Imaging the liver and biliary tract

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Abstract

A variety of modalities is available to image the liver and biliary tract, many offering complementary information; a combination of techniques is often required to make the diagnosis or determine optimal patient management. Ultrasonography (US) is commonly used as the primary investigation as it is safe, cheap and widely available. Computed tomography (CT) has a central role in emergency imaging, cancer diagnosis and staging, surgical planning and assessment of treatment response. Magnetic resonance imaging (MRI) is excellent for interrogating the liver parenchyma, and is the modality of choice for characterizing a focal liver lesion and non-invasive investigation of the biliary tree. Hepatobiliary contrast agents and diffusion-weighted imaging have further improved the accuracy of MRI. This article describes the role of each of these modalities, highlighting several common benign and malignant hepatobiliary disease processes. Other less commonly used modalities such as positron emission tomography-CT, cholescintigraphy and endoscopic ultrasound/cholangioscopy are summarized.

Keywords Bile ducts; biliary tract diseases; cholangiography; computed tomography; liver; liver diseases; magnetic resonance imaging; MRCP; positron emission tomography; ultrasonography

Key points

- US is widely used as the first-line imaging investigation for surveying the liver and biliary tree. Additional techniques including elastography, Doppler scanning and contrast-enhanced ultrasound can provide supplementary information
- CT provides a fast and accurate means of imaging the liver parenchyma and vasculature, and is widely used in oncological and emergency medicine
- MRI has superior soft tissue contrast with the facility to quantify parenchymal liver disease. It is the imaging modality of choice for complex biliary disease and for detecting and characterizing lesions in normal or cirrhotic liver
- Nuclear medicine, including PET-CT, has restricted but specific uses in imaging the liver and biliary tree, and can provide additional functional information, particularly related to malignancy.

Ultrasonography

Ultrasonography (US) remains the most widely performed primary investigation for suspected hepatobiliary disease, owing to its wide availability and avoidance of ionizing radiation.

Biliary disease

In the fasted state, the gallbladder appears on US as an oval hypoechoic structure with a smooth thin wall. Gallstones usually appear as mobile echogenic foci with posterior acoustic shadowing; they are identified with >95% accuracy in the gallbladder, but less so in the common bile duct owing to adjacent bowel gas. US findings in acute cholecystitis include mural thickening (>3 mm), pericholecystic fluid and a positive sonographic Murphy's sign (the eliciting of tenderness with pressure by the ultrasound probe while visualizing the gallbladder) (Figure 1)

Gallbladder polyps appear as fixed luminal defects without acoustic shadowing. Adenomyomatosis and chronic cholecystitis are other common benign causes of mural thickening demonstrated on US. Carcinoma of the gallbladder can present as a polypoid luminal tumour or as diffuse wall thickening and is often difficult to differentiate from benign conditions. Gallbladders containing polyps >1 cm are thought to carry a higher risk of malignancy and are generally resected. Smaller polyps should be considered for follow-up depending on the presence of other risk factors including age >50 years or a history of primary sclerosis cholangitis.

US has a major role in identifying biliary dilatation[1] in the context of jaundice or right upper quadrant pain, which can be caused by obstructive pathology (duct stones, benign or malignant strictures); however, dilatation is also found after cholecystectomy, after prolonged fasting or with sphincter of Oddi dysfunction and opiate use. The common hepatic duct normally measures up to 6 mm until age 60 years, with a further 'allowance' of 1 mm per decade thereafter.

Liver disease

The normal liver has a uniform and homogenous echotexture. Fatty infiltration gives a diffusely echogenic (bright) liver compared with adjacent normal renal tissue, with attenuation of the US beam as it passes deep into the organ. In advanced parenchymal liver disease (i.e. cirrhosis), the liver usually appears coarse and echogenic; common morphological features include surface nodularity, atrophy of the right lobe, hypertrophy of the caudate lobe and enlargement of the gallbladder fossa and umbilical fissure. Features of portal hypertension may also be

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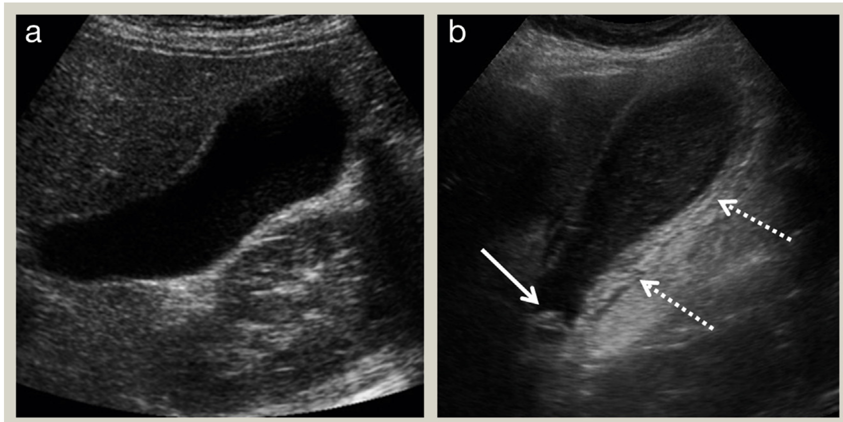

Figure 1 (**a**) US image showing a normal thin-walled gallbladder. (**b**) Acute calculous cholecystitis. The gallbladder wall is diffusely thickened (dashed white arrows) and contains echogenic bile, with a gallstone impacted in the neck (solid white arrow).

identified, with reduced, reversed or absent portal venous flow, varices, splenomegaly and ascites. In patients with cirrhosis, US is used as the primary modality to screen for hepatocellular carcinoma (HCC).[1]

There is increasing benefit to identifying patients with lesser degrees of fibrosis.[2] Increasing liver stiffness correlates with higher stages of fibrosis, which can be quantified by measuring 'shear' waves passing through the liver using US or magnetic resonance imaging (MRI). Measured stiffness values vary between US manufacturers and with the underlying aetiology of liver fibrosis. Multiple guidelines support its use in staging fibrosis (e.g. in viral hepatitis), significantly reducing the requirement for biopsy, with its attendant risks.

Doppler ultrasound

The frequency shift of an ultrasonic wave (Doppler effect) that occurs when it is reflected from a moving target (such as blood) can be used to create a colour map of blood flow and direction (colour Doppler) or a targeted waveform of blood flow (spectral Doppler). This is commonly used to interrogate the major hepatic vessels in chronic liver disease and after liver transplantation.

Contrast-enhanced ultrasound (CEUS)

Grey-scale US has modest sensitivity (50–65%) for metastatic disease and HCC, and can reliably characterize cysts; however, it is limited in the characterization of solid focal lesions.[1] CEUS improves both lesion detection and characterization. It involves the intravenous injection of microbubble contrast media.

Some benign lesions, such as haemangiomas and focal nodular hyperplasia, have characteristic enhancement patterns. Haemangiomas are usually iso- or hyperechoic to background liver in the late phase of enhancement (Figure 2). Although comparable to computed tomography (CT) and MRI for detecting and characterizing lesions in ideal circumstances, multiple lesions and lesions near the diaphragm or obscured by bowel gas are difficult to evaluate.

Computed tomography

Multi-detector CT is widely used and versatile, allowing rapid imaging of a large volume with high spatial resolution, and thus facilitating accurate multiphase imaging of the liver and biliary tree. Iodinated contrast is used for most examinations; it is contraindicated in individuals with severe renal impairment or a history of anaphylactic reaction. The high radiation dose of CT should be considered (especially with multiphase imaging), although increased computing power has facilitated iterative reconstruction techniques that enable decreased dose parameters (peak kilovoltage and milliamps), while maintaining image quality.

Dual-energy CT techniques are now available, simultaneously acquiring images at two different X-ray energies. Complex processing then allows the generation of mono-energetic images. This can improve lesion detection, particularly for highly vascularized tumours such as HCC, by increasing contrast between lesions and the adjacent liver, and reducing artefacts. Material-specific iodine maps that demonstrate the concentration and distribution of iodine can help with lesion characterization.

Imaging the acute abdomen

CT retains an important role for imaging in emergency situations.[1] In major trauma, dual-phase imaging or a single biphasic contrast injection (a protocol developed by the military) has a high accuracy for traumatic liver injuries and active arterial bleeding. High-quality three-dimensional reformats of the hepatobiliary vascular anatomy (Figure 3) are useful for planning endovascular intervention in vascular injury. Whereas US is the first-line investigation for acute pathology of the gallbladder,[1] CT demonstrates complications of cholecystitis such as necrosis, perforation or pericholecystic abscess. Intrahepatic or perihepatic fluid collections and abscesses are accurately depicted.

Hepatobiliary oncology imaging

Metastases are by far the most common malignant liver lesions, exceeding primary liver tumours by a factor of at least 20. CT is used for staging, and to assess response to treatment for most malignancies that metastasize to the liver and for primary tumours arising from the liver, pancreas and biliary tree.

The blood supply to the liver is via the hepatic artery (25%) and portal vein (75%), with most tumours taking their blood supply from the hepatic artery and displaying a varying degree of

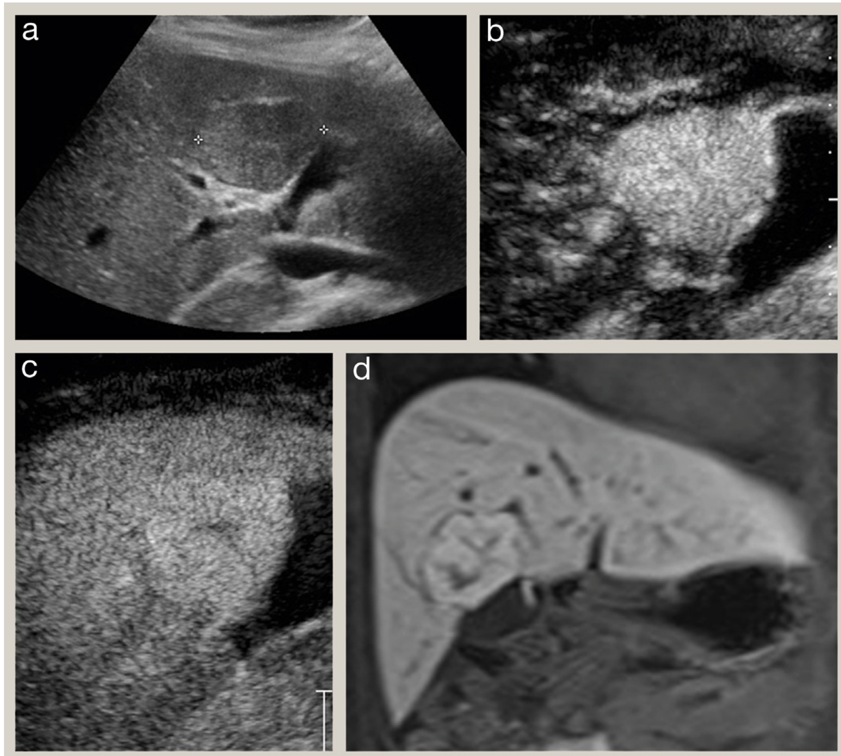

Figure 2 (**a**) Grey-scale US image in a 24-year-old woman shows a well-defined isoechoic mass adjacent to the gallbladder fossa. (**b**) CEUS images shows avid homogenous arterial enhancement within the lesion, (**c**) which is near-isointense in the delayed phase, with a faint central scar visible. (**d**) A subsequent coronal hepatobiliary phase MRI image shows persisting uptake of contrast with a central scar, confirming focal nodular hyperplasia.

vascularity. Hypervascular tumours such as HCC or neuroendocrine malignancy should be imaged in the arterial phase to maximize contrast enhancement between tumour and background liver. Most metastases from other sources (e.g. colorectal cancer) are hypovascular and best depicted on portal venous phase scanning. Triple-phase CT (unenhanced, arterial and portal venous phases) can be used to clarify the cause of biliary obstruction identified on US (when stones are not suspected).

Surgical assessment

The high spatial and temporal resolution of CT makes it suitable for evaluating patients before major surgery, including liver transplantation, and often in conjunction with MRI for liver resection. Thorough anatomical assessment of potential transplant recipients is required to reduce the risk of complications and increase the chance of surgical success. Multiphase CT is used to assess for variant hepatic arterial anatomy, exclude portal venous or superior mesenteric venous thrombus, identify portosystemic shunts, and look for other arterial complications (e.g. stenosis of the celiac origin, splenic artery aneurysm). CT is also used to assess potential live donors. Assessment of the segmental arterial, venous and biliary anatomy in addition to liver volumes is essential as a significant number of potential donors are unsuitable.

Magnetic resonance imaging

MRI is a versatile imaging technique, allowing manipulation of sequence parameters to vary soft tissue contrast or obtain

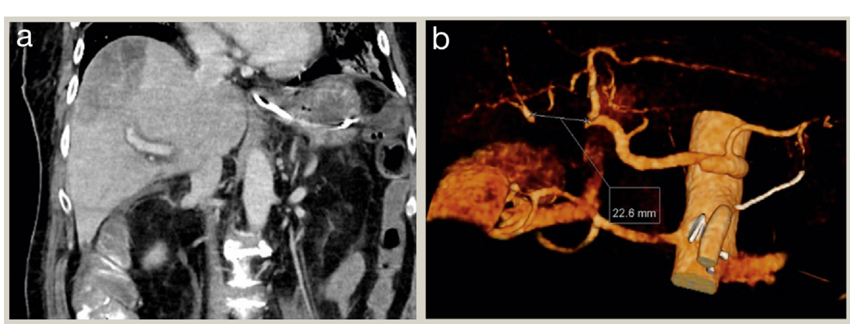

Figure 3 Segmental liver infarction after total pancreatectomy and splenectomy. (**a**) Coronal CT demonstrating a wedge-shaped area of reduced attenuation in segment 8 of the liver. (**b**) Three-dimensional surface projection of a mesenteric angiogram showing a 2.3 cm defect in the right hepatic artery.

structural data. It is the examination of choice for imaging complex biliary disease and characterizing liver lesions in both normal and cirrhotic liver. MRI can characterize both diffuse liver disease and focal liver lesions, in certain cases obviating the need for biopsy. MRI has excellent liver-to-lesion contrast resolution and does not involve ionizing radiation. The use of hepatocyte-specific contrast agents, diffusion-weighted imaging (DWI) and multiphase arterial enhancement has further improved its sensitivity and specificity. Limitations include cost, length of examination (particularly for unwell patients who cannot lie still) and contraindications such as pacemakers and implants.

Biliary disease

Magnetic resonance (MR) cholangiopancreatography (MRCP) uses heavily weighted T2 sequences to display static or slow-moving fluid within the biliary tree and pancreatic duct.[3] MRCP can identify ductal stones as small as 2 mm with comparable accuracy to endoscopic retrograde cholangiopancreatography (ERCP) (Figure 4).[1] Flow artefacts, intraductal gas and adjacent pulsatile vascular compression can lead to false-positive interpretations. Both benign (iatrogenic, post-inflammatory, secondary to primary sclerosing cholangitis) and malignant strictures can be identified.[3] Malignant biliary strictures tend to be longer, with wall thickening and an irregular margin.

Diffuse liver disease

In- and out-of-phase T1 imaging is used to identify cellular fat and iron in hepatic steatosis, haemochromatosis and haemosiderosis. Chemical shift, MR spectroscopy and T2* relaxation techniques can be used to accurately identify and quantify fat and iron in the liver. A number of methods have been developed for the non-invasive grading of liver fibrosis using MRI.[2] MR elastography has been shown to be more accurate than US elastography but requires hardware to generate a shear-wave within the liver. Innovative techniques such as T1-mapping, corrected for the presence of fat and iron, are currently being evaluated as an indicator of the degree of fibrosis.[2]

Focal liver disease

MRI allows accurate characterization of benign liver lesions, such as haemangiomas, adenomas and focal nodular hyperplasia, and their differentiation from primary and secondary malignant lesions.[1] In both the cirrhotic and non-cirrhotic liver, MRI is the investigation of choice for demonstrating the anatomical distribution of disease with high accuracy before liver resection and transplantation.

Typical liver protocols usually include T2-weighted sequences that provide an overview of anatomy and the identification of simple cysts or haemangiomas. In- and out-of-phase T1 imaging identifies intracellular fat within a lesion (e.g. adenoma, HCC,[4] areas of focal fatty infiltration). Contrast agents are used to obtain arterial, portal venous and delayed phases of liver enhancement to detect and characterize lesions and assess the vasculature. The lack of ionizing radiation enables more acquisitions than with CT, which is particularly advantageous in the arterial phase when multiple datasets can be obtain in a single breathhold. Gadolinium chelates are confined to the extracellular space, and behave in a similar way to iodinated contrast used in CT. Hepatocyte-specific contrast agents (gadobenate dimeglamine, gadoxetic acid) are actively taken up by lesions with hepatocyte function and excreted into the bile, providing additional information about the cellular constituents of a lesion.[4] DWI gives unique information about the movement of water molecules at the cellular level. Malignant lesions have a significantly lower apparent diffusion coefficient and display greater diffusion restriction than benign lesions. DWI is particularly useful for detecting malignant lesions in the non-cirrhotic liver.

Multiple organizations have published criteria for the non-invasive diagnosis of HCC using MRI (or CT when MRI is contraindicated). The key diagnostic criteria include arterial

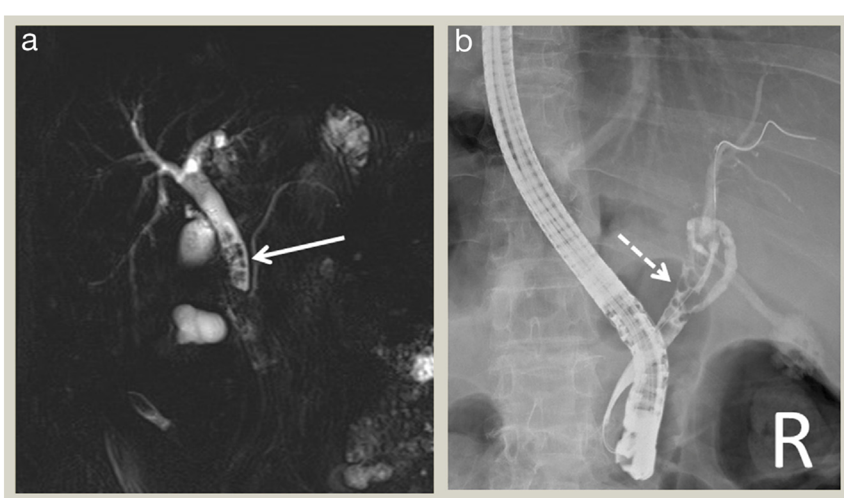

Figure 4 Choledocolithiasis in a patient with cholangitis and obstructive jaundice. (**a**) Reconstructed magnetic resonance cholangiopancreatography maximum intensity projection showing proximal biliary dilatation with multiple small calculi in the common bile duct (solid white arrow). (**b**) Subsequent endoscopic retrograde cholangiopancreatography confirmed the presence of multiple calculi (dashed white arrow). This was followed by sphincterotomy and trawling of the common bile duct to remove the calculi and relieve the biliary obstruction.

enhancement with 'washout' in the portal venous phase. The recently updated Liver Imaging Reporting and Data System (LI-RADS)[5] developed by the American College of Radiology provides a comprehensive diagnostic algorithm to allow risk stratification for any abnormalities detected in the liver of a high-risk patient. In addition to hypervascularity (Figure 5a, b) and washout (Figure 5c), LI-RADS also uses the size of the mass, the presence of an enhancing capsule and threshold growth as major criteria. Using these major criteria along with multiple ancillary features (Figure 5d), the radiologist can grade observations on a scale from 'definitely benign' (LR-1) to 'definitely HCC' (LR-5), with LR-2 to LR-4 representing different probabilities of malignancy. This can then be used to guide further investigation, follow-up and intervention.

Positron emission tomography (PET)-CT

FDG (2-[^{18}fluorine]fluoro-2-deoxy-D-glucose) PET with CT (PET-CT) is a functional imaging technique using a glucose analogue that is taken up by metabolically active tissues and tumour cells. PET-CT is frequently used for demonstrating disseminated malignant disease and can identify occult primary tumours in patients with metastatic liver disease from an unknown primary. PET-CT is commonly used to identify occult metastatic disease in patients with colorectal liver metastases being assessed for liver resection.

It is unreliable for the identification of HCC (although a high standardized uptake value correlates with poor differentiation) and is inferior to MRI for identifying liver metastases. It can improve the detection rate of occult metastatic disease in HCC (as these tend to be less well differentiated tumours). PET-CT has a role in cholangiocarcinoma and gallbladder carcinoma where other cross-sectional imaging is equivocal for metastatic disease and radical surgery is being considered. Limitations include cost, low spatial resolution, large radiation burden and lack of specificity.

Cholescintigraphy

This technique involves an intravenous injection of ^{99m}technetium-labelled hepatobiliary iminodiacetic acid (^{99m}Tc-HIDA), or a related compound, which is taken up by the liver and excreted in the bile. The technique retains an important role in the paediatric setting, differentiating between biliary atresia and neonatal hepatitis. In biliary atresia, there is good hepatic uptake but no excretion into the bowel 24 hours after injection. The technique can also be used to evaluate biliary excretion in adults, and although rarely used as an investigation in the diagnosis of acute cholecystitis, it is highly sensitive. Absence of activity in the gallbladder after 4 hours is diagnostic as HIDA cannot enter through an inflamed and oedematous cystic duct. False-positive results can occur with underlying liver disease or after a prolonged fast.

Endoscopic imaging

Endoscopic ultrasonography (EUS) is an invasive technique in which a high-frequency transducer is attached to the tip of an endoscope. The left lobe of the liver, pancreas, biliary tree and associated nodal chains can be evaluated. EUS is more sensitive than US or CT for detecting early chronic pancreatitis, biliary microlithiasis and strictures, and small pancreatic or ampullary masses. Fine needle aspiration of lymph nodes and solid and cystic pancreatic lesions can be performed. Direct cholangiography (ERCP) has now been largely replaced as a diagnostic test, being reserved for tissue biopsy, stone extraction (Figure 4b) or stent insertion. Cholangioscopy using the SpyGlass® system can be used to directly inspect the biliary tree, evaluate indeterminate

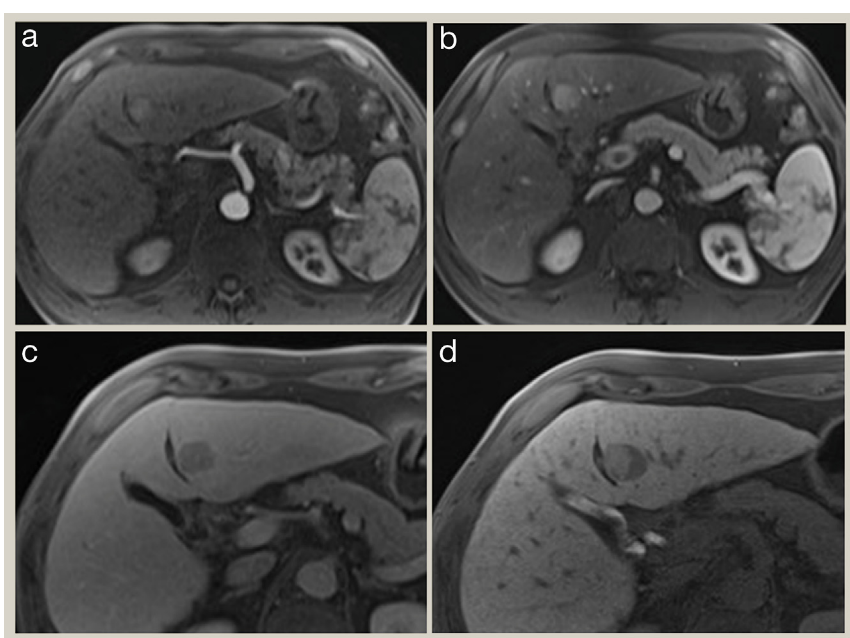

Figure 5 A 2.7 cm focal liver lesion in a patient with cirrhosis. (**a**) An early arterial phase image shows faint hypervascularity in a segment 3 lesion. (**b**) A late arterial phase image confirms strong hypervascularity. (**c**) A portal venous phase image demonstrates washout. (**d**) A delayed image shows heterogeneously reduced uptake of the hepatobiliary contrast agent with a 'nodule-in-nodule' appearance. Applying the liver imaging reporting and data system diagnostic algorithm, this lesion can be safely diagnosed as an hepatocellular carcinoma without invasive testing.

strictures, take targeted biopsies and assess biliary complications after transplant. ◆

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online here.

Question 1

A 32-year-old woman presented with a 3-day history of right upper quadrant pain and a 1-day history of rigors. Her past medical history included type-I diabetes mellitus. On clinical examination, there was mild jaundice, temperature 37.0°C, heart rate 98 beats/minute, and severe right upper quadrant tenderness.

Investigations

- Haemoglobin 125 g/litre (115–165)
- White cell count 16.2 × 10^9/litre (4–11)
- Bilirubin 77 micromol/litre (1–22)
- Alkaline phosphatase 158 U/litre (45–105)
- Alanine aminotransferase 420 U/litre (5–35)

What is the next most appropriate investigation for the likely diagnosis?

A. Abdominal ultrasound
B. CT of the abdomen and pelvis with intravenous contrast
C. Endoscopic retrograde cholangiopancreatography (ERCP)
D. Hepatobiliary iminodiacetic acid (HIDA) scan
E. Magnetic resonance cholangiopancreatography (MRCP)

Question 2

A 63-year-old man presented for review. He had been found to have abnormal liver function tests. He had been drinking approximately 50 units of alcohol a week and had a number of home-made tattoos.

Investigation

- Ultrasonography of the liver showed a coarse, nodular outline with features of portal hypertension. No focal lesions were identified

What is the most appropriate modality for follow-up?

A. Multiphase CT of the abdomen
B. Ultrasonography of the liver
C. MRI of the liver with hepatobiliary contrast agent
D. Transient elastography using a FibroScan® device
E. Positron emission tomography with CT (PET-CT)

Question 3

A 27-year-old woman presented with pleuritic chest pain and shortness of breath. She had no relevant past medical history and the only medication she was taking was the oral contraceptive pill.

Investigation

- CT pulmonary angiography demonstrated no pulmonary embolus. At the bottom of the acquired volume, there was a 3 cm uniformly hypervascular lesion high within the right lobe of the liver

What is the most appropriate investigation to confirm the most likely underlying diagnosis?

A. Contrast-enhanced US of the liver
B. MR scan of the liver using a hepatocyte-specific contrast agent
C. Percutaneous biopsy of the lesion under ultrasound guidance.
D. Multiphase CT of the upper abdomen including arterial, portal venous and delayed phases
E. PET-CT

