Contrast-enhanced sonography versus contrast-enhanced helical CT in the evaluation of hepatocellular carcinoma in cirrhotic patients

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Key words: Hepatocellular carcinoma, cirrhosis; Ultrasound, contrast medium, Microbubbles; Ultrasound, comparative studies

Aim. To evaluate the usefulness of contrast-enhanced ultrasonography (CEUS) using a newer generation of contrast agent for hepatocellular carcinoma evaluation in cirrhotic patients by comparing the results to contrast-enhanced helical Computed Tomography (CT).

Subjects and methods. Between October 2002 and April 2003, 78 cirrhotic patients (64 men and 14 women; age range, 45-80 years; mean age, 66 years) with a single nodule of hepatocellular carcinoma selected from a cohort of 457 cirrhotic patients were studied. The 78 nodules ranged in size 9-65 mm (mean, 28.2 mm). Twenty-eight (36%) were smaller than or equal to 20 mm (range, 9-20 mm; mean, 16.6 mm), and 50 (64%) were larger than 20 mm (range, 21-65 mm; mean, 35.2 mm). CEUS was performed at low mechanical index after SonoVue™ (BR1, Bracco, Milan, Italy) injection. CT scans were performed in all patients. The enhancement pattern related to tumor hypervascularity was analyzed. Chi-square test was used for statistical analysis.

Results. Hepatocellular carcinomas smaller than or equal to 20 mm:

- On CEUS 15/28 (53.6%) hepatocellular carcinomas were hypervascular, 10/28 (35.7%) avascular, and 3/28 (10.7%) missed.

- On CT 12/28 (42.9%) hepatocellular carcinomas were hypervascular, 13/28 (46.4%) hypovascular, and 3/28 (10.7%) missed.

Hepatocellular carcinomas larger than 20 mm:

- On CEUS, 46/50 (92%) hepatocellular carcinomas were hypervascular, and 4/50 (8%) avascular.

- On CT, 39/50 (78%) hepatocellular carcinomas were hypervascular, 8/50 (16%) hypovascular, and 3/50 (6%) missed.

Differences between CT and CEUS were not statistically significant. Concordance between CEUS and CT was observed in 65/78 (83%) cases.

Conclusion. CEUS is roughly comparable to CT in detecting hepatocellular carcinoma hypervascularity. Therefore, it could be complementary to sonography for evaluation of liver nodules.

Ecografia con mezzo di contrasto di seconda generazione (CEUS) nella valutazione dell’epatocarcinoma su cirrosi: confronto con la TC spirale con mezzo di contrasto

Scopo. Studiare prospetticamente l’efficacia dell’ecografia con mezzo di contrasto di seconda generazione (CEUS) nella valutazione dell’epatocarcinoma su cirrosi epatica, confrontando i risultati con quelli della TC spirale con mezzo di contrasto.

Materiali e metodi. Tra Ottobre 2002 e Aprile 2003 sono stati studiati 78 pazienti cirrotici consecutivi (64 uomini e 14 donne; età 45-80 anni; età media 66 anni) con un nодulo singolo di HCC, selezionati da una serie di 457 pazienti cirrotici. I 78 noduli avevano dimensioni comprese tra 9 e 65 mm (media 28.2 mm). 28 noduli (36%) avevano un diametro ≤ 20 mm (range 9-20 mm; media 16.6 mm), e 50 noduli (64%) erano > 20 mm (range 21-65 mm; media 35.2 mm). Tutti i pazienti hanno praticato ecografia con mezzo di contrasto a basso indice meccanico, dopo somministrazione endovenosa di 2.4 ml di SonoVue™ (BR1, Bracco, Milano) ed una TC spirale con mezzo di contrasto. In tutti i pazienti è stato analizzato il pattern di impregnazione del nodulo con il mezzo di contrasto in relazione al parenchima epatico circostante. Per l’analisi statistica è stato utilizzato il test del chi-squared. Concordanza tra CEUS e TC è stata osservata in 65/78 (83%) casi.

Conclusioni. CEUS è in grado di confrontare efficacemente la TC nella visualizzazione dell’HCC come pattern ipervascolare. La CEUS, pertanto, potrebbe essere proposta come esame complementare a quella di base per la valutazione dei noduli epatici.

Introduction

Hepatocellular carcinoma is the most common primary liver cancer that usually occurs as a complication of chronic liver disease and most often arises in a cirrhotic liver (1-3). Therefore, accurate surveillance of patients with liver cirrhosis is of great clinical importance,
because they are at increased risk for hepatocellular carcinoma (4, 5). On the other hand, the accurate and early diagnosis of hepatocellular carcinoma is important for the treatment of the affected patients.

Surgical resection, liver transplantation, percutaneous alcohol ablation, or radiofrequency ablation in selected patients are potentially curative therapies (6-9).

Findings of a liver solid mass on ultrasonography imaging studies are often non-specific, thus requiring contrast-enhanced computed tomography or magnetic resonance characterization (10-16). In addition to imaging studies, for all the nodules presenting a diameter smaller than two centimeters a needle-biopsy is recommended (9).

On the other hand, concerns have been raised about the risk of seeding following fine-needle biopsy aspiration of hepatocellular carcinoma in patients who will undergo liver transplantation or surgical resection (17-19) that has been estimated to be up to 3.4% (20).

In the last few years, to improve the low specificity of sonography in the characterization of focal liver lesions, a wide variety of sonographic contrast agents have been developed by using different gases and coating materials. Levovist (SH U 508A, Schering, Berlin, Germany), a sonographic contrast agent first employed for the enhancement of Doppler ultrasound signals, has been tested to differentiate hepatic lesions on the basis of their appearance after the IV injection (21-23).

Levovist-enhanced sonography imaging requires interval-delay imaging, that is the imaging process is interrupted for several seconds. A newer generation of sonographic intravascular contrast agents, which shows a higher reflectivity compared to the previous one, is now available. SonoVue™ (BR1, Bracco, Milan, Italy) is a sulphur hexafluoride gas stabilized with phospholipids that presents a high reflectivity at a low mechanical index, and is characterized by a low solubility in water and a low diffusion in blood. Like other newer available contrast agents such as Definity™, after IV injection SonoVue™ persists in the bloodstream much longer than the previous sonographic contrast agents, so it can actually be considered a blood pool agent. The contrast-enhancing effect of SonoVue™ does not require the rupture of the microbubbles but is based on the continuous resonance of the microbubbles under a low mechanical index ultrasound field. This mechanism of enhancement allows a real-time imaging of the microcirculation that lasts several minutes, so that the early arterial phase and the late parenchymal phase of the contrast medium diffusion can be analyzed.

The purpose of this study was to investigate the sonographic appearance of hepatocellular carcinoma using non-destructive contrast agent imaging techniques to define the imaging characteristics of hepatocellular carcinoma by comparing the technique to contrast-enhanced helical Computed Tomography (CT).

**Subjects and methods**

**Design of the study**

This study was designed to investigate the sonographic appearance of hepatocellular carcinoma using non-destructive contrast agent by comparing the technique to contrast-enhanced helical Computed Tomography. To study a focal lesion with contrast-enhanced sonography it is necessary to choose the scanning plane where the lesion is located, so only one lesion at a time could be investigated. Thus, for the purpose of the study, patients with a single liver nodule were selected from a series of cirrhotic patients suspected of having at least one nodule of hepatocellular carcinoma on the basis of ultrasonographic findings who were referred to our Interventional Service for further evaluation. Contrast-enhanced ultrasonography and contrast-enhanced helical CT were performed in all patients in two consecutive days.

Percutaneous sonographically-guided needle biopsy of the liver nodule was obtained in all patients the following day, after both imaging studies. Biopsies were performed using a 19-gauge modified Menghini needle or a fine-needle-aspiration technique.

**Subjects**

Between October 2002 and April 2003, a total of 457 cirrhotic patients (331 males and 126 females; age range, 42-85; mean age, 65 years) suspected of having at least one nodule of hepatocellular carcinoma on the basis of ultrasonographic findings were referred to our Institution for further evaluation.

Between them, 83 consecutive patients with a single liver nodule were selected to enter into the study. Five patients were excluded because the nodule histology or cytology results were not conclusive (three cases) or the lesion turned out not to be hepatocellular carcinomas (two cases).

Thus, our study group consisted of 78 patients (64 men and 14 women; age range, 45-80 years; mean age, 66 years). On contrast enhanced helical CT, there were two additional lesions in two patients in the study group that were both localized in the subcapsular portion of segment 8 (size 13 mm, and 15 mm).

These patients were included in the subsequent analysis, and only the nodule seen on conventional ultrasonography was studied with the contrast agent.

The diagnosis of liver cirrhosis was based on liver biopsy findings in 63 of the 78 patients and on clinical data in the remaining patients. The cause of cirrhosis was HCV-associated in 63 patients, alcoholic in 4 patients, alcoholic and HCV-associated in 2 patients, HBV-associated in 7 patients, and cryptogenic in 2.

The tumors were located in the right lobe of the liver in 59 patients, and in the left lobe in 19 patients. The 78 tumors ranged in size from 9 to 65 mm (mean, 28.2 mm). Twenty-eight (36%) hepatocellular carcinomas were smaller than or equal to 20 mm in diameter (range, 9-20 mm; mean, 16.6 mm), and 50 (64%) were larger than 20 mm (range, 21-65 mm; mean, 35.2 mm). According to the impairment of liver function related to cirrhosis, 43 patients were in Child-Pugh class A, and 36 in class B. Serum levels of alpha-fetoprotein were below 20 ng/mL in 60 patients, and between 20 and 40 ng/ml in 18 patients. The treatment was approved by the institutional review board and informed consent was obtained from all patients after the nature of the procedure had been fully explained.
Equipment

All abdominal sonography scans were performed using a commercially available sonography machine with a software for contrast media (Aloka Prosound SSD-5500 PHD Extended, Tokyo, Japan) with a 3.0-6.0 MHz convex array broad-band probe. Triphasic contrast-enhanced helical CT scans were performed using the helical CT scanner Somatom Balance (Siemens Medical System, Erlangen, Germany).

Contrast agent

SonoVue™ is a suspension of stabilized sulphur hexafluoride (SF6) microbubbles in saline (0.9% sodium chloride) commercially available in Europe. SonoVue™ was supplied as a sterile lyophilized powder (25 mg) in a gaseous atmosphere (SF6) in 10-mL vials. The SonoVue™ preparation was reconstituted just before administration by adding 5 mL sterile saline to the vial using standard clinical aseptic techniques.

Procedure

Before contrast agent injection, a scanning plane of the liver including the nodule was obtained. After the baseline sonographic examinations, all patients underwent US imaging after the IV administration of the contrast agent SonoVue™.

A volume of 2.4 mL of SonoVue™ was injected intravaneously in bolus via a 20-gauge needle followed by a 5.0 mL saline flush. Contrast-enhanced ultrasonography (CEUS) studies were carried out using a low-pressure setting (mechanical index, 0.09) that was automatically defined by the contrast media software of the ultrasound equipment. Gain ranged from 30 to 90 dB according to the body habitus, the dynamic range was set up to 184 dB, and the frame rate was 13/sec. The line density and frame rate were set to a high level. Images were stored on S-VHS videotapes. Immediately after contrast medium injection, the hepatic lesion to be studied was continuously scanned sonographically for up to five minutes until the enhancement effect began to decrease.

The contrast enhancement pattern was determined by evaluating the behavior of the hepatic lesion throughout the sonographic examination after IV injection of the contrast agent. The whole vascular phase was studied, consisting of the arterial phase (15 to 30 sec following the injection), the portal phase (30 to 60 sec) and the sinusoidal phase (60 to 240 sec). Washout was evaluated as a criterion on contrast-enhanced ultrasonography as it was on CT studies, and this estimated as a change from a hyperechoic lesion relative to the liver at arterial phase to an iso- or hypoechogenic lesion relative to the liver at portal and sinusoidal phases.

The same operator with an experience on sonography of more than 20 years, and who was unaware of CT findings, performed all CEUS studies. He was only requested to describe the pattern of nodule vascularity if any.

A second injection of Sonovue™ was needed in one patient.
## Table. I. Baseline pre-contrast sonographic patterns of hepatocellular carcinomas.

**Tab. I. Pattern degli HCC all’ecografia convenzionale.**

<table>
<thead>
<tr>
<th>Size</th>
<th>No of Tumors</th>
<th>Hypoechoic tumors (%)</th>
<th>Hyperechoic tumors (%)</th>
<th>Isoechoic tumors (%)</th>
<th>Complex tumors (%)</th>
<th>Infiltrative tumors (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.0 cm</td>
<td>28</td>
<td>23/28 (82.1%)</td>
<td>3/28 (10.7%)</td>
<td>1/28 (3.6%)</td>
<td>2/28 (7.1%)</td>
<td>-</td>
</tr>
<tr>
<td>&gt; 2.0 cm</td>
<td>50</td>
<td>25/50 (50%)</td>
<td>4/50 (8%)</td>
<td>3/50 (6%)</td>
<td>15/50 (31%)</td>
<td>2/50 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>48/78 (61.5%)</td>
<td>7/78 (8.9%)</td>
<td>4/78 (5.2%)</td>
<td>17/78 (21.8%)</td>
<td>2/78 (2.6%)</td>
</tr>
</tbody>
</table>

## Table. II. Contrast-enhanced sonographic patterns of hepatocellular carcinomas.

**Tab. II. Pattern degli HCC dopo somministrazione di mezzo di contrasto.**

<table>
<thead>
<tr>
<th>Size</th>
<th>No of Tumors</th>
<th>Hypervascular (%)</th>
<th>Avascular (%)</th>
<th>Missed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.0 cm</td>
<td>28</td>
<td>15/28 (53.6%)</td>
<td>10/28 (35.7%)</td>
<td>3/28 (10.7%)*</td>
</tr>
<tr>
<td>&gt; 2.0 cm</td>
<td>50</td>
<td>46/50 (92%)</td>
<td>4/50 (8%)</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>61/78 (78.2%)</td>
<td>14/78 (17.9%)</td>
<td>3/78 (3.8%)</td>
</tr>
</tbody>
</table>

*one case was technically inadequate.
* un caso è stato tecnicamente impossibile da studiare.

## Table. III. Contrast-enhanced helical CT patterns of hepatocellular carcinomas.

**Tab. III. Pattern degli HCC alla TC spirale con mdc.**

<table>
<thead>
<tr>
<th>Size</th>
<th>No of Tumors</th>
<th>Hypervascular (%)</th>
<th>Hypovascular (%)</th>
<th>Missed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2.0 cm</td>
<td>28</td>
<td>12/28 (42.9%)</td>
<td>13/28 (46.4%)</td>
<td>3/28 (10.7%)</td>
</tr>
<tr>
<td>&gt; 2.0 cm</td>
<td>50</td>
<td>39/50 (78%)</td>
<td>8/50 (16%)</td>
<td>3/50 (6%)</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>51/78 (65.4%)</td>
<td>21/78 (26.9%)</td>
<td>6/78 (7.7%)</td>
</tr>
</tbody>
</table>
Before the injection of the contrast agent, on baseline sonography all lesions appeared as solid masses with different sonographic patterns. The most common sonographic appearance of overall hepatocellular carcinomas was a hypoechoic mass (48/78 tumors, 61.5%). The remaining nodules showed the sonographic pattern of a complex mass in 17/78 cases (21.8%), of a hyperechoic mass in 7/78 cases (8.9%), of an isoechoic mass in 4/78 cases (5.2%), and of an infiltrative mass in 2/78 cases (2.6%). A hypoechoic halo was present in 3 of 78 tumors, two of them were hyperechoic lesions.

When the low mechanical index contrast media setting of the ultrasound machine was switched on, no backscattering from tissues was seen except for the diaphragm’s echoes. 11±2 sec after the injection of the contrast agent, the hepatic arterial vascular bed was visualized in real-time as hyperechoic lines going from the hepatic hilum into the liver parenchyma.

We observed two patterns of tumor hypervascularity:
I) a homogeneous and rapid filling of the lesion (15-20 sec following the injection) that became intensely hyperechoic compared to the surrounding liver tissue with a rapid washout of the contrast agent and thus an appearance of hypoechoic lesion in the portal and sinusoidal phases (Fig. 1);
II) a reticular, inhomogeneous filling of the lesion that became hyperechoic compared to the surrounding liver tissue during the arterial phase (15-20 sec following the injection) and that showed a delayed (up to four minutes) washout thus remaining hyperechoic respect to the surrounding liver tissue during the portal and sinusoidal phases (Fig. 2).

After IV injection of the contrast medium, some lesions did not show any enhancement whereas others lost the appearance of nodular masses and were not seen any more. Therefore, the tumors were classified as follows:
I) hypervascular either when the nodule showed an early, intense, and homogeneous enhancement during the arterial phase (15 to 30 seconds from the IV bolus) with a rapid washout of the contrast agent so that it was hyperechoic to liver on the arterial phase and hypoechoic to liver on the portal phase, or when the nodule showed an early and heterogeneous enhancement during the arterial phase lasting longer time so that the lesion was hyperechoic to liver on the arterial, portal and sinusoidal phases;
II) avascular when no enhancement of the tumor was observed after the injection of the sonographic contrast agent, that is the lesion was hypoechoic to liver on the arterial, portal and sinusoidal phases (Fig. 3);
III) missed when the nodular lesion seen on conventional pre-contrast sonography was not visible as a occupying-space lesion after contrast agent injection.

CEUS was technically inadequate in one case even after a second IV injection of the contrast agent.

After IV injection of the contrast agent SonoVue™, 61 of 78 hepatocellular carcinomas (78.2%) showed a hypervascular pattern, and 14 of 78 tumors (17.9%) were avascular. Three of 78 tumors (3.8%) were missed.

Contrast-enhanced helical CT showed hypervascular tumors in 51 of 78 cases (65.4%) and hypovascular tumors in 13 of 78 (26.9%). Six of 78 tumors (7.7%) were missed.

All differences between contrast-enhanced helical CT and CEUS were not statistically significant.

Hepatocellular carcinomas with a diameter smaller than or equal to 20 mm.

Contrast-enhanced sonographic patterns of hepatocellular carcinomas are reported in Table II. On CEUS 15 of 28 tumors (53.6%) showed a hypervascular pattern, and 10 of 28 tumors (35.7%) were avascular. Three of 28 tumors (10.7%) were missed. Six of the 15 (40%) hypervascular tumors showed a reticular pattern. Contrast-enhanced CT patterns of hepatocellular carcinomas are reported in Table III.

Contrast-enhanced helical CT showed hypervascular tumors in 12/28 cases (42.9%), and hypovascular tumors in 13/28 (46.4%). Three of 28 tumors (10.7%) were missed. All differences between contrast-enhanced helical CT and CEUS were not statistically significant.

Contrast-enhanced sonographic patterns of hepatocellular carcinomas are reported in Table II. On CEUS, 46 of 50 tumors (92%) showed a hypervascular pattern, and four of 50 tumors (8%) were avascular. Two of the 46 (4.3%)
hypervascular tumors showed a reticular pattern. Contrast-enhanced CT patterns of hepatocellular carcinomas are reported in Table III. Contrast-enhanced helical CT showed hypervascular tumors in 39 of 50 cases (78%), and hypovascular tumors in eight of 50 cases (16%). Three of 50 tumors (6%) were missed. All differences between contrast-enhanced helical CT and CEUS were not statistically significant. There was concordance between CEUS and contrast-enhanced helical CT in 65 of 78 (83%) cases (Table IV).

Discussion
Contrast-enhanced helical CT is the most commonly used method for the characterization and staging of hepatocellular carcinoma mainly because of increased ability of arterial phase enhancement to visualize hypervascular lesions (11-16). Although sonography is able to detect focal lesions of the liver, the assessment of the nature of the lesion is disappointing (26,27). Detection and characterization of tumor vascularity are important in the differential diagnosis, the choice of treatment method, and the evaluation of the therapeutic response for hepatocellular carcinoma.
In selected patients, potentially curative therapies for small lesions are currently available (6-9). Therefore, an early detection of the tumor in high-risk patients is mandatory. The guidelines of the European Society for the Study of Liver Disease (EASL) recommend that the imaging detection of a liver nodule smaller than 2 cm should always be confirmed by needle-biopsy, whereas the coincident findings in at least two imaging techniques (US, CT or MRI) of a tumor larger than 2 cm may confidently establish the diagnosis without needing confirmation with a positive biopsy (9).

However, the risk of seeding of hepatocellular carcinoma following needle-biopsy can’t be disregarded because tumor seeding may have a major impact on patients prognosis hindering liver transplantation or surgical resection (17-20). Therefore, there is a need for the availability of accurate and sensitive imaging techniques to confidently depict subtle nodules of hepatocellular carcinoma.

The use of conventional or contrast-enhanced Doppler sonography to provide vascular information is often limited by hepatic masses that are deep in the abdomen, are small, or are subject to motion artifacts from either respiratory or cardiac activity (25). Helical CT is so far-
Contrast-enhanced sonography versus contrast-enhanced helical CT in the evaluation of hepatocellular carcinoma in cirrhotic patients

Figure 3. Subcostal sonogram of the liver.
A. Conventional sonography shows a 25 mm liver nodule in segment VIII.
B. After IV injection of contrast agent no enhancement of the nodular lesion is observed. Tumor has become anechoic respect to surrounding liver parenchyma.

Fig. 3. Scansione sottocostale ascendente del fegato.
A. L’ecografia convenzionale evidenzia un nodulo di 25 mm nel segmento VIII.
B. La somministrazione e.v. del mezzo di contrasto non determina enhancement del nodulo che appare anecogeno.

considered the imaging modality of choice for the diagnosis and staging of hepatocellular carcinoma on cirrhosis (10-16).

Sonographic contrast agents can provide information about microvascular flow and perfusion not currently obtainable using conventional ultrasound techniques. Microbubble contrast agents interact with the scanning process. The nature of this interaction depends on the scanning parameters, mainly the peak rarefractional pressure and the ultrasound frequency. A combination of these parameters is expressed by the mechanical index (25). Using a very low mechanical index to minimize the harmonic response from tissues, the second generation of ultrasound contrast agents produces images of the microcirculation based only on the response of microbubbles.

In the present study, the 28 tumors with a diameter smaller than or equal to 2 cm showed a hypervascular pattern in 53.6% (15/28) of cases at CEUS and in 42.9% (12/28) of cases at helical CT. For the 50 tumors with a diameter larger than 2 cm, the hypervascular pattern was observed in 92% (46/50) of cases at CEUS and in 78% (39/50) of cases at helical CT. There were no statistically significant differences between CEUS and contrast-enhanced helical CT in the visualization of the hypervascular pattern, which is considered specific of hepatocellular carcinoma.

In our series of patients, about 10% of small hepatocellular carcinomas were seen as hypervascular lesions on CEUS whereas they showed a hypovascular pattern on contrast-enhanced CT, this difference was not statistically significant. Probably there is an advantage of CEUS respect to contrast-enhanced helical CT that could be due to a continuous real-time imaging, thus permitting the detection of a fleeting hypervascularity that could be missed in a technique such as CT which is dependent upon interval-delay imaging acquisition.

On the other hand, increased real time imaging potentially increases overall exam time. For this reason, CT may remain preferable due to issues of time.

There are some limitations when using sonographic imaging technique. Sonography is a procedure still operator dependent, strongly influenced by the skillfulness of the operator, and susceptible to patient body habitus. Moreover, to study the characteristics of a focal lesion with CEUS it is necessary to choose the scanning plane where the lesion is located. Therefore, in patients with multiple lesions it is not possible to study all of them simultaneously but only one at a time could be investigated because of the rapid contrast filling and washout of the majority of the hypervascular lesions. CT has the advantage of following patients with multiple liver lesions, as many cirrhotics have.

For the purpose of this study, only patients with a single liver nodule were selected.

A contrast-enhanced dynamic study is considered an important factor in the detection of hepatocellular carcinoma. Of paramount importance is the observation of an early tumor enhancement, which is determined by its hypervascularity, as observed on angiography (28). In this study, both operators were unblinded with respect to the presence of the liver nodules but they were unaware of the findings of the other imaging technique.

The use of a multidetector CT scanner could have improved the detection rate of hepatocellular carcinomas. Nonetheless, the design of the study was to compare CEUS appearance of hepatocellular carcinomas with that of a standardized widely available imaging technique.
such as helical CT.

Lesions hyperenhancing at arterial phase CT that were proven not to be hepatocellular carcinomas have been reported (29). On the other hand, hypervascular metastases should be taken into account (30). All patients included in our study had a biopsy-proven hepatocellular carcinoma, thus excluding any false-positive detection rate.

The information concerning the sonographic appearance of hepatocellular carcinomas using non-destructive contrast agent imaging techniques obtained in this study can be used in further studies to investigate how well contrast-enhanced sonography characterizes liver lesions and to see whether it can be used to supplant biopsy.

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