Received:
14 February 2018

Revised:
29 March 2018

Accepted:
01 May 2018

<https://doi.org/10.1259/bjr.20180182>

Cite this article as:

Jeong SY, Kim KW, Kim JS, Lee S, Kim SY, Song GW, et al. Doppler ultrasonography in liver transplant recipients with hepatic artery dissection: association of Doppler abnormalities with disease severity. *Br J Radiol* 2018; **091**: 20180182.

FULL PAPER

Doppler ultrasonography in liver transplant recipients with hepatic artery dissection: association of Doppler abnormalities with disease severity

¹SO YEONG JEONG, MD, ¹KYOUNG WON KIM, MD, PhD, ²JIN SIL KIM, MD, PhD, ¹SUNYOUNG LEE, MD, ¹SO YEON KIM, MD, PhD, ³GI WON SONG, MD, PhD and ³SUNG GYU LEE, MD, PhD

¹Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, Ulsan, South Korea

²Department of Radiology and Medical Research Institute, School of Medicine, Ewha Womans University, Seoul, South Korea

³Division of Liver Transplantation and Hepatobiliary Surgery, and Departments of Surgery, University of Ulsan College of Medicine, Asan Medical Center, Seoul, South Korea

Address correspondence to:

Assistant Professor Kyoung Won Kim

E-mail: kimkw@amc.seoul.kr

So Yeong Jeong

E-mail: jungsy27@hanmail.net

Objectives: Role of Doppler ultrasonography in determining radiologic and clinical significance of hepatic artery dissection (HAD) is not known. To determine the frequency of abnormalities on Doppler ultrasonography in liver transplant recipients with HAD and to evaluate association between Doppler abnormalities and disease severity.

Methods: 107 liver transplant (LT) recipients with HAD between January 2008 and December 2016 were included, in whom Doppler ultrasonography was performed within the week of diagnosis. Patients with HAD were subdivided into with/without Doppler abnormality groups, and intergroup differences in frequency of graft ischemia/infarction, laboratory values, and frequency of progressive interval change on follow up were evaluated.

Results: 18 (16.8%) of 107 LT recipients with HAD had Doppler abnormalities [tardus-parvus waveform ($n = 8$, 7.5%), no flow ($n = 10$, 9.3%)]. HAD with Doppler abnormality group more commonly showed graft

ischemia/infarction ($p < 0.0001$), had significantly higher mean peak laboratory values, including for aspartate aminotransferase, alanine aminotransferase, total bilirubin, and direct bilirubin (all $p < 0.05$), and were more likely to show progressive interval change ($p < 0.001$). All eight (7.5%) HAD patients requiring revascularization or retransplantation were in Doppler abnormality group.

Conclusion: Doppler abnormalities are occasionally found in LT recipients with HAD and indicate disease severity. Patients with HAD and Doppler abnormalities are more likely to show graft ischemia/infarction, laboratory abnormalities, and progressive changes on follow up that often require revascularization or retransplantation.

Advances in knowledge: Doppler ultrasonography abnormalities are frequently found in liver transplant recipients with HAD, and are a strong indicator of disease severity, such as graft ischemia/infarction, laboratory abnormalities, and progressive changes on follow up that often necessitate revascularization or retransplantation.

INTRODUCTION

Liver transplant (LT) is widely accepted as an important therapeutic option in the management of end-stage liver disease. LT recipients have a high risk of vascular complications, especially those who receive a living donor LT because of the small size and complex nature of reconstruction of vascular structures, and these complications are a major cause of mortality and morbidity after LT.^{1–4} Hepatic artery (HA) complications, which include thrombosis, stenosis, pseudoaneurysm, and dissection, are the

most threatening complications after LT, and may lead to ischemia or necrosis of the transplanted graft and various biliary complications, causing variable degrees of morbidity and even mortality.^{5–10} Early detection and timely treatment of HA complications are critical for survival of the graft and the recipient.

HA dissection (HAD) is a rare type of HA complication for which the clinical significance, treatment strategies, and outcomes are not well-known.^{11–13} Therefore, predicting

Figure 1. Flow diagram showing the categories in the study population. HAD, hepatic artery disease.

the disease course and generating a treatment plan can be difficult in patients with this complication.^{12,14,15} Doppler ultrasonography (US) is the primary screening method used to detect HA complications both in the early postoperative period and in long-term follow-up because of its non-invasive, cost-effective, and non-radioactive nature and availability at the bedside.^{16–22} However, the role of Doppler ultrasonography in determining the radiologic and clinical significance of HAD is not known.

The purpose of this study is to determine the frequency of Doppler ultrasonography abnormalities in LT recipients with HAD and to evaluate the association between these Doppler ultrasonography abnormalities and graft ischemia/infarction, laboratory abnormalities, and prognosis.

METHODS AND MATERIALS

The protocol for this retrospective study was approved by the institutional review board at University of Ulsan College of Medicine, Asan Medical Center (Seoul, Korea). The requirement for informed consent was waived.

Study population

We reviewed the radiologic reports of 3311 consecutive patients who had undergone whole or partial single-lobe LT at our hospital between January 2008 and December 2016 and identified 107 patients who were diagnosed with HAD based on post-operative contrast-enhanced CT findings. Post-operative contrast-enhanced CT scans were performed according to clinical need (*i.e.* for the evaluation of post-operative bleeding or unexpected elevation of liver enzymes and bilirubin) or at intervals as part

of a clinical practice; CT was, in general, performed weekly at 1 month post-living donor liver transplantation (LDLT); at 3, 6, and 12 months post-LDLT; and finally, once or twice a year. A diagnosis of HAD was made when any of the following were detected on hepatic arterial phase scan:^{12,23–25} (1) a double HA lumen with an intimal flap and opacification of both the true lumen and false lumen; (2) an HA with the appearance of a double lumen and an eccentric round-shaped hyperdensity corresponding to a true lumen and a surrounding crescentic hypodensity corresponding to a false lumen; or (3) an HA of increased diameter with hypodensity (presumably a thrombosed false lumen) and faulty visualization of the lumen. We classified HAD into low-grade and high-grade stenosis groups according to the degree of HA narrowing in the dissection segment and the patency of distal flow in the HA: high-grade stenosis was defined as the stenosis with <1 mm in diameter and with no visible or faintly visible discontinuous enhancement of intragraft HA.

Among them, we enrolled those in whom Doppler ultrasonography was performed within a week of the diagnosis of HAD, and all of the 107 LT recipients with HAD fulfilled the criteria. In our institution, we perform Doppler ultrasonography daily for the first week, weekly for the first month, monthly, and the frequency of the exams are reduced (>monthly) after the discharge in general. The intervals between Doppler ultrasonography and the diagnosis of HAD was 0.86 ± 1.6 (range 0–7) days. There were 71 males [mean age 52.52 ± 7.0 (range 31–69) years] and 36 females [mean age 54.94 ± 7.10 (38–69)] years with an overall mean age of 53.3 ± 7.03 (range 31–69) years. Of these, four underwent deceased-donor LT and the remainder underwent LDLT using

a modified right lobe ($n = 102$) or left lobe ($n = 1$). Indications for LT included liver cirrhosis associated with hepatitis B or C virus ($n = 58$), hepatocellular carcinoma ($n = 25$), acute fulminant hepatitis ($n = 4$), autoimmune hepatitis ($n = 1$), cryptogenic liver cirrhosis ($n = 6$), chronic rejection after previous transplantation ($n = 1$), and primary sclerosing cholangitis ($n = 1$). A flow diagram describing the categories of the study population is shown in [Figure 1](#).

Doppler ultrasonography and analysis

All Doppler ultrasonography examinations were performed by abdominal radiologists using a Sequoia 512 machine (Acuson Siemens, Mountain View, CA) with a 1–4 MHz transducer. Each patient was placed in the supine position with the head elevated and right arms abducted, and most examinations were performed by oblique intercostal scanning. Color and spectral Doppler sonograms of the post-anastomotic HA were obtained near the first order portal vein during the expiratory phase. The standard Doppler parameters were adjusted to maximal gain without background noise, lowest pulse-repetition frequency without aliasing artifacts, and a 2–5 mm Doppler sample gate for optimal signal detection from the HA.

On a Doppler spectrogram of the HA, several indices, including peak systolic velocity, end diastolic velocity, resistive index (RI), and systolic acceleration time (SAT), were measured 2–3 times and averaged, with manual angle correction. All measurements were acquired on waveforms that could be reproduced for at least three consecutive heartbeats. Pathologic HA findings were defined as follows: (1) a combination of $RI \leq 0.5$ and $SAT \geq 80$ ms (the so-called tardus-parvus waveform); (2) a high velocity peak ($\geq 2 \text{ m s}^{-1}$); or (3) no detectable flow.^{19,20} The patients with HAD were subdivided into two groups according to the Doppler ultrasonography findings, *i.e.* an HAD with Doppler abnormality group and an HAD without Doppler abnormality group.

Graft ischemia/infarction

CT scans acquired during the portal venous phase at the time of diagnosis of HAD were anonymized, coded, and put into a picture archiving and communication systems folder, randomized in order, and were retrospectively evaluated by blinded reviewers (BLINDED, with more than 10 years of experience in LT imaging; and BLINDED, with 2 years of experience in LT imaging) for graft ischemia/infarction. Graft ischemia/infarction was considered when the liver showed segmental or subsegmental wedge-shaped, rounded, or irregularly shaped tubular areas of low attenuation lesion(s) with no abnormalities in the hepatic or portal veins.^{26,27}

CT scans were obtained on a 16-channel or 64-channel multi-detector row CT scanner (LightSpeed 16, GE Healthcare, Milwaukee, WI; Somatom Sensation 16 or Somatom Definition, Siemens Medical Solutions, Erlangen, Germany). Portal venous phase CT scans were obtained with a standard dose (200 effective mAs, and 120 kVp; the actual radiation dose was adjusted according to the patient's body size and shape by automatically modulating the tube current (CARE-Dose, Siemens Medical Solutions, Malvern, PA) and detector configurations of $1.5 \times$

16 mm or 0.6×64 mm, a beam pitch of 1, and a gantry rotation time of 0.5 s. The images were reconstructed with a slice thickness and interval of 3–5 mm.

Analysis of laboratory findings

Another reviewer evaluated the laboratory findings, including for aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, and international normalized ratio of prothrombin (INR). Peak levels of these laboratory indices in the 7 days before and after diagnosis of HAD were recorded.

Follow up

In the LT recipients diagnosed as having HAD, follow-up CT scans were performed weekly thereafter using the same protocol as described above. We evaluated the interval change on CT according to time between diagnosis of HAD and follow-up CT scans (1 and 2 weeks, if available), and the results were categorized as either stable or progressive. Progressive interval change was deemed to have occurred when there was a substantial increase in graft ischemia/infarction or other complications such as formation of a biloma or abscess. Otherwise, the interval change was defined as stable.

The clinical course, the method of management, and outcome after diagnosis of HAD were investigated for each patient using medical records.

Statistical analysis

The statistical analyses were performed using SPSS v. 21.0 (IBM Corp., Armonk, NY). All tests were two-sided and $p < 0.05$ was considered to be statistically significant.

Fisher's exact test was used to evaluate the relationship between CT grading (HAD with low-grade stenosis or high-grade stenosis) or Doppler ultrasonography abnormalities (HAD with Doppler abnormality and HAD without Doppler abnormality) and graft ischemia/infarction. The differences between the groups by CT grading and Doppler ultrasonography abnormalities in terms of the association with graft ischemia/infarction were analyzed using the McNemar test. Differences in mean peak bilirubin (total and direct), AST, ALT, and INR between the two groups according to CT grading or Doppler ultrasonography abnormalities were evaluated using the independent samples *t*-test.

Differences in interval change at 1 and 2 weeks of follow up after diagnosis of HAD by CT grading or Doppler ultrasonography abnormalities were compared between the two groups using Fisher's exact tests.

RESULTS

A total of 107 HAD was diagnosed at a mean of 12 ± 10.7 postoperative (range 0–72) days, and mostly involved recipient arteries ($n = 106$, 99%). There were 78 patients in the low-grade stenosis group and 29 in the high-grade stenosis group.

Of the 107 LT recipients with HAD (78 with low-grade stenosis and 29 with high-grade stenosis), 18 (16.8%) had abnormalities

Table 1. Differences in Doppler indices of the hepatic artery in subgroups of liver transplantation recipients with HAD according to CT grading and Doppler abnormality

Indices	CT grading			Doppler abnormality		
	HAD with low-grade stenosis (<i>n</i> = 76) ^a	HAD with high-grade stenosis (<i>n</i> = 21) ^a	<i>p</i> -value	HAD with tardus-parvus waveform of HA (<i>n</i> = 8) ^b	HAD without Doppler abnormality group (<i>n</i> = 89) ^b	<i>p</i> -value
PSV ^c	66.04 ± 38.24 cm s ⁻¹ (11–191 cm s ⁻¹)	55.57 ± 34.36 cm s ⁻¹ (15.7–153 cm s ⁻¹)	0.236	46.26 ± 31.59 cm s ⁻¹ (11–108 cm s ⁻¹)	65.35 ± 37.76 cm s ⁻¹ (15.7–119.6 cm s ⁻¹)	0.142
EDV	18.22 ± 13.67 cm s ⁻¹ (0–64 cm s ⁻¹)	16.82 ± 16.05 cm s ⁻¹ (2.4–79.3 cm s ⁻¹)	0.718	27.65 ± 19.27 cm s ⁻¹ (6–64 cm s ⁻¹)	17.10 ± 13.46 cm s ⁻¹ (0–51 cm s ⁻¹)	0.189
RI	0.718 ± 0.147 (0.36–1)	0.703 ± 0.156 (0.44–0.94)	0.684	0.41 ± 0.04 (0.36–0.46)	0.74 ± 0.12 (0.51–1)	0.000
SAT	77.82 ± 35.7 ms (28–250 ms)	80.48 ± 32.62 ms (33–184 ms)	0.748	119.75 ± 57.09 ms (82–250 ms)	74.67 ± 30.01 ms (28–144 ms)	0.061

EDV, end diastolic velocity; HAD, hepatic artery dissection; PSV, peak systolic velocity; RI, resistive index; SAT, systolic acceleration time.

^aDoppler indices were available in 76 recipients of HAD with low-grade stenosis and in 21 with high-grade stenosis. The other 10 recipients with no flow of HA on Doppler were excluded from this Table.

^bOnly the eight patients with measurable Doppler flow at graft hepatic artery were included.

^cThe values are presented as the mean ± standard deviation (range, minimum value–maximum value).

on Doppler ultrasonography of the intrahepatic artery [tardus-parvus waveform (*n* = 8, 7.5%) or no flow (*n* = 10, 9.3%)]. Doppler ultrasonography abnormalities were more common in the high-grade stenosis group (34.5%, 10/29) than in the low-grade stenosis group (10.3%, 8/78; *p* = 0.007). Table 1 shows the mean ± standard deviation (range) values for the HA Doppler indices in the patients with HAD according to CT grading and Doppler abnormalities.

Graft ischemia/infarction was found in 20 (18.7%) of the 107 LT recipients with HAD. Graft ischemia/infarction was more common in the group that had HAD with high-grade stenosis on CT than in the group with HAD and low-grade stenosis (10/29 vs 10/78, *p* = 0.023). Graft ischemia/infarction was also more common in the HAD with Doppler abnormality group than in the HAD without Doppler abnormality group (17/18 vs 3/89, *p* < 0.0001). Graft ischemia/infarction was more strongly associated with Doppler abnormality than CT-grade (*p* = 0.156; Figures 2 and 3).

The mean ± standard deviation (range) for peak laboratory values in 7 days before and after diagnosis of HAD were as follows: 478.28 ± 1148.66 (20–8402) international units per liter for AST, 456.46 ± 728.75 (10–4747) international units per liter for ALT, 7.01 ± 7.36 (0.8–43.8) mg dl⁻¹ for total bilirubin, 4.03 ± 4.75 (0.5–25.8) mg dl⁻¹ for direct bilirubin, and 2.28 ± 2.28 (0.95–18.88) for INR. Table 2 provides a summary of the laboratory findings for HAD according CT grading and Doppler abnormalities. The mean peak AST, ALT, total bilirubin, direct bilirubin, and INR values were slightly higher in the HAD with high-grade stenosis group than in the HAD low-grade stenosis group, but not significantly so. The mean peak AST, ALT, total bilirubin, and direct bilirubin values were significantly higher in the HAD with Doppler abnormality group than in the HAD without Doppler abnormality group. Although the mean peak INR value was slightly higher in the HAD with Doppler abnormality group than

in the HAD without Doppler abnormality group, the difference was not statistically significant.

Follow-up CT scans at 1 and 2 weeks after diagnosis of HAD were available for 90 and 59 patients, respectively. On 90 follow-up CT 1 week after diagnosis of HAD, progressive interval change was noted in 7 (7.8%) patients, with no interval change detected in the remaining 83 patients (92.2%). Progressive interval change was noted in four patients (4/69, 5.8%) in the low-grade stenosis group and in three patients (3/21, 14.3%) in the high-grade stenosis group, with no statistically significant difference between the groups (*p* = 0.347). In contrast, while progressive interval change was noted in seven patients (7/16, 43.8%) in the HAD with Doppler abnormality group, none (0/74) in the HAD without Doppler abnormality group showed a progressive interval change (*p* < 0.0001). Of 59 patients who had follow-up CT after 2 weeks, progressive interval change was noted in 9 (15.3%) patients and not in the other 50 (84.7%). Progressive interval change was noted in five patients (5/42, 11.9%) in the low-grade stenosis group and four patients (4/17, 23.5%) in the high-grade stenosis group, respectively, with no statistically significant difference between the groups (*p* = 0.424). However, progressive interval change was significantly more common in the HAD with Doppler abnormality group than in the HAD without Doppler abnormality group (8/15 vs 1/44, *p* < 0.001).

Table 3 summarizes the information of eight patients with HAD who underwent surgical or interventional revascularization or explantation. All these patients were in the Doppler abnormality group and five were in the high-grade stenosis group.

DISCUSSION

HAD is an uncommon complication after LT. One previous study reported the incidence of HAD after LDLT to be 5.8%.¹² In our study, HAD occurred in 3.2% of LT recipients overall (107/3311). Most were recipients of LDLT (96.2%, 103/107) and most cases

Figure 2. A 55-year-old female who underwent LDLT using a right lobe graft. (a) On CT scans obtained 12 days after LDLT, an axial image during the hepatic arterial phase shows that the HA has a double-lumen appearance with eccentric hyperdensity of the true lumen and a surrounding hypodensity corresponding to the false lumen (arrows), suggestive of HAD. (b) On CT angiography, a maximal intensity projection image shows mild narrowing in the dissection segment (arrows), but patent distal HA flow (arrowheads), suggestive of low-grade stenosis associated with HAD. (c) An axial CT image during the portal venous phase shows a subsegmental geographic low attenuation lesion in the periphery of the graft (arrows), suggestive of graft ischemia/infarction. There were no abnormalities in the hepatic or portal veins. (d) On Doppler ultrasonography, no detectable flow signal was found at intragraft HA. (e) On follow-up CT scans (5 days later), progressive interval change with a substantial increase in graft ischemia/infarction was noted. HAD, hepatic artery dissection; LDLT, living donor liver transplantation.

of HAD occurred in recipient arteries (99%, 106/107). Possible explanations for the frequent occurrence of HAD in recipient HA vessels after LDLT are as follows: (1) HAD may be related to a honeycomb-like intimal deformity of the HA in recipients with chronic liver disease and be vulnerable to dissection and ligation or clamp injury;^{25,28} (2) in such cases, if possible, surgeons may try repeatedly to cut the recipient's HA towards the root of the celiac trunk until the normal wall appears in deceased donor LT, but this approach is frequently limited in LDLT surgery because the graft HA is often not long enough.^{25,29}

Treatment strategies and the prognosis of HAD have not been clearly established. Several authors have demonstrated spontaneous improvement of HAD on follow up without serious complications in patients who undergo conservative management, and it has been speculated that the true lumen is restored over time with resorption of the hematoma or thrombus in the false lumen.¹² Because of the risk of morbidity or adverse events associated with surgical revascularization and endovascular treatment, a wait-and-see strategy may be favored if an uncomplicated recovery is strongly expected.^{12,14,15} However, our study demonstrated that not all patients with HAD after LT had a favorable clinical course, with 8 (7.5%) of 107 patients requiring revascularization or re-LT. Therefore, it would be important for

radiologists to characterize HAD radiologically and to identify relevant features when predicting the prognosis.

Doppler ultrasonography is a primary surveillance method for detecting complications of HA in LT recipients.^{16,20,30,31} The value of Doppler ultrasonography in the diagnosis of significant HA stenosis or thrombosis in LT recipients cannot be overemphasized.^{16,30} However, the role of Doppler ultrasonography in estimation of the severity of HAD in LT recipients has not been established. It has been suggested that multidetector row CT, with its superb spatial and time resolution, may facilitate diagnosis of HA complications in LDLT recipients.²⁵ Previous studies have demonstrated the usefulness of CT in the diagnosis and follow up of HAD in LT recipients.²⁵ In this study, we evaluated the association of Doppler ultrasonography abnormalities, including the so-called tardus-parvus waveform (a combination of RI ≤ 0.5 and SAT ≥ 80 ms), high velocity peak (≥ 2 m s⁻¹),^{19,20} and no detectable flow, with disease severity in LT recipients with HAD and made a comparison with CT grading by the degree of HA narrowing in the dissection segment and patency of distal HA flow.

The results of our study demonstrated that Doppler ultrasonography abnormalities are occasionally seen in LT recipients

Figure 3. A 57-year-old male who underwent LDLT using a right lobe graft. (a) On CT performed 17 days after LDLT, an axial image during the hepatic arterial phase shows that the HA has a double-lumen appearance with eccentric hyperdensity of the true lumen and a surrounding hypodensity corresponding to the false lumen (arrows), suggestive of HAD, along with marked narrowing in the dissection segment and scant flow in the distal HA, suggestive of high-grade stenosis associated with HAD. (b) An axial CT image during the portal venous phase shows homogenous enhancement of the parenchyma. There were no abnormalities in the hepatic or portal veins. (c) A Doppler spectrogram of the HA scanned on the same day as CT shows that flow in the HA has a normal waveform. The patient had an uneventful post-operative recovery. HAD, hepatic artery dissection; LDLT, living donor liver transplantation.

with HAD and that patients with these abnormalities tend to show graft ischemia/infarction on CT, liver function-related laboratory abnormalities, and interval progression of graft

ischemia/infarction on follow-up CT more often than those without Doppler ultrasonography abnormalities. Surgical or interventional revascularization or explantation was eventually

Table 2. Differences in peak laboratory values in subgroups of liver transplantation recipients with HAD according to CT grading and Doppler abnormality

Laboratory parameter	CT grading			Doppler abnormality		
	HAD with low-grade stenosis (n = 78)	HAD with high-grade stenosis (n = 29)	p-value	HAD with Doppler abnormality (n = 18)	HAD without Doppler abnormality (n = 89)	p-value
AST (IU/l) ^a	396.06 ± 868.25 (20–5098)	699.41 ± 1688.89 (57–8402)	0.226	1871.39 ± 2371.03 (48–8402)	196.53 ± 161.29 (20–724)	0.000
ALT (IU/l)	389.42 ± 634.29 (10–3721)	636.76 ± 926.25 (73–4747)	0.119	1420.06 ± 1353.16 (55–4747)	261.57 ± 240.09 (10–1717)	0.000
Total bilirubin (mg dl ⁻¹)	7.29 ± 7.90 (0.8–44)	6.27 ± 5.71 (1.3–22.9)	0.525	10.63 ± 11.87 (1.9–43.8)	6.28 ± 5.90 (0.8–37)	0.021
Direct bilirubin (mg dl ⁻¹)	4.14 ± 5.10 (0.5–26)	3.74 ± 3.75 (0.6–14.8)	0.703	6.94 ± 8.00 (0.9–25.8)	3.35 ± 3.54 (0.5–21)	0.003
INR	2.2 ± 2.06 (1–19)	2.37 ± 2.81 (1.1–16.4)	0.794	3.18 ± 4.11 (1.17–18.88)	2.10 ± 1.67 (1–16)	0.660

ALT, alanine transaminase; AST, aspartate transaminase; HAD, hepatic artery dissection; INR, international normalized ratio of prothrombin; IU, International unit.

^aThe values are presented as the mean ± standard deviation (range, minimum value—maximum value).

Table 3. Demographic and laboratory findings in graft failure cases after diagnosis of HAD

Patient	Sex	Age (y)	HAD onset ^a	Stenosis grading by CT ^b	Graft ischemia/infarction	Doppler ultrasonography findings ^c	Laboratory findings					Intervention (interval) ^d	Outcome
							AST (IU/l)	ALT (IU/l)	TB (mg dl ⁻¹)	DB (mg dl ⁻¹)	INR		
1	M	31	2	Low	+	Tardus-parvus waveform (RI 0.36, SAT 117 ms)	4916	3291	32.1	25.8	18.88	Re-LT (7 days)	Mortality related to multiorgan failure (post-re-LT day 10)
2	F	55	12	Low	+	No detectable flow	3534	2586	20.3	15.2	2.33	Re-LT (26 days)	Mortality related to sepsis (post-re-LT day 2)
3	F	57	10	High	+	No detectable flow	150	311	4.3	3.1	1.39	Re-LT (44 days)	Uneventful postoperative recovery
4	M	53	9	High	+	No detectable flow	128	294	4.2	2	1.63	Revascularization (4 days)	Uneventful postoperative recovery
5	M	52	1	High	+	No detectable flow	507	700	6	3.2	2.24	Revascularization (1 days)	Uneventful postoperative recovery
6	M	60	12	High	+	No detectable flow	3161	4747	2.5	1.7	1.81	Revascularization (4 days)	Uneventful postoperative recovery
7	M	69	0	High	+	No detectable flow	3374	1241	22.9	13.6	4.3	Re-LT (4 days)	Uneventful postoperative recovery
8	M	45	13	Low	+	No detectable flow	79	213	2.7	0.9	1.17	Re-LT (77 days)	Mortality related to sepsis (post-re-LT day 5)

ALT, alanine transaminase; AST, aspartate transaminase; DB, direct bilirubin; HAD, hepatic artery dissection; INR, international normalized ratio of prothrombin; IU, International unit; LT, liver transplantation; TB, total bilirubin.

^aThe data indicate the time interval (postoperative day) between LT and diagnosis of HAD.

^bStenosis grading was performed based on degree of hepatic artery narrowing in the dissection segment and patency of flow in the distal hepatic artery on CT.

^cA Doppler spectrogram could not be obtained in those with hepatic artery obstruction.

^dThe data indicate the time interval (postoperative day) between LT and radiologic or surgical intervention.

required in eight LT recipients with HAD, all of whom were in the Doppler abnormality group. While graft ischemia/infarction in LT recipients with HAD was frequently associated with high-grade stenosis (10/20, 50%), it was more significantly associated with Doppler ultrasonography abnormalities (17/20, 85%; $p = 0.0156$). However, there were no significant differences in liver function-related laboratory abnormalities or interval progression of graft ischemia/infarction on follow-up CT between the high-grade and low-grade stenosis groups. Surgical or interventional revascularization or explantation was required in five LT recipients with HAD in the high-grade stenosis group and was also required by three patients in the low-grade stenosis group. Therefore, we suggest that Doppler ultrasonography abnormalities are a stronger indicator of disease severity than CT grading in LT recipients with HAD. More aggressive clinical and radiologic monitoring is warranted in these patients and the possibility of revascularization or retransplantation should be considered to prepare.

This study has several limitations. First is its retrospective nature, which meant that although a relatively large number of LT recipients with HAD were included, the type, etiology, predisposing factor(s), and mechanism(s) for development of HAD in LT recipients could not be elucidated further. There was also no systematic evaluation of the HA using intraoperative ultrasonography in our study population. Therefore, the previous suggestion that the honeycomb-like deformity of the HA in LT recipients with chronic liver disease may be related to HAD could not be confirmed in our study, although we believe that this would be a promising line of investigation in a future prospective study. Second, because of the relatively long period over which patients were enrolled, various CT scanners were used and Doppler studies were performed by many abdominal radiologists, which increased the subjective heterogeneity of our study sample. However, there was no great step change in CT protocol during

the study period and all radiologists were trained in using a standard Doppler protocol for LT recipients under the supervision of a dedicated radiologist experienced in LT imaging. Third, in our institution, we frequently obtained contrast-enhanced CT as well as Doppler ultrasonography as a part of clinical practice. The most common indication of contrast-enhanced CT within a week was for the evaluation of postoperative bleeding or unexpected elevation of liver enzymes and bilirubin. Besides, CT scans were also frequently performed to survey for non-vascular complications or those difficult to diagnose by Doppler ultrasonography, such as HAD and related abnormality, ABO incompatibility-related bile duct injury, unexpected gastrointestinal complication, veno-occlusive disease/sinusoidal obstruction syndrome, portal steal syndrome, and during the late postoperative period, relapse of portal hypertension or recurrent hepatocellular carcinoma. Although there are some issues about the justification of radiation exposure and cost-effectiveness, they are beyond the scope of this study, warranting a further well-design study in the future.

In conclusion, Doppler ultrasonography abnormalities are occasionally seen in LT recipients with HAD, and are a strong indicator of severe disease, including graft ischemia/infarction, laboratory abnormalities, and progressive changes on follow up that may require revascularization or retransplantation.

FUNDING

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (No. 2017R1E1A1A03070961).

IRB STATEMENT

The study protocol was approved by Institutional Review Board at our institution.

REFERENCES

1. Sugawara Y, Makuuchi M. Technical advances in living-related liver transplantation. *J Hepatobiliary Pancreat Surg* 1999; **6**: 245–53. doi: <https://doi.org/10.1007/s005340050114>
2. Moray G, Boyvat F, Sevmiş S, Karakayali F, Ayvaz I, Dalgıç A, et al. Vascular complications after liver transplantation in pediatric patients. *Transplant Proc* 2005; **37**: 3200–2. doi: <https://doi.org/10.1016/j.transproceed.2005.08.045>
3. Duffy JP, Hong JC, Farmer DG, Ghobrial RM, Yersiz H, Hiatt JR, et al. Vascular complications of orthotopic liver transplantation: experience in more than 4,200 patients. *J Am Coll Surg* 2009; **208**: 896–903. doi: <https://doi.org/10.1016/j.jamcollsurg.2008.12.032>
4. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, et al. Surgical techniques and innovations in living related liver transplantation. *Ann Surg* 1993; **217**: 82–91. doi: <https://doi.org/10.1097/0000658-199301000-00014>
5. Vaidya S, Dighe M, Kolokythas O, Dubinsky T. Liver transplantation: vascular complications. *Ultrasound Q* 2007; **23**: 239–53. doi: <https://doi.org/10.1097/ruq.0b013e31815d6e1d>
6. Pérez-Saborido B, Pacheco-Sánchez D, Barrera-Rebollo A, Asensio-Díaz E, Pinto-Fuentes P, Sarmentero-Prieto JC, et al. Incidence, management, and results of vascular complications after liver transplantation. *Transplant Proc* 2011; **43**: 749–50. doi: <https://doi.org/10.1016/j.transproceed.2011.01.104>
7. Raby N, Karani J, Thomas S, O'Grady J, Williams R. Stenoses of vascular anastomoses after hepatic transplantation: treatment with balloon angioplasty. *AJR Am J Roentgenol* 1991; **157**: 167–71. doi: <https://doi.org/10.2214/ajr.157.1.1828649>
8. Orons PD, Sheng R, Zajko AB. Hepatic artery stenosis in liver transplant recipients: prevalence and cholangiographic appearance of associated biliary complications. *AJR Am J Roentgenol* 1995; **165**: 1145–9. doi: <https://doi.org/10.2214/ajr.165.5.7572493>
9. Hom BK, Shrestha R, Palmer SL, Katz MD, Selby RR, Asatryan Z, et al. Prospective evaluation of vascular complications after liver transplantation: comparison of conventional and microbubble contrast-enhanced US. *Radiology* 2006; **241**:

- 267–74. doi: <https://doi.org/10.1148/radiol.2411050597>
10. Wozney P, Zajko AB, Bron KM, Point S, Starzl TE. Vascular complications after liver transplantation: a 5-year experience. *AJR Am J Roentgenol* 1986; **147**: 657–63. doi: <https://doi.org/10.2214/ajr.147.4.657>
11. Paz-Fumagalli R, Jia Z, Sella DM, McKinney JM, Frey GT, Wang W. Percutaneous retrograde transhepatic arterial puncture to regain access in the true lumen of the dissected and acutely occluded transplant hepatic artery. *Am J Transplant* 2017; **17**: 830–3. doi: <https://doi.org/10.1111/ajt.14092>
12. Hwang JY, Kim KW, Lee SJ, Kim SY, Lee JS, Kim HJ, et al. The computed tomographic angiography finding of hepatic artery dissection after living donor liver transplantation; what is the clinical significance? *Clin Imaging* 2016; **40**: 130–6. doi: <https://doi.org/10.1016/j.clinimag.2015.06.007>
13. Wildgruber M, Matevossian E, Stock K, Umgelter A, Kornberg A, Berger H. Dissection of the hepatic artery and the celiac trunk after a liver transplant: description of a complication and endovascular management. *Exp Clin Transplant* 2013; **11**: 565–8. doi: <https://doi.org/10.6002/ect.2012.0252>
14. Vennarecci G, Guglielmo N, Busi Rizzi E, Ettorre GM. Hepatic artery dissection with retrograde extension to the celiac trunk and splenic artery after liver transplantation: A clinical challenge. *Dig Liver Dis* 2015; **47**: e15. doi: <https://doi.org/10.1016/j.dld.2015.03.023>
15. Mun HS, Kim KW, Song GW, Ahn CS, Kim SY, Hwang S, et al. Evaluation of the hepatic artery anastomosis by intraoperative sonography with high-frequency transducer in right-lobe graft living donor liver transplantation. *J Clin Ultrasound* 2010; **38**: 10–16. doi: <https://doi.org/10.1002/jcu.20628>
16. Abdelaziz O, Attia H. Doppler ultrasonography in living donor liver transplantation recipients: Intra- and post-operative vascular complications. *World J Gastroenterol* 2016; **22**: 6145–72. doi: <https://doi.org/10.3748/wjg.v22.i27.6145>
17. Sidhu PS, Ellis SM, Karani JB, Ryan SM. Hepatic artery stenosis following liver transplantation: significance of the tardus parvus waveform and the role of microbubble contrast media in the detection of a focal stenosis. *Clin Radiol* 2002; **57**: 789–99. doi: <https://doi.org/10.1053/crad.2002.0969>
18. Park YS, Kim KW, Lee SJ, Lee J, Jung DH, Song GW, et al. Hepatic arterial stenosis assessed with doppler US after liver transplantation: frequent false-positive diagnoses with tardus parvus waveform and value of adding optimal peak systolic velocity cutoff. *Radiology* 2011; **260**: 884–91. doi: <https://doi.org/10.1148/radiol.11102257>
19. García-Criado A, Gilabert R, Berzigotti A, Brú C. Doppler ultrasound findings in the hepatic artery shortly after liver transplantation. *AJR Am J Roentgenol* 2009; **193**: 128–35. doi: <https://doi.org/10.2214/AJR.07.3919>
20. Dodd GD, Memel DS, Zajko AB, Baron RL, Santaguida LA. Hepatic artery stenosis and thrombosis in transplant recipients: Doppler diagnosis with resistive index and systolic acceleration time. *Radiology* 1994; **192**: 657–61. doi: <https://doi.org/10.1148/radiology.192.3.8058930>
21. Someda H, Moriyasu F, Fujimoto M, Hamato N, Nabeshima M, Nishikawa K, et al. Vascular complications in living related liver transplantation detected with intraoperative and postoperative Doppler US. *J Hepatol* 1995; **22**: 623–32. doi: [https://doi.org/10.1016/0168-8278\(95\)80218-5](https://doi.org/10.1016/0168-8278(95)80218-5)
22. Platt JF, Yutzky GG, Bude RO, Ellis JH, Rubin JM. Use of Doppler sonography for revealing hepatic artery stenosis in liver transplant recipients. *AJR Am J Roentgenol* 1997; **168**: 473–6. doi: <https://doi.org/10.2214/ajr.168.2.9016229>
23. Jung SC, Lee W, Park EA, Jae HJ, Chung JW, Park JH. Spontaneous dissection of the splanchnic arteries: CT findings, treatment, and outcome. *AJR Am J Roentgenol* 2013; **200**: 219–25. doi: <https://doi.org/10.2214/AJR.11.7877>
24. Soper JR, Parker GD, Hallinan JM. Vertebral artery dissection diagnosed with CT. *AJNR Am J Neuroradiol* 1995; **16**(4 Suppl): 952–4.
25. Kim SY, Kim KW, Kim MJ, Shin YM, Lee MG, Lee SG. Multidetector row CT of various hepatic artery complications after living donor liver transplantation. *Abdom Imaging* 2007; **32**: 635–43. doi: <https://doi.org/10.1007/s00261-006-9145-5>
26. Torabi M, Hosseinzadeh K, Federle MP. CT of nonneoplastic hepatic vascular and perfusion disorders. *Radiographics* 2008; **28**: 1967–82. doi: <https://doi.org/10.1148/rg.287085067>
27. Smith GS, Birnbaum BA, Jacobs JE. Hepatic infarction secondary to arterial insufficiency in native livers: CT findings in 10 patients. *Radiology* 1998; **208**: 223–9. doi: <https://doi.org/10.1148/radiology.208.1.9646817>
28. Adani GL, Avellini C, Baccarani U, Lorenzin D, Risaliti A, Gasparini D, et al. Graft vessel wall pathology in a case of hepatic artery pseudo-aneurysm in a liver transplant recipient. *Transplant Proc* 2008; **40**: 3800–3. doi: <https://doi.org/10.1016/j.transproceed.2008.06.095>
29. Asonuma K, Ohshiro H, Izaki T, Okajima H, Ueno M, Kodera A, et al. Rescue for rare complications of the hepatic artery in living donor liver transplantation using grafts of autologous inferior mesenteric artery. *Transpl Int* 2004; **17**: 639–42. doi: <https://doi.org/10.1111/j.1432-2277.2004.tb00399.x>
30. Vit A, De Candia A, Como G, Del Frate C, Marzio A, Bazzocchi M. Doppler evaluation of arterial complications of adult orthotopic liver transplantation. *J Clin Ultrasound* 2003; **31**: 339–45. doi: <https://doi.org/10.1002/jcu.10190>
31. Noltén A, Sproat IA. Hepatic artery thrombosis after liver transplantation: temporal accuracy of diagnosis with duplex US and the syndrome of impending thrombosis. *Radiology* 1996; **198**: 553–9. doi: <https://doi.org/10.1148/radiology.198.2.8596865>