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Original Article

Characterization of Focal Liver Lesions Using SonoVue, Contrast-enhanced Ultrasound

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Abstract

Introduction: Focal liver lesions are frequently discovered in daily practice owing to extensive use of imaging methods. Their nature must be elucidated for prognosis assessment and to decide on therapeutic strategy.

Aim: The aim of this article is to study the sonographic characterization of focal liver lesions can be improved using SonoVue®-enhancement.

Materials and Methods: This prospective study was conducted in 30 patients with focal liver lesions identified in conventional gray-scale ultrasound at Barnard Institute of Radiology, Madras Medical College.

Results: Out of total 30 cases, contrast-enhanced real-time ultrasonography (CEUS) identified 9 hepatocellular cancer (HCC) cases and 8 cases were confirmed by fine-needle aspiration cytology (FNAC) as HCC. Four cases of HCC were identified by both contrast-enhanced computed tomography (CECT) and conventional gray-scale ultrasonography (USG). Out of the 17 cases of metastatic deposits confirmed by FNAC CEUS, CECT and conventional gray-scale USG identified 16 (94%), 14 (82%), and 11 (65%) cases, respectively.

Conclusion: CEUS is a promising approach in the non-invasive characterization of focal liver lesions and can be useful as a first-line imaging technique clinically when a focal liver lesion is detectable on USG.

Key words: Contrast-enhanced ultrasound, Enhancement pattern, Focal liver lesions, Ultrasound contrast agents

INTRODUCTION

The characterization of focal liver lesions forms a key element in the majority of radiological practices. While B-mode imaging is useful for the identification of focal liver lesions, it is often difficult, even with the use of color Doppler, to accurately characterize a focal liver lesion.[1] Contrast-enhanced real-time ultrasonography (CEUS) is a promising approach in the non-invasive characterization of focal liver lesions and can be useful as a first-line imaging technique clinically when a focal liver lesion is detectable on ultrasonography (USG).[2] Microbubble CEUS utilizes ultrasound contrast agents (UCAs), which perform as blood pool tracers, have overcome the limitations of conventional B-mode and color or power Doppler ultrasound (US) and enable the display of parenchymal microvasculature.[3] Dependent on contrast agent and US-mode, the dynamic lesion enhancement pattern is visualized during intermittent or continuous insonation. Enhancement patterns are described during subsequent vascular phases (e.g. arterial, portal-venous, and late phase for liver lesions), similar to contrast-enhanced computer tomography (CECT) and/or contrast-enhanced magnetic resonance imaging (MRI).[4] UCA remains in the intravascular space, whereas the majority of currently approved contrast agents for CT and MRI are rapidly cleared from the blood pool into the extracellular space. An inherent advantage of CEUS is the possibility to assess the contrast enhancement patterns in real time, without the necessity to predefine scan-time points or to perform bolus-tracking and the possibility to perform repeated examinations due to the excellent patient toleration of UCA.[5-7]

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Aim

The aim of this study is to characterize focal liver lesions by CEUS using SonoVue, an UCA, and to assess sensitivity, specificity, and positive predictive value of CEUS in detecting benign and malignant focal liver lesions in comparison with CECT and histopathological correlation.

MATERIALS AND METHODS

This prospective study was conducted in 30 patients with focal liver lesions identified in conventional gray-scale US at Barnard Institute of Radiology, Madras Medical College.

Inclusion Criteria

Those with focal liver lesions detected by conventional USG abdomen and those in renal or hepatic failure were included in the study.

Exclusion Criteria

Pregnant and breastfeeding women, severe hypersensitivity or previous allergic reactions, critically ill patients, severe coronary artery disease, post-extracorporeal shock wave lithotripsy patients within 24 h, under 18 years, uncontrolled systemic hypertension, and adult respiratory distress syndrome were excluded from the study. Triple-phase CECT abdomen was done for 23 patients, and enhancement patterns of focal liver lesions were obtained and analyzed during arterial, portal venous, and delayed phases. CECT abdomen was not done for 7 patients (5 had renal failure, and 2 had hepatic failure) since intravenous contrast was contraindicated in them. Then, a bolus of 1.0-2.4 ml of SonoVue was administered intravenously for all the 30 patients including those with hepatic and renal failure, since SonoVue is not contraindicated in patients with hepatic and renal failure. Real-time imaging of focal liver lesions was done continuously for 3 min using harmonic imaging mode with low mechanical index (MI) (0.08-0.11) in Siemens Acuson Antares USG machine, and enhancement patterns of focal liver lesions in CEUS were obtained, recorded, and analyzed during arterial, portal venous, and delayed phases. Thereafter, both the results were compared. Out of 30 patients, 25 patients were subjected to pathological examination and results obtained. Five patients with hemangioma were not subjected to pathological examination since those lesions are highly vascular.

RESULTS

The study population consisted of 30 consecutive patients with suspected focal liver lesions. The study group consisted of 18 male and 12 female patients, between the age of 11 and 70 years (with a mean age of 40 years). Out of the 30 patients, 5 patients had renal failure, and 2 patients had hepatic failure, so CECT not done. In Table 1, out of total 30 cases, CEUS identified 9 hepatocellular cancer (HCC) cases, and 8 cases were confirmed by fine-needle aspiration cytology (FNAC) as HCC. Four cases of HCC were identified by both CECT and conventional gray-scale USG. Out of the 17 cases of metastatic deposits confirmed by FNAC CEUS, CECT, and conventional gray-scale USG identified 16 (94%), 14 (82%), and 11 (65%) cases, respectively. 12 of the 16 metastases in CEUS were "hypovascular" and showed rim enhancement in the arterial phase; the most common primaries in this group were colorectal (n = 7), stomach (n = 2), and bronchogenic carcinoma (n = 3). The remaining 4 metastases were "hypervascular" on arterial phase imaging with homogeneous enhancement; the primaries in these patients were small-cell lung cancer (n = 1), thyroid carcinoma (n = 2), and renal cancer (n = 1). In the portal venous and delayed phase, all 16 metastases were hypoechoic compared with normal liver. Five cases of hemangioma were identified by both CECT and CEUS, and 4 cases were identified by conventional gray-scale USG. The results of this study show that SonoVue improves sensitivity and specificity in discrimination between benign and malignant focal liver lesions when compared with baseline B-mode sonography. Out of total 30 cases, 5 of the lesions were benign; correct diagnosis of benignity was made in 4 (80%) of these on baseline US and in 5 (100%) after SonoVue. One benign lesion was misinterpreted as malignant after contrast: One benign cyst which did not fill with contrast after the arterial phase. Homogeneous SonoVue enhancement in the late phase is a parameter for benign lesions, whereas more conspicuousness of the lesion due to washout in the late phase is a parameter for malignant lesions. Late-phase imaging with SonoVue is important for differentiation between benign and malignant lesions and early-phase imaging is important for characterizing final diagnosis of the lesions. Peripheral globular-nodular enhancement is predictive for hemangioma and was found in 17% (5 cases) of hemangioma cases in this study. This parameter is comparable with the peripheral globular nodular

Table 1: Distribution of diagnosis

Diagnosis	Gray-scale USG	CECT	CEUS	Final diagnosis
HCC	4	4	9	8
HCC/metastasis	5	-	-	-
Metastasis	11	14	16	17
Hemangioma	4	5	5	5
Normal	5		-	
Begin cyst	1		-	
Total	30	23*	30	30

CECT: Contrast-enhanced computed tomography, CEUS: Contrast-enhanced real-time ultrasonography, HCC: Hepatocellular cancer, USG: Ultrasonography

enhancement found on CT. However, the results observed with real-time examination of SonoVue are better than findings reported with gray-scale USG, which showed only 4 of 5 patients with hemangioma. The higher sensitivity of SonoVue is due to the advantages of the low-MI real-time examination with a second-generation contrast agent. The typical enhancement pattern of primary liver carcinoma was an early intranodular enhancement and early washout with whole-lesion or mosaic enhancement.

On CEUS, the typical hemodynamic pattern of HCC was the whole-lesion enhancement or mosaic enhancement in the arterial phase with washout in the late phase (sensitivity 100%; specificity 77%; and positive predictive value 61%).

Diagnostic accuracy of contrast enhancement patterns in characterizing HCC in CEUS (sensitivity 100%; specificity 77%; and positive predictive value 61%) is higher when compared to that of CECT (sensitivity 80%; specificity 73%; and positive predictive value 44%).

On CEUS, the typical hemodynamic pattern of metastasis was the whole-lesion or peripheral rim enhancement in the arterial phase with washout in the late phase (sensitivity 100%; specificity 61.5%; and positive predictive value 77.3%).

Diagnostic accuracy of contrast enhancement patterns in characterizing metastasis in CEUS (sensitivity 100%; specificity 61.5%; and positive predictive value 77.3%) is higher when compared to that of CECT (sensitivity 100%; specificity 30%; and positive predictive value 65%).

Homogeneous enhancement in the late phase was predictive for benign lesions ($P < 0.0001$). Diagnostic accuracy of characterizing benign lesions in CEUS (sensitivity 100%; specificity 100%; and positive predictive value 100%) is higher when compared to that of gray-scale USG (sensitivity 40%; specificity 88%; and positive predictive value 40%).

Conversely, no contrast enhancement in the late phase was predictive for malignant lesions ($P < 0.0001$). Diagnostic accuracy of characterizing malignant lesions in CEUS (sensitivity 100%; specificity 100%; and positive predictive value 100%) is higher when compared to that of gray-scale USG (sensitivity 72%; specificity 60%; and positive predictive value 90%).

Diagnostic accuracy of characterizing HCC in CEUS (sensitivity 87%; specificity 90.9%; and positive predictive value 80%) is higher when compared to that of CECT (sensitivity 37.5%; specificity 93.3%; and positive predictive value 75%) and gray-scale USG (sensitivity 25%; specificity 68.18%; and positive predictive value 22.2%).

Diagnostic accuracy of characterizing metastasis in CEUS (sensitivity 94%; specificity 100%; and positive predictive value 100%) is higher when compared to that of CECT (sensitivity 92%; specificity 79%; and positive predictive value 85%) and gray-scale USG (sensitivity 65%; specificity 62%; and positive predictive value 69%) (Figures 1 and 2).

Diagnostic accuracy of characterizing hemangioma is similar in CEUS and CECT (sensitivity 100%; specificity 100%; and positive predictive value 100%), and it is higher when compared to that of gray-scale USG (sensitivity 40%; specificity 92%; and positive predictive value 50%) (Figures 3-5).

DISCUSSION

The characterization of a focal liver lesion requires the assessment of morphological characteristics as well as vascularity and enhancement patterns within the lesion. Therefore, the administration of a contrast agent,

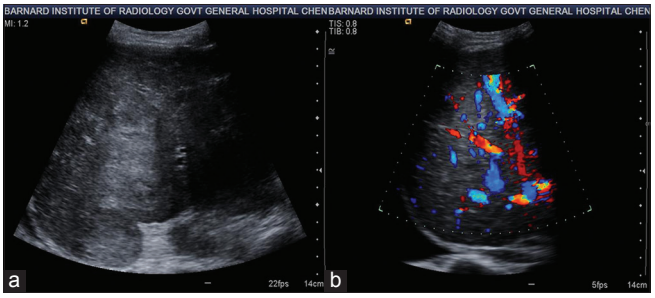

Figure 1: (a and b) Conventional gray-scale ultrasonography - large heteroechoic lesion in right lobe of the liver with high vascularity. Hypervascular metastasis

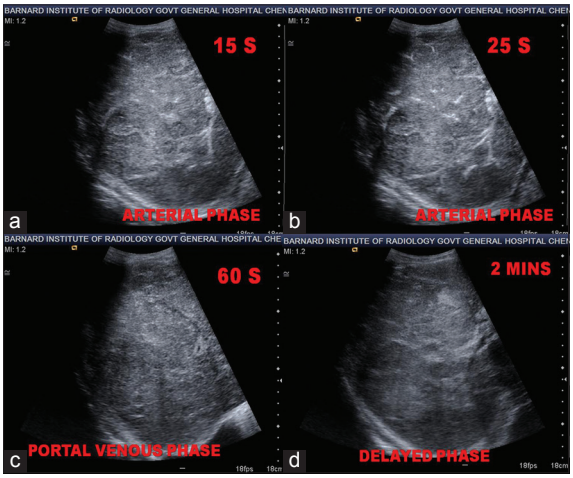

Figure 2: (a-d) Contrast-enhanced real-time ultrasonography - hypervascular metastasis - arterial phase: Hyperenhancing, complete; portal vein phase: Iso- to hypo-enhancing; parenchymal phase: Hypoenhancing or washout. Hypervascular metastasis

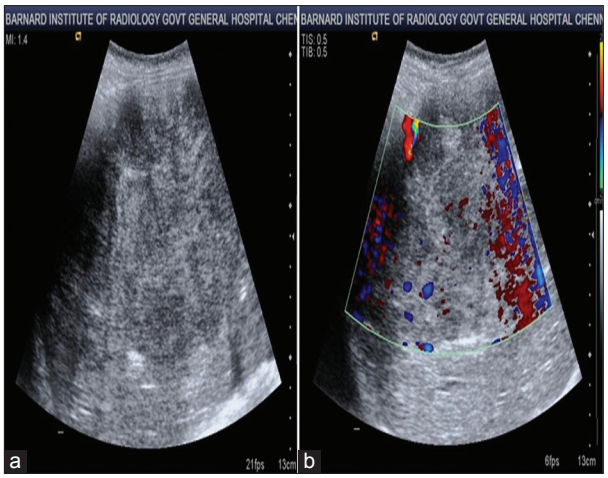

Figure 3: (a and b) Conventional gray-scale ultrasonography - large hyperechoic lesion noted involving both lobes of the liver. Typical hemangioma

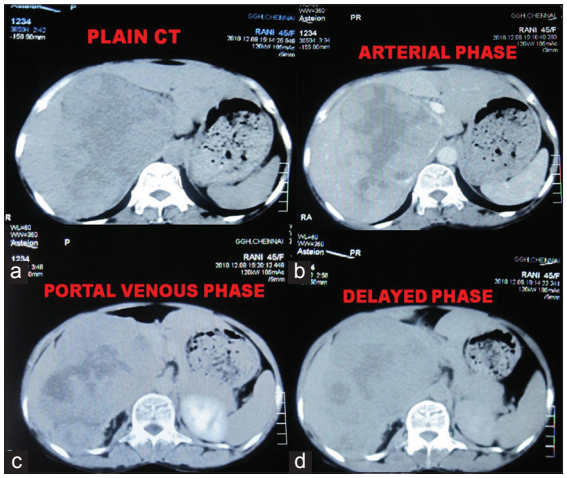

Figure 4: (a-d) Contrast-enhanced computer tomography - Arterial phase: Peripheral nodular or globular enhancement, no central enhancement, rim enhancement; portal vein phase: Partial/complete centripetal filling; parenchymal phase: Persistent enhancement. Typical hemangioma

demonstrating the intratumoral vascularity and blood flow, gives essential information for the characterization of focal liver lesions. Contrast-enhanced imaging with US has two major advantages.[5] The microbubble contrast agents are real blood-pool agents, not leaving the intravascular space, and[6] a continuous imaging over the whole-enhancement period with high temporal resolution is possible, not limited to distinct, pre-defined time points.[8,9] Furthermore, CEUS has many other advantages, such no exposure to radiation, and absence of nephrotoxic contrast agents and large availability of machines. There are already several studies published, demonstrating the safety and efficacy of this method for the diagnosis of focal liver lesions; however, most of these studies were single-center studies performed with just one type of machine. The results of this study confirm the excellent performance of real-time

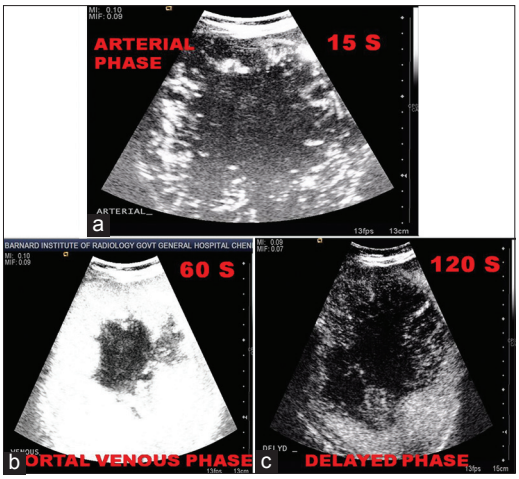

Figure 5: (a-c) Contrast-enhanced real-time ultrasonography - Arterial phase: Peripheral nodular or globular enhancement, no central enhancement, rim enhancement; portal vein phase: Partial/complete centripetal filling; parenchymal phase: Persistent enhancement. Typical hemangioma

CEUS for focal liver lesion characterization which is clearly superior to that of unenhanced US, as shown already in other studies with SonoVue® and other microbubble contrast agents.[10-13]

CONCLUSION

Conventional US, being readily available, economical, and safe, remains the imaging modality most widespread worldwide in detecting hepatic focal lesions. CEUS gas has greater sensitivity, specificity, and positive predictive value in characterizing focal liver lesions than CECT and conventional gray-scale USG. SonoVue-enhanced sonography has greater sensitivity and specificity than baseline sonography for the differentiation of benign and malignant liver lesions. CEUS is a promising approach in the non-invasive characterization of focal liver lesions and can be useful as a first-line imaging technique clinically when a focal liver lesion is detectable on USG.

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