OPEN ACCESS

ISSN: 2676-7473

RBMS.2019;24(1):e22

ORIGINAL RESEARCH

Diagnostic value of early postoperative color doppler ultrasonography to predict vascular complications following liver transplantation

Seyed Mohammad Reza Nejatollahi [1], Maryam Khoshkholgh Sima [2*], Habibollah Peirovi [1], Farhad Niaghi [2]

1. *Hepato-Pancreato-Billiary/Transplant Surgeon, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Radiologist, Department of Radiology Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

*Corresponding Author:
Address: Department of Radiology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Email: maryambahar68@yahoo.com

Date Received: July, 2018 *Date Accepted: July, 2019* *Online Publication: October 15, 2019*

Abstract

Introduction: Blood flow and hemodynamic of the transplanted liver has an important predictive role in the survival of the patients. We aimed to determine the diagnostic value of early post-operative color doppler ultrasonography (CDU) for detecting vascular complications following liver transplantation at our center.

Materials and Methods: In this prospective study, consecutive patients who underwent deceased donor liver transplantation between March 2016 and March 2017 were enrolled. Color Doppler ultrasonography was performed within the first week following surgery. The follow-up CDU was performed after 1 year from the liver transplantation. Using the findings of follow up CDU as the reference standard, we calculated values of the capability of the initial CDU in the diagnosis of the hepatic artery, portal vein and intrahepatic veins' stenosis, including the level of agreement, sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

Results: The data of 50 patients were analyzed in this study (mean age=38.9±13.2 years, 26 [52%] men). In the initial ultrasonography, 16 cases had hepatic artery stenosis, 4 cases had portal vein stenosis and 4 patients had IVC stenosis. The diagnostic value of the early postoperative CDU for hepatic artery stenosis, portal vein stenosis, and other vascular stenosis were 71.9, 96.0, and 62.0, respectively.

Conclusion: Early post-operative CDU is a safe and feasible method that can detect the development of hepatic artery or portal vein stenosis in liver transplant recipients with a low to moderate positive predictive value and a high negative predictive value.

Keywords: Liver transplantation; Color doppler ultrasonography; Portal vein stenosis; Hepatic artery stenosis; Diagnosis

Introduction

Liver transplantation has been recognized as a definitive treatment for end-stage liver diseases [1]. By the advent of the surgical techniques and immunosuppressive drugs, postoperative complications have decreased and the survival of the patients have been prolonged during the past decades[1]. However, vascular complication, particularly thrombosis or stenosis of hepatic vessels has remained as a major predictor for transplant survival as well as the need for re-transplantation [2,3]. Therefore, the use of imaging techniques for early detection of vascular complications following liver transplantation can help to minimize the adverse events and improve the patients' survival [4].

Color Doppler ultrasonography (CDU) has been utilized successfully as a practical imaging modality in the postoperative management of liver transplantation [5]. CDU is a non-invasive, cost-effective, affordable and radiation-free imaging technique that can be employed at the bedside for early and late follow-up of the transplant complications [6,7]. Viability and function of a liver transplant can be assessed using CDU, although it lacks optimal sensitivity for diagnosing acute rejection [8]. CDU has the potency to evaluate the hemodynamic status, such as patency, direction, velocity, and spectrum of the blood flow in the transplanted liver [9]. Hepatic artery and portal vein thrombosis can be detected by CDU even before the development of the clinical symptoms [10,11]. The sensitivity of CDU in the diagnosis of hepatic artery thrombosis has been reported to be between 75% and 100%, while its diagnostic accuracy for portal vein thrombosis has been reported to be 97-100% [12]. Also, CDU can diagnose hepatic artery stenosis with a sensitivity of 72%-97% and a specificity of 64%-99.1% [13,14]. As for the portal vein stenosis, CDU can diagnose it with a sensitivity of up to 100% and a specificity of 84% [15]. However, these values depend on various factors such as the clinical setting, experience of the ultrasonography operator and the used diagnostic criteria. Therefore, more studies are still required to fully describe the role of CDU in the surveillance of liver transplant patients, particularly shortly after the transplantation. In the present study, we aimed to determine the diagnostic value of early postoperative CDU for detecting vascular complications following liver transplantation at our center.

Materials and Methods

In this prospective study, consecutive patients who referred to Taleghani hospital for deceased donor liver transplantation between March 2016 and March 2017 were enrolled. The inclusion criteria were the candidate patients for liver transplantation due to cirrhosis and age <60 years. The exclusion criteria were death after surgery due to acute respiratory distress syndrome, hemorrhage or unsuccessful transplantation within the first 24 hours following surgery. All patients signed a written informed consent to be enrolled in the study before surgery. The research board of the Taleghani hospital and committee of medical ethics of Shahid Beheshti University of Medical Sciences approved our study protocol. The study protocol conforms to the declaration of Helsinki.

Demographic and clinical data of the patients were collected by the researchers that included age, sex, the reason for liver transplantation and the underlying disease. All patients received deceased donor liver allograft. All transplantations were performed according to the standard protocols at our hospital with modified right lobe with middle hepatic vein reconstruction. Hepatic artery reconstruction was performed by connecting the graft right hepatic artery to the recipient's right hepatic artery, left hepatic artery or a proper hepatic artery based on diameter, length, and status of the intima. End-to-end anastomosis was done using interrupted sutures (nylon #9) under a microscope. Piggyback technique was used for inferior vena cava anastomosis. The patients were transferred to the intensive care unit after the operation and were managed based on the routine protocols.

Color Doppler ultrasonography was then performed for all the patients within the first week following liver transplantation. All CDU procedures were executed by an expert radiologist using a GE Voluson 730 machine (GE Healthcare, Zipf, Austria) with a 3-5 MHz

transducer. The patients were in the supine position during CDU with head elevation and abduction of the right arm. Oblique intercostal scanning was used for most of the measurements. The operator adjusted standard Doppler parameters to gain maximal results with no background noise. CDU was used to determine the changes in the hepatic artery, portal vein, and intrahepatic veins for stenosis, thrombosis, and ischemia, based on the spectral waveform and measurements. In normal hepatic artery, resistive index (RI) was considered between 0.5 and 0.7. RI above 0.8 or pre- to post-anastomosis PSV ratio more than 2-3 times with the presence of aliasing was in favor of significant stenosis at the site of anastomosis in the hepatic artery. As an indirect sign, the presence of Tardus-Parvus wave (RI<0.5 or acceleration time > 100 msec) was in favor of stenosis in the proximal region of the hepatic artery. Accordingly, the velocity of the hepatic vein before and after anastomosis and the triphasic waveform of the hepatic veins and inferior vena cava were measured. In the hepatic vein, three times increase in the peak velocity before and after the anastomosis with the presence of aliasing at the site of anastomosis was in favor of stenosis. Moreover, the presence of reverse flow in the hepatic vein or IVC or absence of normal triphasic wave and change to monophasic wave were other signs of hepatic vein stenosis. Portal vein stenosis was defined as PSV>125 cm/s or the pre- to post-anastomosis ratio above 3:1.

The final follow-up CDU was performed after 1 year from the liver transplantation by the same operator and under a similar situation. Stenosis of the hepatic artery, portal vein, and inferior vena cava were evaluated as the study endpoints in both CDUs and their results were compared together.

Statistical analysis

Data analysis was performed using SPSS version 24.0 (IBM corp., USA). Continuous variables were shown as mean ± standard deviation while categorical variables were shown as frequency (percentage). Using findings of the 1-year follow up CDU as the reference standard, we calculated values of the capability of the initial CDU in the diagnosis of hepatic artery, portal vein and intrahepatic veins' stenosis, including level of agreement, sensitivity, specificity, positive predictive value (PPV), negative predictive value, and diagnostic accuracy. We also calculated 95% confidence intervals (CIs) for each of these parameters.

Results

Within the study period, 60 patients underwent liver transplantation, of which 10 patients died due to peritoneal hemorrhage or acute respiratory distress syndrome. The remaining 50 patients entered the study. The mean age of the patients was 38.9±13.2 years (min: 11 years, max: 58 years) and 26 (52%) patients were men.

The cause of cirrhosis or the reason for liver transplantation included: Cryptogenic cirrhosis (n=20); autoimmune hepatitis alone (n=10); primary sclerosing cholangitis alone (n=8); primary sclerosing cholangitis and autoimmune hepatitis (n=4); autoimmune hepatitis and primary biliary cirrhosis (n=3); Primary sclerosing cholangitis and primary biliary cirrhosis (n=1); Wilson's disease (n=1); hyperoxaloria (n=1); congenital fibrosis (n=1); and, alcoholic cirrhosis (n=1).

In 7 patients, both the right and left hepatic arteries were implanted, so we studied 57 hepatic arteries. Hepatic artery or portal vein thrombosis was not detected in our patients. In the initial ultrasonography, 16 cases had hepatic artery stenosis, 4 cases had portal vein stenosis and 4 patients had IVC stenosis. In the follow-up CDU and from the 16 patients who had hepatic artery stenosis in their initial CDU, 5 patients showed hepatic artery stenosis and 11 other patients had normal findings.in addition follow-up CDU showed 5 patients with late onset stenosis in hepatic artery despite the initial normal CDU. Moreover, 2 patients had portal vein stenosis and none of the cases had IVC stenosis (Table-1). Diagnostic Values of postoperative color Doppler ultrasonography for vascular stenosis following liver transplantation, including sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy, are shown in table-2.

Discussion

In the present study, we observed that early postoperative CDU following liver transplantation can predict vascular stenosis

with a low to moderate positive predictive value and a high negative predictive value. However, some of the observed stenosis in the early post-operative CDU were due to post-operative inflammatory change or edema and resolved by time.

Hemodynamic status of a transplanted liver can significantly predict the survival of the patients [16]. Vascular complications have shown to be associated with lower graft survival [17]. These complications are very much related to surgical techniques and can lead to death. Additionally, the incidence of vascular complications has been observed more significantly among the living donor transplant recipients compared with the deceased donor transplant recipients [17]. Hepatic artery and portal vein are the two main vessels that need surveillance following liver transplantation [12,16]. The most common Doppler parameter used for the evaluation of hepatic artery is RI that we also used in this study. This index is a semi-quantitative measurement of the resistance to arterial flow into the liver with a normal range of 0.5 to 0.7 [18]. Results of a study on 60 liver transplant recipients showed that utilization of the Tardus-Parvus waveform of the hepatic artery was accompanied by a low to moderate positive predictive value and a high false-positive rate [19]. But after the combination of the Tardus-Parvus pattern and an optimal PSV cutoff, the positive predictive value improved and the false positive rate decreased for the diagnosis of hepatic artery stenosis. It should be noted that transient high-resistance arterial flow is often observed in patients with normal hepatic artery and an experienced ultrasonographer should be aware of this phenomenon and distinguish it from any probable pathology [16].

Doppler criteria of stenotic ratio and velocity ratio have a high sensitivity but a less specificity in detecting portal vein thrombosis following liver transplantation [20]. In a study that compared the results of CDU with portal venography for diagnosing portal vein stenosis in 13 adult patients with liver transplantation, CDU had a sensitivity of 100% and specificity of 84% to detect hemodynamically significant portal vein stenosis [15]. In another study on 284 liver transplant recipients, preoperative complete portal vein thrombosis was accompanied by a significantly higher rate of vascular complications following liver transplantation and all these complications could be detected successfully by CDU [21].

Ultrafast doppler has also been shown a feasible method for post-transplantation evaluation of the hepatic artery in liver recipients, with reduced examination time at the bedside [22]. The sensitivity and specificity of post-operative CDU for detecting hepatic artery stenosis in our study was comparable to previous studies[13,14].

One of the best achievements of our study is that it can assist the surgeons in decision making for the patients within the first week of transplantation regarding vascular complications. According to our result and due to the moderate positive predictive value of CDU in the diagnosis of vascular stenosis, we can say that a later follow-up CDU should be performed to reach to a clear-cut diagnosis, as many of the reported stenosis dissolved through time. This can be due to postoperative structural changes and edema at the site of anastomosis. Similar studies have also reported that initial hepatic artery abnormalities in the early post-operative CDU are transient and generally resolve in the follow-up CDUs [23,24]. We also showed that the same issue can be true for IVC stenosis in the early post-operative CDU, as all cases of IVC stenosis resolved in the follow-up CDU in our study. On the other hand, due to the high negative predictive value of CDU in our study, in patients with normal CDU within the first week, follow-up CDUs can be only performed selectively in the presence of specific signs and symptoms, which will be more cost-effective.

The major limitation of this study is its sample size. Also, 10 patients died after transplantation and we could not perform CDU on these patients. However, liver transplantation is not a frequent surgery and our center is one of the few centers in Iran that has a professional team for liver transplantation. Moreover, we used the 1-year follow-up CDU as our reference. In order to prove the presence of vascular complications, we would better have the data of multi-slice triphasic CT scan or angiography. However, as we have compared the results of two CDUs and checked for their consistency, our results are reliable.

Conclusion

Early post-operative CDU is a safe and feasible way to rule out the vascular complications in patients with a liver transplant. CDU can detect the development of hepatic artery, portal vein, and intrahepatic veins stenosis, as well as non-vascular complications, with a low to moderate positive predictive value and a high negative predictive value. We recommend further larger studies to reach a definite diagnostic value for CDU in liver transplantation.

Conflict of interest

Authors declare no conflict of interest.

References:

1. Maynard E. Liver Transplantation: Patient Selection, Perioperative Surgical Issues, and Expected Outcomes. *The Surgical clinics of North America.* 2019;99(1):65-72.
2. Mourad MM, Liossis C, Gunson BK, et al. Etiology and management of hepatic artery thrombosis after adult liver transplantation. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society.* 2014;20(6):713-723.
3. Zanetto A, Rodriguez-Kastro KI, Germani G, et al. Mortality in liver transplant recipients with portal vein thrombosis - an updated meta-analysis. *Transplant international : official journal of the European Society for Organ Transplantation.* 2018;31(12):1318-1329.
4. Rubenthaler J, Paprottka KJ, Hameister E, et al. Vascular complications in liver transplantation: Beneficial role of contrast-enhanced ultrasound (CEUS) in the postoperative phase. *Clinical hemorheology and microcirculation.* 2016;64(3):475-482.
5. Chung Y, Choi H, Na G, You Y, Park I. Postoperative Doppler Ultrasonography in Liver Transplantation. Paper presented at: Transplantation proceedings2018.
6. Sanyal R, Zarzour JG, Ganeshan DM, Bhargava P, Lall CG, Little MD. Postoperative doppler evaluation of liver transplants. *The Indian journal of radiology & imaging.* 2014;24(4):360-366.
7. Stell D, Downey D, Marotta P, et al. Prospective evaluation of the role of quantitative Doppler ultrasound surveillance in liver transplantation. *Liver transplantation: official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society.* 2004;10(9):1183-1188.
8. Bolognesi M, Sacerdoti D, Mescoli C, et al. Acute liver rejection: accuracy and predictive values of doppler US measurements--initial experience. *Radiology.* 2005;235(2):651-658.
9. Crossin JD, Muradali D, Wilson SR. US of liver transplants: normal and abnormal. *Radiographics : a review publication of the Radiological Society of North America, Inc.* 2003;23(5):1093-1114.
10. Garcia-Criado A, Gilabert R, Nicolau C, et al. Early detection of hepatic artery thrombosis after liver transplantation by Doppler ultrasonography: prognostic implications. *Journal of ultrasound in medicine.* 2001;20(1):51-58.
11. Rossi S, Rosa L, Ravetta V, et al. Contrast-enhanced versus conventional and color Doppler sonography for the detection of thrombosis of the portal and hepatic venous systems. *AJR American journal of roentgenology.* 2006;186(3):763-773.
12. Ma L, Lu Q, Luo Y. Vascular complications after adult living donor liver transplantation: Evaluation with ultrasonography. *World journal of gastroenterology.* 2016;22(4):1617-1626.
13. Sidhu P, Ellis S, Karani J, Ryan S. 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. *Clinical radiology.* 2002;57(9):789-799.
14. Vit A, De Candia A, Como G, Del Frate C, Marzio A, Bazzocchi M. Doppler evaluation of arterial complications of adult orthotopic liver transplantation. *Journal of clinical ultrasound.* 2003;31(7):339-345.
15. Mullan CP, Siewert B, Kane RA, Sheiman RG. Can Doppler sonography discern between hemodynamically significant and insignificant portal vein stenosis after adult liver transplantation? *AJR American journal of roentgenology.* 2010;195(6):1438-1443.
16. Abdelaziz O, Attia H. Doppler ultrasonography in living donor liver transplantation recipients: Intra-and post-operative vascular complications. *World journal of gastroenterology.* 2016;22(27):6145.
17. Khalaf H. Vascular complications after deceased and living donor liver transplantation: a single-center experience. *Transplantation proceedings.* 2010;42(3):865-870.
18. Lafortune M, Patriquin H. The hepatic artery studies using Doppler sonography. *Ultrasound Quarterly.* 1999;15(1):9-26.
19. Park YS, Won Kim K, Lee SJ, 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(3):884-891.
20. Huang TL, Cheng YF, Chen TY, et al. Doppler ultrasound evaluation of postoperative portal vein stenosis in adult living donor liver transplantation. *Transplantation proceedings.* 2010;42(3):879-881.
21. Jia Y-P, Lu Q, Gong S, et al. Postoperative complications in patients with portal vein thrombosis after liver transplantation: evaluation with Doppler ultrasonography. *World Journal of Gastroenterology: WJG.* 2007;13(34):4636.
22. Kim SY, Kim KW, Choi SH, et al. Feasibility of UltraFast Doppler in Post-operative Evaluation of Hepatic Artery in Recipients following Liver Transplantation. *Ultrasound in medicine & biology.* 2017;43(11):2611-2618.
23. Sanyal R, Lall CG, Lamba R, et al. Orthotopic liver transplantation: reversible Doppler US findings in the immediate postoperative period. *Radiographics : a review publication of the Radiological Society of North America, Inc.* 2011;32(1):199-211.
24. García-Criado Á, Gilabert R, Berzigotti A, Brú C. Doppler ultrasound findings in the hepatic artery shortly after liver transplantation. *American Journal of Roentgenology.* 2009;193(1):128-135.