Diagnostic Performance for Hepatic Artery Occlusion After Liver Transplantation: Computed Tomography Angiography Versus Contrast-Enhanced Ultrasound

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The purpose of this study was to compare the diagnostic performance of computed tomography angiography (CTA) and contrast-enhanced ultrasound (CEUS) when used to diagnose significant hepatic artery occlusion (HAO) in patients that was suspected on Doppler ultrasound (US). Among 3465 adult liver transplantations (LTs) performed between January 2010 and February 2018, 329 recipients were suspected of having HAO by Doppler US. In these patients, 139 recipients who had undergone both CTA and CEUS as second-line studies were included. CTA and CEUS were retrospectively reviewed using the criteria for HAO used in previous studies (CTA, ≥50% stenosis at the anastomosis; CEUS, no HA enhancement or delayed and discontinuous enhancement). The diagnostic values of CTA and CEUS were compared using the McNemar test. CEUS showed statistically significant better accuracy and specificity than CTA in patients with Doppler US abnormality seen after LT (accuracy, 99.3% versus 89.2%, P < 0.001; specificity, 100% versus 83.1%, P < 0.001). CTA had 15 false-positive diagnoses, and CEUS had 1 false-negative diagnosis. In conclusion, CEUS showed higher specificity and positive predictive value than CTA for the diagnosis of HAO in selected patients with a Doppler US abnormality. However, even if there is no HAO diagnosed on CEUS, continuous monitoring and follow-up imaging are required when HAO is strongly suspected in the clinical setting and on CTA.

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Hepatic artery occlusion (HAO) after liver transplantation (LT) is a devastating complication1,2 that can rapidly progress to early graft failure or acute biliary duct necrosis with or without biliary sepsis and can sometimes lead to patient mortality.1,3-5 Therefore, an immediate therapeutic intervention, such as surgical anastomotic revision or angiographic intervention, is required in most patients with HAO, and even retransplantation may be indicated if the ischemic damage to the hepatic graft is extensive and irreversible. Early detection of HAO and its timely management are crucial for favorable outcomes in LT recipients.6,7

It is generally agreed that Doppler ultrasound (US) is suitable as a surveillance method with acceptable sensitivity for HAO in LT recipients.8,9 However,
it should be remembered that previously published studies also showed that Doppler US has a low positive predictive value (PPV) and a high false-positive rate.\textsuperscript{(10,11)} When HAO is suspected on Doppler US, hepatic arteriography is commonly indicated for a confirmative diagnosis. However, considering the invasiveness and potential complications of hepatic arteriography, an appropriate second-line imaging tool that could complement the low specificity of US would be very helpful for reducing unnecessary hepatic arteriography used to make an accurate diagnosis of HAO.

Three-dimensional computed tomography angiography (CTA) has also been considered a useful evaluation tool in the diagnosis of HAO after LT.\textsuperscript{(12-14)} Contrast-enhanced ultrasound (CEUS) is an imaging technique that provides real-time, angiographic-like images of vessels using a microbubble contrast agent. The efficacy of CEUS as a noninvasive technique for diagnosing HAO after LT has been validated by several clinical investigators.\textsuperscript{(15-17)} However, to our knowledge, there is no sufficiently large study comparing CTA and CEUS as a second-line imaging tool for the diagnosis of HAO in high-risk patients in whom HAO is suspected on Doppler US. Determining the pearls and pitfalls that are often encountered in clinical practice along with the diagnostic value of CTA and CEUS in these situations would be helpful for establishing the potential role of these imaging methods in the clinical algorithm. Therefore, we aimed to evaluate the diagnostic performance of CTA and CEUS and to compare the 2 imaging modalities and their capacity to diagnose significant HAO in LT recipients suspected of having HAO by Doppler US.

Patients and Methods

Our institutional review board approved this study, and informed consent was waived due to the retrospective nature of the analyses.

PATIENTS

Between January 2010 and February 2018, 3465 adults (18 years old or older) received LTs (615 deceased donor liver transplantation [DDLT] and 2850 living donor liver transplantation [LDLT]) at a single medical institution. Among these patients, 329 recipients (69 DDLTs [69/615, 11.2%] and 260 LDLTs [260/2850, 9.1%]) were suspected of having HAO by Doppler US. As part of an extensive radiologic postoperative complication surveillance program in the institution where this study was conducted, Doppler US was performed daily during the first 3 postoperative days, and once or twice per week thereafter during hospitalization. Additional Doppler studies were performed at any time under clinical necessity at the discretion of the treating physicians. The Doppler US parameters for HAO were defined as no Doppler signal or a tardus parvus waveform (with resistive index [RI] <0.5 and systolic acceleration time >0.08 seconds) at the graft HA or a focal high velocity jet >2 meter/second at the anastomosis based on previous studies.\textsuperscript{(8,9)} Among those patients with suspected HAO on Doppler US, we included recipients for whom both CTA and CEUS were successfully obtained as second-line imaging tools for HAO within a week of the Doppler abnormality presentation (Fig. 1).

Finally, 139 recipients with a mean age of 52.4 ± 10.7 years were included for comparing the 2 modalities; 93 were men (age, 52.0 ± 10.4 years; range, 19-74 years), and 46 were women (age, 53.1 ± 11.4 years; range, 21-68 years). Doppler abnormalities were found in 125 patients during their hospitalization and in 14 patients at follow-up visits after discharge. If the patients had undergone multiple CTA and/or CEUS examinations within 1 week of the Doppler abnormality, the earliest examination(s) were selected for each patient. There were 22 patients with HAO who repeatedly underwent the tests while they awaited retransplantation or because they could not undergo angiography or revision operation immediately because of unstable vital signs.

To evaluate the incidence of HAO in the whole cohort, we also searched for patients diagnosed as
having HAO without Doppler US examinations or with negative Doppler US findings. Figure 1 is a flow diagram of the study population.

COMPUTED TOMOGRAPHY AND CEUS METHODS

Computed tomography (CT) scans were obtained using 16–128 multidetector CT scanners (Somatom Sensation 16, Definition, Definition AS, Definition AS+, or Edge, Siemens Medical Solutions, Erlangen, Germany; LightSpeed 16, GE Medical Systems, Milwaukee, WI) in the unenhanced, arterial, and portal phases with a standard dose (200 effective mAs and 120 kVp). The actual radiation dose was adjusted based on the patient’s body size and shape by automatically modifying the tube current. After nonenhanced CT scans were obtained, each patient was intravenously administered 120-150 mL of iopromide (Ultrasound 370; Schering, Berlin, Germany) at a rate of 3 mL/second via the antecubital vein using a mechanical injector (Percupump II, E-Z-Em, Westbury, NY). Arterial phase images were obtained using a bolus-tracking technique with a trigger enhancement threshold at the upper abdominal aorta of 100 Hounsfield units. A delay time of 10–15 seconds was used for the arterial phase after the threshold was reached. The parameters used for hepatic arterial phase CT scanning included a detector configuration of 0.75 mm × 16 for a 16-channel CT scanner and 0.6 mm × 64-128 for a 64-128 channel CT scanner. The CT images were reconstructed with section thicknesses and intervals of 3 mm for the axial images and 5 mm for the coronal images. In addition, the images were reconstructed at 1-mm section thicknesses and 0.70-mm intervals for the Somatom series or 0.625-mm section thicknesses and 0.625-mm intervals for the LightSpeed 16 scanner and were then downloaded to a workstation (Advantage Windows, version 4.6; GE Medical Systems, Milwaukee, WI; AquariusNet, TeraRecon, Inc., Foster City, CA) for 3-dimensional reconstruction of HAs. Volume-rendering and maximum intensity projection techniques were used as standard algorithms.

CEUS was performed by board-certified, abdominal radiology fellows (5 or 6 in each academic year; <2 years of experience in LT imaging) under the supervision of a staff radiologist (>10 years of experience in LT imaging) after administration of SonoVue (Bracco Imaging, Milan, Italy) using a Sequoia 512 scanner (Acuson Siemens, Mountain View, CA) with a 1-4–MHz transducer or Toshiba Aplio 500 (Toshiba Medical Systems Cooperation, Tokyo, Japan) with a 1.6–6.0–MHz transducer. After manually mixing a bottle of SonoVue with 5 cm³ of saline, half of the mixture was administered via a bolus injection through the central venous route, and

FIG. 1. A flow diagram describing the categories of this study population.
the graft HA was evaluated using a contrast pulse sequencing (contrast-coherent imaging) or contrast harmonic imaging mode. Patients were placed in the supine position with their head elevated and the right arm abducted, and most examinations were performed using oblique intercostal scanning. We evaluated 2 phases: the hepatic arterial phase and the portal parenchymal phase. The hepatic arterial phase was qualitatively defined as the time from contrast agent arriving in the graft HA to partial opacification of the main portal vein (half of the area of the vein on visual assessment). The portal venous phase was qualitatively defined as the time from complete opacification of the main portal vein to peak enhancement of the hepatic parenchyma.\(^{(18)}\)

**INTERPRETATION OF IMAGES**

We used diagnosis criteria of HAO based on previous studies, and the criterion for CTA was defined as $\geq 50\%$ stenosis at the anastomosis.\(^{(10,12)}\) For CEUS, the criterion was defined as no HA enhancement or abnormal HA enhancement, ie, delayed and discontinuous enhancement (Fig. 2).\(^{(17)}\)

CTA or CEUS images were anonymized, coded, and put into a picture archiving and communication system folder. Window levels were not standardized, thus allowing the observers to choose their preferred window values on the picture archiving and communication system workstation. There were 2 board-certified radiologists who were blinded to the final outcome and to each other’s results and who independently evaluated all of the CTA and CEUS examinations. Reviewer 1 had $>10$ years of clinical experience with LT imaging, and reviewer 2 had 4 years of clinical experience with LT imaging. For all of the patients, in a second reading, agreement was reached in consensus with an interval of at least 30 days between both readings.

**CLINICAL OUTCOMES**

A board-certified radiologist (with 4 years of clinical experience) and a LT surgeon (with 4 years of clinical experience) reviewed the radiologic and medical records of the patients in order to determine the clinical outcome and categorized them according to the presence or absence of HAO (Fig. 1). We defined HAO as a totally occluded HA or partially occluded HA that was causing complications. A reference diagnosis of HAO was made by surgery, hepatic arteriography, or follow-up imaging findings as follows:

1. Surgical findings of HAO that necessitated HA revision or retransplantation due to graft failure related to HAO (usually accompanying multifocal infarction).
2. Hepatic arteriographic findings of HAO from near-total or total occlusion to luminal diameter $<50\%$ and flow disturbance.

**FIG. 2.** A true-positive diagnosis using CT angiography and CEUS in a 68-year-old female with HAO after LDLT using a right liver graft. The patient underwent retransplantation due to graft failure with multifocal infarction by HAO. (A) The coronal maximal intensity projection shows $\geq 50\%$ stenosis at the anastomosis of the HA (arrows). (B) CEUS shows faint and delayed enhancement of the HA at a later vascular phase (arrows).
3. Persistent no flow or progressive change from tardus parvus waveform to no flow on Doppler US follow-up studies associated with the development of multifocal, wedge-shaped ischemia or infarction or a nonanastomotic biliary complication, such as bile duct necrosis/biloma, presumably as a complication of HAO seen on follow-up CT.

We defined non-HAO as the normalization of Doppler US abnormalities and no association with graft ischemia or infarction within 1 month of follow-up.

**STATISTICAL ANALYSIS**

All statistical analyses were performed using commercially available statistical software (PASW Statistics for Windows, version 21.0, SPSS Inc., Chicago, IL). A $P$ value of $<0.05$ was considered statistically significant. The demographics of the 2 groups, ie, HAO versus non-HAO, were compared using the Student $t$ test for continuous variables and the chi-square test for discrete variables. For evaluation of the diagnostic value of CTA and CEUS for HAO, the sensitivity, specificity, PPV, negative predictive value (NPV), and accuracy were used. Interobserver variability was determined using kappa statistics. Agreement was considered to be poor, when $\kappa$ was $\leq 0.20$; fair, when $\kappa$ was between 0.21 and 0.40; moderate, when $\kappa$ was between 0.41 and 0.60; good, when $\kappa$ was between 0.61 and 0.80; and excellent, when $\kappa$ was $>0.80$. We also evaluated the discordance between the primary reports of CTA or CEUS at the time of clinical practice and the results of retrospective analyses. The diagnostic performance of CTA and CEUS were compared using the McNemar test in the subgroup of 139 patients evaluated with both methods.

**Results**

Figure 1 illustrates the distribution of the study population in each category. Among the 3465 patients with LT, 73 (2.1%) patients had true HAO. The incidence of HAO was 3.1% (19/615) in DDLTs and 1.9% (54/2850) in LDLTs. Recipients with HAO first had a documented abnormality on Doppler US at a mean of $25.5 \pm 64.7$ days (range, 1-379 days; median, 7 days; interquartile range, 2-18 days) after LT, except 2 patients without Doppler abnormality. HAO was confirmed by surgical findings of HAO necessitating a revision operation of HA ($n = 24$) or liver retransplantation due to graft failure related to HAO (accompanying multifocal infarction; $n = 13$), angiography ($n = 17$), and persistent no flow or a progressive change from tardus parvus waveform to no flow that was seen on Doppler US follow-up studies and associated with multifocal infarction seen on follow-up CT or CEUS ($n = 19$). Two patients were diagnosed as HAO with negative Doppler US findings. Table 1 shows the recipient characteristics in each category (HAO and non-HAO groups). HAO occurred more frequently in females than in males ($P < 0.001$).

Among the 73 patients with HAO, 17 (23.3%) patients had mortality including those who received retransplantation due to HAO and died within 1 week after retransplantation. Of those 17 patients, 6 (35.3%) patients received DDLT; 11 (64.7%) patients received LDLT; and 4 (23.5%) patients died of hepatic graft

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients With HAO ($n = 73$)</th>
<th>Patients Without HAO ($n = 3392$)</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Male</td>
<td>38</td>
<td>2519</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>35</td>
<td>873</td>
<td></td>
</tr>
<tr>
<td>Body weight, kg*</td>
<td>$63.9 \pm 13.1$ (30.5-102.0)</td>
<td>$65.8 \pm 11.8$ (30.7-121.5)</td>
<td>0.18</td>
</tr>
<tr>
<td>Body mass index, kg/m$^2$*</td>
<td>$24.1 \pm 4.3$ (13.8-40.7)</td>
<td>$23.8 \pm 3.6$ (13.6-43.1)</td>
<td>0.48</td>
</tr>
<tr>
<td>Transplantation type</td>
<td></td>
<td></td>
<td>0.08*</td>
</tr>
<tr>
<td>DDLT</td>
<td>19</td>
<td>596</td>
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<td>LDLT</td>
<td>54</td>
<td>2796</td>
<td></td>
</tr>
<tr>
<td>Dual graft</td>
<td>3</td>
<td>36</td>
<td></td>
</tr>
</tbody>
</table>

NOTE: Data are given as n or mean ± standard deviation (range).
*The $P$ value compared the number of DDLTs with the number of LDLTs in the HAO group and the non-HAO group.
failure directly caused by HAO (Table 2). Most of the HAOs with mortalities (15/17, 88.2%) showed Doppler abnormalities and were confirmed within 1 month after LT. In an exception, 1 patient who showed HAO 379 days after LT had an ABO-incompatible LT with biliary cast syndrome and died within 1 week after retransplantation due to pseudoaneurysm rupture.

In 272 patients with CTA, the mean interval between the Doppler US showing abnormalities and CTA as a second-line test was 2.5 ± 4.1 days, except for 2 patients with HAO with negative Doppler US findings. The diagnostic values of CTA in 272 patients who underwent CTA as a second-line test with Doppler US abnormalities were as follows: accuracy, 86.8% (236/272); sensitivity, 100% (65/65); specificity, 82.6% (171/207); PPV, 64.4% (65/101); and NPV, 100% (171/171). There was excellent interobserver agreement for CTA diagnosis (κ = 0.88). Category discordance between the 2 readers was observed in 16/272 (5.9%) using CTA. Discordance between a primary report and reanalysis was 1.8% (5 patients).

In 154 patients with successful CEUS, the mean interval between the Doppler US showing abnormalities and CEUS as a second-line test was 0.7 ± 2.4 days. The diagnostic values of CEUS were as follows: accuracy, 99.4% (153/154); sensitivity, 98.1% (53/54); specificity, 100% (100/100); PPV, 100% (53/53); and NPV, 99.0% (100/101). There was excellent interobserver agreement for CEUS diagnosis (κ = 0.91). Category discordance between the 2 readers was observed in 6/154 (3.9%) using CEUS. Discordance between a primary report of the bedside US examiner and reanalysis was found in 1 (0.6%) patient, who did not have HAO.

In 139 patients with both CTA and successful CEUS, the mean interval between the Doppler US showing abnormalities and CTA or CEUS as a second-line test was 2.0 ± 3.7 days and 1.0 ± 2.9 days, respectively (P = 0.01). The mean duration between the CTA and angiography or HAO revision was 1.0 ± 2.3 days, and the duration between the CEUS and angiography or HAO revision was 1.0 ± 2.8 days. The sensitivity, specificity, PPV, NPV, and accuracy

### Table 2. Patients With Mortality After Diagnosing HAO

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Sex</th>
<th>Age, years</th>
<th>Transplantation Type</th>
<th>Interval Between Transplantation and Doppler Abnormality, days</th>
<th>Interval Between Transplantation and Confirmation of HAO, days</th>
<th>Interval Between Transplantation and Mortality, days</th>
<th>Presumed Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>55</td>
<td>DDLT</td>
<td>20</td>
<td>22*</td>
<td>29</td>
<td>AMI</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>62</td>
<td>DDLT (left)</td>
<td>2</td>
<td>5*</td>
<td>11</td>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>53</td>
<td>DDLT (right)</td>
<td>24</td>
<td>26</td>
<td>69</td>
<td>HAO</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>54</td>
<td>DDLT (right)</td>
<td>21</td>
<td>21</td>
<td>33</td>
<td>HAO</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>53</td>
<td>DDLT</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>HAO</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>47</td>
<td>DDLT (right)</td>
<td>15</td>
<td>15</td>
<td>22*</td>
<td>ICH</td>
</tr>
<tr>
<td>7</td>
<td>Female</td>
<td>68</td>
<td>DDLT (right)</td>
<td>62</td>
<td>63*</td>
<td>63</td>
<td>Biliary sepsis</td>
</tr>
<tr>
<td>8</td>
<td>Male</td>
<td>54</td>
<td>DDLT (right)</td>
<td>30</td>
<td>30*</td>
<td>96</td>
<td>Multiorgan failure</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>58</td>
<td>DDLT (right)</td>
<td>379</td>
<td>379*</td>
<td>405*</td>
<td>Pseudoaneurysm rupture after retransplantation</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>31</td>
<td>DDLT (right)</td>
<td>7</td>
<td>7</td>
<td>10*</td>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>11</td>
<td>Female</td>
<td>57</td>
<td>DDLT (right)</td>
<td>13</td>
<td>13</td>
<td>39*</td>
<td>Sepsis</td>
</tr>
<tr>
<td>12</td>
<td>Female</td>
<td>44</td>
<td>DDLT</td>
<td>11</td>
<td>11</td>
<td>39*</td>
<td>Sepsis</td>
</tr>
<tr>
<td>13</td>
<td>Female</td>
<td>54</td>
<td>DDLT (right)</td>
<td>18</td>
<td>20</td>
<td>29</td>
<td>Myocarditis</td>
</tr>
<tr>
<td>14</td>
<td>Female</td>
<td>50</td>
<td>DDLT</td>
<td>3</td>
<td>3</td>
<td>75</td>
<td>SAH</td>
</tr>
<tr>
<td>15</td>
<td>Female</td>
<td>56</td>
<td>DDLT (right)</td>
<td>18</td>
<td>18</td>
<td>20*</td>
<td>Sepsis</td>
</tr>
<tr>
<td>16</td>
<td>Male</td>
<td>53</td>
<td>DDLT</td>
<td>4</td>
<td>4*</td>
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<td>ICH</td>
</tr>
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<td>17</td>
<td>Male</td>
<td>64</td>
<td>DDLT</td>
<td>2</td>
<td>2*</td>
<td>5</td>
<td>HAO</td>
</tr>
</tbody>
</table>

*HAO was confirmed with angiography.
†Transplantation using a dual graft. The type of hemiliver graft is in parentheses.
‡Patients were confirmed with a revision operation of the HA. The other remaining patients were confirmed as having HAO by follow-up imaging studies including CT and Doppler US.
§Patients received retransplantation and died within 1 week after retransplantation.
of CTA and CEUS for patients with Doppler US abnormalities are summarized in Table 3. The accuracy of CEUS was higher than that of CTA with statistical significance (99.3% versus 89.2%; \( P < 0.001 \)). Although the sensitivity did not differ significantly between them, the specificity of CEUS was significantly higher than that of CTA (100% versus 83.1%; \( P < 0.001 \)). CTA had 15 false-positive diagnoses (Fig. 3), but it missed no instances of HAO. CEUS had no false-positive diagnosis, but it missed 1 instance of HAO (Fig. 4). Of 15 false-positive diagnoses on CTA, 7 (46.7%) patients had dissection of the recipient HA without a significant clinical outcome.

### Discussion

HAO is considered to be a serious threat to graft survival after LT. Therefore, early diagnosis and treatment are important for successful management.\(^{(1)}\) HAO is a wide spectrum entity, from partial HAO, ie, significant stenosis, to near-complete or complete HAO, ie, complete thrombotic occlusion. Partial HAO can proceed rapidly to near-complete or complete HAO. Because clinical or laboratory findings of patients with HAO may not show any abnormality until severe damage of the liver parenchyma has occurred and ischemic bile duct injury could rapidly progress, routine radiologic surveillance is important for early postoperative periods with a high frequency of HAO.

In clinical practice, most HAOs are first seen in Doppler US, which is generally accepted as the first-line radiologic surveillance method. Then, if there is an abnormality, CTA and CEUS could be used as a second-line study. Hepatic arteriography and surgery are used to confirm HAO and are used for treatment.

As CT technology advances, it becomes possible to obtain CT images without a moving artifact in early postoperative patients with shallow and unstable breathing, and it allows high-quality images to be generated with excellent anatomical visualization of HA in LT recipients. CTA is a fairly rapid and standardized test. Several previous studies of HAO have used CTA as a reference,\(^{(10,15)}\) and in most studies,
>50% diameter reduction was defined as positive.\textsuperscript{(12,13)} However, our study showed that using this criterion, the specificity and PPV for clinically significant HAO were low. Approximately half of the false-positive diagnoses on CTA were attributed to dissection of the recipient HA around the anastomosis. In such an entity, we assume that morphologic abnormality of the anastomosis may not correlate with significant hemodynamic abnormality.\textsuperscript{(19)} Also, even with the advanced CT technology, there may still be a limitation in stable delineation of small HAs, especially in LDLT CT sometimes exaggerates or overestimates the narrowing around the anastomosis. 

With the advantage of it being a bedside examination, CEUS has complemented Doppler US in many previous studies, particularly those of patients who cannot undergo contrast-enhanced CT because of azotemia or whose vital signs are not stable.\textsuperscript{(20-22)} CEUS provides intuitive real-time images like angiography shortly after the administration of microbubble contrast agents with high frame rates (10-20 frames per seconds), and typically 4-6 images during the arterial phase and a dozen of images during the parenchymal phases are captured with a single injection (video clips can be stored as well). The recommended dose of SonoVue emulsion is 2.5 cm\textsuperscript{3} per injection in humans, permitting the 2 opportunities. In general, there is no significantly challenging step in imaging of a posttransplant hepatic artery (HA) with CEUS if a radiologist or sonographer is already accustomed
to posttransplant hepatic Doppler studies. At Asan Medical Center, CEUS is performed by board-certified abdominal radiology fellows who are acquainted with posttransplant hepatic Doppler studies, and the captured images are reviewed and supervised by a specialist radiologist dedicated for LT imaging. However, it should be mentioned that CEUS may not always be possible particularly in recipients of LDLT with dual grafts because of the small grafts and the poor sono-

graphic window (2 out of 141 patients, 1.4%). Previous

studies have generally used the criterion for HAO as the nonvisualization of the HA on CEUS. In those studies, the reported accuracy, sensitivity, and specificity of CEUS was 100%, 100%, and 100%, respectively.\(^\text{11,20}\) However, in most of the previous studies that focused on the role of CEUS in patients with no flow on Doppler US, the role of CEUS in patients with the tardus parvus pattern seen on Doppler US has been not well addressed. In a recent study, modified criteria of CEUS for HAO was suggested and worked well even in patients with the tardus parvus pattern seen on Doppler US. Using this criterion, in our study, the accuracy of CEUS was statistically significantly higher than that of CTA.

In the diagnosis of HAO after LT, Doppler US, which has high sensitivity, is suitable as a screening tool even though the specificity is low.\(^\text{10,11}\) Alternatively, specificity is as important as sensitivity as a second-line imaging tool. In the present study, CEUS showed significantly higher specificity than CTA in high-risk patients with suspected HAO seen on Doppler US (100% versus 83.1%; \(P < 0.001\)). Therefore, CEUS could be expected to contribute to reducing unnecessary hepatic arteriography or surgical exploration in this clinical setting. However, it should still be noted that there was 1 missed HAO by CEUS. Even though the amount and the speed of microbubble movement in HAs can be assessed, the morphological change of the anastomosis is not directly seen on CEUS. Therefore, in the case of a rapidly progressing type of HAO, CEUS may not show a blood flow abnormality at the beginning. Therefore, even if the CEUS is negative, continuous monitoring and follow-up imaging are required when the HAO is strongly suspected in the clinical setting.

There is a limitation to the present study. First, the mean interval between the Doppler US showing abnormalities and CTA or CEUS as a second-line test was 2.0 ± 3.7 days and 1.0 ± 2.9 days, respectively. This difference reached statistical significance \((P = 0.01)\). This kind of difference in time intervals was attributed to the pattern of clinical workflow and would be an inherent limitation of retrospective study, whereas CEUS could be immediately applied at the bedside when there was Doppler US abnormalities with the same US machine. However, such a workflow is not the case with CTA, and any abnormality might have become more apparent over time in HAOs, at the time of CTA examination. Therefore, even though CEUS showed a better performance than CTA in our series, the difference between the 2 methods may be larger with control of this bias. We think that such a bias can be neutralized by randomization of the study sequence, which would be anticipated in the future prospective study for validation. Second, the standard of reference of HAO was a composite outcome of positive angiography, surgical findings, or clinical progression of HAO. Although 19 of 73 cases of HAO (26.0%) were diagnosed with clinical progression, this would be questionable because clinical outcomes may not exactly reflect HAO or the absence thereof.

In conclusion, CEUS showed higher specificity and PPV than CTA in selected patients for the diagnosis of HAO with a Doppler US abnormality. However, even if there is no HAO on CEUS, continuous monitoring and follow-up imaging are required when HAO is strongly suspected in the clinical setting and on CTA.

REFERENCES


