Comparison of contrast-enhanced ultrasonography with grey-scale ultrasonography and contrast-enhanced computed tomography in diagnosing focal fatty liver infiltrations and focal fatty sparing

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ABSTRACT

Purpose: Fatty liver infiltrations and fatty sparing impair diagnostic performance of grey-scale ultrasonography in differentiating malignant and benign focal liver lesions. In the study, we present our experience in diagnosing focal fatty liver infiltrations and focal fatty sparing with contrast-enhanced ultrasonography (CEUS) in comparison to grey-scale ultrasonography and contrast-enhanced computed tomography (CECT).

Material and Method: The retrospective study group (n=82 patients), included 44 (53.7%) men, 38 (46.3%) women (aged 29-81 years, mean 55.8 years) with 48 focal fatty liver infiltrations and 34 focal fatty sparing. All patients underwent grey-scale ultrasonography (US), CEUS using SonoVue® and CECT executed within the 7 days.

Results: With US, CEUS and CECT focal fatty liver infiltrations were diagnosed in 22, 46 and 44 cases, respectively. The following values were obtained: sensitivity - 45.8%, 95.8% and 91.7%, specificity - 100% for all, accuracy - 95.2%, 99.6% and 99.3%, respectively. Focal fatty sparing was diagnosed in 16, 31 and 30 cases, respectively. The following values were obtained: sensitivity - 47.1%, 91.2% and 88.2%, specificity - 99.8%, 100% and 100%, accuracy - 95.6%, 99.4% and 99.3%, respectively. No statistically significant differences were found in sensitivity of diagnosing focal fatty liver infiltrations and focal fatty liver sparing between CEUS and CECT. Sensitivity of grey-scale ultrasonography was significantly lower when compared to those of CEUS and CECT (p<0.001).

Conclusion: CEUS is as sensitive as CECT in focal fatty infiltrations and focal fatty sparing diagnosing. However, CEUS provides more information than CECT about the vasculature and enhancement pattern of focal fatty liver infiltrations.

Key words: Contrast-enhanced ultrasonography, Contrast-enhanced computed tomography, Focal fatty liver infiltrations, Focal fatty sparing
INTRODUCTION

Focal fatty liver infiltration and focal fatty liver sparing are among the most common benign liver entities in clinical practice. Focal fatty infiltrations have been detected in up to 25.6% of young adults [1], while the prevalence of focal fatty sparing was reported in 13-77.6% of patients with liver steatosis, which is found in 20-30% of the general adult population of the western world [2,3]. Focal fatty infiltrations as well as focal fatty sparing may impair diagnostic performance of grey-scale ultrasonography (US) and computed tomography (CT) in differentiating malignant and benign focal lesions and provoke the use of more sophisticated diagnostic techniques such as magnetic resonance imaging (MRI) or biopsy [4-8]. Nowadays US is the first-line technique of investigation in evaluating liver pathologies. For further diagnosis contrast-enhanced computed tomography (CECT) is usually used [9-11]. Unfortunately, this technique involves exposure to radiation and results in adverse effects after contrast media administration [12-14]. Technical advances in ultrasonography and contrast media result in widespread application of the contrast-enhanced ultrasonography (CEUS) [15-22]. Nowadays second generation contrast agents are used. Among them SonoVue® is well known. The agent contains sulfur hexafluoride gas stabilized with phospholipids which presents a high reflectivity at low mechanical index and persists in the blood stream much longer after intravenous injection in comparison with the previous generation contrast agent – Levovist [23-25]. SonoVue® is characterized by low solubility in water and low diffusion in blood. It does not disperse into the extracellular space (as iodinated contrast agents in computed tomography) and therefore permits a more accurate demonstration of persisting blood flow in the lesion. CEUS and the above mentioned properties of SonoVue® allow real time and continuous imaging of the microarchitecture of the liver for up to 11 minutes [26]. Ultrasound imaging using an inverted pulse with the contrast medium administration has been proved useful in diagnosing liver lesions [27-30]. Xie et al. based on meta-analysis of 25 studies have even concluded that sensitivity and specificity of CEUS (87% and 89%, respectively) is not significantly different than that of CECT (86% and 82%, respectively) in diagnosing focal liver lesions [31]. However, only a few papers have reported application of CEUS for evaluation of focal fatty infiltrations and focal fatty sparing and they have presented a limited number of patients with these entities [32-34].

The aim of the study was to compare diagnostic performance of contrast-enhanced ultrasonography versus grey-scale ultrasonography and contrast-enhanced computed tomography in evaluation of focal fatty liver infiltrations and focal fatty liver sparing.

MATERIALS AND METHODS

This was a retrospective study performed with the approval of the Ethics Committee of our institution. Fully informed consent was obtained from all patients.

We searched our institutions systems to identify patients who were examined with US, CEUS and CECT and diagnosed with focal fatty liver infiltrations or focal fatty sparing. Patients with coexisting liver neoplasm were excluded.

The study group consisted of 82 patients (44 (53.7%) men, 38 (46.3%) women), aged between 29 and 81 years (mean age 55.8 ± 10.9 years) with solitary focal fatty liver infiltrations or focal fatty liver sparing, selected from the group of 544 patients investigated between 2006 and 2011 year because of suspicion of the liver neoplasm. Tab. 1 presents conditions and clinical disorders coexisting with examined entities in the studied group. In 10 subjects no clinical disorders were found. The final diagnosis of fatty liver infiltrations and fatty liver sparing were based on imaging techniques: CECT (74 cases), MRI (12 cases) and biopsy (12 cases). Tab. 2 and Tab.

<table>
<thead>
<tr>
<th>Conditions and disorders</th>
<th>Number (n)</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>20</td>
<td>24.4</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19</td>
<td>23.2</td>
</tr>
<tr>
<td>Steroids use</td>
<td>12</td>
<td>14.6</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>7</td>
<td>8.5</td>
</tr>
<tr>
<td>Viral infection</td>
<td>6</td>
<td>7.3</td>
</tr>
<tr>
<td>Alcohol overuse</td>
<td>8</td>
<td>9.7</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>87.9</td>
</tr>
</tbody>
</table>

Table 1. Conditions and clinical disorders in the examined group

<table>
<thead>
<tr>
<th>Conditions and disorders</th>
<th>Number (n)</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grey-scale ultrasonography (US)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphology: hyperechoic area with wedge-shaped or geographic margin in normal liver, no mass effect, undisturbed vessels traversing through the lesion. Localization: adjacent to falciform ligament, portal vein, gallbladder fossa, subcapsular.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast-enhanced ultrasonography (CEUS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogenous and iso-enhancing in all vascular phases.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast-enhanced computed tomography (CECT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypodense area (values &lt; 40 HU, and at least 10 HU lower than density of the spleen). Homogenous and iso-enhancing in all vascular phases.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnetic resonance imaging (MRI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area of increased signal on T1-weighted image. In-phase/out of phase: signal drop-out in out of phase imaging.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Diagnostic criteria of focal fatty sparing [20,35,37,38].

<table>
<thead>
<tr>
<th>Area of hyperintense signal on opposed-phase images, appears normal and similar to the rest of the liver on T2 weighted images and magnetic resonance imaging (MRI)</th>
<th>Homogenous and iso-enhancing in all vascular phases.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnetic resonance imaging (MRI)</td>
<td>Area of hyperintense signal on opposed-phase images, appears normal and similar to the rest of the liver on T2 weighted images and contrast enhanced sequences. The rest of the liver demonstrates signs of hepatic steatosis.</td>
</tr>
</tbody>
</table>

Table 4. Postinjection time of vascular phases in contrast-enhanced ultrasonography (CEUS) and contrast-enhanced computed tomography (CECT) of the liver.

<table>
<thead>
<tr>
<th>Time (s)</th>
<th>CEUS</th>
<th>CECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
<td>Start</td>
<td>End</td>
</tr>
<tr>
<td>Arterial</td>
<td>10 - 20</td>
<td>25-35</td>
</tr>
<tr>
<td>Portal-venous</td>
<td>30 - 45</td>
<td>120</td>
</tr>
<tr>
<td>Late</td>
<td>&gt; 120</td>
<td>240 - 350</td>
</tr>
</tbody>
</table>

show diagnostic criteria of focal fatty liver infiltrations and focal fatty sparing in US, CEUS, CECT and MRI. All examinations were carried out within the period of 7 days.

US and CEUS examinations were performed by senior radiologists with over 9 years’ experience in contrast-enhanced ultrasonography, using Sonoline Elegra scanner (Siemens Ultrasound, Erlangen, Germany) equipped with Ensemble Contrast Imaging (ECI) software or Toshiba Apio scanner (Toshiba Medical Systems Corporation, Otawara, Japan) equipped with Contrast Harmonic Imaging (CHI) software, both with use of the wide-band, multi-frequency convex array abdominal transducers. During US examination the following parameters were assessed: echogenicity of the liver, morphology of focal fatty liver infiltrations and focal fatty sparing (echogenicity, size, margins, shape, and mass effect). Lesions were identified as typical-looking (in shape: wedge-shaped, geographic and location: periportal, subcapsular, near falciform ligament, in gallbladder fossa) and non-typical looking – nodular or mass-like [4]. A commonly referred to three point scoring system for fatty liver was used [35]. Localization of nodular lesions was assessed according to Couinaud’s and Bismuth’s classification systems [36]. Dynamic real-time CEUS was performed using low mechanical index (MI) (SIEMENS Elegra - MI 0.1, TOSHIBA Apio - MI 0.07) to avoid microbubble disruption. A bolus of 2.4 ml of SonoVue® (Bracco, Italy) was administered with a 21-gauge peripheral intravenous cannula, followed by a 10 ml saline flush. After SonoVue® injection, lesions were scanned continuously for up to 10 min until the enhancement effect began to subside. Recognition of focal fatty liver infiltrations and focal fatty sparing with CEUS was based on enhancement: wash-in and wash-out patterns of the lesion, relative to normal hepatic parenchyma during three vascular contrast phases (Tab. 4) according to the guidelines for contrast-enhanced ultrasonography by Claudon et al. [20].

Computed tomography examinations of the liver were performed with a multi-slice CT scanner Aquilion 16(Toshiba Co. Ltd., Tokyo, Japan). Images were reconstructed with a 1-mm slice thickness at 0.8 mm intervals. Non enhanced imaging was first performed through the liver. Contrast agent (jomeprol, Iomeron 400, Bracco Imaging, Germany) was administered by infusion pump through the antecubital vein followed by saline infusion flush. Contrast volume was estimated according to the rule [time of scanning+10] x 4 and infusion rate of 4 ml/s was set. The start of image acquisition was adjusted automatically by bolus tracking (SUREStart ) when 150 HU of contrast concentration was detected at a region of interest located in descending aorta. Triphasic contrast-enhanced CT scanning protocol was used: late arterial phase, portal phase and equilibrium phase. Computed Tomography scans started with a 10 s delay after the enhancement in the trigger ROI exceeding 150 HU. Tab. 3 shows the time of the start and the end of all phases of CECT examination. CECT images were analysed by a radiologist with 11 years of experience in abdominal imaging on available workstation (Vitrea 4.2 Vital Inc.). The liver density measurements were carried out by drawing elliptical regions of interest (ROI) in the axial scans at several locations and different levels. Unenhanced CT images were assessed for qualitative evaluation of steatosis and the spleen density was used as the reference organ for comparison. Fatty liver was diagnosed if the attenuation of the liver was at least 10 HU less than that of the spleen or if the attenuation of the liver was less than 40 HU [37]. Severe cases were diagnosed when intrahepatic vessels have appeared hyperattenuated in relation to the fat-containing liver tissue [38]. To assess focal liver lesions, average densities of ROI from pre- and post-contrast phases were estimated and then compared.

All continuous variables in statistical format were presented as a summary: mean, standard deviation and range. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for assessment of focal fatty liver infiltrations was calculated for US, CEUS,
CECT using the final diagnosis as a reference. Differences between US, CEUS and CECT were analyzed using the McNemar test-sided test. P<0.05 was considered as being statistically significant.

RESULTS

There were 48 (58.5%) cases of focal fatty liver infiltrations and 34 (41.5%) of focal fatty sparing in the examined group. Dimensions of focal fatty liver infiltrations were 8-135 mm (33.2 ± 23.2 mm). Dimensions of focal fatty sparing were 35-73 mm (54.6± 9.2 mm). In the group with sparing areas the liver steatosis was found to be moderate in 32 (94%) cases and severe in 2 (6%) cases. In the group with focal fatty liver infiltrations in 24 (50%) patients nodular pattern was observed, while in the group with focal fatty sparing lesions nodular pattern was detected in 18 (53%) patients. Nodular fatty liver infiltrations were most often detected in segment VI, while nodular fatty sparing in segment V (Table 5). Wedge-shaped and geographical-shaped fatty liver infiltrations were found periportally in 9 (18.7%) cases, subcapsularly in 5 (10.4%) cases, near falciform ligament in 4 (8.4%) cases, in gallbladder fossa in 2 (4.2%) cases, in segment III in 1 (2%) case and VI in 1 (2%) cases. Wedge-shaped and geographical-shaped focal fatty sparing was detected close to the portal vein in 5 (14.7%) cases, falciform ligament in 4 (11.8%) cases, in gallbladder fossa in 7 (20.6%) cases, in segment II in 2 (5.9%) cases. In 1 (2.9%) case focal fatty sparing was detected around the focal nodular hyperplasia.

Grey-scale ultrasonography

With US focal liver lesions were diagnosed in 38/82 (46.3%) cases, including 22/48 (45.8%) cases of focal fatty liver infiltrations and 16/34 (47%) cases of focal fatty sparing. Among undiagnosed with US there were 2/34 (5.9%) cases of focal fatty sparing areas in severe steatosis and 1/34 (2.9%) case, which was recognized as a focal fatty sparing instead of the perilesional sparing around focal nodular hyperplasia (FNH).

Contrast-enhanced ultrasonography

With contrast-enhanced ultrasonography 77/82 (93.9%) focal liver lesions were diagnosed, including 46/48 (95.8%) cases of focal fatty liver infiltrations (Fig. 1) and 31/34 (91.2%) cases of focal fatty sparing. CEUS enabled diagnosis of a mass-like fatty liver infiltration within the cirrhotic liver, as well as FNH masked by fatty sparing (Fig. 2 and Fig. 3), both lesions not diagnosed with US. CEUS, as well as US, has failed to visualize focal fatty sparing in 2 (5.9%) cases with severe steatosis. In both patients the liver parenchyma was visible only to the depth of about 4 cm.

In 2 (4.1%) cases of focal fatty liver infiltrations and 1 (2.9%) case of focal sparing diagnosed with US the dynamics

Table 5. Distribution of nodular focal fatty liver infiltrations and nodular focal fatty sparing in the liver segments.

<table>
<thead>
<tr>
<th>Segment</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
<th>VIII</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal fatty liver infiltration (n)</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>5</td>
<td>1</td>
<td>26</td>
</tr>
<tr>
<td>Focal fatty sparing (n)</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

n - number of nodular focal fatty liver infiltrations and nodular fatty sparing

Table 6. Number (n) of focal fatty liver infiltrations diagnosed with US, CEUS, CECT and sensitivity (%), specificity (%), accuracy (%), PPV (%), NPV (%) of these techniques.

<table>
<thead>
<tr>
<th>Diagnostic technique</th>
<th>Number (n)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>22</td>
<td>45.8</td>
<td>100</td>
<td>95.2</td>
<td>100</td>
<td>95</td>
</tr>
<tr>
<td>CEUS</td>
<td>46</td>
<td>95.8</td>
<td>100</td>
<td>99.6</td>
<td>100</td>
<td>99.6</td>
</tr>
<tr>
<td>CETK</td>
<td>44</td>
<td>91.7</td>
<td>100</td>
<td>99.3</td>
<td>100</td>
<td>99.2</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Number (n) of focal fatty sparing diagnosed with US, CEUS, CECT and number (n), sensitivity (%), specificity (%), accuracy (%), PPV (%), NPV (%) of these techniques.

<table>
<thead>
<tr>
<th>Diagnostic technique</th>
<th>Number (n)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>16</td>
<td>47.1</td>
<td>99.8</td>
<td>95.6</td>
<td>94.1</td>
<td>96.6</td>
</tr>
<tr>
<td>CEUS</td>
<td>31</td>
<td>91.2</td>
<td>100</td>
<td>99.4</td>
<td>100</td>
<td>99.4</td>
</tr>
<tr>
<td>CETK</td>
<td>30</td>
<td>88.2</td>
<td>100</td>
<td>99.3</td>
<td>100</td>
<td>99.2</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
of enhancement after contrast media administration did not correspond with the commonly accepted pattern. In the arterial phase these lesions were homogenous and hypo-enhanced while in the portal and late phase homogenous iso-enhancement compared with the surrounding liver parenchyma was found (Fig.4).

No pathological angioarchitecture was detected using CEUS in 80 (97.5%) cases. Only in 2 (2.4%) cases the pattern of vasculature failed to be assessed due to severe steatosis.
Contrast-enhanced computed tomography

With CECT 74/82 (90.2%) focal liver lesions were diagnosed, including 44/48 (91.7%) cases of focal fatty liver infiltrations and 30/34 (88.2%) cases of focal fatty sparing. In 4 (8.3%) cases focal fatty infiltrations have not been recognized with CECT. They were diagnosed as non-specific small hypodense lesions (metastases or primary liver tumor could not be ruled out). In 4 (11.8%) cases focal fatty sparing was mistakenly recognized as liver tumors. Among these unrecognized focal fatty liver infiltrations there were 2 cases of focal fatty liver infiltrations and 3 cases of focal fatty sparing unrecognized with CEUS. FNH surrounded and masked by fatty sparing was diagnosed with CECT and CEUS, while unrecognized with US.

There were no adverse events related to CEUS or CECT examinations.

Grey-scale ultrasonography is the first-line imaging modality in evaluation of liver diseases, but accurate quantification of fatty infiltration needs ultrasound system.

DISCUSSION

Fatty liver infiltration occurs when deposits of macronodular fat droplets fill the liver parenchyma cells [39]. Focal sparing in fatty liver may result from several mechanisms: regionally decreased portal flow with the following less fat or toxins (e.g. alcohol or chemotherapeutic drugs) delivery to the hepatocytes in regions of decreased portal flow; only hepatocytes that are metabolically normal are susceptible to fat deposition [40]. Several conditions are associated with fatty liver infiltrations including alcoholism, obesity, diabetes mellitus, malnutrition, hepatitis [41,42]. However, steatosis of the liver may be found in patients who are completely asymptomatic [43].

Grey-scale ultrasonography is the first-line imaging modality in evaluation of liver diseases, but accurate quantification of fatty infiltration needs ultrasound system.
US, CEUS and CECT in diagnosing fatty liver infiltrations and focal fatty sparing

Fitted to a custom-built interface card and a work-station for post-processing [44]. Steatosis appears bright (hyperechoic) relative to adjacent cortex of the kidney or spleen [45]. Fatty liver infiltrations as well as fatty sparing can present variable forms in morphology and localization, which makes evaluation of the liver difficult [6,46-48]. They may modify the ultrasonographic appearance of liver tumors, mask them or even mimic the neoplasm [4,49-51]. Quai et al. [10] reported focal fatty liver infiltration and focal fatty sparing mistakenly recognized with grey-scale ultrasonography as metastases. Fatty sparing in caudate lobe seen as a pseudotumor have been also reported by White et al. [8] and Kawashima et al. [52]. The cause of misrecognized lesions of the caudate lobe was most probably the result of different and multisource blood supply to the caudate lobe when compared against other liver parenchyma [53].

In our study, there were fatty liver infiltrations and fatty liver sparing of typical morphology and localization but atypical, nodular and mass-like lesions have occurred. All focal fatty liver infiltrations and focal fatty sparing of typical appearance including these infiltrations in caudate lobe were diagnosed using grey-scale US. However, we have found the lowest sensitivity of US in diagnosing focal fatty liver infiltrations (45.8%) and focal fatty sparing (47.1%) when compared with CEUS (95.8% and 91.2%, respectively) or CECT (91.7% and 88.2%, respectively). Similar disproportions between sensitivity and specificity of US (49%-58.8% and 25%-50.7%, respectively) and CEUS (68.7%-93% and 67%-75%, respectively) were reported in diagnosing other liver lesions [10,33,54,55]. Ooi et al. [56] reported that CEUS can be accurate in differentiating malignant from benign focal liver lesions and may become a useful first-line imaging tool where CT or MRI are not available or contra-indicated.

Homogenous iso-enhancement in all vascular phases is regarded as a distinctive feature of fatty liver infiltrations and fatty liver sparing [20]. The specificity of CEUS in diagnosing focal fatty sparing in our study conformed with that reported by Liu et al. and was 100% [57]. We obtained higher NPV and the accuracy when compared with those reported by Liu et al. (99.4% vs. 95.1% and 99.4% vs.97%, respectively). On the other hand, the sensitivity was slightly lower (91.2 vs. 92.6%, respectively), and PPV was equal (100%). Specificity

Figure 4. Focal fatty sparing:

a. Gray scale sonogram shows a round shape hypoechoic area (arrow) located periportaly.

b. Duplex Doppler sonogram shows hepatopetal venous flow within the area (arrow).

c. CEUS sonogram obtained in the arterial phase (23 s p.i.) shows hypoenhancement of the area (arrow) and the vessel within it (corresponding with the Duplex Doppler sonogram).

d. CEUS sonogram obtained in the late phase (111 s p.i.) shows isoenhancement of the area (arrow) with the surrounding liver parenchyma.
of focal fatty infiltrations evaluation in our study and in that reported by latter authors were 100%, while the sensitivity and accuracy were higher (91.2 vs. 88% and 99.4 vs. 96%, respectively) [34]. Our results correspond with those by Xie et al. [31] who found that sensitivity and specificity of CEUS (87%, 89%) are similar to those of CECT (86%, 82%) in diagnosing focal liver lesions.

However, in diagnosing focal fatty infiltrations and fatty sparing CEUS enabled higher sensitivity than CECT (95.8 vs. 91.7% for focal fatty infiltrations and 91.2 vs. 88.2% for focal fatty sparing), but the difference is not statistically significant. Nevertheless, the application of CEUS, as in the case of US, may be limited by severe fatty infiltration. We have observed 2 cases of focal fatty sparing in severe steatosis, which were omitted using CEUS. In both cases they were too deeply located in the 4th segment. In our study CEUS also failed in diagnosing 2 cases of focal liver infiltrations and 1 focal fatty sparing, which were located in the 4th segment. In the arterial phase these lesions presented hypoenhancement and isoenhancement in the later phases, which was inconsistent with the European Guidelines in Liver Contrast Ultrasound [58]. Similar pattern of enhancement was reported by Liu et al. [34]. The delayed enhancement in the arterial phase is most likely a result of anatomical variants of vascularization of the 4th segment [33].

In contrast to US, with CEUS and CECT we were able to diagnose 1 case of FNH masked by fatty sparing. Peritumoral sparing areas were also reported by Kim et al. [9], Grossholz et al. [40] and Itai et al. [59]. We do agree with Kim et al. [27] who pointed out that focal fatty sparing seen on US examination may be a sign of an adjacent various focal hepatic lesion.

Our study demonstrates that sensitivity of the CEUS (93.9%) is as high as that of CECT (90.2%) with regard to assessment of fatty liver infiltrations. No statistically significant differences between these two methods could be established. Ambiguous and incorrect diagnoses were results of CEUS as well as CECT. However, inaccurate results of CEUS were mostly due to delayed enhancement of focal liver lesions in the arterial phase, which had no effect on recognizing malignancy, while with CECT low density of fatty lesions in the native phase and hypodense appearance of these lesions in portal and late phase may suggest wash out when compared against the surrounding liver parenchyma and gives the suspicion of malignant tumor [5].

Indisputable advantage of CEUS is continuous monitoring of enhancement which gives the opportunity to visualize vascular architecture of the lesion more precisely than CECT, when vascular phases are determined by specific time intervals. Some enhancement patterns, therefore, during arterial phase may not be captured on CECT. In addition, Faccioli et al. [60] have found CEUS the most cost-efficient when compared to the mentioned above techniques. The minimal invasive nature of CEUS with few contraindications for the administration of SonoVue® and the reported low incidence of side effects make this technique a safe alternative to CECT in diagnosing fatty liver infiltrations and fatty liver sparing [36,29,61].

CONCLUSIONS

In conclusion, US is a sufficient technique in diagnosing fatty liver infiltrations and fatty liver sparing of typical appearance. Results of our study show that the sensitivity of CEUS is as high as that of CECT in diagnosing focal fatty liver infiltrations and focal fatty sparing. CEUS, however, provides more information about the vasculature and enhancement pattern of the fatty liver infiltrations and fatty liver sparing than CECT.

ACKNOWLEDGEMENTS

Authors disclose no commercial interest in the subject of the study and in the source of support.

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