◇Original Contribution◇

Tissue Harmonic Imaging in the Diagnosis of Small Hepatocellular Carcinoma: Usefulness for Detecting Posterior Acoustic Enhancement

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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.[1] The characteristic findings of mosaic pattern, hypoechoic halo, lateral shadowing, and posterior acoustic enhancement of such small HCC nodules are seldom visualized, however.[2)3)] 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.[4] 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[7] 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,[8] US angiography with intra-

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arterial CO_2 microbubbles[9], 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.

Table Ultrasonographic Findings of 16 HCC Nodules

	Echogenicity			Mosaic	Halo	LS	PAE*
	Hypo	Iso	Hyper				
FI	6	4#	6	0	4	0	0
HI	5	4	6	0	5	1	5

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).

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.[1] The hypoechoic halo corresponds to a fibrous capsule around the nodule.[1] Lateral shadowing may be related to this fibrous capsule.[1] Posterior acoustic enhancement indicates good transmission of ultrasonic waves through the nodule[1]; however, the kind of histologic changes that produce this enhancement remain unclear.[1] Although findings of mosaic pattern, hypoechoic halo, lateral shadowing, and posterior acoustic en-

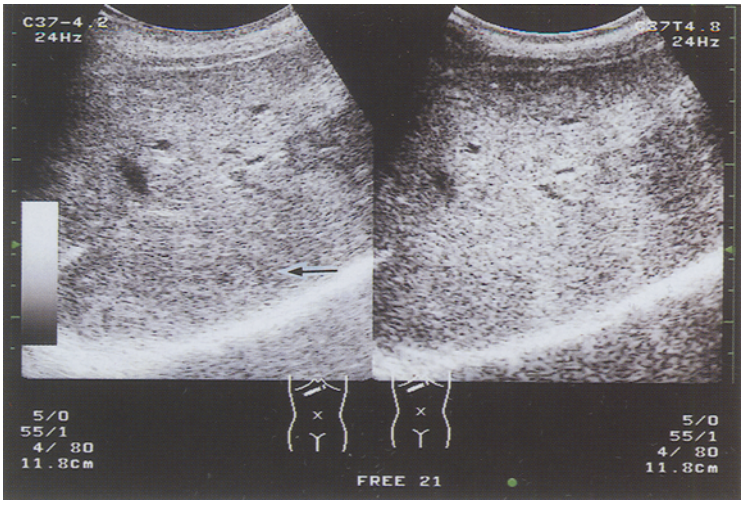

Fig.1 A case of HCC in which the nodule was 8 cm below the abdominal wall. FI (left) shows a isoechoic nodule with a hypoechoic halo (arrow) that remains undetectable on HI (right).

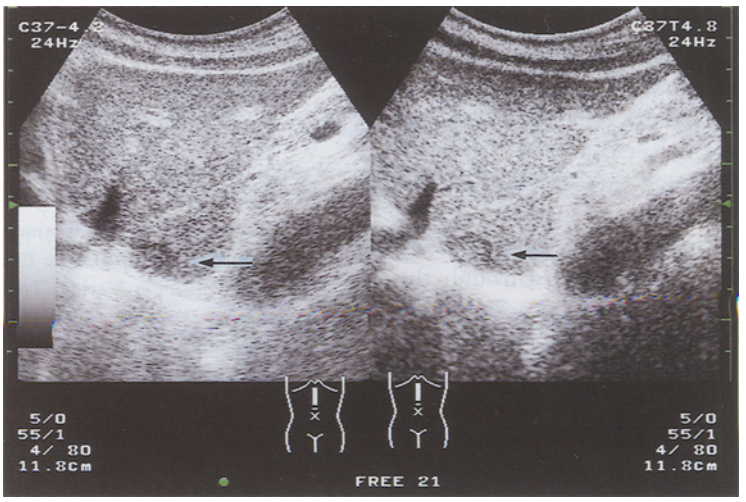

Fig.2 A small HCC measuring 15 mm in diameter. HI (right) demonstrates boundary of the nodule (arrow) more clearly than FI (left).

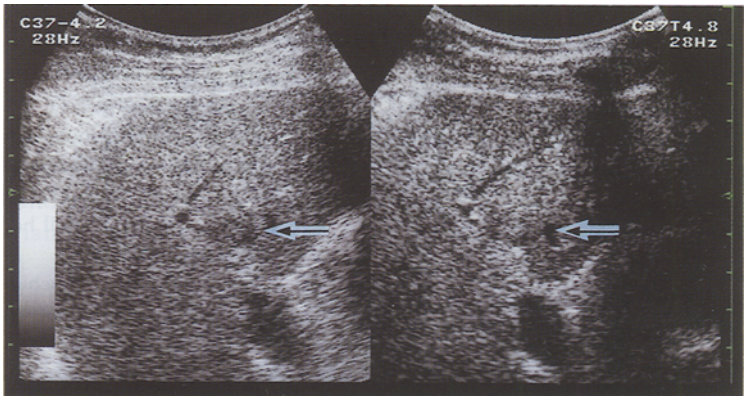

Fig.3 A small HCC measuring 13 mm in diameter. FI (left) shows a hypoechoic nodule with no hypoechoic halo or posterior acoustic enhancement (arrow). However, HI (right) shows an isoechoic nodule with both hypoechoic halo and posterior acoustic enhancement (arrow).

hancement are characteristic of HCC,[1)-3)10)] such findings in small HCC nodules are difficult to discern on FI.[2)3)]

HI is a new modality. Soft tissue is a nonlinear propagation medium in which pulse distortion increases with distance traveled and increases in size and steepness of the positive half-cycles. Echoes from such distorted pulses are rich in harmonics, and frequencies are two, three, or four times greater than those in the transmitted pulse.[11)] In the HI equipment used in this study, the receivers were tuned to twice the transmitted frequency (second harmonic). The width of the reflected harmonic beam decreases with distance traveled, and the levels of the sidelobes on the reflected beams decrease. These two effects correspond to enhancement of the lateral resolution of the system and reduction in clutter. In HI, moreover, because the length of the reflected pulse echoes decreases, axial resolution is moderately enhanced.[4)] HI therefore improves total image quality. In fact, the boundaries of 14 HCC nodules were clearer on HI than on FI. Moreover, only HI demonstrated hypoechoic halos from two HCC nodules, and lateral shadowing from one.

Neither FI nor HI demonstrated a mosaic pattern from any of the HCC nodules studied. Nakashima[12)] reported that septa were present in HCC nodules larger than 15 mm in diameter. Most of the HCC nodules in this study were 15 mm or less in diameter, which may explain why the rate of detection of septa, which account for the mosaic pattern,[1)] was low.

Although the nature of the histologic changes that produce posterior acoustic enhancement remains obscure, acoustic enhancement is known to indicate good transmission of ultrasonic waves through the nodule.[1)] Approximately half of small HCC nodules,

those less than 20 mm in diameter, are histologically uniform,[13] while the surrounding cirrhotic parenchyma contains distorted lobules, enlarged portal tracts, and fibrous tissue.[14] These HCC nodules may transmit ultrasound waves better than the surrounding cirrhotic parenchyma, and better transmission produces less attenuation. Because the ultrasonic beam passes back and forth through the nodule, there is less attenuation of the reflected beam through the nodule than through the surrounding cirrhotic parenchyma. Finally, the echogenicity of the parenchyma behind the nodule may become enhanced. The reason why HI, and not FI, was able to visualize posterior acoustic enhancement in some of the nodules, remains unclear, however. Whatever the reason, posterior acoustic enhancement, which is a diagnostic finding of HCC, was found in only 5 nodules, and only by HI.

On the other hand, the possibility that HI may show posterior acoustic enhancement in other hepatic nodules needs to be addressed. In metastatic liver tumors, hemangiomas, adenomatous hyperplasias, and focal nodular hyperplasias, however, none of the nodules demonstrated posterior acoustic enhancement. We thus conclude that posterior acoustic enhancement is a characteristic finding of HCC, even when using HI. To fully substantiate this conclusion, additional studies will be necessary to determine if any other types of hepatic nodule demonstrate posterior acoustic enhancement.

Furthermore, HI failed to detect the nodule that was located 8 cm below the abdominal wall, although FI did visualize it. The reflected harmonic beam is attenuated more quickly because of the frequency-dependent attenuation of tissue,[6] perhaps explaining cases in which HI fails to produce a clear image in a deep section. HI did visualize liver parenchyma more than 8 cm below the abdominal wall in the same patient, however. Consequently, the reason why the nodule was not detected on HI remains obscure. However, this may be an atypical case.

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