Vascular complications after adult liver transplantation: Evaluation with Doppler ultrasound

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Learning objectives

To illustrate the normal hemodynamic features of liver transplants and the spectrum of postoperative complications.

To retrospectively assess our center Doppler findings in 346 patients after liver transplantation.

Background

Liver transplantation in our country has developed with success in recent years and it is the treatment of choice in patients with liver dysfunction due to chronic disease or acute failure. Worldwide, hepatitis C, alcoholic liver disease and cryptogenic cirrhosis are among the most common disorders demanding transplantation [1,2]. Other conditions treated with hepatic transplantation comprise cholestatic, metabolic or vascular diseases as exposed in Table 1. Malignancy is a problem that requires careful consideration in the evaluation of the liver transplant candidate. Initially well accepted for transplantation, hepatic malignancy is currently an indication only in highly selected individuals.
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<th>Liver cirrhosis</th>
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<td>Vascular conditions</td>
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<td>Acute liver failure</td>
<td>Intoxication [mushroom – (amanita phalloides), acetaminophen]</td>
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<td>Other:</td>
<td>Pylcystic liver disease</td>
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**Table 1**: Common indications for liver transplantation.

**References**: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

The generally accepted guidelines for patients with hepatocellular carcinoma are the Milan criteria of no single lesion greater than 5 cm in diameter or three or fewer lesions each less than or equal to 3 cm in diameter. However some studies, as the one developed by the liver transplant group at the University of California at San Francisco (UCSF), claim that Milan criteria are very restrictive and have attained similar outcomes with least restrictive data: Single lesion # 6.5 cm; multiple lesions # 3 cm;
largest tumor diameter if multiple # 4.5 cm; total tumor diameter if multiple # 8 cm [3]. As long-term survival increased, the absolute and relative contraindications to liver transplant transformed, are gradually becoming fewer. Relative contraindications include ischemic cardiac disease, primary tumors other than hepatic, portal vein thrombosis and psychosocial and economic factors in which patients are now elected on a case-by-case basis.

The presence of one or more of the following absolute contraindications will frequently preclude acceptance for liver transplantation:

- uncontrolled systemic infection
- severe cardiovascular or pulmonary disease
- extrahepatic malignancy
- multisystem organ failure
- active substance abuse
- acquired immunodeficiency syndrome

Despite technical advances, improvements in organ preservation and immunosuppressive therapy, postoperative complications remain a major cause of graft loss. Besides acute graft rejection, there are other postoperative risks that can change the hemodynamics of a grafted liver. Vascular complications, with an overall incidence of 9% are the third cause of graft loss, include thrombosis and stenosis of the hepatic artery, portal vein, or inferior vena cava, as well as hepatic artery pseudoaneurysms and arteriovenous fistulae [4].

The clinical signs of vascular complications depend on the timing during the post-transplant course and usually are nonspecific with overlapping features with sepsis and rejection, so radiologic diagnosis is required.

Most transplantation centers perform postoperative ultrasound (US) (gray-scale and Doppler) as the first imaging modality to evaluate the integrity of the graft vasculature, since it can be performed with portable equipment, it is widely available, does not involve exposure to ionizing radiation, is cost effective and has a high sensitivity and specificity for detection of arterial and venous disorders. At our institution we complete a baseline study within the first 24h after transplantation and if a complication is demonstrated that does not require immediate intervention it is followed up every 24/48 hours thereafter. Otherwise and without clinical or laboratorial changes, we only repeat the ultrasound prior to discharge.

Optimization for each patient of the various operator-dependent technical controls (baseline, filters, gain, angle correction, gate size, velocity scale) will allow maximum results. When ultrasound results are equivocal, confirmation is required or clinical suspicion for a complication persists despite normal findings, cross-sectional imaging studies are performed [magnetic resonance, computed tomography angiography (angio-CT)].
In our study the records of 346 patients who underwent post-transplant Doppler US between November 2007 and November 2011 were reviewed retrospectively. Doppler US findings were correlated with angiographic results or surgery.

**Imaging findings OR Procedure details**

Knowledge of the surgical technique of hepatic transplantation and acquaintance of the normal US appearance of liver allows prompt detection of complications and prevent misdiagnosis (figure1).

The normal parenchyma of a liver transplant has a homogeneous or slightly heterogeneous pattern at gray-scale imaging. However for a proper evaluation of the vascularization the examination is performed with both gray scale and Doppler evaluation. The normal Doppler waveform in the hepatic artery is of a broad systolic peak (<200 cm/s) with continuous diastolic flow. The acceleration time, which represents the time from end diastole to the first systolic peak, should be below 80 msec, and the resistive index must be between 0.5 and 0.7. Any deviation from this pattern should be carefully investigated or followed-up [5].

Normal hepatic vein usually has a triphasic pattern with hepatofugal flow while the expected portal vein waveform is a constant flow pattern toward the liver with slight variations of velocity linked to respiration.
Fig. 1: - Normal gray- (a) and Doppler US (b-c) appearance. a: the hepatic parenchyma appears slightly heterogeneous with the left, middle and right hepatic veins draining into the inferior vena cava (IVC). b: intra-hepatic arterial waveform with an adequate low resistance profile. c: shows anterograde (hepatopetal) flow in the portal vein, a finding that appears red on the color Doppler image and is displayed above the baseline on the spectral waveform It has a normal continuous waveform with mild velocity variations.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

In the study group conducted at our institution there were 346 individuals ranging in age from 17 to 73 years - mean of 45 years and 8 months. Alcoholic liver disease was the most common disease requiring transplantation, soon followed by alcoholic liver disease, familial amyloidotic polyneuropathy and Hepatitis C (figure2).
Fig. 2: Indications for liver transplant presented by our patients. Some individuals have overlapping conditions.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Of the 518 Doppler US examinations performed in these patients, 39 (11.3%) had vascular complications. Twenty one of these were hepatic artery thrombosis and 7 were stenosis. Hepatic vein complications, including stenosis and thrombosis, occurred in 5 of our patients. Disorders of the portal vein were reported in 6 individuals, accounting for approximately 15% of all post-transplant vascular complications (Figure 3).
Fig. 3: Vascular complications detected in our center between November 2007 and November 2011.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Fig. 4: A schematic drawing of the illustrated vascular complications.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Hepatic Artery Thrombosis

Currently, in standard techniques, the donor hepatic artery is typically anastomosed to the recipient hepatic artery in an end-to-end fashion.

Hepatic artery thrombosis according to our results, which were similar to those reported on different medical studies, is the most common vascular complication of liver transplantation with a peak incidence during the first two weeks.

The importance of complications involving the hepatic artery in liver grafts is grounded on the fact that the intrahepatic biliary epithelium is perfused purely by small branches of the hepatic artery. Therefore, arterial thrombosis may lead to biliary ischemia and consequent necrosis. As a result, it is a complication that should be supposed face to sudden high fever, elevation of liver enzymes, biliary leaks, fulminant liver failure or intermittent episodes of sepsis without an evident source. Prompt diagnosis is vital.
allowing early intervention (thrombectomy, reconstruction) in an attempt to avoid the necessity of retransplantation [4,6].

At Doppler examination, there is usually complete absence of both proper hepatic and intrahepatic arterial flow. Nolten and Sproat [7] have showed a condition of "impending thrombosis" occurring in the 3rd to 10th day in the post-operative period: initially normal waveform, with follow-up examinations progressively revealing no diastolic flow followed by decreased peak systolic velocity and lastly loss of the hepatic waveform. At times, intrahepatic waveforms may show a tardus parvus pattern, which is characterized by an increased acceleration time (AT) of more than 0.08 second and a resistive index (RI) of less than 0.5. (figs. 5,6) This finding is probably due to the formation of collateral vessels that take at least three weeks to become apparent. Therefore we have to be careful as the use of these parameters may result in false-positive cases [1]. When an intrahepatic tardus-parvus waveform is demonstrated, it may be due to severe hepatic edema (24-72 hours after surgery), marked aortoiliac atherosclerosis, systemic hypotension or high-grade hepatic artery stenosis.

Fig. 5: 26 years old, female. Tardus parvus intra-hepatic arterial waveform. Image obtained in a patient who had undergone liver transplantation 1 month earlier shows a prolonged AT (0.087 s) greater than 0.08 s and a RI value (0.34) less than 0.5 indicative of a hepatic arterial disease.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Fig. 6: Same patient as in figure 5. a, b: angio-ct. a: axial image (*) showed a peripheral parenchymal infarct. The presence of a tardus-parvus waveform pattern in the Doppler ultrasound is suggestive of hepatic artery stenosis. b: however this examination confirmed hepatic artery thrombosis by demonstrating abrupt cutoff (#) with lack of opacification of distal branches with some collateral arterial vessels.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Hepatic Artery Stenosis

As in hepatic artery thrombosis, clinical manifestations vary noticeably, ranging from elevation of liver enzyme levels to bile leak, ischemic changes or even fulminant hepatic necrosis [4].

Caution is needed since mild degrees of hepatic artery narrowing may be present without Doppler impact. Therefore, if the clinical suspicion is high, normal results should not avoid follow-up with angiography/angio-CT/angio-MR, although in such cases the hepatic artery stenosis, if detected, will tend to be of a minor degree with no management repercussion. On the other side spectral analysis at the site of narrowing primary may reveal a focal accelerated velocity greater than 200 cm/sec with associated turbulence distal to the stenosis. However, the site of narrowing is difficult to identify, and the diagnosis is usually made on the basis of the findings distal to the stenosis. Intrahepatic waveforms may show a tardus-parvus pattern with a prolonged acceleration time and decreased resistive index, identical to the one that may be seen in hepatic artery thrombosis with collateralization (figs. 7-9).
Fig. 7: a: Spectral Doppler. The presence of proximal stenosis was inferred by an assessment of the arterial waveform distal to the stenosis, which shows the characteristic tardus-parvus waveform. b: Color Doppler with focal color aliasing (#). References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Fig. 8: Same patient as in figure 7. a,b: Angio-CT demonstrated multiple hemodynamically significant hepatic artery stenosis (») associated with post-stenotic dilatation. References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Fig. 9: a: Doppler US exhibited a peak systolic velocity greater than 240 cm/sec b: angio-TC with Maximum Intensity Projection (MIP), proved what could be initially misdiagnosed as a stenosis because of the more tortuous course of the hepatic artery causing a stenosing effect

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Pseudoaneurisms and Fistulae

Hepatic artery pseudoaneurysm may be intra or extra-hepatic and is a rare condition after transplantation, occurring in 1% of patients [1,4]. The potential for rupture and subsequent hemorrhage makes early diagnosis and treatment vital. Arteriography is the gold standard for detection but any hypoechoic collection in the proximity of the hepatic artery must raise the suspicion.

Fistula formation between the hepatic artery and the portal or hepatic veins can also occur following trauma or iatrogenic procedures (figure 10).

Fig. 10: a,b: Doppler US. Hepatic artery-Hepatic vein fistula. Fistula formation between intra-hepatic artery and right hepatic vein after percutaneous liver biopsy

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Portal vein Stenosis/Occlusion

Similarly to the hepatic artery, the portal vein is also formed in an end-to-end anastomosis between the portal vein of the donor and that of the receptor. Complications affecting the portal vein after liver transplantation include thrombosis and anastomotic stenosis of the venous lumen, which are detected by the absence or acceleration of blood flow. Clinical signs are non-specific, such as, elevated values of transaminases, portal hypertension, massive ascites, severe encephalopathy, renal dysfunction and gastrointestinal bleeding. The clinical presentation includes portal hypertension, hepatic failure, edema, and massive ascites. Treatment options range from balloon angioplasty, thrombolysis, stent placement, mechanical thrombectomy, placement of a venous jump graft or creation of a portosystemic shunt to retransplantation[8,9].

Ultrasound findings associated with thrombosis are an echogenic or eventually anechoic filling defect in the portal vein with absence of Doppler signal (figure 11). Reduction in the hepatic artery RI accompanies portal vein occlusion and may be a helpful secondary sign for the determination of portal vein thrombosis. Caution must be taken since occasionally, reversed flow in the intrahepatic branches may be observed in patients with thrombosis and complete absence of flow in the main portal vein. This finding is due to arterioportal shunts that develop rapidly after the thrombosis [4].

Fig. 11: Portal vein thrombosis in a 18 year old female. a: On a B-mode US image a hypoechoic thrombus («) is seen in the lumen of the main portal vein. b: Axial angio-CT in the venous phase showed a complete low-attenuation filling defect (#) in the portal vein. Both techniques demonstrated staples (*) of the end-to-end portal vein anastomosis.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

In gray-scale mode a difference in caliber between donor and recipient portal veins may be normal and can be helpful in locating the portal venous anastomosis. However in portal vein stenosis, there is focal color aliasing with more than a three-to-fourfold increase in
velocity at the stenotic segment relative to that at the prestenotic segment (figures 12-14) [4,8].

Fig. 12: Portal vein stenosis in a 33 year old female. B-mode ultrasound image of the porta hepatis demonstrated a marked stenosis at the anastomotic site of the portal vein (#).

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Fig. 13: Same patient as in figure 12. a,b: Spectral Doppler revealed an accelerated flow velocity (90.7 cm/s) at the stricture (a) that was greater than 4 times of the values estimated (20.5 cm/s) in the prestenotic segment (b), a finding consistent with significant stenosis.
Fig. 14: Same patient as in figs. 12 and 13. Angio-CT with MIP reconstruction reveals significant portal vein stenosis (#) at the anastomosis.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

The donor suprahepatic inferior vena cava (IVC) can be attached to the recipient and the donor infrahepatic IVC to the recipient infrahepatic IVC by means of an end-to-end anastomosis. A common variation of this is the piggyback technique, commonly applied in the familial amyloidotic polyneuropathy patient, with conservation of the recipient vena cava which is anastomosed to the graft hepatic veins having a common trunk of the left and middle hepatic veins separated from the right.
The clinical signs are once again nonspecific and include congestion of the liver parenchyma with anomalous laboratory values, hepatomegaly and refractory ascites. Early detection of hepatic vein stenosis is important because it can lead to prompt intervention and thereby increase the probability of successful outcome [4]. After the interventional procedure (stent placement or balloon angioplasty) is also necessary to reevaluate the restoration of normal hepatic venous flow (fig. 15).

Fig. 15: a, b: Spectral doppler confirming a well-functioning stent with flow intra and distal to it.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Hepatic vein thrombosis appears as an absence of flow on colour Doppler ultrasound and echogenic thrombus may be seen within the hepatic vein (fig.16-18).

Fig. 16: Right hepatic vein thrombosis. a: Color Doppler. b: Spectral Doppler. Oblique color and spectral Doppler US images obtained through the hepatic vein confluence show absence of flow in the right hepatic vein (#) even with adequate technical parameters.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Fig. 17: Axial angio-CT. Same patient as in figure 16. Ultrasound findings indicative of right hepatic vein thrombosis were corroborated by the absence of filling at enhanced CT. Middle and left hepatic veins maintain normal permeability.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Fig. 18: Same patient as in figs. 16, 17. In spite of stent placement hepatic vein remained completely with no flow at Doppler studies (a). Angio-CT (b) revealed the presence of surgical material (») in an obstructed stent of the right hepatic vein.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

As referred, normal hepatic veins usually show a triphasic waveform with both respiratory variation and cardiac pulsatility. Once proper technique has been assured, pathologic causes of nonphasicity may be deliberated, including cirrhosis, peritonitis, atrial thrombus, hepatic vein thrombosis (Budd-Chiari syndrome), hepatic veno-occlusive disease and hepatic venous outflow obstruction from any cause. In this way Rossi et al reported that monophasic waveform is a sensitive, but not specific, indicator of hepatic vein stenosis/upper IVC obstruction after liver transplantation. However a persistent
triphasic wave pattern on Doppler ultrasound images can exclude the possibility of substantial stenosis with a high negative predictive value [1, 5, 10] (figs. 19, 20).

**Fig. 19**: a: B-Mode b: spectral Doppler. Male patient with 38 years old with refractory ascites (a) and persistent monophasic venous flow (b) in several studies suggesting right hepatic vein stenosis. Did these images represent a false-positive Doppler US result? No. Outcome was confirmed by CT angiogram (see figure 19a,b).

**References**: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL
Fig. 20: Same patient as in figure 19. CT angiogram (a,b) showed severe stenosis (#) in the right hepatic vein with a thrombus partially extending to inferior vena cava («), which was treated with endovascular balloon dilation and metallic stent placement. The referring clinician decided to monitor the individual with Doppler US follow-up (c,d) that revealed intra-stent restenosis.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Conclusion

Early recognition of these complications is essential for graft salvage. Doppler ultrasound is the main screening technique used in our institution, while angiography and computed tomography angiography are performed when ultrasound findings are equivocal.

Because of the wide spectrum of vascular complications and the inherent complexity of the anatomy in hepatic transplants, continuing education, knowledge of the current surgical techniques and experience are keys to success.
Fig. 21: Practical guidelines for postoperative liver transplant US at our center.

References: M. S. C. Sousa; Radiology, Atouguia da Baleia, PORTUGAL

Personal Information

References


