ORIGINAL PAPERS

Adv Clin Exp Med 2014, **23**, 1, 85–89
ISSN 1899–5276

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Characteristics of Focal Liver Lesions in Arterial Phase on Contrast-enhanced Ultrasound and Contrast--enhanced Computed Tomography – Comparative Study*

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. To compare the features of focal liver lesions in the arterial phase on contrast-enhanced ultrasonography (CEUS) and contrast-enhanced computed tomography (CECT).
Material and Methods. A total of 38 lesions in 29 patients with focal liver lesions (FLL) were examined with CEUS and CECT. The characteristics of the enhancement were determined, especially in the early arterial phase (0~25 s). The enhancement of FLL in CEUS and CECT graded as follows: grade 0 – no enhancement; grade I – peripheral enhancement or spotty enhancement at the center; grade II – spoke-like, honeycomb-like or heterogeneous enhancement; grade II – entire enhancement.
Results. On CEUS, the arriving time within 25 s was found in 36 out of 38 lesions (94.73%) and the peak time within 25 s in 29 lesions (76.32%). The number of grade II–III FLL was 25 (65.79%) on CEUS, and 13 (34.21%) on CECT showing a significant difference ($p < 0.05$).
Conclusions. Compared with CECT, CEUS plays an important role in the diagnosis of FLL with enhancement in the early arterial phase (< 25 s) (**Adv Clin Exp Med 2014, 23, 1, 85–89**).

Key words: ultrasonography, helical computed tomography, contrast, focal liver lesions.

The conventional ultrasonography is a preferred method for the diagnosis of focal liver lesion (FLL) and has been widely used in screening liver lesions. However, due to the lack of data on enhanced images, ultrasonography is found to be less accurate than contrast enhanced computed tomography (CECT) in identifying liver neoplasms [1–3]. With its great advantages of imaging techniques, the contrast enhanced ultrasonography (CEUS) has made a breakthrough and plays crucial roles in the diagnosis of FLL [4–9]. CEUS allows a whole-course observation of contrast enhancement, whereas CECT is performed at pre-designed time points (generally in arterial, portal and equilibrium phases). On CECT, the arterial phase usually occurs from 25 s to 30 s and the presentations before the arterial phase (0–25 s) is often overlooked, although it may provide important diagnostic information. Therefore, in the present study, the characteristics of FLL on CEUS and CEUT were compared in an effort to improve diagnostic accuracy.

Material and Methods

Subjects

A total of 29 patients with FLL (38 lesions) were recruited from our hospital from August 2009 to April 2011. There were 17 males and 12 females with a mean age of 50.3 ± 6.9 years (range: 24~76 years). The mean diameter of lesions was 4.7 ± 0.8 cm (range: 1.4~14.2 cm). For patients with multi-lesions, 2~3 lesions which were clearly

This research project was supported by Shanxi Scholarship Council of China (Grant 2013-058).

displayed on CEUS were selected for further analysis. Procedures were explained to each subject and informed consent was obtained before the study. The whole study was approved by the Ethics Committee of the Shanxi Medical University.

The 38 lesions were confirmed by pathological examination, angiography or follow-up and included hepatic cell carcinoma (HCC) (n = 9), metastatic liver cancer (n = 10), hepatic hemangiomas (n = 9), focal nodular hyperplasia of the liver (n = 4), hepatic abscess (n = 1), liver tuberculosis (n = 1), regenetrative nodules in the liver (n = 3) and heterogeneous fatty liver (n = 1).

Material and Methods

CEUS was performed with a Philips iU22 Ultrasound System along with a 2~5-MHz probe at a low mechanical index (0.06–0.08) using a contrast pulse sequence. The contrast agent was SonoVue. Before CEUS, the contrast was added to 5 mL of normal saline for preparation of contrast suspension. Firstly, the entire liver was detected in the conventional grey-scale ultrasound mode to search FLL. The location, size and number of FLLs were observed and the appearance, boundary and inner echo were recorded. Then, the liver was observed in a color ultrasound mode to observe the blood flow inside and surrounding the FLL. After the optimal section was identified, the probe was fixed and the contrast enhanced mode was switched. Then, 2.4 mL of SonoVue suspension was injected intravenously as a bolus through the elbow vein, followed by a 5 mL injection of normal saline. The time and patterns of enhancement and the changes in enhancement over time were observed. Especially, the arrival time, peak time, and the patterns of enhancement in early arterial phase (0–25s) were observed, and were carried out for at least 4 min. The characteristics of enhancement in the arterial phase were compared on CEUS and CECT.

CECT was conducted with a GE 16-slice helical CT scanner. The plain scanning and subsequent contrast-enhanced scanning were applied. The contrast agent was 90–100 mL of Iohexol, which was injected with a high-pressure injector at a rate of 3 mL/s through the elbow vein. The entire liver was scanned in 3 phases, which included arterial phase (postinjection 25–30 s), portal phase (60–70 s) and equilibrium phase (120–180 s). The patterns of FLL enhancement were recorded. All the data was entered into a computer.

The enhancement varies among FLLs with different blood supply. The contrast filled area exhibited enhancement and the contrast free area was slightly or not enhanced. According to the patterns of enhancement in the arterial phase, these lesions were graded: grade 0 – no enhancement; grade I – peripheral enhancement or spotty enhancement at the center; grade II – spoke-like, honeycomb-like or heterogeneous enhancement; grade III – entire enhancement.

Statistical Analysis

SPSS13.0 (SPSS, USA) was used for statistical analysis. Qualitative data was compared using chi square test. A value of $p < 0.05$ was considered statistically significant.

Results

Time of Enhancement

CEUS showed that 36 of 38 lesions (94.73%) had the enhancement time of < 25 s and 29 (76.32%) had the peak time of < 25 s. The information on blood perfusion before 25 s (arterial phase) was absent on CECT and thus not provided in the present study.

Patterns of Enhancement

The patterns of enhancement of 38 FLLs are shown in Table 1 and the results of comparison of enhancement patterns between CEUS and CECT in Table 2. On CEUS, the proportion of grade 0–I lesions was significantly lower and that of grade II–III markedly higher than those on CECT ($P < 0.05$) (Table 2).

Table 1. Patterns of enhancement of 38 FLLs in arterial phase

	Grade 0	Grade I	Grade II	Grade III
CEUS	1	12	9	16
CECT	2	23	7	6

Table 2. Enhancement patterns between CEUS and CECT

	Grade 0–I	Grade II–III	χ^2	P value
CEUS	13 (34.21%)	25 (65.79%)	7.579	0.006
CECT	25 (65.79%)	13 (34.21%)		

Misdiagnosis

Of 38 lesions, 6 were identified by CEUS but misdiagnosed by CECT. All 6 lesions had the arrival time of < 25 s, of which 5 had the peak time of < 25 s. The ultrasound images in the first 25 s provided important information for an accurate diagnosis. These 6 lesions included blood supply-rich small liver cancer (n = 1, Fig. 1), blood supply-rich metastatic liver cancer (n = 1, Fig. 2) and focal nodular hyperplasia of the liver (n = 3).

Of 38 lesions, 3 were identified by CECT but misdiagnosed or not identified by CEUS, including

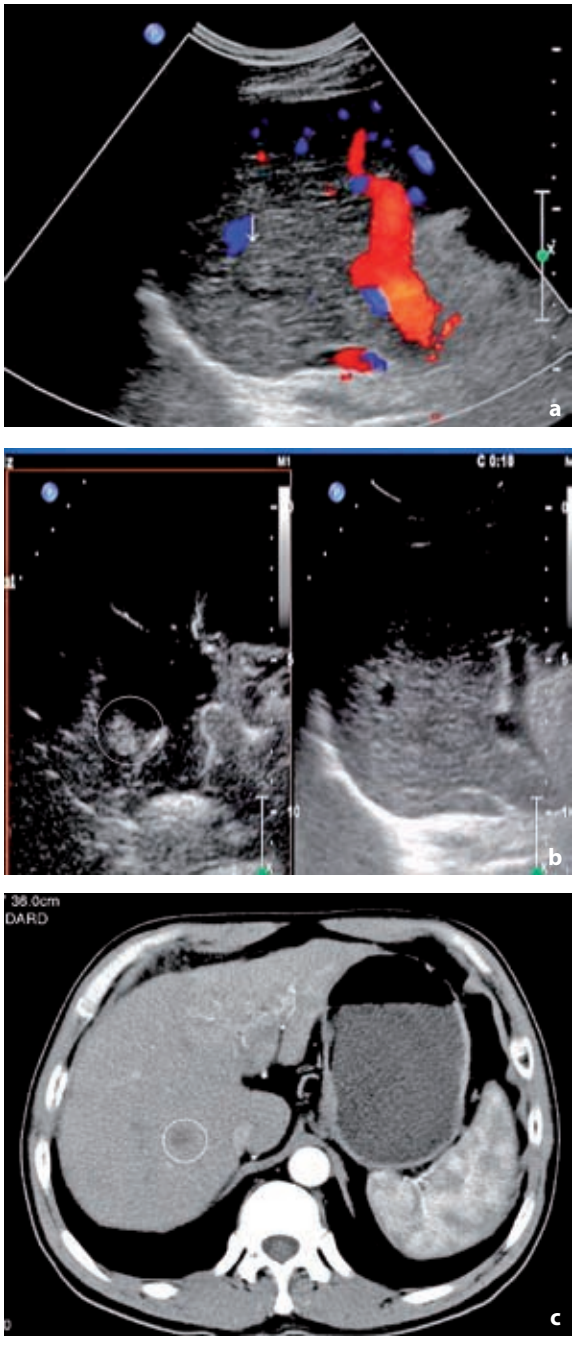

Fig. 1. Small liver cancer: A – conventional ultrasound showed a 1.0 0.9 cm isoecho in the right lobe of the liver, unclear boundary (white arrow) and no blood flow signal; B – CEUS showed diffuse enhancement within 18 s (white circle); C – CECT displayed non-enhancement in arterial phase (white circle) and the liver abscess was considered

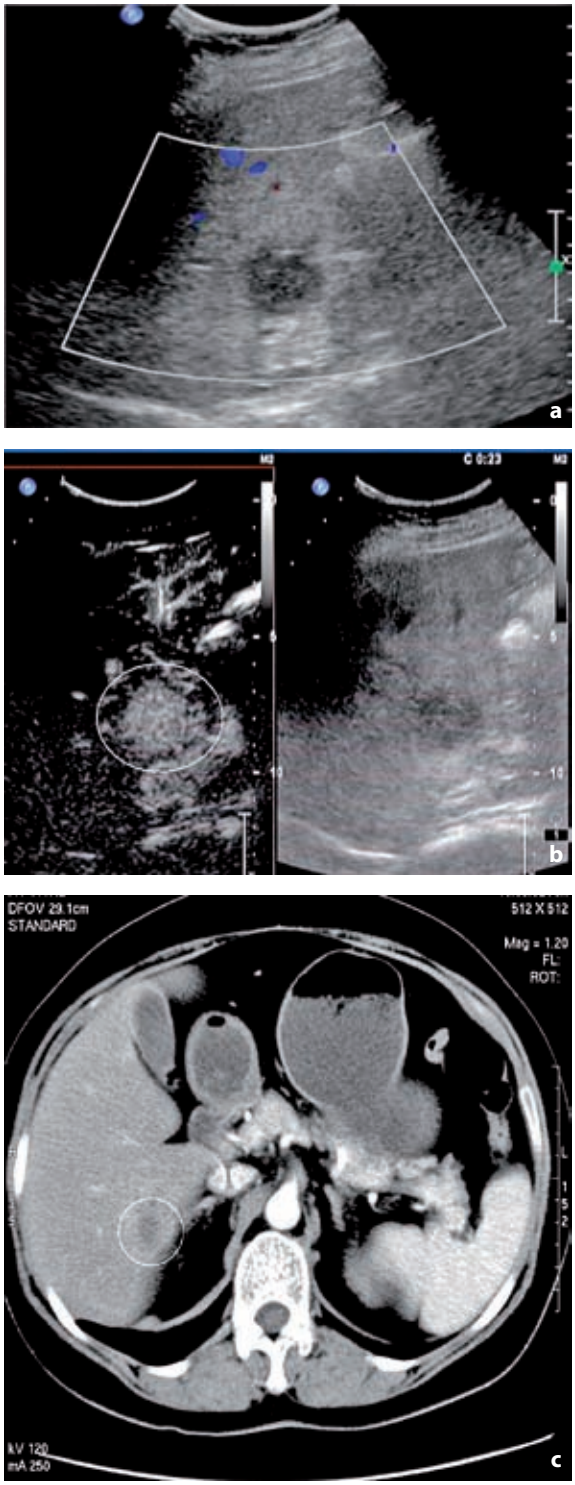

Fig. 2. Metastatic liver cancer with rich blood supply: A – conventional ultrasound showed hypoecho in the right lobe of the liver and no evident blood flow signals (white circle); B – CEUS showed diffuse enhancement within 23 s (white circle); C – CECT displayed peripheral enhancement in arterial phase (white circle) and the hemangioma was considered

2 HCCs secondary to hepatic cirrhosis and 1 right hepatic hemangioma close to the diagram. All 3 lesions did not present evident space-occupying features on CEUS and had hypointense on the plain CT.

Discussion

CEUS is a novel imaging technique and CECT is one of the major diagnostic modalities of FLL in clinical practice. CEUS can obtain the real-time enhancement of lesions and does not require pre-designing time points for scanning. However, the CECT images are collected intermittently at different time points starting from 25~30 s (arterial phase), to 60~70 s (portal phase) and to 120~180 s following contrast injection. CEUS allows continuous assessment of the overall enhancement course – starting from the injection of contrast to the excretion of contrast from the body, especially at the early stage of enhancement (first 25 s following the injection). The enhancement at the early stage may provide important information on lesions, particularly about severe arteriosclerosis and lesions occurring in the early arterial phase such as blood supply-rich small liver cancer and focal nodular hyperplasia of the liver. However, these cannot be presented on CECT. Hemodynamic features are the important basis of imaging examination to identify FLL. The characteristics of enhancement in the arterial phase are crucial for the differential diagnosis. CEUS and CECT have their own advantages in the early stage (first 25 s following contrast agent injection), resulting in differences in the characteristics of enhancement which is beneficial for the final diagnosis.

Some studies have been conducted to compare the ability of CECT and CEUS to identify FLL and predominantly focus on the specificity, sensitivity and accuracy of both techniques [10–14]. However, the characteristics of enhancement in the arterial phase between 2 techniques are seldom reported. Most studies [9–14] demonstrate that the patterns of enhancement in the same phase are comparable between 2 techniques and the ability of both techniques to identify FLL is also similar. In addition, other studies [15] suggest that CEUS is more sensitive, specific and accurate in displaying FLLs and more likely to display the small liver cancer as compared to CECT.

In this study, 36 of 38 lesions (94.73%) had the arrival time of < 25 s and 29 (76.32%) had the peak time of < 25 s. In the arterial phase, the proportion of Grade II~III lesions on CECT was significantly lower than that on CEUS (25 vs.13) ($P < 0.05$). We further analyzed 6 lesions which were identified by CEUS but misdiagnosed by CECT and the results showed that all lesions were severe arterial diseases, including blood supply-rich small HCC (n = 2), blood supply-rich metastatic liver cancer (n = 1) and focal nodular hyperplasia of the liver (n = 3). The 6 lesions had the arrival time of < 25 s, of which 5 had the peak time of < 25 s. The accuracy of CEUS in the diagnosis of 6 lesions is attributed to the enhancement in the first 25 s, which provides the important information for diagnosis. The scanning in CECT is intermittently done and information within the first 25 s cannot be obtained, which may cause a misdiagnosis of lesions with enhancement in the early arterial phase.

In this study, three lesions were misdiagnosed or not identified by CEUS. Two were HCC in the same patient. They were identified as hepatic cirrhosis companied by multiple nodules in the right lobe of the liver on CECT; 2 selected nodules had no rapid enhancement and were identified as cirrhotic nodules by CEUS. However, these 2 nodules were identified as huge lesions occupying the whole right lobe of the liver on plain CT, which displayed an irregular, slight enhancement in the arterial phase but no rapid extinction in the portal and delayed phases. These lesions were identified as a giant hepatic carcinoma by CECT. The 2 nodules were confirmed as a giant hepatic carcinoma in the follow-up period. CECT is superior to CEUS in displaying the entire liver and the giant hepatic carcinoma. The 2 nodules located in the giant space-occupying lesions in the right lobe of the liver. The CEUS cannot display the outline of space-occupying lesions, and the liver parenchyma surrounding the nodules is virtually the tumor tissue. Another lesion was the hepatic hemangioma in the context of severe cirrhosis. It is located in the right lobe of the liver close to the diaphragm. The conventional ultrasonography cannot display this region and thus fails to find this lesion, thus causing a misdiagnosis.

In conclusion, CEUS has several advantages: (1) Real-time images in CEUS allows the continuous assessment throughout the enhancement phase and are particularly suitable to display lesions with the arrival time of < 25 s such as severe arteriosclerosis and lesions with enhancement in the first 25 s (blood supply-rich small HCC and focal nodular hyperplasia of the liver). The patterns of enhancement within the first 25 s may provide key diagnostic information. (2) CEUS is safe and cheap, and requires low dose contrast and can be applied repeatedly. However, as compared to CECT, it is not suitable in displaying the entire liver and simply focuses on lesions in one section. The dynamic helical CECT can acquire the images of the entire liver at one scan in different phases and the

targeted lesions in different sections. In addition, CEUS is based on the two-dimensional ultrasound and generally visualize the lesions which are found in the two-dimensional ultrasound whereas CECT can diagnose independently and display lesions which are undetectable in the plain CT.

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Conflict of interest: None declared

Received: 19.02.2013
Revised: 29.08.2013
Accepted: 20.02.2014