Abdominal Imaging REVIEW

Imaging of hepatic incidentalomas with CT and MRI

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ABSTRACT

The increasing and widespread use of imaging techniques has led to an increase in the detection of incidental focal liver lesions. Most hepatic incidentalomas are benign lesions which do not require further investigation or intervention; however, few of them may prove malignant. Although conventional ultrasonography is usually the first imaging method, it lacks the diagnostic performance of multidetector computed tomography (CT) or magnetic resonance imaging (MRI) in the detection and characterisation of hepatic incidentalomas. In this review, the role of CT and MRI in the investigation of hepatic incidentalomas will be presented. The guidelines of the American College of Radiology regarding the management of focal liver lesions incidentally detected on CT will be discussed. Finally, the typical CT and MRI features of common hepatic incidentalomas, including both benign and malignant, will be reviewed.

KEY WORDS

Liver; Hepatic neoplasms; MR imaging; Multidetector computed tomography; Incidentalomas

1. Introduction

The increasing use and widespread availability of cross-sectional imaging techniques has resulted in the detection of incidental liver lesions that are mostly asymptomatic prior to their discovery [1-30]. Hepatic incidentalomas (HIs) were first reported by Little et al in 1990 as a new entity, described as "an unexpected solid filling defect in the liver of a well patient detected incidentally by scanning". The authors of this study assessed 36 HIs, 29 (81%) of which were benign, with hepatic haemangioma (HH) representing the most common histologic type, and seven (19%) were malignant [2].

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HIs are found in up to 30% of individuals aged more than 40 years [4]. The commonest way to be detected is during conventional ultrasonography (US), an examination widely performed for the assessment of abdominal symptoms [3, 11, 25, 29]. Choi et al evaluated the clinical significance of 681 focal hepatic solid lesions incidentally detected on initial US in 542 asymptomatic patients. From these lesions, 674 (99.0%) were benign, and only seven (1.0%) proved malignant [11]. HIs may also be detected during screening investigations, such as computed tomography (CT) colonography [3, 8, 9]. Alternatively, incidental focal liver lesions may be seen during laparoscopy or at laparotomy [3].

Although, most incidentally discovered liver lesions in asymptomatic and healthy individuals without any previous history of malignancy are benign, HIs require careful and accurate investigation to suggest a differential diagnosis and even a histologic characterisation [1, 3, 23, 24, 27, 29]. In oncologic patients, the probability that a focal liver lesion will be malignant is significantly higher. In these patients, focal hepatic lesions are mainly detected on multidetector CT (MDCT), which represents the primary imaging technique for staging and follow-up of most malignancies. It must be emphasised that approximately 51-88.8% of liver lesions detected by CT with a maximal diameter of 10-15 mm are metastases in oncologic patients. However, even in this group at least 65% of single liver lesions less than 15 mm are benign [26].

Focal hepatic lesions can usually be characterised on the basis of history, physical examination, simple laboratory tests and imaging examinations [1, 3, 23]. The outcomes of investigation include discharge, follow-up imaging or tissue diagnosis either by biopsy or lesion excision [3].

The most commonly used imaging technique is conventional B-mode US, combined with colour Doppler. However, the diagnostic performance of conventional US for the characterisation of focal liver lesions is usually insufficient, with the exception of simple hepatic cysts and HHs, the latter when presenting with the typical echogenic appearance [24, 29, 31-33]. Therefore, HHs with indeterminate US features must be further investigated [4].

MDCT provides satisfactory results in the characterisation of focal liver lesions. One of the advantages of CT is the ability to evaluate the whole abdomen, including also the basal lungs in one examination. Another advantage is the reduced examination time. When performed for liver lesion evaluation, CT may include the following phases: unenhanced imaging and contrast-enhanced late arterial, portal venous, and delayed-phase imaging [4].

Although most liver tumours can be reliably evaluated with MDCT, nowadays magnetic resonance imaging (MRI) is considered as the most sensitive and specific examination for the detection and characterisation of focal liver lesions [4, 24-26, 29, 34-36]. The American College of Radiology (ACR) recommends the use of MRI over CT for the characterisation of HIs [4]. In most cases, MRI enables better characterisation of the internal features of the lesions and more reliable detection of contrast enhancement. Lack of radiation exposure is another advantage of MRI [4]. The addition of diffusion-weighted imaging (DWI) and liver-specific contrast agents improves the diagnostic performance of the technique in differentiating liver lesions [26, 36]. However, gadolinium-enhanced MRI is primarily recommended for the assessment of HIs, with the exception of distinguishing between focal nodular hyperplasia (FNH) and hepatocellular adenoma (HCA), where gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) is endorsed [4].

Chung et al in a retrospective study of 127 HIs assessed the diagnostic efficacy of MDCT and Gd-EOB-DTPA-enhanced MRI in lesion characterisation [28]. The authors reported that both MDCT and EOB-MRI had similarly high diagnostic performances for HH and hepatocellular carcinoma (HCC), while EOB-MRI provided better diagnostic accuracy for differentiation between benign and malignant liver lesions and for the characterisation of FNH [28].

Contrast-enhanced US (CEUS) represents an alternative option for the evaluation of HIs [29, 37, 38]. In large multicenter studies, CEUS revealed a diagnostic accuracy of more than 90% in characterising focal liver lesions. CEUS performs better than CT and at least equivalent to MRI in differentiating liver tumours [29, 37-44]. Soussan et al in a prospective study of 50 HIs reported similar high diagnostic accuracies for both CEUS and Gd-MRI in the characterisation of HH and FNH [29]. However, both imaging techniques were of limited value in characterising HCA. The authors concluded that CEUS and MRI are complimentary imaging techniques for the characterisation of HIs [29].

In cases of focal liver lesions, 18F-FDG PET/CT may help in characterisation, especially in patients with known extrahepatic malignancy [45, 46]. The ACR considers 18F-FDG PET/CT appropriate with a rating point of 7 (max value, 8) for the characterisation of HIs in patients with a history of malignancy [45]. However, in healthy individ-

uals the technique is recommended as a complimentary tool in cases of indeterminate findings on MRI or CT [46].

In this review, we comment on the role of CT and MRI in the investigation of HIs. Guidelines regarding their imaging evaluation are also presented. Common benign and malignant HIs and their CT and MRI features will be reviewed.

2. Recommendations for management of HIs

Recently, recommendations of the ACR Incidental Findings Committee on management of incidental liver lesions found on CT were published [4]. These recommendations should be applied for HIs detected in asymptomatic adult patients (more than 18 years of age) for whom CT was requested for an unrelated reason [4].

2.1 Risk categories for patients with HIs

Prior to assessing the imaging features of a focal liver lesion, it is important to know patient's clinical history. Recommendations require designation of patients as of low, average or high-risk for having a hepatic malignancy. Patients with "hepatic risk factors" and patients with a history of primary carcinoma with a propensity to metastasise to the liver are considered as high-risk patients. "Hepatic risk factors" refer to conditions that increase the risk for primary liver malignancy, including hepatitis, alcoholism, nonalcoholic steatohepatitis, sclerosing cholangitis, primary biliary cirrhosis, choledochal cysts, haemochromatosis, haemosiderosis and long-term oral contraceptive or anabolic steroid use. Low-risk patients have no history of malignancy, hepatic dysfunction, or hepatic risk factors. Within this category, patients more than 40 years of age are considered as of average risk for liver malignancy [4].

2.2 Imaging features

When assessing the imaging characteristics of a HI on CT, the following should be reported:

1. Lesion size. Most liver lesions smaller than 1 cm in maximal diameter, even in high-risk patients, are benign. 2. CT density. The following CT criteria are considered as diagnostic of a simple liver cyst in low-risk patients: homogeneous, sharply demarcated, hypodense lesion, with a mean CT density of 10-20 HU, without mural thickening, nodularity, or septations and absence of contrast enhancement. However, low density should not always be considered suggestive of a simple cyst, especially in patients with malignancies in whom liver metastases may have a cystic appearance. 3. Lesion homogeneity versus heterogeneity. Wall thickening, peripheral enhancement, mural nodules, and thick septa increase the likelihood of malignancy. It is important to place multiple ROIs throughout the lesion, including the areas with highest density to assess its internal features. 4. Contrast enhancement patterns. Simple hepatic cysts should enhance less than 20 HU, although this may be difficult to appreciate in small-sized cystic lesions. To confirm the presence of a liver cyst with indeterminate CT findings, MRI is recommended. The enhancement patterns of HH and FNH are often characteristic. The "flash-filling" phaenomenon, detected as strong, uniform enhancement in the arterial-phase (including late arterial or venous-phase) should be separately reported, especially if it is the only imaging characteristic. Based on ACR's recommendations, such lesions should be managed separately, in cases where no additional multiphasic imaging is available. 5. Lesion margins. Benign lesions usually have smooth margins, whereas malignant lesions may have smooth, irregular, or ill-defined margins. 6. Lesion multiplicity. The presence of multiple hepatic lesions in patients with a known history of cancer often raises suspicion for metastases. However, differential diagnosis should include benign entities, for example biliary hamartomas. In these cases, index lesions that are largest in diameter and/or show the most suspicious features should be selected to guide management. 7. Lesion growth pattern. Enlargement of a hepatic lesion is suspicious for malignancy, but both benign and malignant lesions may grow over time. Absence of growth over a 1-year time period strongly favours the diagnosis of benignity. Therefore, comparison with prior studies can help to establish lesion stability. 8. Location. Specific regions of the liver are susceptible to effects of perfusional changes and fatty infiltration or fatty sparing of the liver.

2.3 Recommendations

The ACR white paper considers HIs smaller than 1 cm as benign in low and average-risk patients and recommends no further investigation or follow-up. MRI should be considered in the presence of incidental small liver lesions with suspicious features, such as ill-defined margins, heterogeneous CT density, mural thickening or nodularity, or thick septa. Follow-up MRI after 3-6 months, or more shortly in some cases, is advocated in high-risk group patients with very small hepatic lesions. CT may be used as an alternative in oncologic patients, who are already un-

der CT surveillance [4].

Liver lesions between 1-1.5 cm in diameter should be grouped as being either "flash-filling", hypodense with benign imaging features and hypodense with suspicious features. Lesions with the "flash-filling" phaenomenon are probably benign, typically representing HHs in low or average-risk patients, and no further investigation or follow-up is warranted. However, if such a lesion is detected in a high-risk patient, a hypervascular malignancy could not be excluded and immediate further imaging is recommended. MRI with liver specific agent is considered the investigation of choice. Hypodense HIs with benign features on CT, such as sharp margins, homogeneity, low density (equal or less than 20 HU on unenhanced and/or portal venous phase imaging), or characteristic imaging features of HH, FNH, focal fatty infiltration or sparing and perfusional changes require no further investigation or follow-up. Prompt MRI is recommended in the presence of suspicious features, including ill-defined margins, heterogeneous density, mural thickening or nodularity, thick septa, and intermediate to high CT density on portal phase imaging. If unenhanced and contrast-enhanced CT images are available, enhancement more than 20 HU is considered a suspicious feature [4].

Large focal liver lesions, measuring more than 1.5 cm are easier to be characterised on imaging. Large, hypodense HIs with benign imaging features require no follow-up. Large "flash-filling" lesions may show characteristic features for the diagnosis of HH, FNH or perfusional changes. "Flash-filling" lesions without diagnostic imaging features or hypodense lesions with suspicious features should be immediately further evaluated with MRI. Direct biopsy instead may be recommended in some cases. If biopsy is pursued, core biopsy is preferred over fine-needle aspiration. EOV-MRI is advised for differentiation of FNH from HCA, especially in lesions larger than 3 cm and subcapsular in location. In large hepatic lesions, PET/CT or PET/MRI may preclude the need for biopsy in some cases [4].

3. Common HIs

Benign HIs include hepatic cysts, HH, FNH perfusional changes and the significantly less common HCA. Common malignant HIs include primary liver malignancies (hepatocellular carcinoma/HCC and cholangiocarcinoma/CHC] and metastases [47-53].

3.1 Hepatic cysts

Simple hepatic cysts are the most commonly encountered liver lesions, occurring in approximately 2.5% of the general population [54]. Hepatic cysts are thought to be of biliary origin. They are lined by a cuboidal, columnar epithelium, filled with serous fluid and surrounded by an outer layer of fibrous tissue. They are usually less than 1 cm in diameter, but may grow up to 30 cm. Most simple cysts are asymptomatic and therefore are discovered incidentally. Rarely, internal haemorrhage, infection, or rapid cyst enlargement may lead to symptoms.

Imaging diagnosis is often straightforward. On conventional US, simple cysts are anechoic, sharply delineated, with imperceptible wall, demonstrating increased through transmission and absence of vascularity. CT demonstrates a well-defined, non-enhancing hypodense lesion, with smooth margins and a mean CT density in the water range. Similarly, MRI shows a well-defined, homogeneous mass lesion with very low and very high T1 and T2 signal, respectively. Differential diagnosis should include biliary cystadenoma/cystadenocarcinoma, hydatid cyst, biliary hamartoma, polycystic liver disease, metastases from primary cystic tumours (eg. neuroendocrine tumours, gastrointestinal stromal tumour, lung adenocarcinoma, colorectal carcinoma, transitional cell carcinoma, adenoid cystic carcinoma, ovarian carcinoma, choriocarcinoma, sarcoma, and metastases treated with chemotherapy) and cystic necrosis of large primary solid neoplasms [3, 23, 26, 54-57].

3.2 Hepatic haemangioma

HHs are the commonest benign solid tumours of the liver, with a prevalence of 0.4-20% as reported on autopsy series. The neoplasm is composed of variably-sized vascular spaces, lined with flat endothelial cells and myxoid or fibrous stroma. These tumours are usually subcapsular in location and single, although multiple HHs may be seen. They affect all age groups, but typically are seen between 30-50 years of age. The majority of HHs is asymptomatic and discovered incidentally during imaging. Clinical symptoms may occur in approximately 11-14% of all HHs. The main clinical manifestations are right upper quadrant pain and/or a palpable mass [3, 4, 23, 26, 58].

Typical HH is detected as a sharply-defined, homogeneous, echogenic focal liver lesion on US. Both CT and

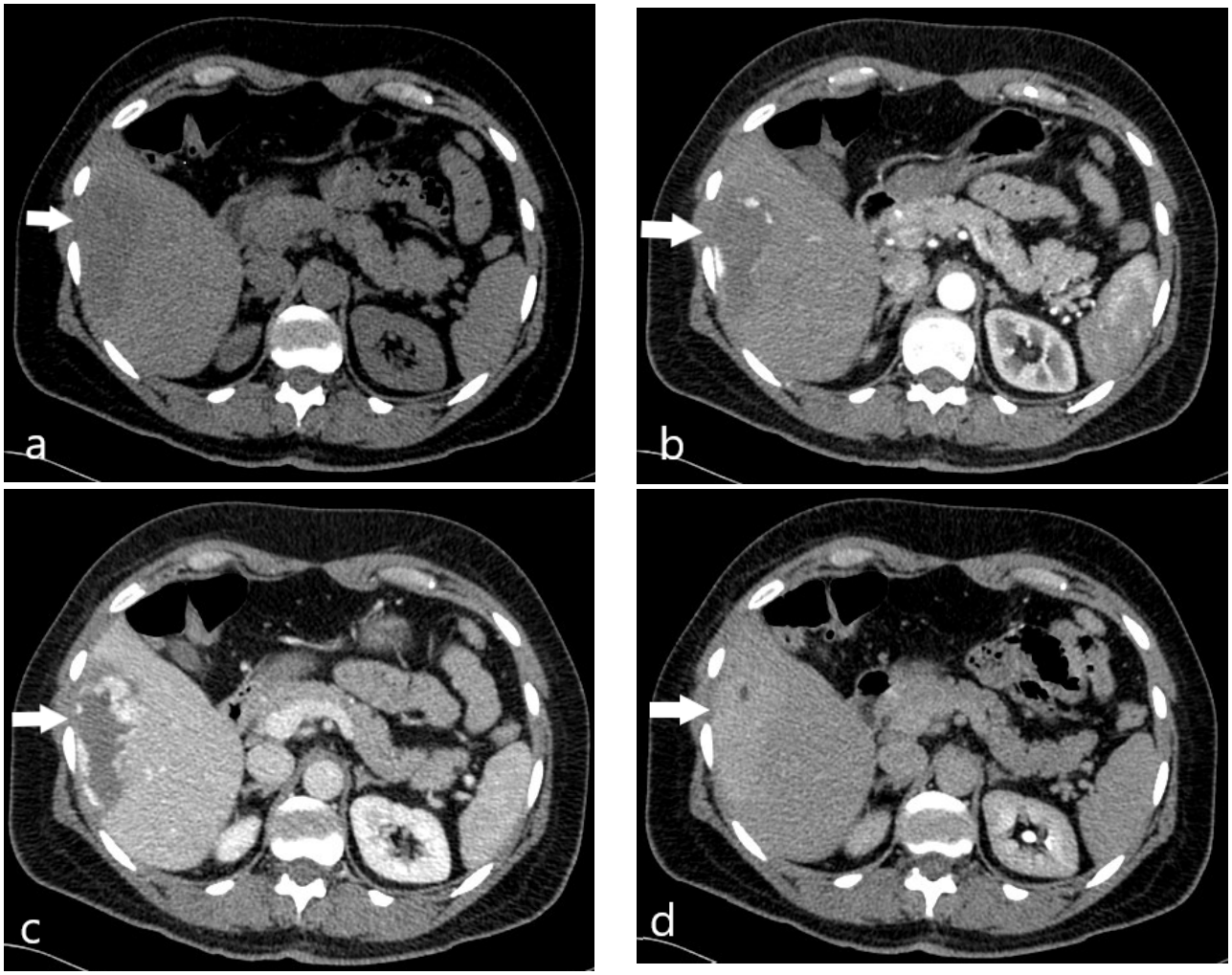

Fig. 1. ***(a)*** *Axial unenhanced CT image shows a well-defined lesion (arrow) in the right liver lobe. The mass appears mainly hypodense, when compared to normal liver parenchyma.* ***(b)*** *Axial contrast-enhanced CT image in the arterial phase shows discontinuous, nodular areas of enhancement in the periphery of the lesion (arrow), almost isodense to the aorta.* ***(c)*** *Portal phase demonstrates progressive peripheral enhancement with more centripetal fill-in (arrow).* ***(d)*** *Delayed phase shows nearly complete fill-in. The lesion (arrow) appears mainly slightly hyperdense compared to the surrounding liver.*

MRI are highly accurate in the characterisation of HHs. On unenhanced CT, haemangiomas are hypodense, similar in density to the blood pool. The classic enhancement pattern of HH is often diagnostic. The tumour presents with peripheral, nodular, discontinuous enhancement, becoming isodense with the aorta in the arterial phase, with progressive centripetal fill-in on subsequent imaging (**Fig. 1**). In the portal phase, HH may become uniformly hyperenhancing and isodense with hepatic and portal veins, and this enhancement persists on delayed imaging. Large HHs may not enhance centrally in the delayed phase, due to the presence of cystic degeneration, thrombosis, and/or fibrosis. When they are smaller than 2 cm, they may appear as homogenous, "flash-filling" lesions in the arterial phase, simulating other hypervacular hepatic lesions, including HCC or hypervascular metastases.

In cases of indeterminate CT findings, MRI may help in diagnosis. On MRI, HHs are hypointense on T1WI and typically bright on T2WI. Enhancement patterns are similar to those described on CT (**Fig. 2**). DWI and liver specific contrast agents do not increase the diagnostic accuracy of MRI in the characterisation of HH.

Follow-up imaging is not recommended in typical HHs, except in the rare cases of uncertain imaging findings.

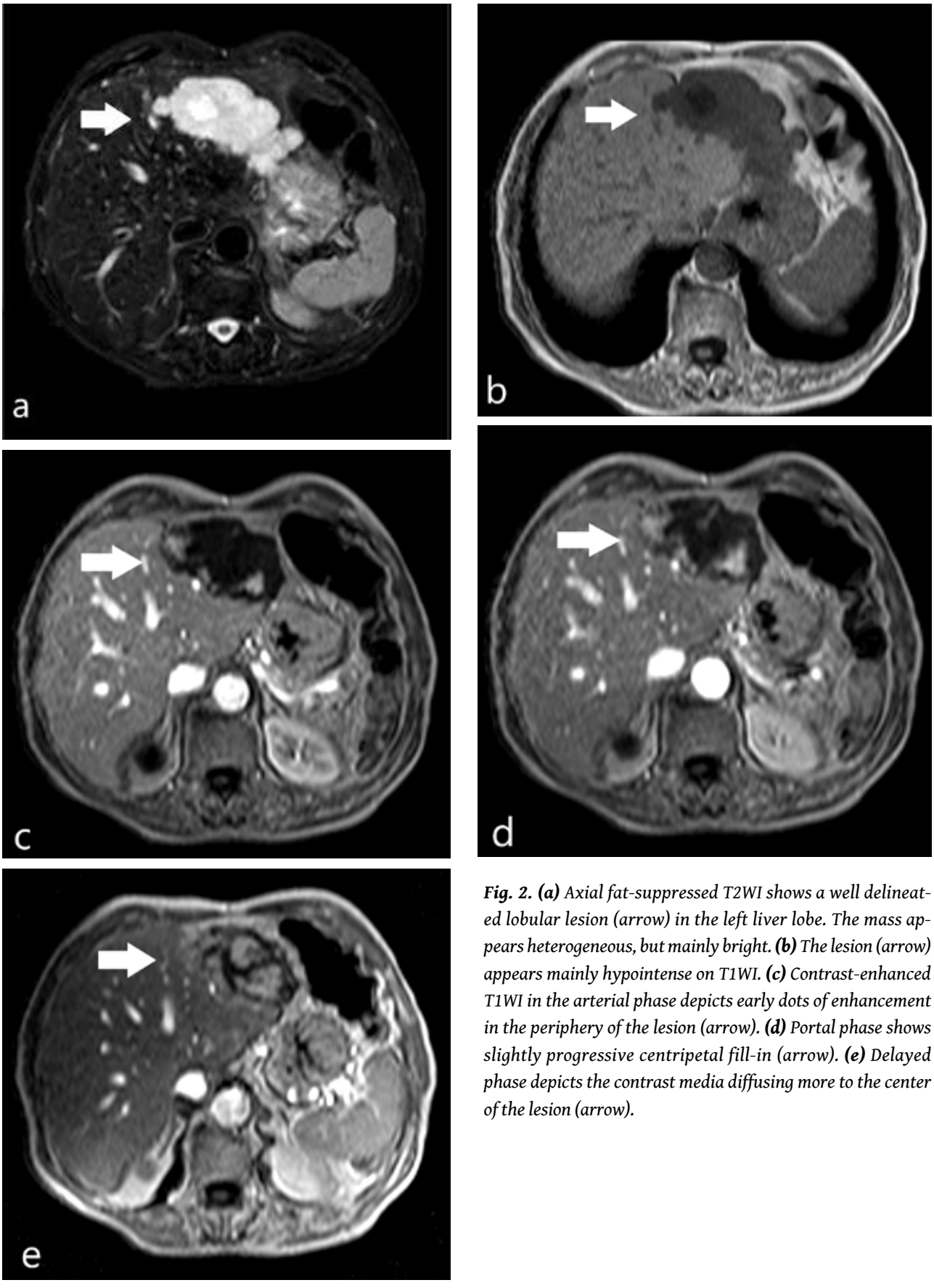

Fig. 2. ***(a)*** *Axial fat-suppressed T2WI shows a well delineated lobular lesion (arrow) in the left liver lobe. The mass appears heterogeneous, but mainly bright.* ***(b)*** *The lesion (arrow) appears mainly hypointense on T1WI.* ***(c)*** *Contrast-enhanced T1WI in the arterial phase depicts early dots of enhancement in the periphery of the lesion (arrow).* ***(d)*** *Portal phase shows slightly progressive centripetal fill-in (arrow).* ***(e)*** *Delayed phase depicts the contrast media diffusing more to the center of the lesion (arrow).*

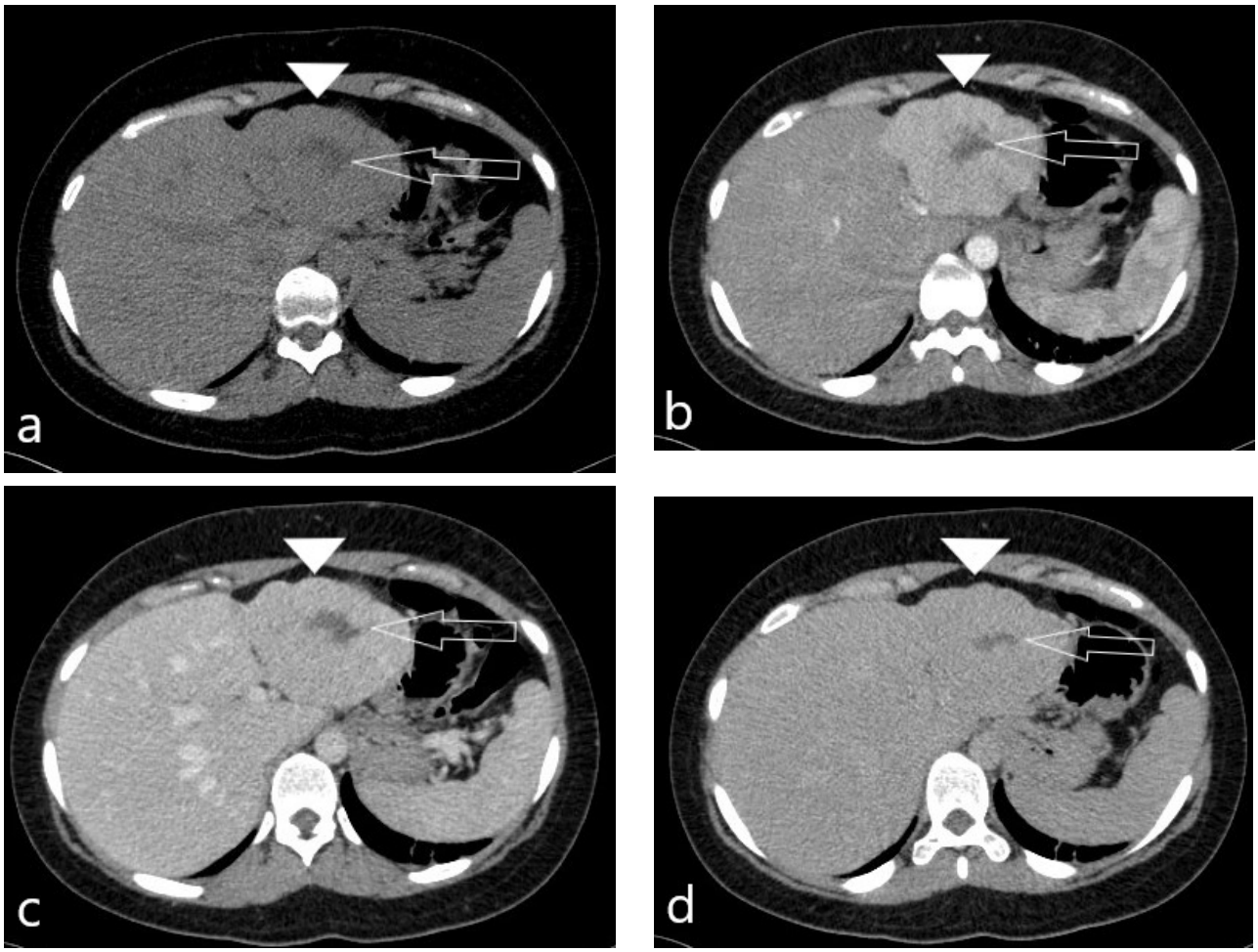

Fig. 3. *FNH detected as a HI on US.* ***(a)*** *Axial unenhanced CT image shows a lobular well-defined lesion in the left liver lobe (arrowhead). The mass appears mainly isodense when compared to normal liver parenchyma, with a hypodense central scar (long arrow).* ***(b)*** *Arterial phase shows liver lesion enhancing, although less than the aorta, detected as a hypervascular mass (arrowhead), with a hypodense, nonenhancing, central scar (long arrow).* ***(c)*** *Portal phase demonstrates lesion isodense (arrowhead) compared to the normal liver. Notice that the central scar is still hypodense (long arrow).* ***(d)*** *Delayed phase shows that the central scar demonstrates enhancement (long arrow).*

HHs often remain stable over time and do not require any treatment. Surgical intervention is recommended in cases of large HHs (measuring more than 10 cm) or in symptomatic cases [3, 4, 23, 26, 47-53, 58].

3.3 Focal nodular hyperplasia

FNH is the second most common benign solid hepatic tumour, with a prevalence of 0.9% in the general population. This tumour is believed to be a hyperplastic reaction of hepatocytes to increased local blood flow, due to an arterial malformation. FNH is typically seen in women in their 40s and 50s. Although 20-40% of patients with FNH may present with symptoms, most are discovered incidentally. Twenty percent of patients will have multiple FNHs and these tumours are often seen in association with HHs. FNH may also be associated with the use of oral contraceptives or the presence of other hypervascular tumours, such as HCA and HCC. Histologically, FNH typically consists of hepatocyte nodules, surrounded by fibrous septa with large malformed arterial branches, not accompanied by interlobular bile ducts or portal veins. It is rarely larger than 5 cm and tends to remain stable or regress over time [3, 4, 23, 26]. A conservative approach is usually recommended. Individuals with a straightforward diagnosis of FNH, not using oral contraceptives, do not require follow-up imaging. Annual US follow-up for 2-3 years is recommended in

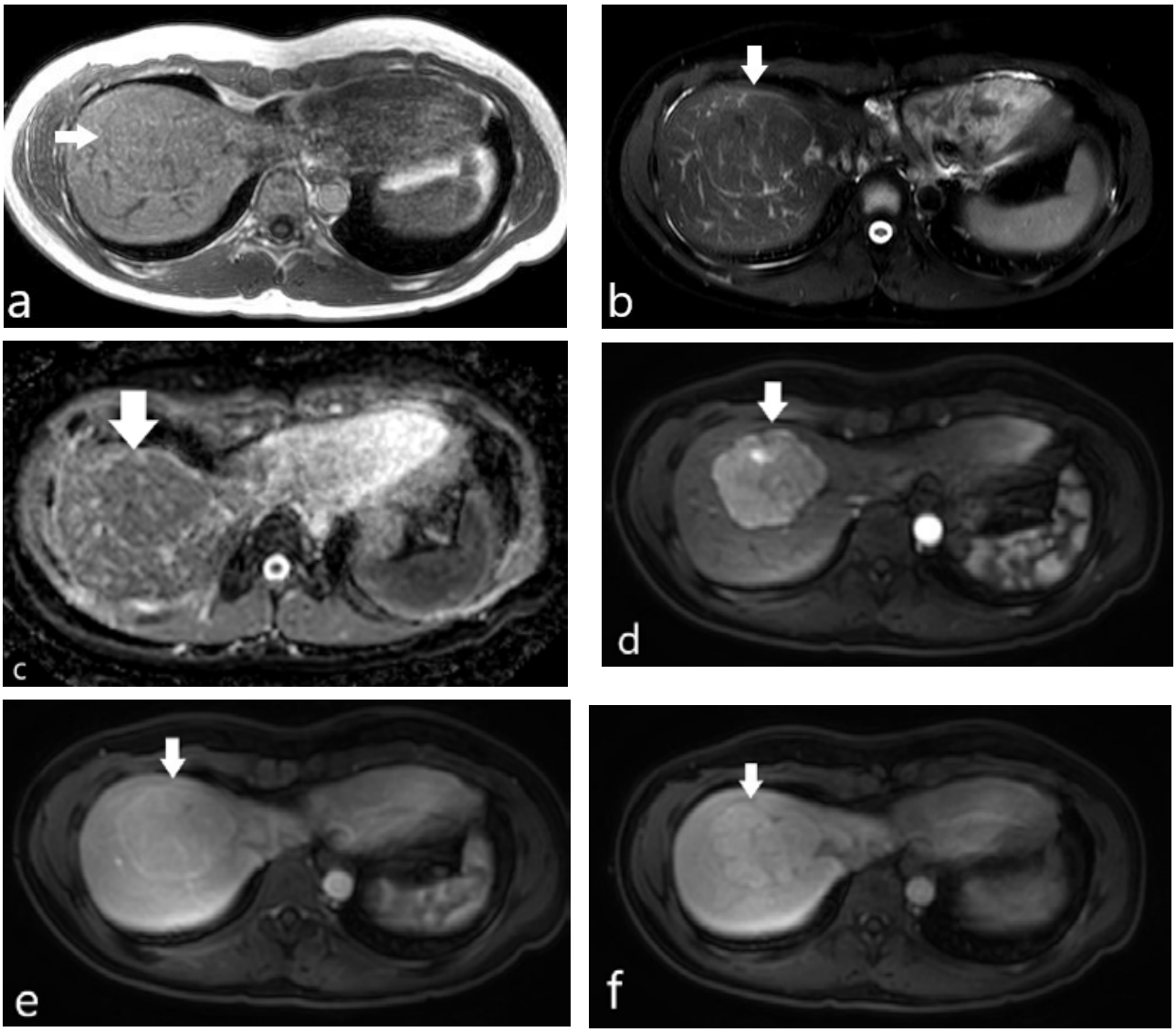

Fig. 4. ***(a)*** *Axial T1WI shows a large, well-defined lobulated mass (arrow) in the right liver lobe, mainly isointense to the surrounding hepatic parenchyma.* ***(b)*** *Axial fat-suppressed T2WI depicts the lesion (arrow) mainly isointense to the liver.* ***(c)*** *Transverse apparent diffusion coefficient map (b=600 s/mm²) demonstrates lesion (arrow) isointense relative to the adjacent liver parenchyma.* ***(d)*** *Axial post-contrast T1WI in the arterial phase shows intense enhancement of the lesion (arrow).* ***(e)*** *Portal phase depicts that the lesion (arrow) has become isointense relative to the surrounding hepatic parenchyma.* ***(f)*** *Axial hepatobiliary phase shows liver lesion (arrow) as a hypervascular mass that appears slightly hyperintense relative to the liver, a finding that is consistent with FNH.*

women with FNH who wish to continue oral contraceptives [23].

The identification of classic FNH by its "spoke-wheel" central scar on cross-sectional imaging is usually diagnostic [3, 4, 23, 47-53, 59-63]. FNH tends to be homogeneously hypodense or isodense on unenhanced CT. The presence of calcifications is rare and may require biopsy for tissue diagnosis. The tumour lobules enhance strongly in the arterial phase and gradually de-enhance on portal and delayed phases, becoming isodense to the surrounding liver. The characteristic hypodense central scar is visible on CT in 32-60% of cases (**Fig. 3**), often enhancing on the delayed phase.

MRI has a higher accuracy compared to CT in the diagnosis of FNH. On MRI, FNH is typically isointense on T1WI and isointense to slightly hyperintense on T2WI. A central scar is visualised in 78% of cases and appears of low T1 and high T2 signal. No areas of restricted diffusion are

typically seen within the tumour. Enhancement patterns are similar to those reported on CT (**Fig. 4**). Occasionally, FNH may exhibit atypical features, including absence of central scar, especially if the tumour measures more than 3 cm, closely simulating HCA, low signal in portal or delayed phases, heterogeneous contrast enhancement, presence of haemorrhage and/or necrosis, presence of a pseudocapsule or low T2 signal of the central scar. MRI with gadoxetate disodium is highly recommended for the characterisation of FNH and especially for the differentiation between FNH and HCA. FNH, unlike HCA, typically demonstrates hyperintensity or isointensity on hepatobiliary phase MRI (**Fig. 4f**) [64-69]. In cases of non-diagnostic imaging findings, immunohistochemical analysis performed on biopsy specimens can usually discriminate FNH from HCA.

3.4 Hepatocellular adenoma

HCAs are rare neoplasms of hepatocyte origin, with an incidence of 0.007-0.012% in the general population. These tumours are seen almost exclusively in females, occurring at any age. The development of HCA is strongly associated with long-term use of oral contraceptives or anabolic steroids. Other risk factors for HCAs are glycogen storage disease Ia and III, obesity and metabolic syndromes such as diabetes mellitus, insulin resistance, hypertension, and dyslipidaemia. HCAs are typically symptomatic, with incidental discovery seen only in 15-25% of cases. These tumours have a small risk for malignant transformation, as well as a propensity for haemorrhage and rupture. Histologically, they contain sheets and cords of normal appearing hepatocytes with abundant intracellular lipid and glycogen. Prominent "free floating" arterial vessels and draining veins are present throughout the tumour. There are three main histologic subtypes of HCAs, based on molecular characteristics, including the inflammatory HCA, which has the greatest risk for haemorrhage, the hepatocyte nuclear factor-1a inactivated HCA, and the type with β catenin activation, which has an increased risk for malignancy [3, 4, 23, 26, 47-53, 63-73].

Of all the benign HIs in an oncologic patient, HCAs are the most difficult to differentiate from liver metastases. Their imaging features depend on the amount of lipid, haemorrhage, or fibrosis within the neoplasm and the status of the surrounding liver parenchyma. HCAs are typically isodense or hypodense on unenhanced CT. Low-density areas within the tumour may correspond to regions of intratumoural fat. Hyperdense areas may also be seen, corresponding to areas of haemorrhage. Unlike FNHs, HCAs do not contain a central scar. Contrast enhancement in the arterial phase is seen in 81-90% of cases, especially in small-sized (less than 3 cm) tumours. The enhancement is moderate and less than that of the arterial vasculature. It is also more heterogeneous and less avid compared to that of FNH. In the portal and delayed phases, the tumour gradually de-enhances.

MRI offers better diagnostic information for the characterisation of HCA. On conventional imaging, the tumour shows variable signal. Hyperintense T1 foci may be seen corresponding to intracellular lipid or haemorrhage. Detection of intratumoural fat with fat-suppressed or in phase/out of phase T1WI helps in differentiating HCA from FNH. DWI usually provides misleading information. The enhancement patterns are similar to those of CT. MRI with gadoxetate disosium is very helpful in distinguishing HCA from FNH. Adenomas are usually hypointense in the hepatobiliary phase [64-69].

Resection should be considered for hepatic adenomas larger than 5 cm. For smaller lesions, withdrawal of oral contraceptives is advised and follow-up with serial imaging.

3.5 Perfusional changes

Perfusional changes, including areas of focal hepatic steatosis or fatty sparing of the liver have characteristic imaging features and locations, which usually permit their accurate characterisation [4, 26, 74-76]. Transient hepatic attenuation differences (THADs, seen on CT) and transient hepatic intensity differences (THIDs, seen on MRI) represent imaging manifestations of regional variations in the balance between arterial, portal, or other venous system of hepatic blood flow. These pseudolesions are typically wedge-shaped, hypervascular regions detected in the arterial phase, which become isodense in the portal and delayed phases. Conditions that cause decrease of portal venous flow, for example venous thrombosis due to hypercoagulable states or septic pyelophlebitis, liver cirrhosis, direct compression of portal vein branches by tumours or abscesses, extrinsic compression of the liver by ribs, subcapsular haematomas, or masses and Budd-Chiari syndrome may result in THADs/THIDs. Markedly hypervascular liver tumours, local inflammation of liver parenchyma caused by cholangitis or abscess, posttraumatic or congenital arteriovenous fistulas, small “flash-filling”

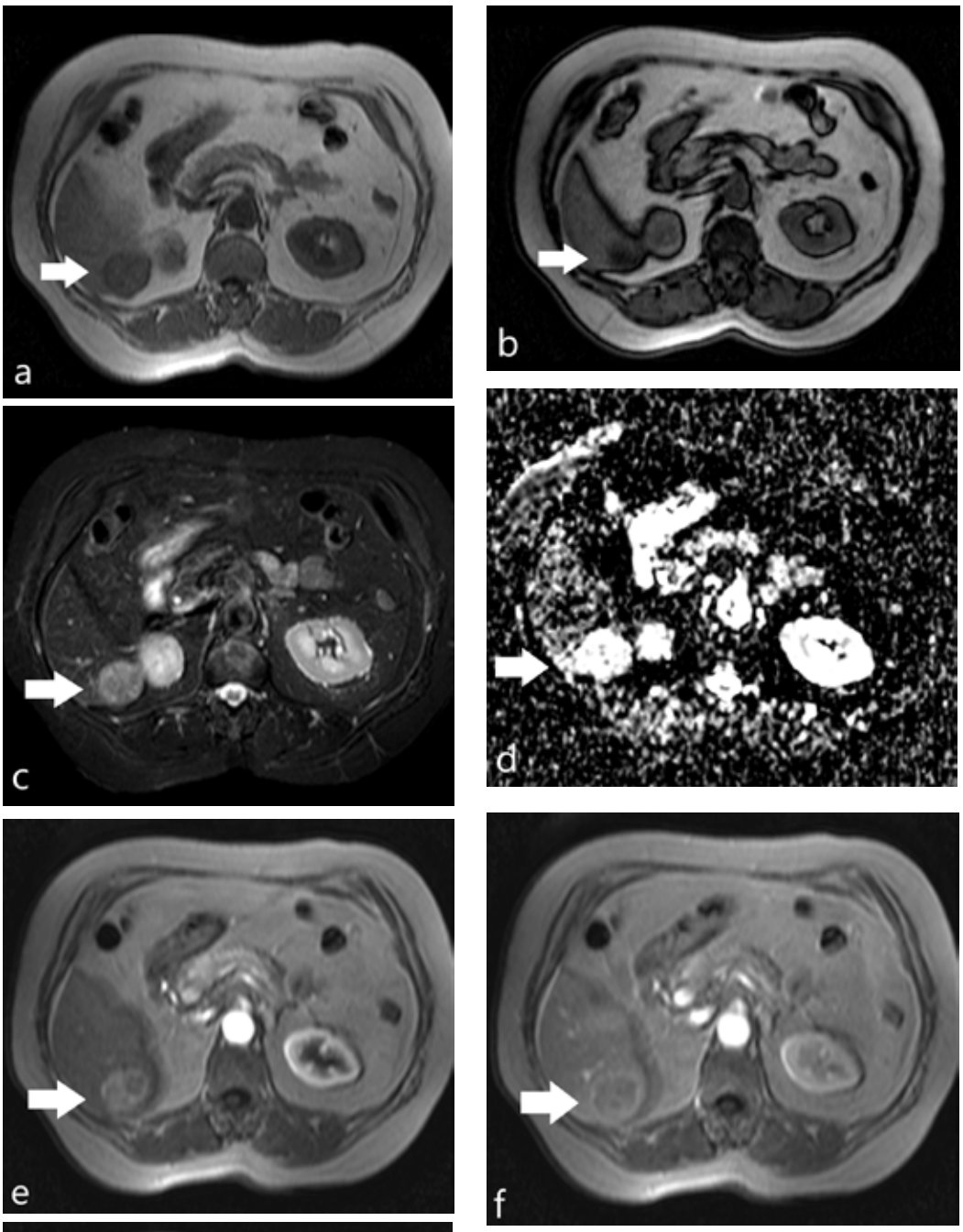

Fig. 5. *Axial* ***(a)*** *in phase and* ***(b)*** *out of phase T1WI demonstrate a focal liver lesion in segment VI (arrow). The mass appears mainly hypointense on T1W1, with significant decrease in signal on out of phase sequence, a finding consistent with the presence of intralesional microscopic fat.* ***(c)*** *Transverse T2WI with fat saturation shows heterogeneous liver lesion (arrow), mainly of high signal intensity.* ***(d)*** *Axial DWI (b=600 s/mm²) shows a bright lesion signal (arrow), due to restricted diffusion. Axial contrast-enhanced T1WI in* ***(e)*** *early arterial,* ***(g)*** *portal and* ***(f)*** *delayed phases. The lesion shows strong, early heterogeneous contrast enhancement, with washout in the portal phase and enhancing tumour pseudocapsule. The lesion was first detected as a hypoechoic nodule on US in a cirrhotic patient and proved to correspond to HCC on histopathology.*

HHs represent other causes of THADs/THIDs due to increased arterial flow [74, 75].

When hepatic steatosis is focal or nodular, differentiation from focal liver lesions, both benign and malignant, may be needed. Focal hepatic steatosis usually has straight margins with the adjacent liver parenchyma, does not cause bulging of liver contour, vessel displacement or invasion and may improve over time. Certain areas of the liver, including the hepatic parenchyma surrounding the gallbladder and adjacent to the falciform ligament in segments II, III and IV, are typical locations for focal fatty infiltration and focal sparing in a normal or diffusely fatty liver. The presence of aberrant venous flow in these areas makes them vulnerable to the above alterations and also to the development of THACs/THIDs [74-76].

3.6 Hepatocellular carcinoma

HCC is the most common primary malignancy of the liver and the second leading cause of cancer-related death worldwide. It occurs more often in men during the fourth and fifth decades of life. The most important risk factors for HCC include cirrhosis, chronic viral B or C hepatitis infection, alcoholic steatohepatitis, and nonalcoholic steatohepatitis. HCC is frequently associated with elevated serum a fetoprotein levels.

Clinical presentation of HCC may vary from asymptomatic cases to patients presenting with right upper quadrant pain, palpable mass, weight loss, ascites, variceal bleeding and paraneoplastic symptoms. It is an aggressive malignancy, with poor prognosis and an overall 5-year survival rate of 15%. However, in cases with disease localised to the liver, a 5-year survival rate of 58% has been reported for patients receiving curative therapy with liver resection or transplantation. The classic histologic features of HCC consist of a well vascularised tumour, typically receiving its blood supply from a branch of the hepatic artery [3, 23, 77-80].

Imaging plays an important role in the management of HCC. Multiphasic CT or MRI allows a reliable non-invasive diagnosis of HCC, with high specificity, helping most patients to avoid biopsy and its potential risks, including bleeding and tumoural seeding. A CT or MRI should be performed in a cirrhotic patient with a newly detected hypoechoic liver nodule, larger than 1 cm on US, an elevated or rising α-fetoprotein in the absence of a liver lesion on US, or in cases of clinical suspicion for the presence of HCC. A characteristic imaging feature of HCC detected in approximately 85% of patients with HCC is that of an arterially hypervascular tumour with washout in the portal venous or delayed phase (**Fig. 5**). On unenhanced CT, HCC is usually hypodense or isodense. The tumour may vary in signal intensity on conventional MRI, depending on the relative lipid content, fibrosis, necrosis and dominant histological pattern. However, HCC is usually hypointense and hyperintense on T1WI and T2WI, respectively, often with decrease of signal on out of phase T1WI, due to intracellular lipid content.

The following imaging findings may also be seen: a mosaic pattern, consisting of multiple nodules of heterogeneous T2 signal, with variable contrast enhancement; hyperintense T1 foci, which may be related to the presence of fatty metamorphosis, copper-binding protein, haemorrhage and/or glycogen; portal or hepatic venous invasion, detected as intraluminal venous material, with enhancement pattern similar to that of primary malignancy; a tumour capsule, consisting of a thick rim of tissue surrounding all or part of tumour, typically enhancing on delayed imaging; and, a central scar, not enhancing after contrast administration [3, 23, 77-80].

DWI increases the detection rate of HCC, particularly for small tumours [81]. Hepatocyte-specific contrast agents have also proved useful in the detection of HCC. Typically, poorly differentiated HCCs do not contain functioning hepatocytes and bile ducts, and therefore demonstrate low signal relative to the surrounding liver parenchyma in the hepatobiliary phase. However, well-differentiated HCCs, accounting for approximately 20% of all HCCs, may show retention of the liver-specific contrast. Features that help in differentiating hyperintense HCC from benign liver lesions such as FNH in the hepatobiliary phase include focal defects of contrast uptake within the tumour and presence of a hypointense rim [81-84].

3.7 Intrahepatic cholangiocarcinoma

Intrahepatic cholangiocarcinoma (ICC) is the second most common primary malignancy of the liver, accounting for about 10% of all cholangiocarcinomas. It arises from the peripheral bile ducts within the hepatic parenchyma, proximal to the secondary biliary radicals. Important risk factors for the development of ICC are primary sclerosing cholangitis, chronic intrahepatic stones, liver fluke infestation, Caroli's disease, choledochal cyst, bile duct adenoma, and cirrhosis. ICC should be strongly suspected in patients with primary sclerosing cholangitis referred for a

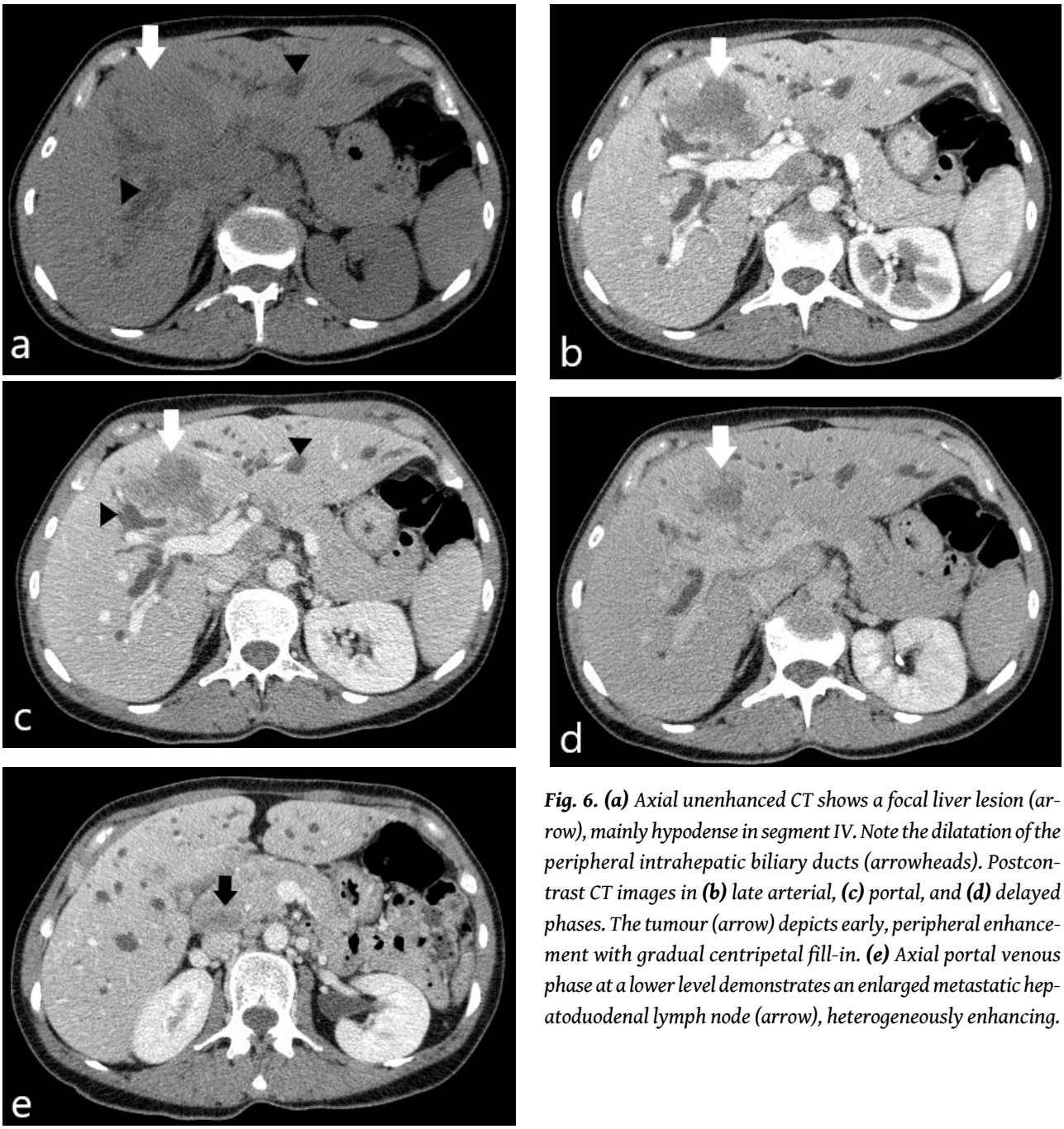

Fig. 6. (a) *Axial unenhanced CT shows a focal liver lesion (arrow), mainly hypodense in segment IV. Note the dilatation of the peripheral intrahepatic biliary ducts (arrowheads). Postcontrast CT images in* ***(b)*** *late arterial,* ***(c)*** *portal, and* ***(d)*** *delayed phases. The tumour (arrow) depicts early, peripheral enhancement with gradual centripetal fill-in.* ***(e)*** *Axial portal venous phase at a lower level demonstrates an enlarged metastatic hepatoduodenal lymph node (arrow), heterogeneously enhancing.*

focal liver lesion.

Patients may present with nonspecific symptoms, including abdominal pain, loss of appetite, weight loss, and malaise. Carbohydrate antigen 19-9 is a serum marker that can be used to identify patients with ICC, with 62% sensitivity and 63% specificity. The prognosis is poor. Only a minority of patients (15%) present with resectable disease, and a median survival of less than three years [3, 23].

The diagnosis of ICC cannot be confidently made with imaging techniques alone. In patients who are poor candidates for surgery, a biopsy specimen should be obtained to confirm the diagnosis if ICC is suspected. However, even on histology, differential diagnosis from a metastatic lesion (especially a colorectal cancer metastasis) may be difficult.

Both CT and MRI may be used for the evaluation of tumour size, presence of satellite lesions, status of vascular structures, assessment of resectability and volumetric

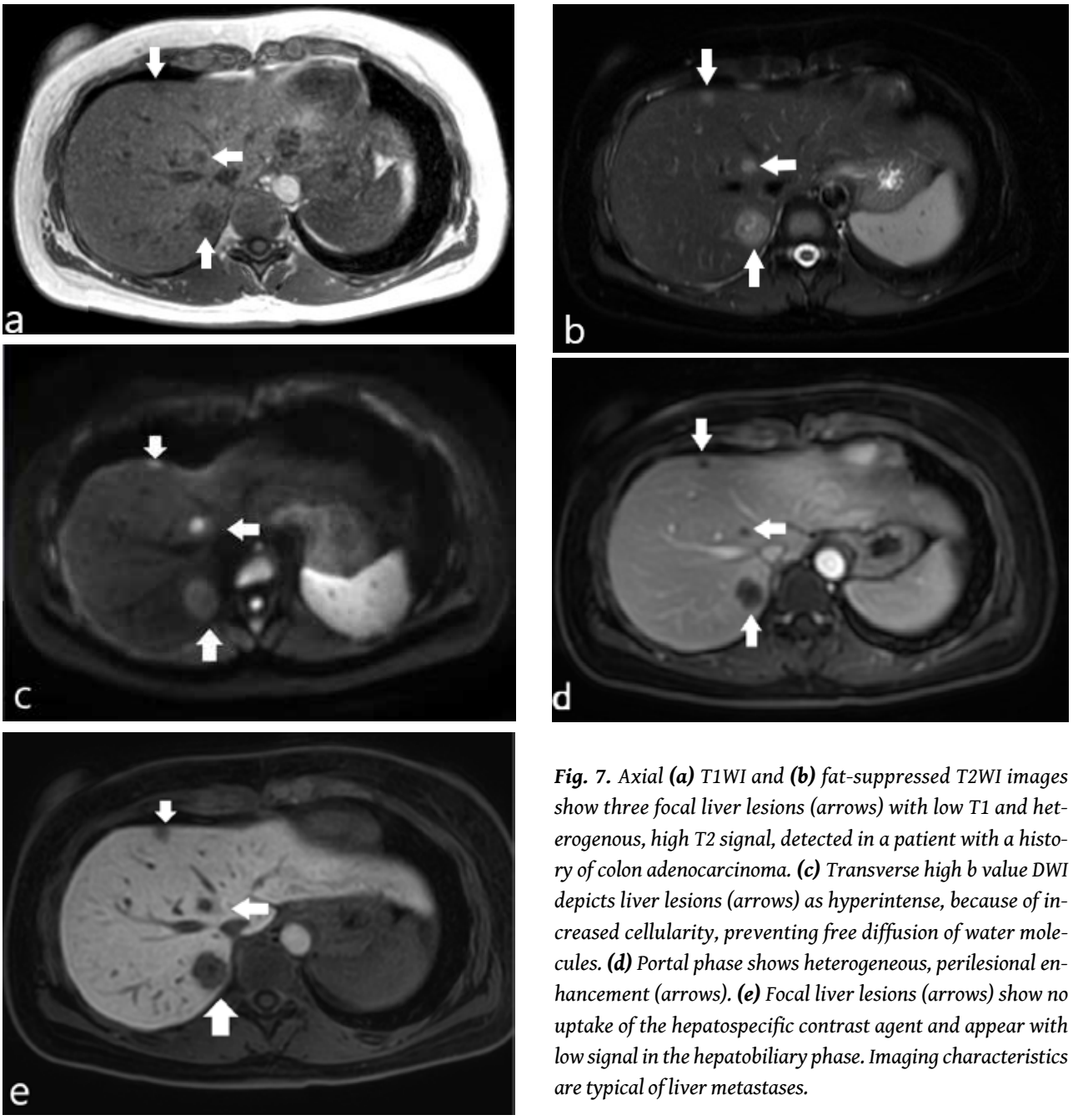

Fig. 7. *Axial* ***(a)*** *T1WI and* ***(b)*** *fat-suppressed T2WI images show three focal liver lesions (arrows) with low T1 and heterogenous, high T2 signal, detected in a patient with a history of colon adenocarcinoma.* ***(c)*** *Transverse high b value DWI depicts liver lesions (arrows) as hyperintense, because of increased cellularity, preventing free diffusion of water molecules.* ***(d)*** *Portal phase shows heterogeneous, perilesional enhancement (arrows).* ***(e)*** *Focal liver lesions (arrows) show no uptake of the hepatospecific contrast agent and appear with low signal in the hepatobiliary phase. Imaging characteristics are typical of liver metastases.*

assessment of potential liver remnants, as these findings can be used to plan treatment [85-88]. CT is the most frequently used imaging modality to assess tumour resectability with a good sensitivity and specificity. MRI is generally comparable to CT and can be used as an alternative imaging technique [87, 88].

Typical appearance of ICC on CT is that of a hypodense mass with irregular margins on unenhanced imaging, minimal or moderate, peripheral incomplete enhancement in early phases, and gradual centripetal enhancement on delayed imaging (**Fig. 6**). This pattern of enhancement closely correlates with the histopathologic characteristics of ICC, namely the presence of abundant viable tumour cells in the periphery of the neoplasm and a varying degree of fibrous stroma centrally, the latter accounting for the delayed enhancement. Other coexisting findings suggesting the diagnosis of ICC include peripheral biliary duct dilatation, capsular retraction, satellite nodules, and invasion of

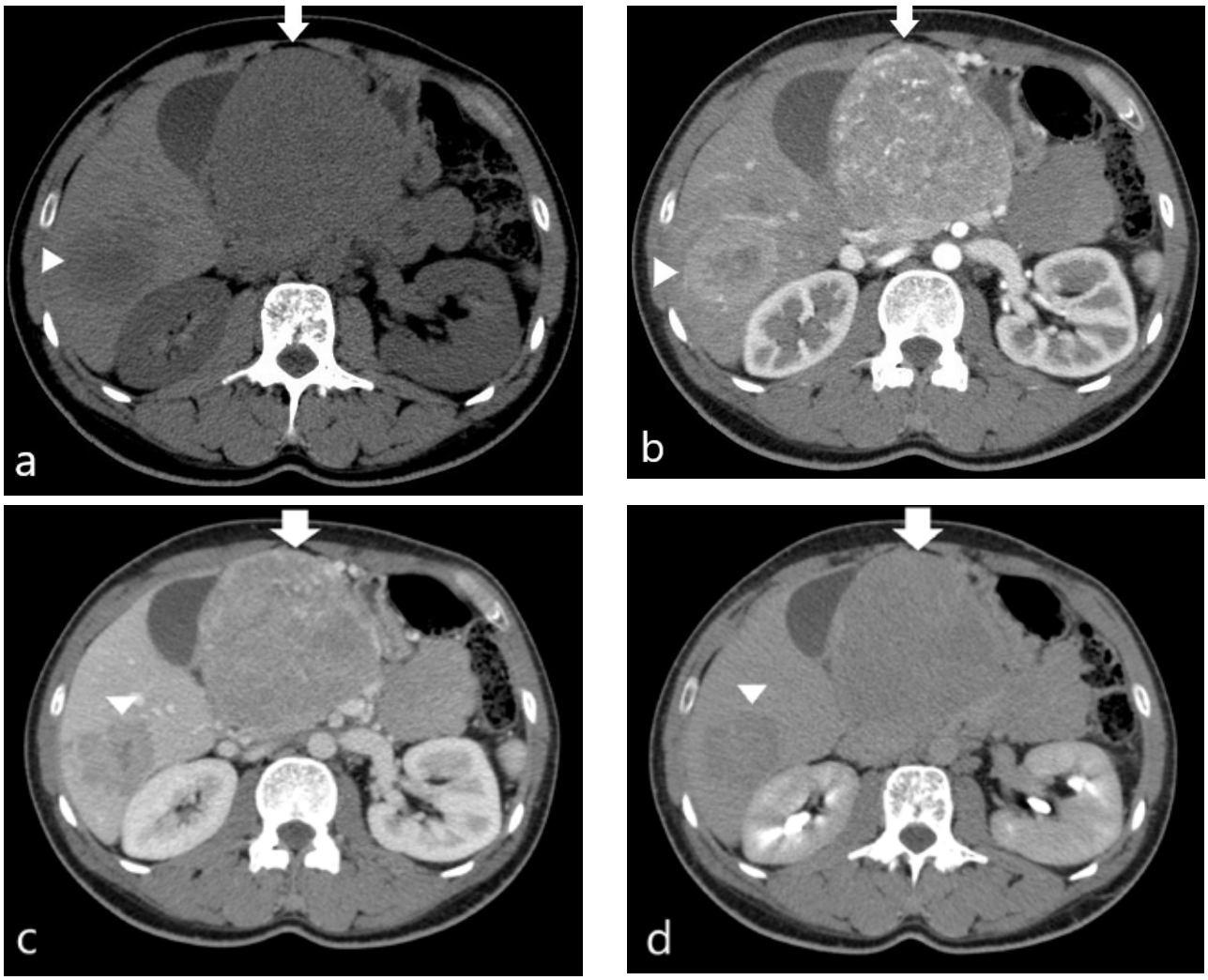

Fig. 8. (a) *Axial unenhanced CT shows a large heterogeneous pancreatic mass (arrow) and a liver lesion (arrowhead) in segment VI. The liver mass lesion appears also inhomogeneous, mainly hypodense when compared to normal liver parenchyma.* ***(b)*** *Axial arterial contrast-enhanced CT image shows both pancreatic and liver lesions avidly and heterogeneously enhancing. Both lesions de-enhance in portal* ***(c)*** *and delayed* ***(d)*** *phases. Imaging findings were suggestive of a neuroendocrine tumour of the pancreas with liver metastasis and were subsequently confirmed on pathology.*

adjacent peripheral portal vein branches.

ICC typically appears with low T1 and high T2 signal. On dynamic imaging, the tumour exhibits the same enhancement patterns, as on CT. On DWI, 52-75% of mass-forming ICCs present with a characteristic target like restriction at high b values. This is caused by a central area, detected hyperintense and hypointense on DWI and apparent diffusion coefficient (ADC) maps, respectively due to the presence of fibrosis, surrounded by peripheral brighter and darker area on DWI and ADC maps, respectively due to highly cellular and vascular tumour cells. This appearance may help to differentiate ICC from HCC. Most ICCs appear hypointense on hepatobiliary phase. However, heterogeneous hypointensity combined with hyperintensity on hepatobiliary imaging, resulting in a target appearance may also be seen, often associated with tumours with abundant central fibrous stroma [3, 23, 85, 86].

3.8 Liver metastases

Liver metastases are 20 times more common than primary liver malignancies. However, HIs are often detected in patients with a history of primary malignancy and not all of these lesions correspond to metastatic foci [3, 26]. Most liver metastases are hypovascular and typically best visu-

alised in the portal venous phase, as hypodense on CT and hypointense on MRI (**Fig. 7**). Colon, lung, breast, and gastric cancers are the most common causes of hypovascular liver metastases. Hypovascular metastases may also have a target appearance due to perilesional enhancement, and this is helpful in differentiating them from benign focal liver lesions. Neuroendocrine tumours, renal cell carcinoma, melanoma, choriocarcinoma, thyroid carcinoma and, less often, breast and pancreatic adenocarcinoma may produce hypervascular metastases. These are most evident in the arterial phase, where they appear hyperdense on CT (**Fig. 8**) and hyperintense on T1WI. Small hypervascular metastases (less than 1.5 cm) may be difficult to differentiate from flash-filling HHs, since both often show rapid, strong enhancement during the arterial phase. However, differentiation is usually possible on subsequent phases. In the portal and delayed phase, hypervascular metastases tend to washout, whereas HHs retain the contrast agent. An additional highly specific distinguishing feature is the target appearance seen in liver malignancies, including hypervascular metastases and HCC. Specifically, malignant lesions often show peripheral washout of contrast medium in the delayed phase, resulting in a target appearance, with the periphery of the lesion detected hypodense, relative to the center [3, 26].

Although the first-line imaging technique for the evaluation of liver metastases is CT, MRI can be used as a problem-solving method. MRI also is recommended as the first-line imaging technique in patients who would undergo curative surgery or metastatectomy. The most sensitive MRI sequences are DWI and hepatobiliary phase imaging. Peripheral rim enhancement, diffusion restriction, and hypointensity on hepatobiliary phase images (**Fig. 7c, e**) are typical findings of liver metastases [89].

4. Conclusion

HIs represent a significant part of modern hepatobiliary imaging. Incidental focal liver lesions are often detected in patients imaged for an unrelated reason. These lesions may represent a source of anxiety and often require an accurate investigation to establish the characterisation of their usually benign nature. Both MDCT and MRI provide satisfactory results in the characterisation of HIs. The following recommendations regarding the management of HIs incidentally discovered on CT were recently reported by the American College of Radiology: 1. no further investigation is needed for HIs smaller than 1 cm, in patients with low risk of having a hepatic malignancy, 2. no further work-up is needed for HIs with distinctly benign features, regardless of patient's risk level, and, 3. further investigation with MRI is recommended for HIs measuring equal or more than 1 cm in high-risk patients. **R**

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Conflict of interest

The authors declared no conflicts of interest.

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