Imaging of the jaundiced patient

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Jaundice is a common condition which has a wide range of causes. Imaging plays a vital role in establishing the underlying aetiology and planning management. Image-guided interventional techniques are used for therapeutic procedures and for diagnostic purposes.

Jaundice is the clinical manifestation of elevated levels of bilirubin within the tissues and becomes visible within the sclera and skin at blood concentrations above 40 µmol/litre. The development of jaundice in adult patients may be caused by a range of pathological conditions. These include both benign and malignant processes but all will require a positive diagnosis to be made of the underlying aetiology. Imaging plays a pivotal role in the investigation of such patients and prompt recognition of obstructive jaundice is particularly important to prevent complications such as cholangitis and septicaemia ensuing.

A number of imaging modalities are used to further assess the cause of the jaundice and its prognosis, including ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) and nuclear medicine. Radiologists and gastroenterologists may use fluoroscopic techniques such as endoscopic retrograde cholangiopancreatography (ERCP) to investigate and treat certain patients. Imaging may also be used to guide percutaneous or transjugular biopsies if histological diagnosis is required. A sound knowledge of the role and limitations of each modality is required to investigate the patient appropriately.

HAEM METABOLISM

Pre-hepatic phase

Bilirubin is formed from the degradation of haem molecules within the spleen and liver. The majority of bilirubin is formed from effete red blood cells with the remainder deriving from ineffective erythropoiesis in bone marrow. The bilirubin is bound to albumin in the plasma and, as it is not water soluble, there is no excretion into the urine; however, it is soluble in fat and it freely crosses both the placenta and the blood–brain barrier.

Intrahepatic phase

Unconjugated bilirubin circulates in the plasma from where there is uptake into hepatocytes. In the liver there is enzymatic conjugation with sugars to form a diglucuronide. This is water soluble and readily excreted from the hepatocytes across the canalicular membrane into the bile.

Post-hepatic phase

The water-soluble conjugated bilirubin drains from the canaliculi into the intrahepatic bile ducts where it may be stored in the gall bladder before passing down the cystic duct into the common bile duct. The common bile duct passes through the head of the pancreas and joins the pancreatic duct at the ampulla of Vater to drain into the second part of the duodenum. Obstruction at any level of the biliary tree may lead to jaundice.

Within the bowel the bilirubin undergoes deconjugation and reduction by gut bacteria to form the brown pigment stercobilinogen which gives faeces their normal colour. The colourless breakdown product urobilinogen is also formed which undergoes enterohepatic recirculation. It is filtered by the kidneys and is detectable in the urine of normal subjects.

In hepatobiliary disease there is reflux of water-soluble conjugated bilirubin into the blood which is filtered at the glomerular membrane in the kidney, giving rise to dark urine (choluria). Similarly, if there is reduced excretion of bilirubin into the intestine then the stools become pale because of the reduced formation of stercobilinogen, and urobilinogen will not be detected in the urine.

The term cholestasis is used to describe the pathological state of reduced bile formation or flow, and it encompasses elements of both intrahepatic and extrahepatic pathology. There are distinctive histological characteristics present with bile seen within the hepatocytes and plugging of the interlobular ducts.

These processes help to explain the clinical and biochemical features of jaundice which are essential to understanding its investigation.

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Pre-hepatic causes

In pre-hepatic jaundice there is an excess of unconjugated bilirubin within the blood. Haemolytic anaemia is the most common underlying cause and is associated with a raised reticulocyte count and characteristic blood-film appearances. In particular, the congenital haemoglobinopathies sickle cell disease and thalassaemia major are associated with a number of important complications. Although imaging does not generally have a role in primary diagnosis there are a number of features of these conditions which may be apparent on imaging studies. For instance, bone marrow hyperplasia may be seen in the skull giving rise to the vertical striations known as 'hair on end' appearance. Extramedullary haematopoiesis may give rise to paravertebral masses (*Figure 1*).

The spleen may be enlarged in children and then undergo autosplenectomy in adulthood because of chronic multiple infarcts. Pigment gallstones are common, even in children, and may lead to obstructive jaundice.

Lastly, sickle cell disease may be associated with complications caused by thrombosis and infarction such as avascular necrosis of the femoral head, dactylitis in the tubular bones of the hand and stroke. Osteomyelitis may occur as a result of the Salmonella bacterium and be difficult to differentiate from certain primary bone neoplasms, e.g. Ewing's sarcoma.

Intra-hepatic causes

Worldwide, the most common cause of hepatocellular disease causing jaundice is viral hepatitis, while in the developed world alcoholic hepatitis is increasingly prevalent. Often there are no specific imaging findings, but on US the liver parenchyma may appear of decreased reflectivity, giving rise to the 'starry sky' appearance of the relatively bright portal triads. Oedema of the gall bladder fossa may also be a feature. Cirrhosis may develop in response to continued exposure to toxic agents such as alcohol, chronic viral infection, or metabolic disorders including haemochromatosis and Wilson's disease. Non-alcoholic steatohepatitis is also increasingly being recognized as an important cause of liver fibrosis and cirrhosis. This is characterized by diffuse fatty change in the liver which makes the parenchyma appear bright on US and of low attenuation on CT. Cirrhosis may also result from the chronic biliary obstruction seen in cystic fibrosis, primary biliary cirrhosis and other autoimmune conditions. Prolonged use of methotrexate, isoniazid and other drugs may also be complicated by cirrhotic change.

The imaging findings reflect the histological changes in the liver of parenchymal necrosis with regenerative nodule formation. Micronodular cirrhosis (less than 3 mm) is seen in alcoholic liver disease, biliary obstruction and haemochromatosis, while macronodular cirrhosis is associated with chronic viral hepatitis and Wilson's disease and may produce nodules several centimetres in diameter. The presence of large regenerative nodules may hamper attempts to reveal hepatocellular carcinoma complicating liver cirrhosis. Following intravenous contrast, regenerative nodules demonstrate a similar enhancement pattern to the surrounding parenchyma on CT and MRI, while hepatocellular carcinoma shows arterial enhancement with rapid washout of contrast. Both dynamic, contrast-enhanced CT and MRI make use of similar differential enhancement characteristics to identify focal tumours. Recently, contrast-enhanced US (*Figure 2*), uti-

Figure 1. A thalassaemic patient with bony hyperplasia and multiple paravertebral masses (arrowheads) secondary to intra- and extramedullary haematopoiesis.

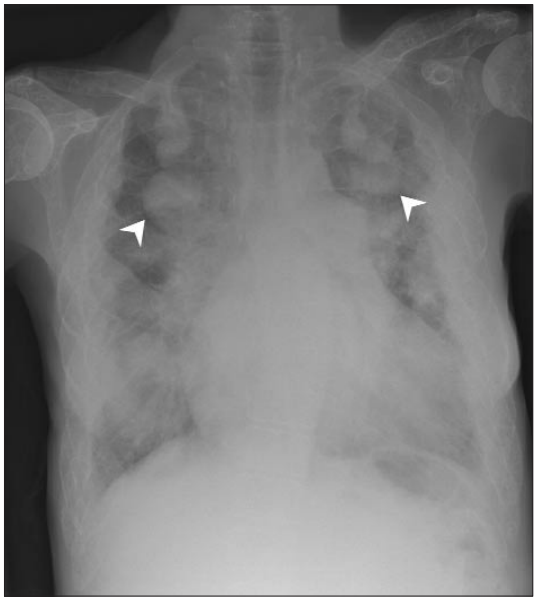
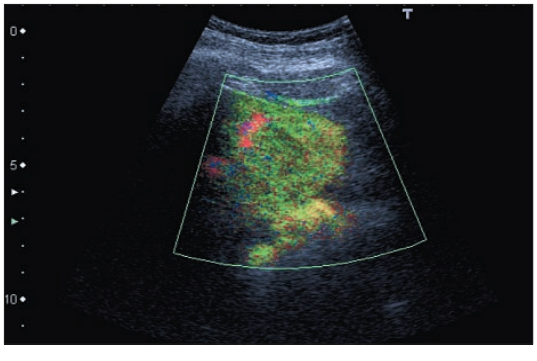


Figure 2. A contrast-enhanced ultrasound showing a hypervascular hepatocellular carcinoma.



lizing intravenous microbubbles, has shown promise in differentiating benign from malignant liver lesions (Quaia et al, 2004).

The abnormal morphology of the cirrhotic liver is demonstrated on cross-sectional imaging which typically shows shrinkage of the right and quadrate lobes with hypertrophy of the left lateral segments and caudate lobe (*Figure 3*). Massive enlargement of the caudate is a feature of cirrhosis as a result of chronic Budd–Chiari syndrome (Mathieu et al, 1987) (*Figure 4*). On US the liver contour may be nodular and the parenchymal echotexture appears heterogeneous. Doppler studies may reveal the vascular changes seen in portal hypertension of reversed portal vein flow, hepatic artery dilatation and dampening of the hepatic vein waveforms (Gorg et al, 2002). High velocity arteriovenous shunts may be demonstrated by shortened hepatic vein transit times of US contrast agents (Albrecht et al, 1999), as well as by early filling of hepatic veins on dynamic CT imaging. The presence of splenomegaly, varices and ascites may be readily apparent (*Figure 5*).

MRI has a specific role in quantifying hepatic iron deposition in haemochromatosis using gradient echo sequences (Alustiza et al, 2004). The autoimmune condition primary sclerosing cholangitis is a progressive inflammatory process that involves the intra- and extrahepatic bile ducts. The typical beaded appearances of alternating segments of ductal dilatation and stenoses may be shown both on ERCP (*Figure 6*) as well as non-invasively with magnetic resonance cholangiopancreatography (MRCP). Lastly, intrahepatic metastases may sometimes be the underlying cause of jaundice if there is extensive parenchymal disease or extrinsic biliary compression. These are readily detectable with CT or US and have variable enhancement characteristics depending on the primary tumour (*Figure 7*).

Figure 3. A contrast-enhanced computed tomogram of a cirrhotic liver demonstrating an irregular capsular contour with atrophy of the left lobe.

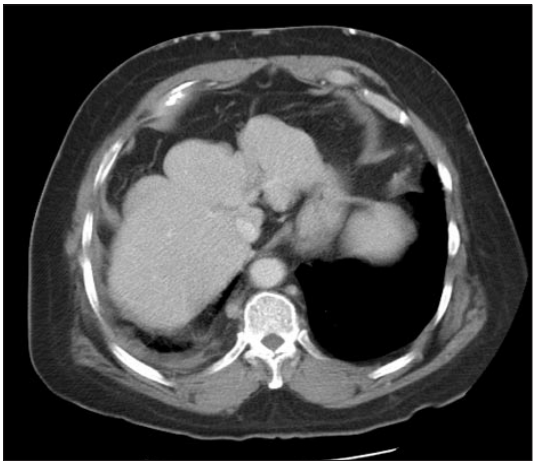


Figure 4. A contrast-enhanced computed tomogram of Budd–Chiari syndrome shows the characteristic variegated enhancement pattern of the liver with caudate hypertrophy (arrowhead).

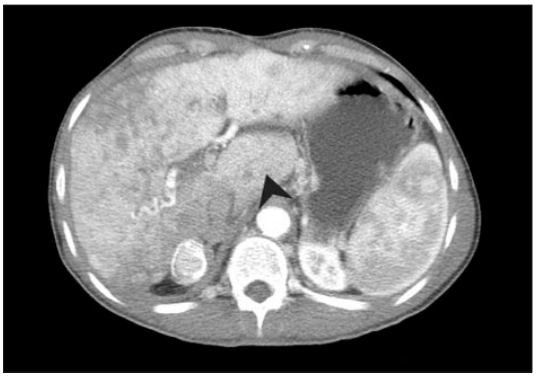


Figure 5. Splenorenal varices in portal hypertension (arrowhead) are shown on this contrast-enhanced computed tomogram.

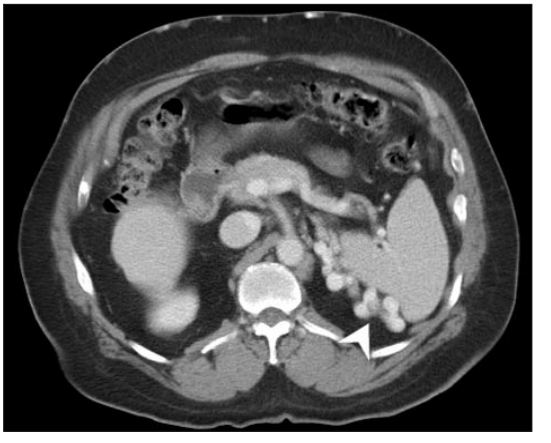
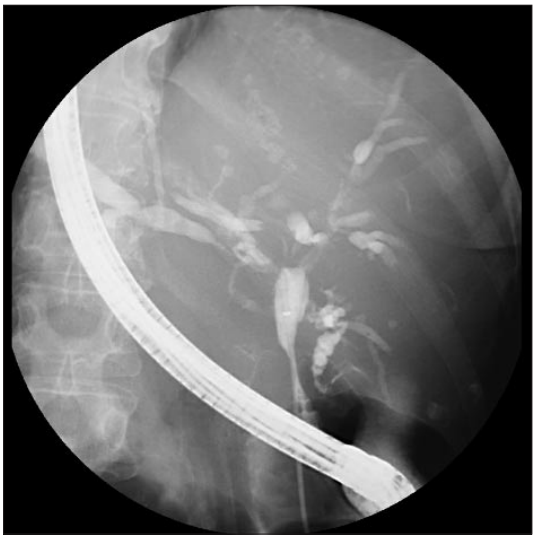


Figure 6. An endoscopic retrograde cholangiopancreatogram shows the beaded appearance of alternating dilatations and stenoses of the biliary tree in primary sclerosing cholangitis.



Extra-hepatic causes

A key role of imaging the jaundiced patient is to recognize those with an obstructive cause. US is particularly well suited to this purpose because of its ability to visualize the intra- and extrahepatic biliary tree in detail and should be the first line of investigation. When distal obstruction is present the proximal biliary ducts become dilated (*Figure 8*). US can reliably confirm the presence of duct dilatation and indicate the level of obstruction in the majority of cases. However, the extrahepatic common bile duct and pancreatic head may sometimes be a blind spot as a result of overlying bowel gas.

Gallstones are a frequent benign cause of extrahepatic obstruction and are often clearly demonstrated with US (*Figure 9*). An important caveat is that gallstones may often not be apparent on CT depending on the size and density of the stones. A nuclear medicine study using a radio-labelled bilirubin analogue – 99m-technetium hepatoiminodiacetic acid (HIDA) – is used in certain cases to obtain functional information about biliary excretion (*Figure 10*) and to confirm the presence of a bile leak following cholecystectomy. MRCP utilizes different signal characteristics of tissues to highlight the biliary tree and thus provide both cross-sectional and three-dimensional images of the bile ducts (*Figure 11*). The same examination may also be tailored to evaluating the liver, pancreas and vascular structures. ERCP, although associated with the risks of sedation, endoscopy and iatrogenic pancreatitis, has the advantage of being potentially therapeutic as there is the ability to retrieve common duct stones following sphincterotomy (*Figure 12*). Other benign causes of obstructive jaundice include traumatic biliary strictures, usually post surgical, and inflammation following acute pancreatitis.

Figure 7. A contrast-enhanced computed tomogram shows multiple target lesions in the liver resulting from metastatic adenocarcinoma of the lung.

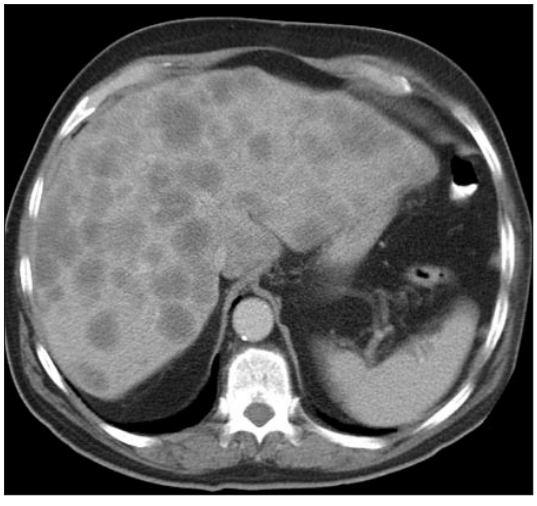


Figure 8. Dilated intrahepatic ducts in the left lobe of the liver (ultrasound).

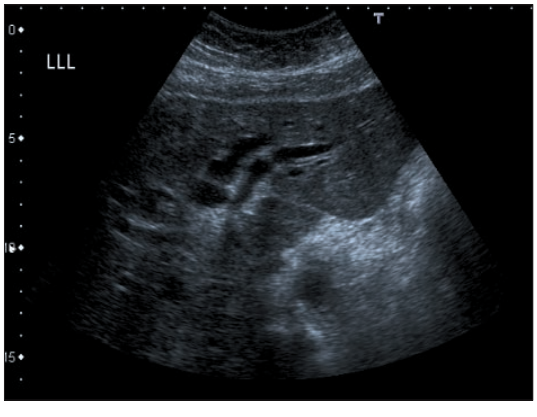


Figure 9. Two gallstones within the gall bladder showing typical posterior shadowing (ultrasound).

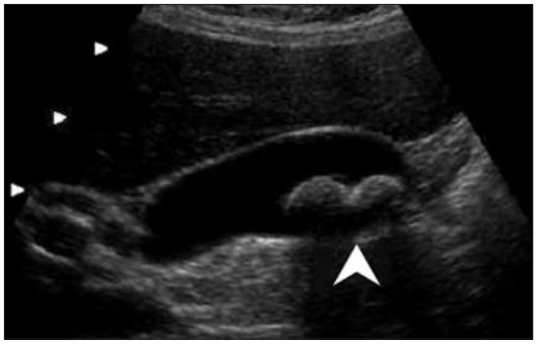
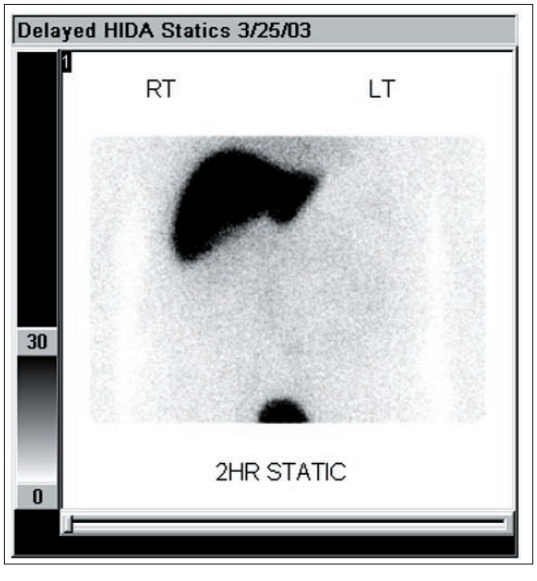


Figure 10. A 99m-technetium hepatoiminodiacetic acid (HIDA) nuclear medicine study showing uptake within the liver but absent activity in the common bile duct or bowel. This is a sensitive method of confirming biliary obstruction in selected cases.



Painless obstructive jaundice raises the possibility of malignant compression of the extrahepatic bile ducts. This is most commonly as a result of a carcinoma arising within the head of the pancreas and compressing the common bile duct and pancreatic duct. Tumours are most commonly ductal adenocarcinomas, but islet cell tumours, lymphoma and metastases may also occur. CT has a high sensitivity for detecting pancreatic neoplasms and permits assessment of local extension, vascular encasement and metastases. Endoscopic US has a useful role as it has a high specificity for assessing unresectable pancreatic malignancy before consideration of surgical resection (Yusoff et al, 2003). Trans-abdominal US may also detect tumours which appear as hypoechoic masses (*Figure 13*) and help to guide a percutaneous biopsy. Relatively rare islet cell tumours often show avid arterial enhancement on CT and may also be demonstrated with radio-labelled somatostatin analogues on nuclear medicine imaging.

Figure 11. Magnetic resonance cholangiopancreatography demonstrating the appearances of normal bile ducts and gall bladder (magnetic resonance imaging).

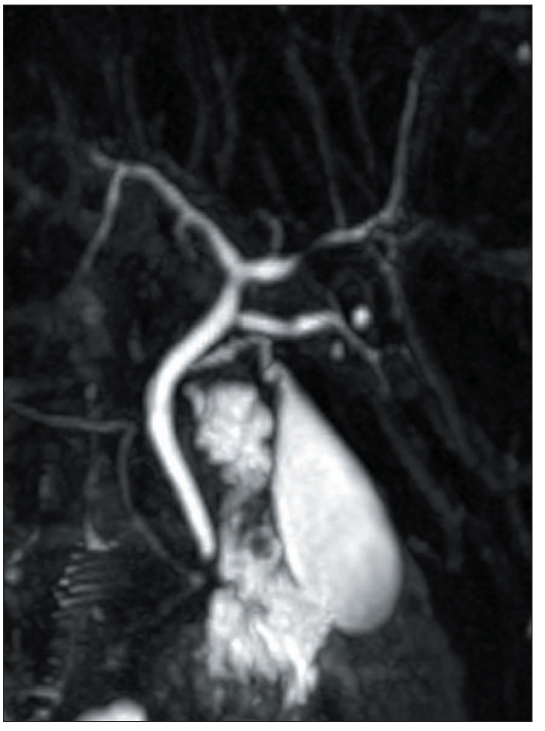
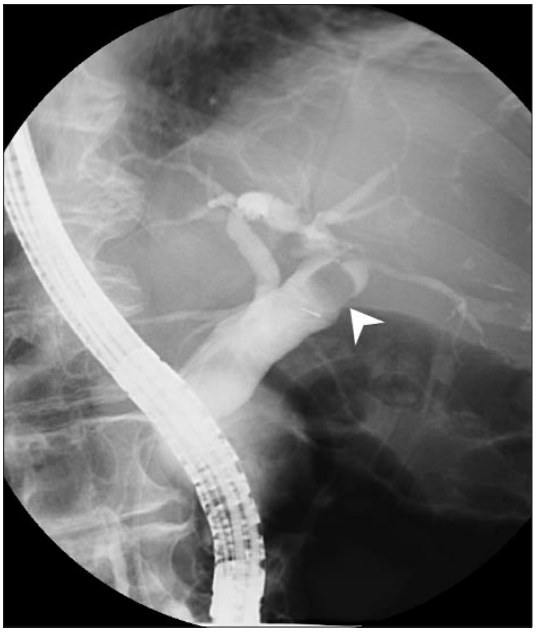


Figure 12. A gallstone (arrowhead) in a dilated common bile duct. This stone was retrieved at endoscopic retrograde cholangiopancreatography and a sphincterotomy performed.

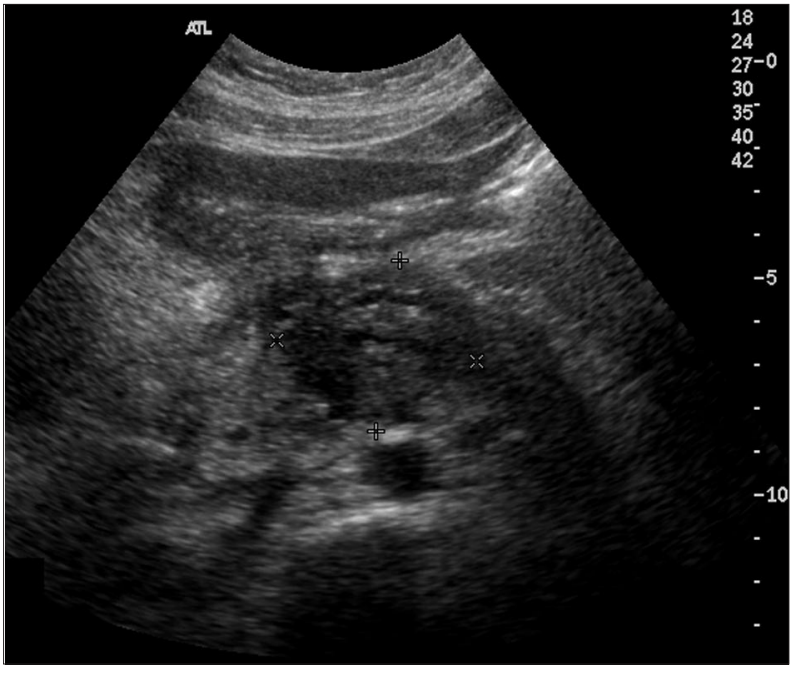


Cholangiocarcinoma is the second most common primary liver tumour after hepatocellular carcinoma, and may arise from the intra or extrahepatic bile duct epithelium. Imaging demonstrates a central mass causing biliary dilatation (*Figure 14*) which frequently has satellite nodules. US may reveal tumour extension along the bile ducts. A tumour at the confluence of the hepatic ducts is called a Klatskin tumour and may cause biliary dilatation in both lobes of the liver. Ampullary or duodenal tumours may also lead to biliary obstruction, as may lymphoma or metastases around the porta hepatis.

INTERVENTIONAL PROCEDURES

Percutaneous transhepatic cholangiography (PTC) is performed to gain access to the biliary

Figure 13. A neoplasm in the head of the pancreas on ultrasound.



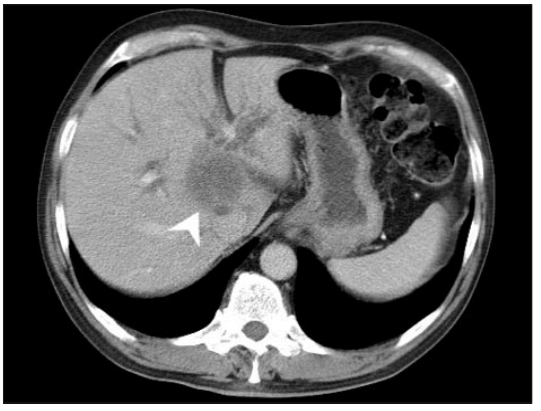
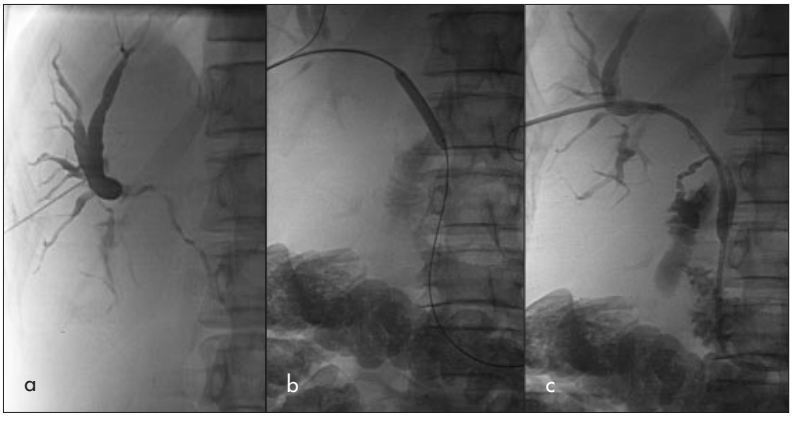


Figure 14. A cholangiocarcinoma causing intrahepatic biliary dilatation on an enhanced computed tomogram.

tree using imaging guidance. Typically the ducts are punctured with a fine needle using US to guide its course. The needle's position can be confirmed by injecting contrast material during real-time fluoroscopy. A drainage catheter can be inserted to provide decompression of an obstructed system. This may prove life-saving in biliary sepsis secondary to obstruction. Treatment options to provide a longer-term result may include balloon dilatation of a stricture or stent insertion to relieve the obstruction (*Figure 15*). A diagnostic PTC may be performed if an ERCP has failed although increasingly MRI is being used as a non-invasive means to evaluate the biliary tree.

Imaging is also used for targeted biopsies of hepatic or pancreatic masses for tissue diagnosis. CT or US may be used depending on the site of the lesion. Fine-needle aspiration biopsy or core biopsy may be taken according to local practice and tumour location. Liver biopsy carries a small but significant risk of haemorrhage which may be life-threatening. If there is an uncorrected coagulopathy or significant ascites a transjugular biopsy may be performed. This involves puncturing the internal jugular vein and passing a catheter into the hepatic veins under fluoroscopic guidance. Through a cannula, a cutting needle is used to obtain the biopsy. Any vessel damage results in a situation where blood will autotransfuse into the systemic circulation, rather than leak into the peritoneum.

Figure 15. Percutaneous transhepatic cholangiogram. a. A fine needle is passed into the right lobe of the liver. Contrast is injected which demonstrates a dilated biliary tree above a long stricture. b. A guidewire is used to cross the stricture and multiple balloon dilatations are performed to open the stricture. c. Last, a temporary plastic stent is inserted to ensure biliary drainage into the small bowel.



KEY POINTS

- Prompt diagnosis of the cause of jaundice is essential.
- Ultrasound is the first-line imaging investigation, and will confirm the presence of an obstructive cause, such as gallstones or tumour.
- Biliary sepsis may complicate obstructive jaundice and decompression may be performed radiologically.
- Contrast-enhanced computed tomography allows staging of malignant disease.
- Magnetic resonance cholangiopancreatography is useful for non-invasive imaging of the biliary tree, as well as the solid upper abdominal organs.
- Contrast-enhanced ultrasound has a developing a role in selected cases.

CONCLUSIONS

Imaging has a crucial role in the diagnostic pathway for jaundiced patients. US is the primary investigation of choice and will confirm the presence and level of obstruction in the majority of patients.

Detailed information about the liver, biliary tract and extrahepatic structures may be gained from a variety of imaging modalities, and image-guided intervention plays an important role in both diagnosis and management. HM

Conflict of interest: none.

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