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Original Research Article

The Diagnostic Performance of Contrast-Enhanced Computed Tomography and Contrast-Enhanced Ultrasound in Hepatocellular Carcinoma

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Abstract

Objective: To investigate the sensitivity, specificity and diagnostic accuracy of contrast-enhanced computed tomography (CECT) and contrast-enhanced ultrasound (CEUS) for hepatocellular carcinoma (HCC). ***Methods*:** The clinical data of patients who underwent hepatectomy in the first Affiliated Hospital of Guangxi Medical University and underwent CECT and CEUS before surgery were retrospectively analyzed. The gold standard was postoperative pathological examination results. ***Results*:** A total of 554 patients were included, and 650 lesions were found. The sensitivity and coincidence rate of CECT and CEUS for lesions were more than 94% and 83%, respectively. 14 lesions with diameter less than 2cm which were detected by CUES were not detected by CT and 26 such lesions which were detected by CT were not detected by CUES. ***Conclusion*:** CUES and CECT have similar high sensitivity and diagnostic accuracy for HCC. Combined CT and CUES detection could find more small lesions in the liver.

Keywords: Computed tomography; contrast-enhanced ultrasound; hepatocellular carcinoma.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for more than 90%, and is the sixth most common tumor worldwide [1, 2]. Hepatocellular carcinoma is clinically diagnosed mainly by history of hepatitis, tumor markers such as AFP and typical imaging characteristics [3].

Conventional ultrasound (US) is an essential imaging technique for the detection or diagnosis of liver lesions, but its sensitivity and specificity are not high [4]. Contrast-enhanced ultrasound (CEUS) is a kind of visual and dynamic observation of liver lesions on the basis of conventional ultrasound detection, with high sensitivity and specificity [5]. Studies have shown that CEUS was highly sensitive to arterial hypervascular lesions [6], and the specificity of CEUS for HCC lesions with hypervascular lesions is higher than that of Contrast-enhanced computed tomography (CECT) [7]. CEUS is inherently more sensitive to microbubbles than CECT was to iodization contrast agents [8]. CEUS was recommended by several guidelines for routine detection of liver cancer [9]. As a conventional first-line detection method of liver, CECT had high sensitivity and specificity for HCC. However, there were also some missed diagnoses and misdiagnosis for small lesions in CECT [10].

We conducted this retrospective study in a single center to compare and analyze the performance of CEUS and CECT in the diagnosis of hepatocellular carcinoma, hoping to improve the basis for the selection of imaging methods for preoperative examination and postoperative monitoring of patients with hepatocellular carcinoma.

PATIENTS AND METHODS

This single-center retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Informed consent was waived for this retrospective study. Postoperative pathological examination was performed for all patients. Our inclusion criteria included patients undergoing CECT and CEUS simultaneously prior to

hepatectomy. A pathological examination is required for the resected liver specimen. Patients with CECT and CEUS imaging intervals of more than 3 weeks were excluded. We also excluded cases in which the exact number and size of liver lesions were not reported in the resected specimens.

CEUS

The patient received ultrasound diagnostic instrument (LOGIQ E9, General Electric Company, USA) was used in CEUS. The contrast agent used in CEUS imaging is a Sulphur Hexafluoride Microbubble (Bracco Suisse SA, Switzerland). Saline was administered after intravenous contrast media. During intermittent imaging, liver lesions were analyzed in early arterial, portal venous phase and late venous phase (120 seconds to 4-6 minutes. Each patient was scanned for at least 5 minutes to ensure that the physiologic features of the contrast agent were fully displayed after injection.

CECT

All patients received a preoperative CECT (64-slice, GE, United States). The contrast agent used was iopromide (Bayer Medical Health Co., Ltd., Germany).

Image analysis and diagnostic criteria

All images were collected from the computer system of our hospital. All imaging data were evaluated by an imaging specialist with many years of clinical experience. The diagnosis of hepatocellular carcinoma is typically "fast-in, fast-out" on CEUS and/or CECT.

Statistical analysis

We analyzed the sensitivity, specificity, positive predictive value, negative predictive value and coincidence rate of CEUS and CECT for HCC. The significant difference was $p < 0.05$. The software SPSS 26.0 was used for statistical analysis.

RESULTS

From March 15, 2017 to October 25, 2019, a total of 554 patients with 650 lesions were enrolled in this retrospective study. There were 440 males and 114 females, with an average age of 51 (17–88) years old (Table 1). The lesions with average diameter were 5.8 cm (0.87- 20.1 cm). The mean time interval between CT and CEUS was 3.89 days (0 to 20 days); CECT was performed first in 286 patients.

In this study, more than 80% of patients and lesions were HCC, whereas 55 patients and 102 lesions were benign, as shown in Table 2. The diagnostic performance of CECT and CEUS for lesions larger than 2 cm were similar, but the specificity of CECT for lesions less than 2cm is better than that of CEUS ($P < 0.001$), as shown in Table 3. CECT detected 636 lesions, but CEUS detected 624 lesions. Lesions larger than 2 cm could be detected by both CECT and CEUS. CECT found 120 whereas CEUS only found 102 lesions smaller than 2 cm. CECT detected 26 lesions that were not detected by CEUS, and 21 of them were HCC. However, CEUS also detected 14 lesions that were not detected by CECT, and 12 of them were HCC.

Table 1. Patient characteristics.

Parameter	Number
Patients	554
Lesions	650
Mean age (range)	51 years (17–88 years)
Sex (male/female)	440 (79.42%)/114 (20.58%)
Diameter of lesions (range)	5.8 cm (0.87–20.1 cm)
Liver cirrhosis	481 (86.8%)

Table 2. Postoperative pathology.

Pathology results	Patients	Lesions
HCC	450	529
ICC	29	32
HCC and ICC	8	9
Hepatic metastasis	10	11
stromal tumors	1	2
carcinosarcoma	1	1
Hemangioma	15	22
FNH	10	12
Inflammatory pseudotumor	23	23
Dysplastic nodule	6	8
PE Coma, Benign	1	1

HCC: Hepatocellular carcinoma; ICC: Intrahepatic cholangiocarcinoma; FNH: Focal nodular hyperplasia, PEComa NOS, Benign: perivascular epithelioid cell tumors, benign.

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Table 3. Comparison of CECT and CEUS in the diagnosis of hepatocellular carcinoma

Lesions	Methods	Sensitivity(95%CI)	Specificity(95%CI)	AUC(95%CI)	PPV(95%CI)	NPV(95%CI)	CR(%)
All lesions (n=650)	CECT	93.31(90.87-95.27)	64.28(54.68-73.12)	0.79(0.76-0.82)	92.62(90.72-94.15)	66.67(58.63-73.83)	88．31
	CEUS	94.24(91.92-96.05)	61.61(51.94-70.64)	0.78(0.75-0.81)	92.18(90.31-93.72)	69.0(60.55-76.34)	87.62
CECT/ CEUS		98.51(97.09-99.36)	54.46(44.78-63.36)	0.76(0.73-0.79)	91.22 (89.97-93.33)	88.41(78.97-93.93）	90.92
Lesion > 2cm (n=516)	CECT	95.59(93.20-97.33)	63.53(52.38-73.71)	0.79(0.76-0.83)	93.0(0.94-94.63)	73.97(64.02-81.95)	90.31
	CEUS	98.84(97.31-99.62)	65.86(54.79-75.83)	0.82(0.79-0.86)	93.63(91.62-95.18)	91.80(82.22-96.45)	93.41
CECT/ CEUS		99.31(97.98-99.86)	75.65(46.45-98.30)	0.79(0.75-0.82)	92.24(90.27-93.84)	94.23(83.90-98.09)	92.44
Lesion <2cm(n=134)	CECT	84.11(75.79-90.46)[a]	66.67(46.04-83.48)[b]	0.75(0.67-0.82)	90.91(85.36-94.49)	51.43(38.84-63.84)	80.60
	CEUS	75.70(66.46-83.47)[c]	48.15(28.67-68.05)	0.62(0.53-.70)	85.26(79.84-89.42)	33.33(23.01-45.56)	70.15
CECT/ CEUS		95.33(89.43-98.47)	44.44(25.48-64.67)	0.69(0.61-0.78)	87.18(82.88-90.52)	70.89(48.04-86.17)	85.07

Note. AUC: Area Under Curve; CECT: contrast-enhanced computed tomography; CEUS: Contrast-enhanced ultrasound; CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value; CR： Coincidence rate; CECT / CEUS: As long as one of the two diagnoses of CECT and CEUS was positive, it was considered positive. [a]$p < 0.05$, [b]$p < 0.05$, CECT *vs* CECT/ CEUS. [c]$p < 0.01$, CEUS *vs* CECT/CEUS.

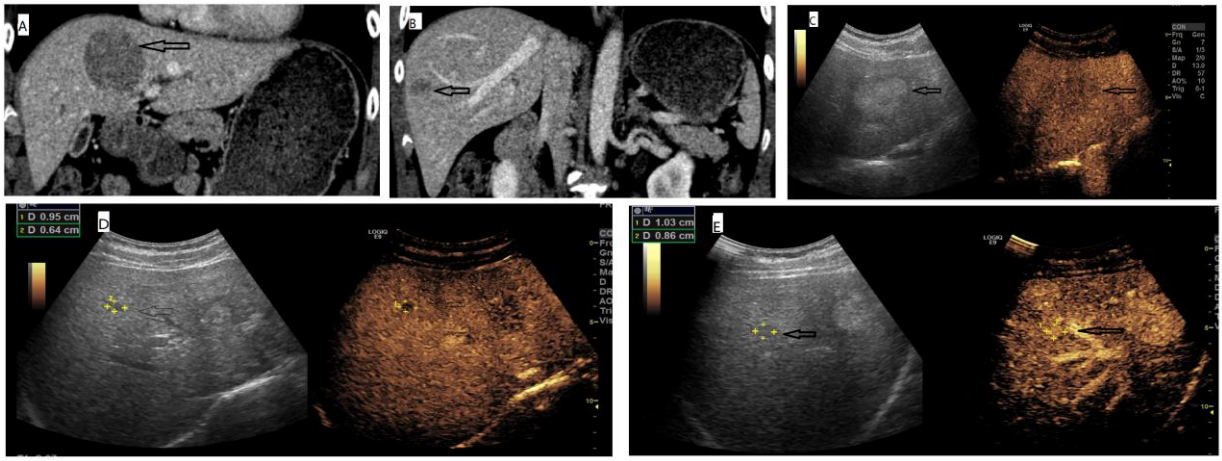

Figure 1: Case 1: The patient was with HCC. In the patient, CECT detected only 2 lesion, while CEUS detected 3 lesions. CECT: Contrast-enhanced computed tomography; CEUS: Contrast-enhanced ultrasound

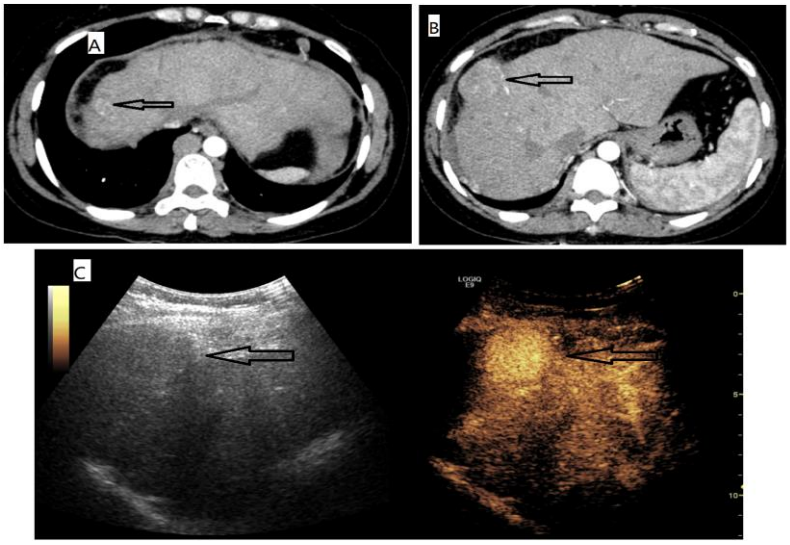

Figure 2: Case 2: The patient was with HCC. In the patient, CEUS detected only 1 lesion, while CECT detected 2 lesions. Contrast-enhanced computed tomography; CEUS: Contrast-enhanced ultrasound

DISCUSSION

In our study, CECT found some small lesions that were not found by CEUS, and CEUS also found few small lesions that were not found by CECT. Both imaging methods detected lesions larger than 2cm. The number of lesions with diameter less than 2cm detected by CECT was significantly more than that of CEUS. At the same time, CEUS found 14/134 small lesions not found by CECT, and there was a significant difference. This indicated that CECT and CEUS were complementary in detecting small lesions. Twelve patients with only one lesion detected by CECT were found with additional lesions in CEUS, and sixteen patients with only one lesion detected by CEUS were found with additional lesions in CECT. And the vast majority of these additional lesions were HCC. This suggested that even patients with only one lesion detected by one of the two imaging methods may need another test.

Even in patients with only one lesion detected by one of the two imaging methods, the other test is necessary.

Our study found that the diagnostic coincidence rate of CECT and CEUS was more than 90% for lesions larger than 2 cm (459/493) and 80% for lesions smaller than 2 cm (41/51). Our results are similar to previous studies [6, 11]. The sensitivity, the positive predictive value and the negative predictive value of CECT and CEUS to the lesions were both greater than 95%, 90% and 70% , respectively, which is similar to previous studies [6, 12, 13]. Compared with the corresponding CT scan results, CEUS showed higher diagnostic accuracy in evaluating HCC [14].

In this study, the specificity of both imaging methods was less than 70%, which is different from some previous studies [6, 12, 13, 15-17]. This may be due to the fact that the vast majority of cases in this study were preoperatively considered to be hepatocellular carcinoma. Moreover, surgical resection is rarely performed in patients whose preoperative imaging diagnosis is considered benign.

There were some limitations in our study. First, this study was a retrospective study in a single-center, so there may be selection bias. Second, CEUS images were non-dynamic images in the retrospective analysis, and it is possible that some lesions were indeed detected but not seen by the readers. A prospective multi-center study with a large sample size is needed in the future.

CONCLUSION

Both CECT and CEUS have high sensitivity and diagnostic coincidence rates for HCC. CECT combined with CEUS can detect more small liver lesions (< 2 cm).

DECLARATIONS

Ethics approval and consent to participate:

This single-center retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Informed consent was waived for this retrospective study**.**

Consent for publication: All listed authors given final approval of the version to be published.

Conflict of Interest:

The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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Authors' Contributions:

Jiangfa Li and Songqing He made substantial contributions to conception and design. Jiangfa Li , Liping Lei, and Xiaofei Ye acquisition of data. Jiangfa Li, Liping Lei, and Xiaofei Ye analysis and interpretation of data. Jiangfa Li, Liping Lei, Xiaofei Ye and Songqing He participated in drafting the article or revising it critically for important intellectual content. All listed authors given final approval of the version to be published.

Availability of data and materials:

If anyone needs data on this article, they can get it from the corresponding author.

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