RESEARCH ARTICLE

Role of doppler ultrasound in detecting vascular complications in recipients of living donor liver transplant (LDLT)

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Abstract

Objective: To determine the role of Doppler ultrasound in the detection of vascular complications in recipients of living donor liver transplant, keeping contrast-enhanced computerised tomography of abdomen as the gold standard.

Method: The retrospective study was conducted from February 16 to April 1, 2022, at the Pakistan Kidney and Liver Institute and Research Centre, Lahore, Pakistan, and comprised data of living donor liver transplant recipients who had undergone contrast-enhanced computerised tomography of abdomen within 24 hours of Doppler ultrasound between January 2021 and January 2022. For the diagnosis of hepatic vascular complications, the diagnostic values of Doppler ultrasound parameters were derived by correlating Doppler ultrasound findings with contrast-enhanced computerised tomography results. Data was analysed using SPSS 20.

Results: Of the 35 patients, 24(68.6%) were men and 11(31.4%) were women. The overall mean age was 45.86±13.8 years. For hepatic artery thrombosis, the use of Doppler ultrasound criteria yielded a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 100%, 96.6%, 83.3%, 100%, and 97.1% respectively. For hepatic artery stenosis, overall sensitivity, specificity, positive predictive value, negative predictive value and accuracy of Doppler ultrasound was 100%, 96.8%, 75%, 100% and 97.1% respectively. Doppler ultrasound parameters resulted in a sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 100% each in detecting portal vein and hepatic venous outflow tract thrombosis. Overall, Doppler ultrasound sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy was found to be 100%, 88.8%, 89.4%, 100% and 94.2% respectively.

Conclusion: Doppler ultrasound was adequate to document vascular complications after living donor liver transplant in majority of the cases with high accuracy and sensitivity.

Key Words: CLD, Doppler US, Vascular complications, LDLT recipients, CECT abdomen.

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Introduction

Chronic illnesses account for over 60% of all deaths worldwide, with chronic liver disease (CLD) accounting for nearly 2 million deaths every year. In Pakistan, CLD is the 5th leading cause of death and the 11th leading cause of disability.[1] CLD is caused by a range of risk factors and diseases, but hepatitis B virus (HBV) hepatitis C virus (HCV) are the major causes leading to liver failure in Pakistan.[2] A wide range of treatment options are available for CLD patients, but liver transplantation (LT) remains the only definitive mode of treatment in patients who fail to respond to all other treatments.[3] Over 2 million people in Pakistan are expected to need LT at some point during their treatment.[4] The allograft for LT can be received from either a cadaveric or a living donor after performing a partial hepatectomy.[5] Living donor liver transplant (LDLT) has evolved over the years to address the scarcity of cadaveric donors. Vascular complications after LT are among the leading causes of death or graft failure.[6] The overall risk of vascular complications in LDLT is greater than in cadaveric donor LT. Their reported incidence is around 13% for LDLT.[7] Vascular complications involve the hepatic artery (HA), the portal vein (PV) and the hepatic vein (HV). HA complications include hepatic arterial stenosis (HAS), hepatic arterial thrombosis (HAT) and pseudoaneurysm formation. PV complications include portal vein thrombosis (PVT), PV stenosis (PVS) and thrombosis of superior mesenteric vein (SMVT) and splenic vein (SVT). HV complications include HV stenosis (HVS) and HV thrombosis (HVT).[8] Timely identification and treatment of these complications are crucial for the survival of the patient and the graft. Early radiological evaluation is necessary to make a diagnosis for which Doppler ultrasonography (US) is the most often used first imaging modality. Doppler US is an ideal technique to evaluate hepatic vasculature patency post-LDLT,

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particularly in intensive care units (ICUs) where conditions are far from ideal.[8] It is economical, non-invasive, uses no ionising radiation, and can be performed at the patient's bedside.

The current study was planned to determine the role of Doppler US in the detection of vascular complications in recipients of LDLT, keeping contrast-enhanced computerised tomography (CECT) of abdomen as the gold standard.

Patients and Methods

The retrospective, descriptive study was conducted from February 16 to April 1, 2022, at the Pakistan Kidney and Liver Institute and Research Centre, Lahore, Pakistan, and comprised data of LDLT recipients who had undergone CECT of abdomen within 24 hours of Doppler US between January 2021 and January 2022.

After approval from the institutional review board, data was retrieved from the hospital database. All LDLT cases done during the designated period were evaluated. In all cases, Doppler US had been performed first intraoperatively after vascular anastomosis post-LDLT and then once a day during the first post-operative week. One of the three radiologists with experience in Doppler US examination of LT recipients performed all ultrasounds by using a 3.5MHZ curvilinear transducer US machine (GE Logic S8 Doppler). Doppler evaluation of the liver recipient comprised assessment of HA and its intraparenchymal branches, main PV and its branches, HVs, and the inferior vena cava (IVC). In cases where the examiner was unable to locate a patent vessel with a normal spectral curve, Doppler US was repeated during the same session by another senior and more experienced radiologist. If the doubt remained about the patency of the vessel, a biphasic CT abdomen was performed. All CT abdominal examinations were carried out in a supine position using a 128-slice multi-detector CT scanner (GE Revolution Evo). Images were acquired with a 1mm slice thickness after injecting 1.25ml/kg of non-ionic iodinated contrast agent (Ultravist 370mgI/mL) at a rate of 5ml per second via a power injector system. In all patients, an early arterial phase at 15-20 seconds and a portal venous phase (PVP) at 60 seconds were acquired. The upper abdomen was scanned in the early arterial phase, and the whole abdomen and pelvis were scanned in the PVP. Two consultant radiologists with more than 5 years of cross-sectional imaging experience independently evaluated the CT images on the workstation for the presence or absence of vascular complications. The Doppler US findings were then correlated with the CECT results.

The data included for detailed analysis related to patients who had CECT abdomen done within 24 hours of Doppler US post-LDLT because of suspicion of vascular and non-vascular complications on US. Data of patients with missing information and those having had a cadaveric graft was excluded, and so was the case with irritable patients in whom spectral waveform could not be acquired.

The findings of post-transplant Doppler US examination were correlated with those of CECT abdomen, which was taken as the gold standard, to calculate the diagnostic values.

Data was analysed using SPSS 20. Data was presented as mean +/- standard deviation, medians with interquartile range (IQR), or as percentages and frequencies, as appropriate. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) for Doppler US for the diagnosis of vascular complications of HA, PV and HVs were calculated.

Results

Of the 121 cases evaluated, data of 35(29%) patients was analysed; 24(68.6%) men and 11(31.4%) women. The overall mean age was 45.86±13.8 years. There were 32(91.4%) right lobe grafts and 3(8.6%) left lobe grafts.

Doppler US detected HAT in 6(13.8%) patients and HAS in 4(11.4%) patients. CECT confirmed HAT in 5(14.3%) cases and HAS in 3(8.6%) cases, with 1(2.8%) false-positive (FP) diagnosis each. For HAT, the use of Doppler ultrasound criteria yielded a sensitivity, specificity, PPV, NPV, and DA of 100%, 96.6%, 83.3%, 100%, and 97.1% respectively. For HAS, overall sensitivity, specificity, PPV, NPV and DA of Doppler ultrasound was 100%, 96.8%, 75%, 100% and 97.1% respectively.

Doppler US detected PVT in 2(5.7%) patients and hepatic vein outflow tract (HVOT) thrombosis in 7(20%) patients. Among them 4(57.1%) patients had no flow detected in HVs on colour Doppler and 3(42.9%) patients showed patchy monophasic flow pattern suggestive of very sluggish flow/thrombosis. Doppler US sensitivity, specificity, PPV, NPV and DA was 100% in detecting PVT and HVOT thrombosis.

Altogether, vascular complications occurred in 13(37.14%) patients. Overall, Doppler US sensitivity, specificity, PPV, NPV and DA was 100%, 88.8%, 89.4%, 100% and 94.2% respectively (Table).

None of the patients underwent digital subtraction angiography (DSA) since all the vascular complications

Table: Comparison of frequency of Malignancy with respect to age groups (years), Gender, BMI and Duration of disease (in weeks).

Complications	True Positive	False Positive	True negative	False negative	Sensitivity (%)	Specificity (%)	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)	Diagnostic Accuracy
HAT	5	1	29	0	100	96.6	83.33	100	97.1
HAS	3	1	31	0	100	96.8	75	100	97.1
PVT	2	0	33	0	100	100	100	100	100
HV outflow tract thrombosis	07	0	21	0	100	100	100	100	100

HAT: Hepatic artery thrombosis, HAS: Hepatic artery stenosis, PVT: Portal vein thrombosis, HV: Hepatic venous.

were obvious on CECT abdomen. Among the 5(14.3%) patients with HAT, 1(20%) died before any intervention, and 1(20%) died after undergoing surgical revascularisation. In 2(40%) cases, surgical revascularisation was used and was effective. Intra-arterial thrombolysis using tissue plasminogen activator (t-PA) was employed in 1(20%) patient with success. Among 2(5.7%) patients with PVT, 1(50%) died, and 1(50%) developed multiple periportal collaterals, and no surgical intervention was performed. Among the 7(20%) HVOT thrombosis patients, 1(14.3%) died, and the rest were kept on anticoagulant therapy.

Discussion

Since the first successful LT in 1967[9], the procedure has advanced rapidly and has become a life-saving surgery to replace livers affected by end-stage cirrhosis. LT from a deceased donor is by far the most common LT method in many parts of the Western world, accounting for >90% of LTs.[10] In Asian nations, such as Pakistan, where deceased organ donation is difficult, LDLT is more prevalent.[11] Vascular complications following LTs are among the most dreaded consequences, which can result in graft failure and recipient mortality.[8] When compared to deceased donor LT, LDLT patients have more chances of vascular problems post-surgery. For deceased donor LT, the stated incidence is around 7%, and for LDLT, it is about 13%.[12] Graft survival depends on the early detection of these complications. Clinical signs of these vascular complications are typically ambiguous, necessitating radiological diagnosis, for which Doppler US is the most frequently used first imaging modality. It provides a quick and thorough examination of the whole hepatic vascular system at the patient's bedside.

After LDLT, vascular complications mainly involve HA, PV

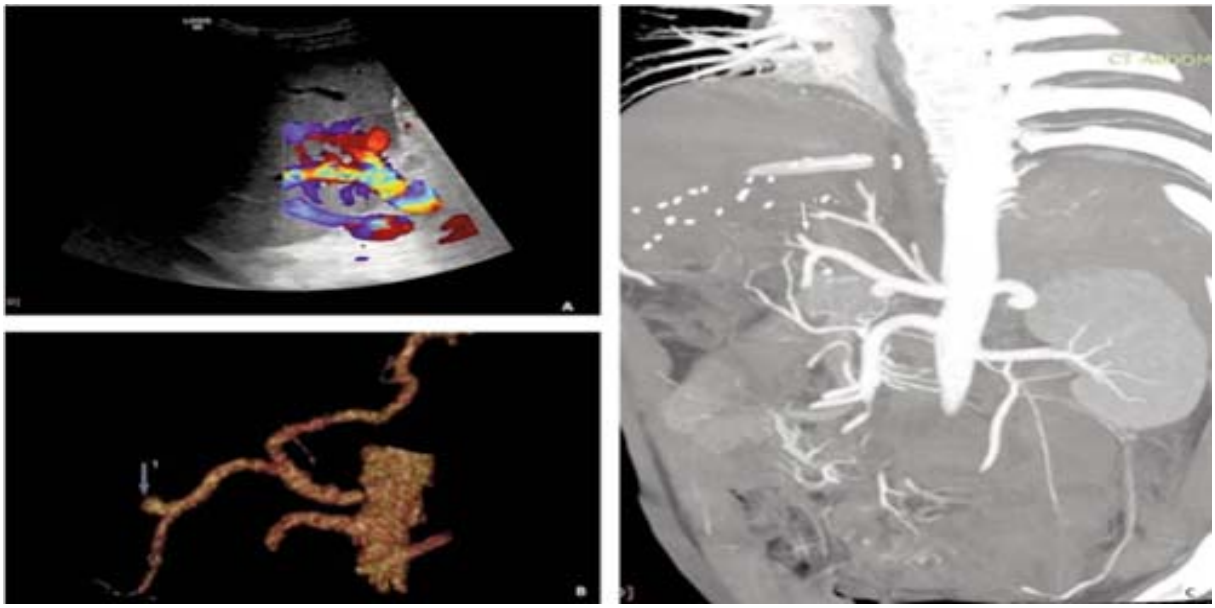

Figure-1: 35-year-old male with hepatic artery thrombosis on 3rd post-operative day after living donor liver transplant (LDLT). A) Colour Doppler ultrasound (US) image of the transplanted liver at porta hepatis demonstrates blood flow in the portal vein, right hepatic veins (RHV) and inferior vena cava (IVC), but no Doppler-detectable blood flow is noted in the hepatic artery, indicative of hepatic artery occlusion. B) Three-dimensional (3D) virtual reality (VR). (C) Coronal Multiplanar reconstruction (MPR) images showing abrupt cut-off of the hepatic artery (arrows) at the porta hepatis without any extension into the liver, hence confirming hepatic artery thrombosis (HAT).

and HVs. Arterial complications are the most common and serious of these, with HAT occurring in 2-12% of cases.[13] It should be diagnosed as soon as possible since graft salvage may be possible with early management, but most patients will eventually need re-transplantation.[14] The mortality rate is still 27-30% even after re-transplantation. Normally, on Doppler US, HA has a rapid systolic upstroke with resistance index (RI) ranging 0.55 to 0.8, peak systolic velocity (PSV) <200cm/sec and systolic acceleration time (SAT) of up to 0.08 seconds in the post-operative period.[5] Diagnostic criteria of early HAT on Doppler US include complete absence of blood flow at porta hepatis and inside the liver[15] (Figure 1). In the current study, HAT was noticed in 5 cases of LDLT with Doppler US, indicating sensitivity, specificity and DA of 100%, 96.6% and 97.1% respectively, which are better than those reported earlier[15,16]. FP or false-negative (FN) outcomes from Doppler US are possible. The most common causes of FP results are reduced HA flow caused by hypotension, narrow calibre HA, early postoperative vasospasm, and incorrect US machine settings.[17] Hom et al. reported FP rate of up to 75%.[18] In contrast, the current study found it to be 3.4%. Collateral circulation is the main cause of FN results, with a study having reported FN rate of 7-29%.[17] In the current study, there was no FN diagnosis of HA occlusion (0%).

The second most common arterial complication is HAS, which occurs largely at the anastomotic location with an incidence rate of 5-11% post-LDLT.[8] If left untreated, it can induce hepatic ischaemia, biliary stricture, infection, and graft loss, as well as HAT due to sluggish flow. Diagnosis of HAS by Doppler US is based on the segment of the artery that is evaluated and its relationship with stenosis. The prestenotic segment has a high RI of >0.8 and a low flow. The stenotic segment shows turbulence and aliasing with a focal increase in PSV to >200cm/s and raised RI. Post-stenotic segment shows tardus parvus waveform (TPW) in intrahepatic arteries demonstrated by reduced RI (<0.55) and prolonged SAT (>0.08s)[8] (Figure 2). The current study found Doppler US sensitivity, specificity, and DA of 100%, 96.8% and 97.1% respectively. Tamsel et al. reported Doppler US diagnostic sensitivity 92% and specificity 97%.[16] Platt et al. reported specificity 96% and sensitivity 67% for Doppler US in detecting HAS.[19] Sanyal et al. mentioned Doppler US sensitivity to be 72-97% and specificity 64-99%.[20] The TPW is acknowledged as an excellent diagnostic parameter for HAS diagnosis, although it is non-specific. It may also be seen in PV occlusion, atherosclerotic disease, and chronic HAT with collateral vessel formation, resulting in FP diagnosis. A relatively high proportion of FP HAS diagnoses based on TPW has been described in literature, ranging from 11.2% to 27%.[21] The current study observed a significantly low FP rate of 3.1%.

PV complications are uncommon and primarily include PVT, PVS and phlebangioma. Normally, PV has hepatopetal flow with a continuous monophasic spectral waveform on Doppler US. Early in the postoperative period, high PV velocities may be seen, which, on follow-up studies, should normalise.[5] PVT is the most common complication, occurring mostly at the anastomotic site, with an overall incidence of 1-3%.[5]. Gray-scale and

Figure-2: 44-year-old male with hepatic artery stenosis (HAT) after living donor liver transplant (LDLT). A) Colour Doppler ultrasound (US) waveform of right hepatic artery showing a prolonged acceleration time (AT) of 0.13s (normal is <0.08s) and resistive index (RI) value of 0.35 (normal is >0.55). B) Three-dimensional (3D) virtual reality (VR) image confirms the presence of marked stenosis (arrow) at the anastomotic site of the donor and recipient hepatic arteries.

Doppler US can be used to easily diagnose PVT. On the gray-scale US, the thrombus appears as anechoic or echogenic material within the PV, with no flow seen on Doppler interrogation. Traditional Doppler ultrasound has a specificity of 97-100% in detecting PVT[17]. However, determining the duration and extent of thrombosis is difficult. The current study observed PVT in 2 LDLT recipients with Doppler US sensitivity, specificity, PPV, NPV and DA of 100% each.

The restoration of the HVOT during LDLT is a challenging task. During a right lobe LDLT, the right hepatic veins (RHVs) are retained in the grafted liver. In the case of left lobe LDLT, the left hepatic veins (LHVs) are kept in the grafted liver. Decision on preserving the middle hepatic vein (MHV) is determined based on the individual's particular situation. Currently, MHV is frequently retained in the donor for the sake of donor safety. Therefore, restoration of segment VIII and segment V tributaries of MHV and the inferior right hepatic vein (IRHV) is frequently required to guarantee appropriate drainage. So, RHV, IRHV, and segment V and VIII tributaries of MHV may provide the outflow tract for right lobe LDLT without MHV.[16] In the current study, the right lobe graft without MHV was used in most cases (n=29), the right lobe with MHV and the left lobe with MHV in 3 cases each. HV complications include HVS and HVT, usually at the site of anastomosis, and occur in 5-13% of LDLT.[22] Early obstruction of the HVOT results in congestion of the drained area. In the normal postoperative period, HVs have a triphasic waveform and anterograde spectrum on Doppler US. On Doppler US, diagnostic criteria for HVOT thrombosis include complete absence of blood flow, patchy monophasic waveform or dampened and barely measurable flow (10cm/s).[23] The monophasic spectrum is a sensitive but non-specific finding and can be seen secondary to extrinsic compression, high intra-abdominal pressure, such as Valsalva, in proximal stenosis or vein thrombosis.[5] In the current study, diagnosis of HVOT thrombosis on Doppler US was suspected in 7 cases, based on patchy monophasic waveforms in 3(42.86%) and absence of blood flow on Doppler US in 4(57.14%). On subsequent CECT abdomen, all of them were found to be thrombosed, indicating sensitivity, specificity, PPV, NPV and DA of 100%. The results are superior to reported values.[24,25]

Overall, the current study resulted in Doppler US sensitivity, specificity, NPV, PPV and DA of 100%, 88.8%, 100%, 89.4%, and 94.2% respectively, keeping CECT abdomen as the gold standard.

The current study has limitations because of its retrospective nature and a small sample. Although 121 patients had LTs during the study period, only 35 were suspected to have vascular and non-vascular complications, and, of them, only 13 actually had vascular complications. This resulted in a small size, but underlines the remarkable advancement in surgical techniques, armoury, skills and experience of the professionals that vascular complications were so rare. A future extension of the current study 2 or 3 years later with a large sample size, particularly of the study limb with vascular complications, may be helpful in further validating the findings.

Conclusion

The use of standard Doppler US was found to be adequate in documenting patent vessels as well as vascular complications after LDLT in majority cases with high accuracy and sensitivity. The most important benefit of Doppler US is that it can be performed intraoperatively or in the early postoperative period in ICUs where conditions are often less than optimal. With such success rates, these low-cost modalities may be able to fully replace CT in the diagnosis of vascular complications post-LDLT. In unclear cases, CT angiography is still considered the gold standard.

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Conflict of Interest: None.

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