Original Research Article

Contrast-enhanced ultrasound for the evaluation of hepatic artery occlusion after liver transplantation

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Abstract

Introduction: Vascular complications after liver transplantation remain a major threat to the survival of recipients.HAT is a major cause of graft loss and patient mortality, with an incidence between 3% to 8% in transplant recipients. Early detection of HAT is critical because urgent revascularization is required to avoid severe graft loss. Although ultrasound is the preferred first-line imaging modality in patients with suspected HAT, the accuracy and positive predictive value of HAT on Doppler US are reported to be low. Moreover, Doppler examination of the hepatic vasculature is time consuming and requires a high level of operator skill. Conventional angiography remains the gold standard for diagnosis. Recently, contrast-enhanced ultrasound (CEUS) has begun providing real-time angiographic-like images of vessels at bed side and allowing the accurate diagnosis of arterial diseases such as hepatic artery thrombosis. The purpose of this study was to evaluate the efficacy of CEUS in detecting HAT after liver transplantation**: Materials and Methods:** This is a retrospective data of the medical records of patients undergoing Liver transplantation in the Osmania General Hospital, Hyderabad between 2016 to 2018. Status of hepatic vascular assessment following liver transplantation done by conventional Doppler Ultra sonography and Contrast Enhanced Ultrasonography tests were obtained from registries of medical records. **Results:** 23 cases of post Liver transplantation aged between 4years and 58 years, with a median age of 30 years were included in the analysis. There were 20 males and 3 females. 14 patients underwent DDLT, 7 patients underwent LDLT, 1underwent split Liver transplantation and another 1 patient underwent Auto liver transplantation. Doppler US was inconclusive regarding patency of the hepatic artery (HA) circulation in 5 (21.7 %) of 23 transplantations. CEUS was performed in these 5 patients and detected HA thrombosis (HAT) in 2 cases and patent HA in 3 transplants. These 5 Transplants were confirmed by CT Angiography /conventional Angiography. In the subset of transplantations examined with CEUS, the sensitivity, specificity and accuracy of CEUS were 100%. CEUS was done at bedside without any Radiation and Nephro toxicity. In approximately 21.7% of cases, conventional Doppler US did not provide sufficient visualization of the HA after liver transplantation. In these cases, correct diagnosis was achieved by supplementary CEUS. **Conclusion:** CEUS may be a new approach for early diagnosis of postoperative vascular complications after Liver Transplantation, and it can be performed at the bedside. It is safe will not cause any nephron toxicity and Radiation. CEUS is a fast, non-ionizing imaging modality for the initial exclusion of vascular complications after liver transplantation. CEUS shows a high specificity and PPV in the detection of vascular complications. In unclear cases CT still is considered as the gold standard

Keywords: Doppler ultra sound, Contrast-enhanced ultra sound, Hepatic artery thrombosis, Liver transplantation, Angiography.

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Introduction

Liver transplantation is a well-accepted therapeutic modality for both acute and chronic liver failure [1].

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Vascular complications after liver transplantation remain a major threat to the survival of recipients. Hepatic artery thrombosis (HAT) occurs in 3–8% of the transplant recipients. It may occur within the first 24 h and is an important cause of re transplantation [2–8].

LDLT recipients (more for paediatric LDLT recipients) are more likely to develop vascular complications because of their complex vascular reconstruction and the slender vessels. Early diagnosis and treatment are critical for the survival of graft and recipients.

Usually, conventional Doppler ultrasonography (CDUS) is the initial imaging technique for identification of vascular complications [2,3,7,9,10]. It is mobile can be done bedside, does not involve ionizing radiation, non-invasive and inexpensive.

Recently, contrast enhanced ultrasound (CEUS) has significantly improved the diagnosis of postoperative vascular complications. CEUS improves the detailed vascular tracing and perfusion visualizationin both the hepatic artery (HA) andportal vein (PV). This article focuses on the role of Doppler ultrasound and CEUS for early diagnosis of vascular complications after liver transplantation

Methods and Materials

In this study, a two-step approach for assessment of livervessel patency was performed, first conventional Doppler US, and then, in case of uncertainty, real-time CEUS witha second-generation contrast agent intravenously In this study, a two-step approach for assessment of livervessel patency was performed, first conventional Doppler US, and then, in case of uncertainty, real-time CEUS witha second-generation contrast agent intravenously.

Place of study and type of study: This is a retrospective data of the medical records of patients undergoing Liver transplantation in the Osmania General Hospital, Hyderabad between 2016 to 2018.

Demographic data, Indications for liver transplantation, type of liver transplantation (DDLT and / or LDLT), Status of hepatic artery flow, Portal vein and Hepatic veins assessmentafter liver transplantation by conventional Doppler Ultra sonography and Contrast Enhanced Ultrasonography tests were obtained from registries of medical records.

In this study, a two-step approach for assessment of liver vessel patency was performed, first conventional Doppler US, and then, in case of uncertainty, real-time CEUS with second-generation contrast agent intra-venously. The radiologists had all been trained to examine liver-transplanted patients with respect to size of the liver and echogenicity of parenchyma, state (open or not) of the HA both intra- and extra-hepatically including measurement of resistive index (RI, normal 0.5–0.7). The normal hepatic artery Doppler waveform should have a rapid systolic upstroke and continuous diastolic flow [9].

Patency and flow direction of portal vein (PV), retro-hepatic vena cava and hepatic veins were also evaluated. In cases where the examiner could not find a patent HA with a normal arterial spectral curve, the Doppler US was repeated by another, more experienced radiologist during the same session.

If still in doubt about the patency of the artery, the more experienced radiologist performed CEUS with the same scanner using one or more 2.4 ml doses of a sulfur hexafluoride-containing second-generation contrast agent (SonoVue, Bracco Suisse SA,Switzerland) given intravenously in an antecubital vein with a 5-ml 0.9% saline flush.

A radiologist with 7 years of experience with CEUS at the start of the study performed the majority (90%) of the CEUS examinations with regard to the patency of HA. A dual screen display with the contrast images and low mechanical grayscale image sidebyside was instructive and often used.

The images were saved as still images and/or video clips. Patients were under medical supervision during and for at least 30 min following the administration of the contrast agent.

Inclusion criteria: All post liver transplantation patients whose blood vessel patency assessed by Doppler US and CEUS were included in this study.

Exclusion criteria: If any post liver transplantation patient did not undergo CEUS evaluation were excluded from this study.

Statistical methods: Continuous data were expressed as median/ range and analysed by Kruskal–Wallis test, and categorical variables were expressed as number/ percentage and analysed by chi-square test.

The sensitivity, specificity, and accuracy for determination of HA occlusion in the subset of patients examined with CEUS were calculated. Sensitivity was defined as the probability of a positive test in a transplant with an occluded artery.

Specificity was the probability of a negative test in a transplant with an open artery.

Results

23 cases of post Liver transplantation aged between 4years and 58 years, with a median age of 30 years were included in the analysis. There were 20 males and 3 females.

14 patients underwent DDLT, 7 patients underwent LDLT, 1underwent split Liver transplantation and another 1 patient underwent Auto liver transplantation.

The indications for liver transplantation are chronic Budd Chiari syndrome in 3, Alcoholic chronic liver diseases in 7, wilsons disease in 3, Auto immune hepatitis in 1, congenital hepatic fibrosis in 1, Algille syndrome in 1, Nonalcoholic liver diseases (NASH) in 2, Hepatitis B related CLD in 1, Hepatitis C induced CLD in 1, Primary sclerosing cholangitis in 1 and cryptogenic cirrhosis in 2.

All patients underwent Doppler US twice daily for10 days following Liver transplantation.

Whenever Hepatic artery, Portal vein or Hepatic veins are not visualized in conventional Doppler US they underwent CEUS. If CEUS also did not show flow in Hepatic artery or Portal vein they underwent CTAngiography / Conventional angiography.

Doppler US was inconclusive with regard to patency of the hepatic artery (HA) circulation in 5 (21.7 %) of 23 transplantations.

CEUS was performed in these 5 patients anddetected HA thrombosis (HAT) in 2 cases and patent HA in 3 patients.

These 5 Transplants were confirmed by CT Angiography /conventional Angiography. In the subset of transplantations examined with CEUS, the sensitivity, specificity and accuracy of CEUS were 100%.

CEUS was done at bedside without any Radiation and Nephro toxicity.

In approximately 21.7% of cases, conventional Doppler US did not provide sufficient visualization of the HA after liver transplantation.

In these cases, correct diagnosis was achieved by supplementary CEUS.

Table-1: Showing results of Hepatic artery status with Doppler USG Abdomen, CEUS and CT Angiography/ Conventional Angiography.

Type of Image	Total number of patients (n=23)	DDLT	LDLT	LTP SPLIT	AUTO LTP
Conventional Doppler Ultrasonography	23	14	7	1	1
CEUSG	5	3 (patent HA)	2 (No flow in HA)	0	0
CT Angiography / conventional Angiography	6	3 (patent HA)	2 (No flow in HA		1 Patent IVC, HV

Table-2: Showing, Post Liver Transplantation Patients Demographic data, Type of transplantation, Indication and findingzs of Doppler US, CEUSG and CTAngiography /Conventional Angiography.

S. No	Sex/ age	DDLT/LDLT	Indication	USG Doppler	CEUSG	CT Angio / Conventional Angio
1	M/22	DDLT	PSC	HA, PV, IVC and HV	-	-
2	M/30	AUTO TRANS-PLANTATION	Chronic. Budd Chiari syndrome	HA,PV,IVC and HV	-	Patent HA,PV and IVC,HV.
3	M/22	DDLT	Chronic. Budd Chiari syndrome	HA, PV, IVC and HV	-	-
4	M/40	DDLT	ALCOHOLIC CLD	Notvisualized HA	Patent vessels	Patent HA
5	F/20	DDLT	WILSONS DISEASE	Doubtful HA patency	Patent vessel	Patent HA
6	M/29	DDLT	Chronic. Budd Chiari syndrome	HA, PV,IVC and HV	-	-
7	M/41	DDLT	Alcoholic CLD	HA Not visualised	HA flow visualized	Patent HA
8	F/27	DDLT	AUTO IMMUNE CLD	HA,PV,IVC and HV	-	-
9	M/27	DDLT	CRYPTOGENIC	HA,PV,IVC and HV	-	--
10	M/56	DDLT	Alcoholic CLD	HA,PV,IVC and HV	-	-
11	M/53	DDLT	Alcoholic CLD	HA,PV,IVC and HV	-	-
12	M/32	DDLT	Alcoholic CLD	HA,PV,IVC and HV	-	-
13	m/11	LDLT	Wilsons	HA,PV,IVC and HV	-	-
14	M/56	LDLT	HBV CLD	HA,PV,IVC and HV	-	-
15	F/4	LDLT	Cong. Hepatic Fibrosis	HA,PV,IVC and HV	-	-
16	M/58	DDLT	NASH	HA,PV,IVC and HV	-	-
17	M/50	LDLT	Alcoholic CLD	HA,PV,IVC and HV	-	-
18	M/10	LDLT	Wilsons	HA,PV,IVC and HV	-	-
19	M/13	SPLIT	Cryptogenic	HA,PV,IVC and HV	-	-
20	M/40	DDLT	NASH	HA,PV,IVC and HV	-	-
21	M/45	DDLT	Alcoholic	HA,PV,IVC and HV	-	-
22	M/54	LDLT	HCC with HCV CLD	HA not visualised	No flow in intra hepatic HA	HA Block at anastomosis
23	M/9	LDLT	Alagille syndrome	HA not visualised	NO flow in HA	HA Block at anastomosis

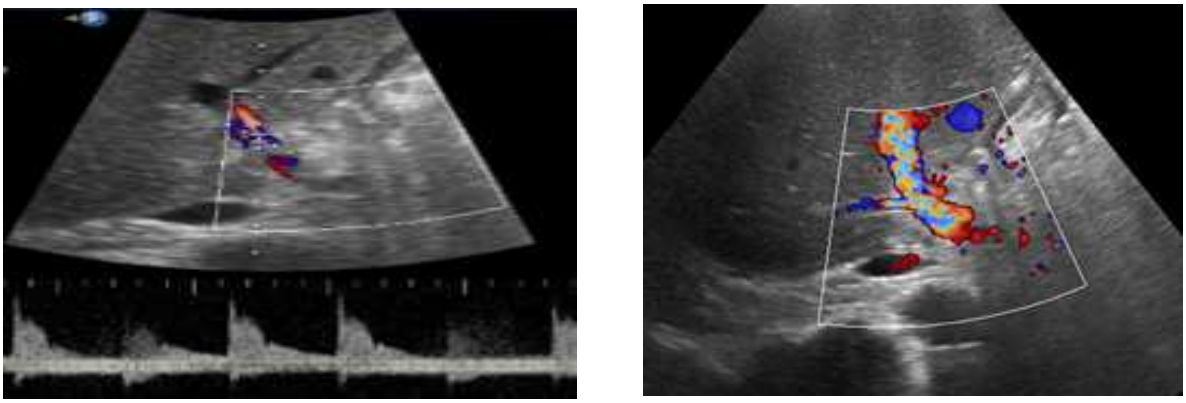

Figure-1: shows Conventional Doppler USG Images of patent Hepatic artery and portal vein.

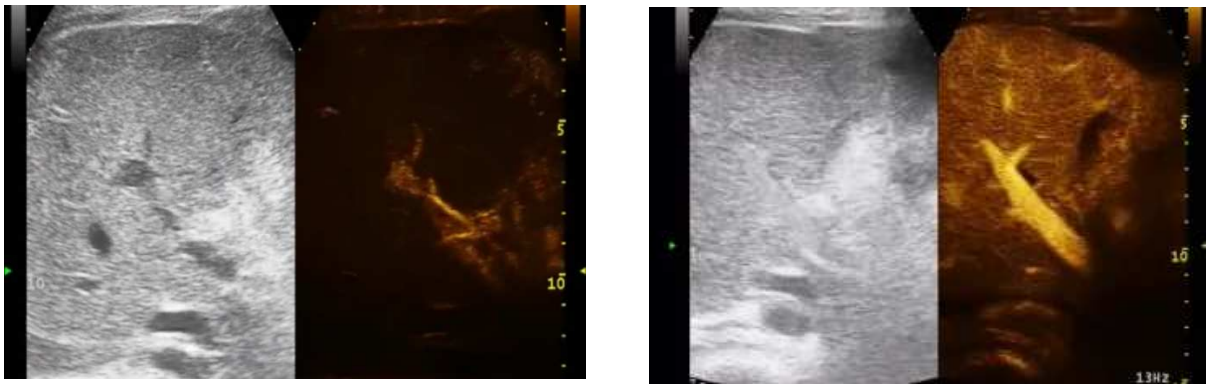

Figure-2: CEUS images of patent Hepatic artery and portal vein

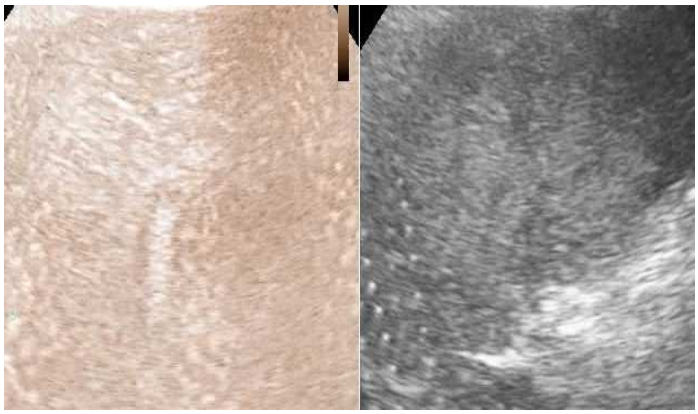

Figure-3 (A): CEUS image of Blocked Hepatic artery Occluded Hepatic arter

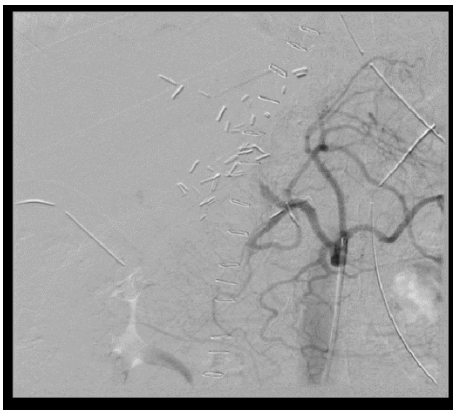

Figure-3 (B): Conventional Angiography shows

Discussion

HAT is a major cause of graft loss and patient mortality, with an incidence between 3% to 8% in adult transplant recipients [2,3]. Early detection of HAT is critical because urgent revascularization is required to avoid severe graft loss. Although ultrasound is the preferred first-line imaging modality in patients with suspected HAT, the accuracy and positive predictive value of HAT on CDUS are reported to be only 64%-82% and 64%-68%, respectively [17,18]. Moreover, Doppler examination of the hepatic vasculature is time consuming and requires a high level of operator skill.

CEUS has been reported to effectively improve flow visualization of the hepatic artery [4,19] and to shorten the scanning time in compared with CDUS [28], with a 100% sensitivity and 97.8% accuracy for the detection of HAT[20].

In this study, a two-step approach for assessment of liver vessel patency was performed, first conventional Doppler US, and then, in case of uncertainty, real-time CEUS with a second-generation contrast agent intravenously. By this approach, 2 HA occlusions that

had occurred in 23 liver transplantations were detected. A prevalence of HA occlusion of 8% agrees with previous studies [2- 8]. HAT is more common in LDLT than DDLT due to slender branches. In our series HAT was noticed in 2 cases of LDLT and none in DDLT. In these patients, this serious complication could be corrected surgically without undue delay because of bed-side documentation of an occluded HA with CEUS. There was no false positive diagnosis of HA occlusion, and in 5 doubtful cases (according to Doppler US), an open artery could be visualized by CEUS in 3, thus avoiding laparotomy or other more expensive imaging procedures. In most cases, conventional Doppler ultrasound was sufficient to document an open HA after liver trans- plantation. Supplementary CEUS provided correct Information in the remaining 21.7% of transplantations. In accordance with previous studies, CEUS improved flow visualization of the HA and PV and correctly differentiated between thrombosis and a patent artery in patients without HA flow at conventional Doppler US [4,6,11–13]. The use of CEUS avoided the need for invasive arteriography in 62.9% of such cases. Thus, HAT has evolved into the most important CEUS application in liver transplantation.

Previous studies have used conventional angiography as a reference standard, whereas we used clinical follow up including repeating Doppler US and, in selected cases, CT angiography /conventional Angiography. Microbubblecontrast was only given to the patients in whom the HA was not visualized with certainty. The most important advantage of CEUSis it can be done in the immediate postoperative period (<24 h) in the operating theatre or in the intensive care unit where conditions are far from ideal. In general, when doubtful about patency of hepatic vasculature withconventional Doppler, CT Angiography/ conventional Angiography may be considered, but may be more cumbersome and time- consuming to perform postoperatively than CEUS. CEUS improved visualization of both extra- and intra-hepatic parts of the HA. This quality of CEUS is particularly valuable in the early postoperative phase when the often-weak Doppler signals from intrahepatic arteries are sometimes obscured by portal venous flow. Doppler US and CEUS should therefore be considered as complementary rather than competitive methods. The main advantage of this study is it will not cause any nephro toxicity and can be done at bed side unlike CT /Conventional angiography.The main drawbacks of this study is retrospective study and hepatic artery stenosis cannotbe detected as clearly as CT angiography/ conventional angiography.

Conclusion

The conventional Doppler US proved sufficient to document open vessels after liver transplantation in most cases. But Supplementary CEUS provided correct information in the remaining doubtful patientsin the operation theatre or in the intensive care unit where conditions are far from ideal.

However, there is a need of randomized control studies that would effectively verify the conclusions of this study.

Message of this study: CEUS is an ideal bed side investigation of choice when conventional doppler US is doubtful about hepatic vasculature patency after liver transplantation particularly in the Operation theatre and ICU where conditions are far from ideal.

Authors Contribution

Author 1. Prepared the manuscript and performed all surgeries.

Author 2. Helped in Conventional doppler and CEUS assessment of liver transplant patients.

Author 3. Helped in Conventional doppler and CEUS assessment of liver transplant patients.

Author 4. Supervised the paper and involved in patient care of these patients.

Author 5. Helped in Conventional doppler and CEUS assessment of liver transplant patients.

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Permission of IRB: Yes

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