Abstract

We attempted to evaluate the usefulness of ultrasonic tissue harmonic imaging (HI) in the diagnosis of small hepatocellular carcinoma (HCC) and compare its effectiveness with that of conventional fundamental imaging (FI) prospectively. Nine patients with 16 nodules of HCC measuring less than 20 mm in diameter were evaluated with both FI and HI. The boundaries of 14 nodules were more clearly visualized on HI than on FI. Posterior acoustic enhancement, which is diagnostic of HCC, was not detected on FI, although it was detected in 5 nodules on HI (p<0.05); however, one nodule located in a section of the liver that was 8 cm below the abdominal wall was visualized only by FI. We conclude that HI is more useful than FI in the diagnosis of small HCC nodules, although HI has minor limitations of the applicable location.

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Keywords
hepatocellular carcinoma, tissue harmonic imaging, ultrasonography, posterior acoustic enhancement

1. Introduction

With the widespread use of conventional ultrasonographic examinations for patients with chronic liver disease, it has become possible to detect nodules of hepatocellular carcinoma (HCC) that are less than 20 mm in diameter. The characteristic findings of mosaic pattern, hypoechoic halo, lateral shadowing, and posterior acoustic enhancement of such small HCC nodules are seldom visualized, however. It is therefore difficult to make a differential diagnosis of small HCC using conventional ultrasonography (fundamental imaging) (FI).

Ultrasonic tissue harmonic imaging (HI) is a new modality that has higher lateral and axial resolution and less clutter than FI. It can thus be expected to provide clearer images than FI. HI has recently been applied in echocardiography to improve endocardial border definition and visualization of cardiac structures. Tanaka et al. have reported, moreover, that HI detected hepatic tumors more frequently than did FI. Here we attempt to evaluate the usefulness of HI in the differential diagnosis of small hepatocellular carcinoma and to compare its effectiveness with that of FI.

2. Materials and Methods

During a 1-month period, nine patients with 16 HCC nodules were evaluated prospectively with both FI and HI. The patients comprised seven men and two women aged 56 to 77 years; mean age, 64 years. All of the patients had liver cirrhosis. Cirrhosis was caused by hepatitis B in two patients and hepatitis C in seven patients. Six of the patients had a single nodule; one had 2 foci, and two had 4 foci. After the evaluation with both FI and HI, 6 nodules were diagnosed by means of ultrasound-guided target biopsy, while the remaining 10 were diagnosed on the basis of hypervascularity, which is a characteristic angiographic finding of HCC, US angiography with intra-
arterial CO₂ microbubbles⁹, or both. All the nodules were less than 20 mm in diameter (range, 10 to 19 mm; mean, 14 mm); 15 of the 16 HCC nodules were 15 mm or less in diameter. FI and HI examinations were both conducted at the same time to evaluate echogenicity, clarity of boundary, presence of a mosaic pattern, hypoechoic halo, lateral shadowing, and posterior acoustic enhancement in these nodules.

On the other hand, in 16 patients with 20 hepatic nodules other than HCC (9 metastatic liver tumors, 6 hemangiomas, 3 adenomatous hyperplasias, and 2 focal nodular hyperplasias), the presence of posterior acoustic enhancement was evaluated on both FI and HI by contrast with HCC.

McNemar's test was used for the statistical analysis. The equipment used was a Power Vision 6000 ultrasound system with a 4.2MHz convex probe for FI (transmitted frequency, 2.4 MHz; received frequency, 4.8 MHz for HI) (Toshiba, Tokyo).

3. Results
FI showed 6 HCC nodules to be hypoechoic; 4, isoechoic; and 6, hyperechoic. HI, on the other hand, showed 5 HCC nodules to be hypoechoic; 4, isoechoic; and 6, hyperechoic (Table). The remaining HCC nodule (an isoechoic nodule with a halo on FI), which was located in a section of the liver that was 8 cm below the abdominal wall, was not visualized by HI (Fig. 1). The boundaries of 14 of the 15 HCC nodules detected on both FI and HI were clearer on HI than on FI (Fig. 2), while the boundary of the remaining nodule was visualized similarly by both FI and HI.

None of the HCC nodules produced a mosaic pattern on either FI or HI. Four HCC nodules produced a hypoechoic halo on FI, while HI showed 5 such nodules to be hypoechoic. None of HCC nodules demonstrated lateral shadowing on FI, although 1 did on HI (Table). Moreover, none of the HCC nodules demonstrated posterior acoustic enhancement on FI, although 5 did on HI (Fig. 3). FI and HI differed significantly (p < 0.05) in rate of detection of posterior acoustic enhancement. On the other hand, the 9 metastatic liver tumors, 6 hemangiomas, 3 adenomatous hyperplasias, and 2 focal nodular hyperplasias showed no posterior acoustic enhancement.

4. Discussion
Ultrasonographic findings of HCC reflect its pathologic conditions. The mosaic pattern is a configuration of confluent, small, viable nodules separated by septa or necrotic areas within the nodule. The hypoechoic halo corresponds to a fibrous capsule around the nodule. Lateral shadowing may be related to this fibrous capsule. Posterior acoustic enhancement indicates good transmission of ultrasonic waves through the nodule; however, the kind of histologic changes that produce this enhancement remain unclear. Although findings of mosaic pattern, hypoechoic halo, lateral shadowing, and posterior acoustic en-

Table | Ultrasonographic Findings of 16 HCC Nodules
<table>
<thead>
<tr>
<th>Echogenicity</th>
<th>Mosaic Halo</th>
<th>LS</th>
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<tr>
<td>FI</td>
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FI indicates fundamental imaging; HI, tissue harmonic imaging; LS, lateral shadowing; and PAE, posterior acoustic enhancement.
# One nodule with a halo was not detected on HI.
* p < 0.05 (McNemar's test).

Fig. 1 A case of HCC in which the nodule was 8 cm below the abdominal wall. FI (left) shows a isoechoic nodule with a hypoechoic halo (arrow) that remains undetectable on HI (right).