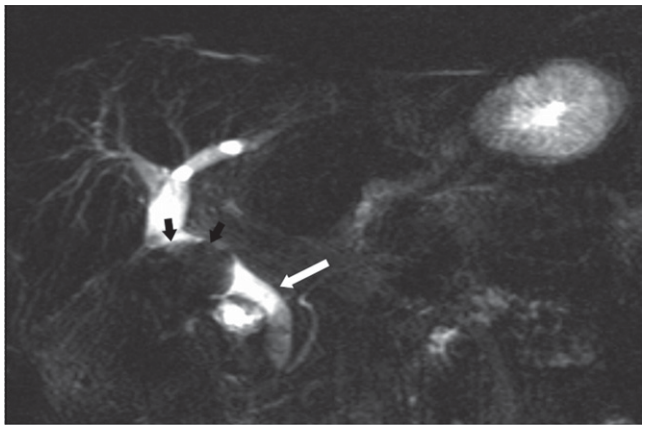
imaging modality of choice for the assessment of the gallbladder wall.

Biliary obstruction from metastatic nodes is mostly related to intra-abdominal malignancies (Figure 16). Although they can be seen well on ultrasound, CT is more useful for staging. On occasion significant biliary obstruction can be caused by very small and difficult to visualise nodes.

Stone disease

Mirrizzi syndrome is an uncommon presentation of a stone impacted in the cystic duct or neck of gallbladder causing inflammation and extrinsic compression of the common hepatic duct leading to obstructive jaundice [45]. This may be subdivided into types 1 and 2. In type 1 there is obstructive jaundice at the common hepatic duct level secondary to extrinsic compression from the inflamed gallbladder (Figure 14a). In type 2, the resulting inflammation leads to a cholecysto-choledocho fistula (Figure 14b). The presence of the stone as well as the level of obstruction can be seen with TAUS. MRCP is the preferred modality that can non-invasively assess the location of the gallstone, level of duct obstruction and presence or absence of fistula or surrounding

(a)



(b)

Figure 14. Coronal magnetic resonance cholangiopancreatography images in two patients with abdominal pain and jaundice. (a) Distended gallbladder with an impacted gallstone in Hartmann's pouch (long arrow) indenting the common hepatic duct. The common hepatic duct is attenuated (short arrow) with proximal intrahepatic duct dilatation consistent with a type 1 Mirrizi's syndrome. (b) A large stone (black arrow) in the gallbladder fistulating into the common bile duct (white arrow) forming a cholecysto-choledocho fistula consistent with a type 2 Mirizzi's syndrome.

inflammatory changes. This technique provides a clear roadmap prior to ERCP and surgical intervention. If not recognised pre-operatively, the common bile duct can potentially be mistaken for the cystic duct and transected.

Bile duct injury

Jaundice is rarely caused by benign, intrinsic bile duct lesions but the most common of these are iatrogenic owing predominantly to bile duct injury during gallbladder surgery.

Pancreatic level

Stone disease

The most common cause of distal duct obstruction is calculi. Biliary calculi predominantly arise in the gallbladder although some calculi can arise in the intrahepatic or extrahepatic ducts. Ultrasound is one of the most effective methods for visualising stones in the gallbladder with a sensitivity of 95–99% [2, 7, 46]. Gallbladder stones are less well seen on other imaging modalities, although these patients present with pain rather than jaundice. The presence of gallbladder stones is not indicative of distal stone obstruction without the clear demonstration of intraduct calculi. There are still a significant number of false negative studies owing predominantly to patient body habitus and bowel gas obscuring the distal CBD (Figure 4a,b). The introduction of tissue harmonic imaging has been shown by some authors to improve bile duct insonation [8], with improvement in the visualisation of ductal stones or intraduct masses, although the sensitivity (75–80%) [2, 9, 13] for detection of stones does not necessarily appear improved.

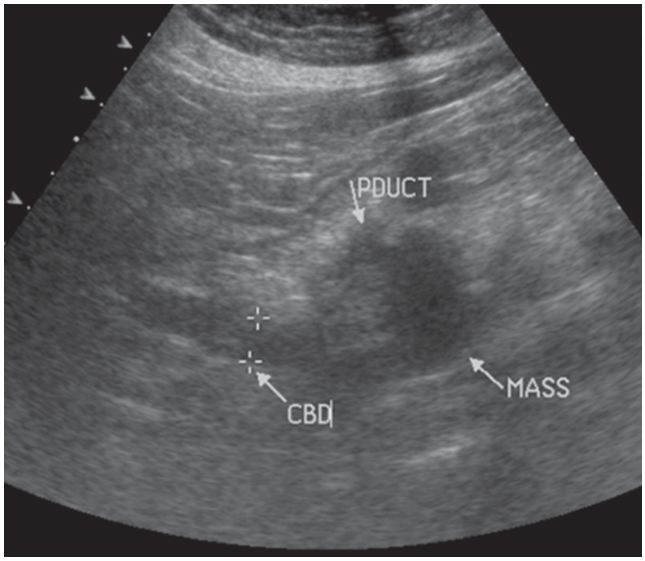
CT has a lower sensitivity in the detection of stones in the gallbladder and CBD [2, 47]. Although calcified gallstones are seen well, the majority of stones are composed of cholesterol with a low density and are not easily visible. CT with neither intravenous nor oral contrast is the most useful method for showing duct stones (Figure 5). Only 20–30% of stones show increased density on CT [39], occasionally with a high attenuation rim. The remainder are difficult to detect, although a large impacted stone may be more easily visualised.

On MRCP, calculi cause low signal filling defects within the high signal fluid within the ducts (Figures 4c and 6b). Good visualisation of stones in all parts of the bile ducts and gallbladder is obtained [33, 48] with a sensitivity of 87–100% and specificity of up to 100% [21, 24, 31, 48]. False negative examinations are more often related to factors such as patient movement and size of calculi with poor detection of calculi <2 mm in diameter [49]. False positive results are related to signal voids from bile flow, adjacent vessel compression and air in the biliary tree [46].

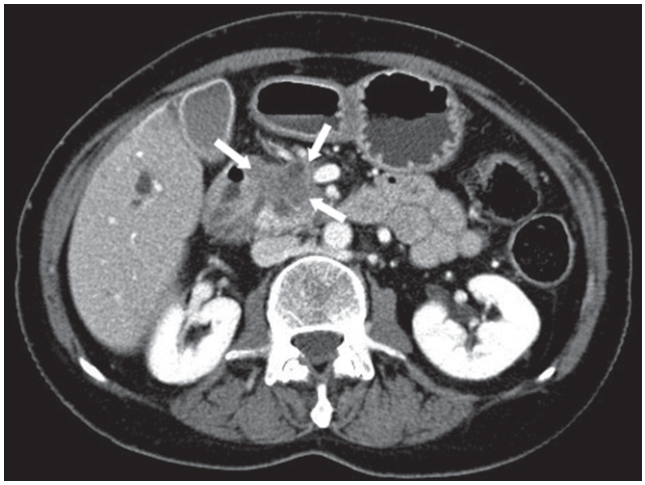
If calculi are seen in intrahepatic dilated ducts, on ultrasound or MRI, then a diagnosis of oriental cholangiohepatitis should be considered. This is a recurrent pyogenic cholangitis owing to strictures and duct stones that are often intrahepatic. The ducts appear dilated and these patients can present with liver abscesses which can help raise the suspicion of the diagnosis.

Cholangitis as a cause of jaundice frequently shows no specific ultrasound findings other than dilated ducts, but usually there is an element of obstruction often related to calculi or blocked biliary endoprostheses. It is most likely to be suggested by the history and clinical evaluation. Occasionally bile duct mural thickening can be identified [13]. Cholangitis rarely causes any detectable changes on CT [14], although a degree of dilatation of the duct with an obstructing gallstone may point to the diagnosis (Figure 1c). Periportal oedema is a non-specific sign that can be seen in unwell patients with acute cholangitis (Figure 1a).

Choledochal cysts occasionally present in adults, with jaundice as the most common presentation in these patients [9]. This condition is actually cystic dilatation of the bile ducts, usually the CBD. Different types have been



(a)



(b)

Figure 15. Ultrasound (a) and axial CT image (b) in a patient with painless jaundice. (a) The typical focal hypoechoic solid mass in the head of the pancreas with abrupt cut off the common bile duct (CBD) and pancreatic duct (PDUCT) referred to as the double-duct sign. (b) Axial CT (white arrows) showing the margins of this locally advanced pancreatic cancer invading the duodenum.

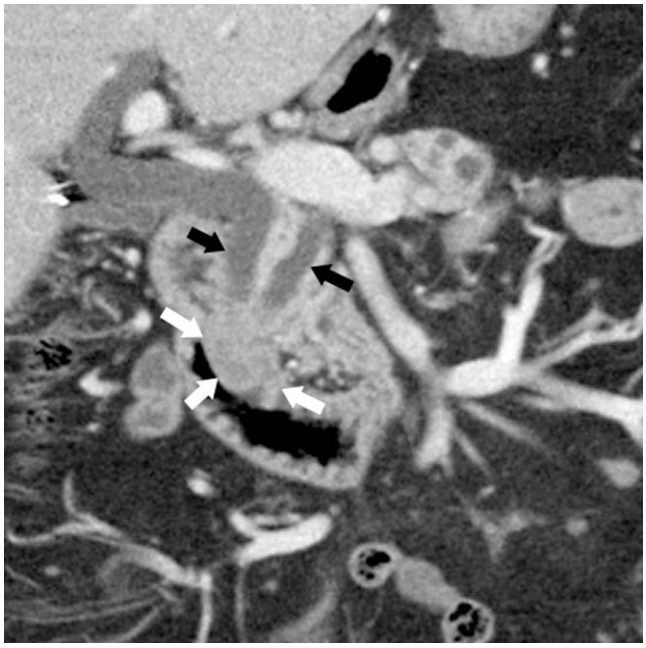


Figure 16. Coronal CT image through the upper abdomen in a 45-year-old male patient with painless jaundice showing a "mushroom"-shaped lesion consistent with an ampullary tumour (white arrows). Note double-duct sign (black arrows) point to abrupt cut off and dilatation of the common bile duct and pancreatic duct.

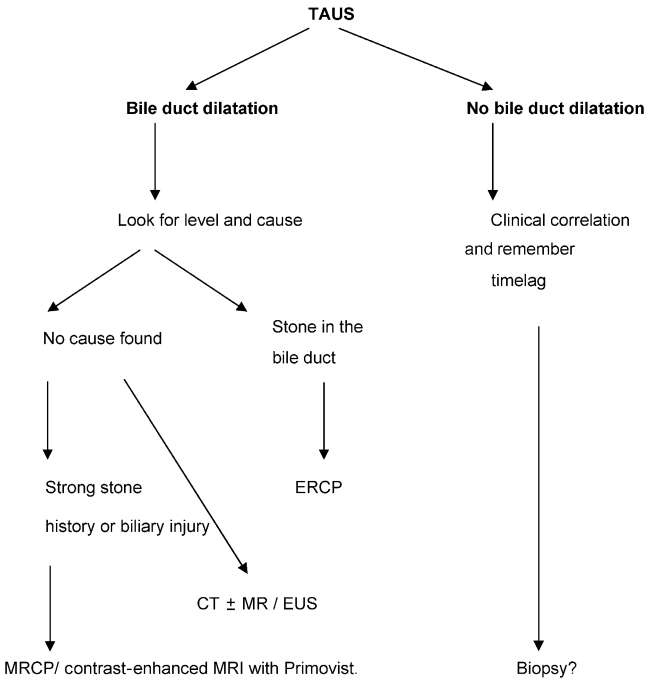


Figure 17. Flow chart for the imaging pathway in the jaundiced patient. TAUS, transabdominal ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; MRCP, magnetic resonance cholangiopancreatography.

described depending on which part of the biliary tree is involved and usually the dilatation is non-obstructive [9, 10]. Ultrasound is useful in the first instance; however, other imaging is often required, particularly in planning treatment. There has been a reported increased incidence of carcinoma, predominantly cholangiocarcinoma, associated with this.

Autoimmune pancreatitis

This entity is a form of chronic pancreatitis that can clinically mimic pancreatic cancer. The diagnosis is often first raised on imaging findings. Prompt recognition is important as this disease is reversible with oral steroid therapy. Elevated serum immunoglobulin subtype 4 (IgG 4) is reported to be specifically high in this group of patients and is associated with disease activity [49].

The characteristic imaging findings include either diffuse or focal enlargement of the pancreas with significant attenuation of the pancreatic duct. The absence of atrophy and visible pancreatic duct are strong distinguishing features from a pancreatic ductal adenocarcinoma [49]. The affected portion can show variable degrees of enhancement. There is often smooth narrowing and elongated appearance of the intrapancreatic portion of the bile duct that leads to obstructive jaundice. Other features include a capsule-like low attenuation rim that can show delayed enhancement. EUS has a role in the evaluation of the pancreas and the performance of FNA.

Carcinoma

Pancreatic carcinoma is the most common malignant cause of distal obstructive jaundice. On ultrasound, pancreatic ductal adenocarcinoma has a characteristic hypoehoic mass-like appearance (Figure 15a). MDCT is excellent in staging the disease and influencing the management (Figure 15b), MR being reserved for selective cases in problem solving. With a good CT technique using water as a negative contrast, ampullary carcinomas can be well demonstrated (Figure 16).

Non-obstructive jaundice

Intrahepatic cholestatic jaundice can occur both with and without structural liver damage.

Acute hepatitis is the most common cause of hepatic jaundice worldwide. Often in these patients with structural damage, no specific change is seen but acute inflammation may manifest as a relative decrease in echogenicity of the parenchyma [13].

Increasingly chronic hepatitis related to alcohol, autoimmune conditions, infections and drugs often leading to cirrhosis presents with episodes of jaundice. In the early stages there is an increase in the echogenicity of the liver parenchyma and coarsening of the texture, which is related to steatosis progressing to a markedly echogenic liver with loss of deep transmission of echoes and lobulation and irregularity of the liver surface in keeping with macro- and micronodular cirrhosis and fibrosis [13]. Ultrasound demonstrates ascites well and is extremely useful in assessing portal vein flow. Cirrhosis can also be seen in chronic biliary diseases such as primary biliary cirrhosis or PSC and also in cystic fibrosis patients as well as some congenital deposition diseases such as haemochromatosis or Wilsons disease.

Pregnancy, hormone treatment and parenteral nutrition can cause jaundice without structural damage.

Some of these cholestatic conditions resolve clinically; however, some require histological confirmation. Imaging, usually ultrasound, is used for guiding biopsy of diffuse liver abnormality or focal lesions.

Conclusion

The rationale for imaging in a jaundiced patient depends to some degree on the biochemical evaluation. Jaundice with bilirubin in the urine or raised liver enzymes require further investigation with radiological imaging. The aim of this is first to establish if obstruction is present, for which ultrasound is an excellent first-line tool. Ultrasound can demonstrate the level and characterise the cause of obstruction. CT or MR are indicated if ultrasound is inconclusive and for further characterisation and staging of lesions. EUS is increasingly being used in patients with suspected bile duct obstruction, in particular when there is a small obstructing lesion such as an ampullary lesion or tiny gallstones not clearly depicted on cross-sectional imaging. Tests do duplicate information and it is important to choose an appropriate pathway for imaging in order for a diagnosis to be made (Figure 17). For neoplastic obstruction, a combination of CT and MR can satisfactorily stage the lesions and plan therapeutic approach with less invasive cholangiographic-guided intervention and/or curative surgery. If choledocholithiasis is the most likely diagnosis, MRCP is superior as a non-invasive investigation. In cases where no bile duct stones are seen on MRCP, EUS can be used to detect small stones, even in the absence of significant bile duct dilatation. The appropriate selection of ERCP or PTC should generally be reserved for therapeutic purposes only when a clear diagnosis has been made with other imaging modalities prior to any radiological or surgical intervention.

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