

Value of Liver Contrast-enhanced Sonography to Diagnose Malignant or Benign Tumors

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Purpose: To evaluate the diagnostic benefit of contrast-enhanced ultrasound for the differential diagnosis of liver tumors in clinical practice.

Methods: From January 2010 to October 2010, 14 patients with focal liver lesions without an accurate diagnosis based on B-mode ultrasound and power Doppler ultrasound were examined by contrast-enhanced ultrasound. All 14 patients were referred for CEUS following identification of 1 or more focal liver lesions on conventional ultrasound or CT imaging. After baseline US examination (GE LOGIQ 9), a bolus of 2.4 ml of SonoVue (Bracco, UK) was administered intravenously. The characterization as benign or malignant liver lesion was assessed based on the vascularity pattern and contrast enhancement seen in focal lesions during the arterial, portal, and late phase.

Result: The final diagnosis of liver lesions included 10 benign lesions (hemangiomas n=6, focal nodular hyperplasia n=1, focal fatty sparing n=1, regenerating nodule n=1, hydatid cyst n=1) and 4 malignant lesions (hepatocellular carcinoma n=3, metastases n=1).

Conclusion: Contrast-enhanced US (CEUS) allows the differentiation between benign and malignant liver lesions based on the vascularity pattern and contrast enhancement seen in focal lesions during the arterial, portal, and late phase. The sensitivity and the specificity of CEUS in detecting hepatic tumors is up to 90%.

Keywords: contrast-enhanced ultrasonography, focal liver lesions

Introduction

The characterization of focal liver lesions represents a key element of radiology practices. Due to its relatively low cost, safety and availability, unenhanced ultrasonography (US) is the most widely used initial imaging modality for patients with known or suspected focal liver disease. In addition, US imaging frequently reveals hepatic lesion as an incidental finding in patients undergoing ultrasonography for screening purposes (hepatic disease) or for investigating a non-hepatic disease. Contrast-enhanced computed tomography (CECT) or contrast-enhanced magnetic resonance imaging (CE-MRI) are performed because B-mode imaging is a useful technique for identification of focal liver lesions, but even with the use of color and/or power Doppler it is often difficult to accurately characterize a lesion. Thus, unenhanced US has limited accuracy in the characterization of focal liver lesions (FLLs) compared with computed tomography (CT) and magnetic resonance imaging (MRI).

The introduction of microbubble-based second generation ultrasound contrast agents, that can be imaged using a low mechanical index together with the development of harmonic imaging has enabled us to visualize the microcirculation in real-time and the different vascular phases of the liver (arterial/portal/late) as shown by dynamic CT or MRI [1]. The differential enhancement of the focal lesions compared to normal surrounding liver parenchyma during the hepatic arterial and portal venous phases of the contrast can therefore be used to characterize the lesions. In addition, the persistent enhancement of the normal liver parenchyma in the late phase produced by the second generation contrast agents adds to the capability of differentiating benign from malignant lesions [2,3]. CEUS increased the accuracy for diagnostic imaging of focal liver lesions.

Important for detection of liver metastases are the portal venous and late phases in which metastases show a wash-out and can be detected as hypoechoic lesions in homogeneous enhanced liver parenchyma. The detection of hepatic metastases is substantially improved by CEUS compared to conventional B-mode sonography. Several studies showed sensitivity in detecting liver metastases comparable to that of contrast-enhanced CT and MRI. Lesions that contain haemodynamically normal liver fill in the same way as the normal surrounding tissue and tend to disappear in the late phase. Examples include focal fatty sparing and the regenerating nodules in liver cirrhosis.

Material and method

All 14 patients were found to have one or more focal liver lesions on conventional ultrasound or contrast-enhanced CT before being referred for CEUS. All contrast-enhanced sonography examinations were performed on a GE LOGIQ 9, using the contrast software True Agent Detection, multi-frequency convex array transducer, and technical settings such as mechanical index, frame rate and focal zone were optimized to obtain images of the best quality.

Target lesions were first identified using B-mode ultrasound, then color or power Doppler was carried out to study the vascularization of target lesions and the surrounding parenchyma.

The second step of sonography was performed after an intravenous bolus injection of SonoVue (Bracco, Italy), the second-generation contrast agent. The agent is provided as a sterile, lyophilized powder contained in a septum-sealed vial. A white, milky suspension of sulphur hexafluoride (SF₆) microbubbles was obtained by adding 5 ml of physiological saline (0.9% sodium chloride) to the powder (25 mg), using standard aseptic techniques, followed by hand



Fig. 1. Typical hyperechoic appearance of a hemangioma on conventional B mode Ultrasound

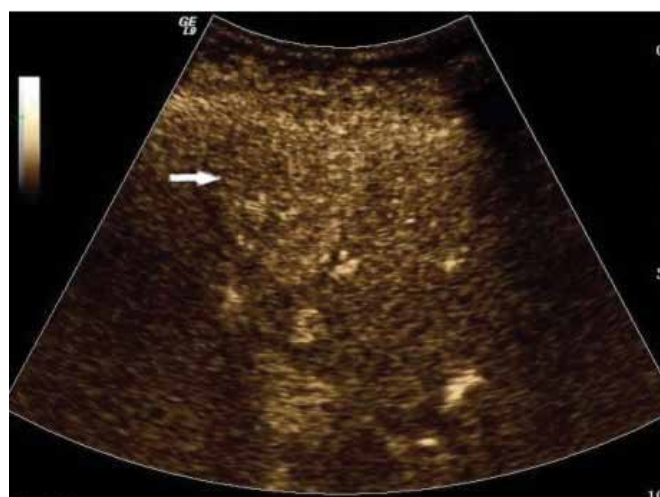


Fig. 2. Hyperechoic appearance of a hemangioma in the late phase in CEUS

agitation. Each patient received 2,4 ml SonoVue via a 20-gauge intravenous catheter placed in the ante-cubital vein followed by 10 ml of saline flush.

The hemodynamic behavior of SonoVue during the hepatic arterial (15–25 seconds), portal venous (25–120 seconds) and late vascular phases (120–300 seconds) was evaluated to characterize the lesion as recommended in European guidelines. All sonographic examinations were recorded on digital disks.

Results

Of the 14 patients, 6 were males and 8 were females. CEUS identified 4 malignant liver tumors and 10 benign lesions.

Of the 6 hemangiomas, 4 had typical appearances of hyperechoic focal lesions on B-mode ultrasound (Figure 1) and showed rapid peripheral filling-in during the arterial phase of contrast enhancement and became isoechoic or hyperechoic with the surrounding liver in the portal venous and late phases (Figure 2). Two hemangiomas were initially hypoechoic, but demonstrated rapid peripheral

filling-in to become isoechoic with the surrounding liver in later phases of the examination.

Focal fatty sparing was shown in one patient to be a hypoechoic, well-defined area on B mode which became isoechoic with the surrounding liver during all phases of CEUS.

The one case of focal nodular hyperplasia demonstrated early central spoke wheel-shaped contrast enhancement, followed by diffuse homogeneous enhancement in the arterial phase.

A focal regenerating nodule was seen to be a well-defined hyperechoic lesion on B mode and was obscured when CEUS was performed.

One hypoechoic lesion on B-mode showed no contrast enhancement and was diagnosed as hydatid cyst.

The 3 hepatocellular carcinomas (2 of them with histological confirmation – Figure 3, 5) demonstrated rapid enhancement in arterial phase and became hypoechoic in the late phase (Figure 4, 6). One case of metastasis demonstrated rapid peripheral enhancement in the arterial phase

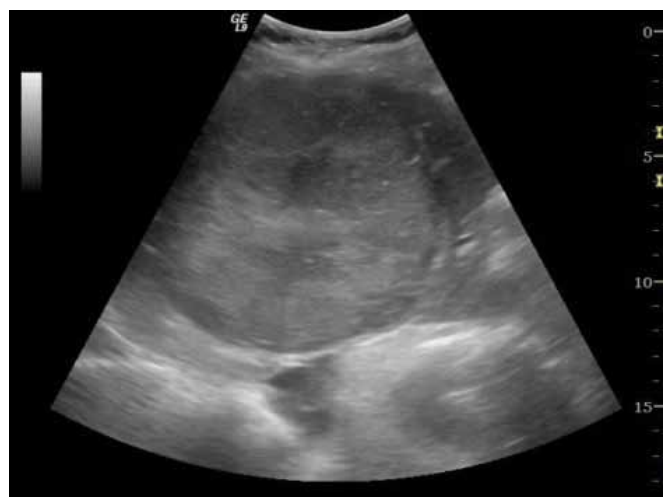


Fig. 3. Hepatocellular carcinoma on conventional B mode Ultrasound



Fig. 4. Contrast wash-out occurred in the same lesion in the late phase



Fig. 5. Hypoechoic tumor in a cirrhotic liver (HCC)

and showed subsequent rapid wash-out of contrast, the lesion becoming hypoechoic to the surrounding liver in the late phase suggesting a hypovascular metastasis.

Discussion

Ultrasound is the first choice of imaging investigation for abdominal disorders and is followed by the discovery of a large number of focal liver lesions. However, conventional US have a low specificity in characterizing FLLs; its specificity in differentiating benign from malignant lesions ranges between 23% and 68% on a baseline study. Color and spectral Doppler US is limited in the detection of tiny vessels and/or low-flow states in all FLLs. CEUS characterization of liver lesions is based on the comparison of enhancement level of the lesion to normal liver parenchyma during all three vascular contrast phases, i.e. arterial, portal-venous and late.

The gold standard for tissue characterization is histology. The sensitivity of fine-needle aspiration cytology (FNAC) for detecting hepatic malignancy is reported to be 90–93% [4], similar to the diagnostic accuracy obtainable with radiological investigations, including CEUS, which have an up to >90% sensitivity [5]. Furthermore, biopsy of hepatic adenomas, focal nodular hyperplasia, and hemangiomas also carries an increasing bleeding risk, so other diagnostic imaging methods must be used. Several studies have demonstrated the value of CEUS in the characterization of FLLs [6].

In all the patients followed in our service, the location and size of the lesion were assessed on unenhanced and CEUS scans. In addition, the vascularity and pattern of contrast enhancement of the lesion (hypo-echoic, hyper-echoic, iso-echoic) compared with the adjacent liver parenchyma during the hepatic arterial, portal venous and sinusoidal phases were evaluated for the CEUS diagnosis. The diagnoses in terms of the nature (malignant or benign) were based on the pre-contrast fundamental and color/power Doppler US, and the contrast enhanced US (CEUS). CEUS images and/or movie clips were stored for



Fig. 6. Contrast wash-out occurred in the same lesion in the late phase

assessment of vascularization patterns in the arterial, portal and late phases. The number, location, size and characterization of the lesions were recorded. The principal difference between benign and malignant liver lesions was their appearance during the late phase of contrast enhancement. Malignant lesions were hypoechoic compared to normal liver parenchyma in this phase, whereas benign lesions were hyperechoic or isoechoic.

CEUS is a real-time imaging technique with important features: provides speed, safety, accurate diagnosis, comfort and cost-effectiveness. Economical impact of CEUS has to be mentioned. In Belgium, for example, the total cost for one abdominal examination (contrast included) is 138,04 Euro for CEUS, 221,70 Euro for CECT, 210,07 Euro for CEMRI [7]. A French study compared the examination costs for the three imaging modalities (CEUS, CT-scan and MRI): 155,20 Euro for CEUS, 191,65 Euro for CT-scan and 322,30 Euro for MRI [8].

Conclusion

Contrast-enhanced real-time ultrasonography is a promising approach in the non-invasive characterisation of focal liver lesions and can be useful as a first-line imaging technique when a focal liver lesion is detectable on ultrasonography. CEUS has the advantages of the absence of ionizing radiation, real-time examination, safety, comfort and cost-effectiveness, it also may limit the need for further investigations and may replace more expensive and invasive imaging technique.

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