

Early Post-Operative Doppler Ultrasound as A Predictive Factor for Vascular Complications after Liver Transplantation

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Abstract

Objective: To evaluate the diagnostic accuracy of early postoperative Doppler ultrasound (DUS) for vascular thrombosis after liver transplantation and to evaluate its impact on clinical outcome.

Materials and Methods: This retrospective study examined 219 patients who underwent liver transplantation at a single reference institution. The results of early postoperative DUS were compared with angiographic, clinical and surgical data through a medical records review. The sensitivity and specificity of DUS for diagnosing vascular complications in the hepatic arteries and portal vein were calculated.

Results: DUS diagnosed vascular complications in 23 out of 210 included patients (10.9%). For the diagnosis of arterial and portal vein complications (stenosis/thrombosis), DUS showed respectively sensitivity of 75% and 90.9% and specificities of 96% and 100%. Overall mortality rate was 10.5% and patients who presented vascular alterations at early postoperative DUS presented a higher mortality (21.7%) rate than those with normal DUS (9.0%), although with no statistically significant difference ($p=0.074$).

Conclusion: DUS is a valuable tool for early vascular complication diagnosis, with high specificity rates for portal and arterial stenosis/thrombosis. Sensitivity rate in this series was lower for arterial complications.

Keywords: Doppler Ultrasonography; Liver Transplantation; Treatment Outcome

Introduction

Over the past 20 years, liver transplantation has proven to be an excellent therapeutic option for patients with advanced liver disease. Vascular complications are the major causes of morbidity and mortality after liver transplantation, mainly in living donor graft recipients. However, the early detection and treatment of these complications may reduce its impact [1,2].

Doppler ultrasound (DUS) is frequently the first imaging exam employed to evaluate vascular complications after liver transplantation, owing to its availability, low cost, and absence of complications. The exam is able to diagnose such vascular complications, including thrombosis and stenosis of the hepatic artery, portal vein, and hepatic veins [3-6]. Angiography is currently further recommended to confirm vascular complications.

The effectiveness of DUS in the diagnosis of vascular complications has been described previously. However, its results at early postoperative period varies, and its correlation with patients' clinical evaluation is controversial [7-10]. For instance, transient high-resistance arterial waveform can be detected by early DUS in the absence of complications or may be the first sign of arterial stenosis. The early detection of vascular complications in patients undergoing hepatic transplantation can allow minimally invasive treatments (e.g., balloon angioplasty for hepatic artery stenosis) or new surgical

procedures to be performed before biliary injury, severe liver failure and/or sepsis develops [11].

The present study aimed to correlate the findings of early postoperative DUS with the clinical and surgical outcome of liver transplantation, concerning vascular complications.

Material and Methods

After approval of the institutional Ethics Review Board, we conducted a retrospective survey on the records of 219 patients who underwent liver transplantation between May 2001 and July 2007. At our institution, DUS is routinely performed within the first 12 hours after transplantation, and when clinically indicated after that period. Another DUS is performed just before the discharge of the hospital. A standard questionnaire was completed for patients with an early postoperative DUS, including epidemiological, clinical, laboratory, and surgical data, as well as the reports of the DUS and, if any, digital angiography results were available. Nine patients were excluded because they did not have early postoperative DUS. Patients were followed for at least 1 year to assess outcomes and survival.

The DUS examinations after transplantation are standardized and evaluate: 1) hepatic parenchyma and biliary tracts; 2) the flow at hepatic artery, portal vein, and hepatic vein; and 3) extra-hepatic changes. Hepatic artery evaluation included the presence or absence of flow. Resistive index (RI) and peak systolic velocities of the hepatic artery were not systematically accessed at every first postoperative Doppler exam, since parenchyma edema, which is common in the

early postoperative period, may alter it [12]. For portal vein, the presence or absence of flow was examined either at the hilus and intrahepatic portal branches. For the hepatic veins, the presence or absence of flow and its waveform were examined. The exams had been performed by one out of three radiologists with at least 5 years practice in Doppler US and all images were reviewed to evaluate the exam quality before inclusion.

For patients with non invasive follow up, clinical outcome (e.g. signs and symptoms related to vascular complications, laboratory tests and sequential DUS) was used as gold standard. When indicated, digital angiography or surgical intervention was performed. Based on the mentioned criteria, the sensitivity, specificity, predictive value, and accuracy of the first postoperative DUS findings in the diagnosis of vascular complications, were calculated.

Statistical analyses were performed using SPSS for Windows, version 12.0 (SPSS Inc. Chicago, Illinois). Frequency analysis was performed to characterize the sample. The following tests were used to compare variables: chi-square test when both variables were categorical, and Student's t-test and Mann-Whitney test when one of the variables was continuous with and without normal distribution, respectively. P value was considered statistically significant when equal to or less than 0.05.

Results

Patient demographics

A total of 210 patients (105 female and 105 male) were included in the analysis, 159 (75.7%) were children (age range: 5 months - 10 years, mean: 34 months) and 51 (24.3%) adults (age range: 24 - 69 years, mean: 52 years). Living and deceased donor grafts were used respectively in 178 (84.7%) and 32 (15.3%) transplants. The most common liver disease leading to transplantation in children was biliary atresia (n=104; 65.4%) and in adults was cirrhosis (n=26; 51.0%).

| Hepatic artery flow at DUS | Arterial thrombosis on follow-up | | Total |
|----------------------------|----------------------------------|-------------|------------|
| | Present | Absent | |
| Absent | 6 (46.1%) | 7 (53.8%) | 13 (100%) |
| Present | 2 (1.0%) | 195 (99.0%) | 197 (100%) |
| Total | 8 (3.8%) | 202 (96.2%) | 210 (100%) |

Table 1: Comparison of DUS findings and diagnosis of arterial thrombosis on clinical/surgical/angiographic follow-up.

All patients who had absence of flow at the hilus and intrahepatic arterial branches (n=5) had confirmed arterial thrombosis on follow-up. From seven patients with presence of flow on hepatic artery at the hilus and absence of flow at the intrahepatic arterial branches, only one (14.3%) had confirmed arterial thrombosis on follow-up. In one case, arterial flow was present at intrahepatic branches but absence at the hilus, which was not confirmed on follow-up. Isolated evaluation

The interval between DUS and liver transplantation varied from one to six days, and most patients (n=192; 91.4%) had DUS performed on the first postoperative day.

Vascular complications on DUS and follow-up

The early DUS demonstrated 24 vascular abnormalities in 22 patients. Of these, 12 (54.5%) displayed arterial thrombosis, 9 (40.9%) patients portal thrombosis and one (4.5%) had arterial, portal and venous thrombosis. Most patients with alterations on DUS were children with living donors transplantation (n=20; 90.9%), however there was no statistically significant difference when compared to deceased donor grafts.

Angiographic/clinical/surgical follow-up detected 22 vascular complications in 20 patients. Nine (45%) had portal, 6 (30%) arterial and 3 patients (15%) venous thrombosis. Associated arterial and portal thrombosis were present in 2 (10%) patients.

In 16 out of 22 patients (72.7%) vascular thrombosis depicted on DUS, had such complication confirmed on invasive or non-invasive follow-up. On the other side, four patients with vascular complications on follow-up have had normal DUS findings.

Hepatic arterial flow evaluation

Of the 13 patients who displayed absence of flow on hepatic artery (hilus or intrahepatic) by postoperative DUS, 6 (46.1%) confirmed arterial thrombosis on follow-up, 1 by clinical follow-up with DUS and 5 by surgery. Two patients had arterial thrombosis on follow-up with normal early postoperative DUS (Table 1). Based on these findings, DUS had a sensitivity of 75%, specificity of 96.5%, positive predictive value of 46.1%, negative predictive value of 96.5% and accuracy of 95.7% in predicting arterial thrombosis.

of the hepatic artery at the hilus had a sensitivity and positive predictive value of 83.3%, specificity and negative predictive value of 83.3% and accuracy of 99.0% in predicting arterial thrombosis. Isolated evaluation of the intrahepatic arterial branches had a sensitivity and negative predictive value of 100%, specificity of 97% and positive predictive value of 50% and accuracy of 97.1% in predicting arterial thrombosis (Table 2).

| Portal vein flow at DUS | Portal vein thrombosis on follow-up | | Total |
|-------------------------|-------------------------------------|--------|-----------|
| | Present | Absent | |
| Absent | 10 (100%) | 0 | 10 (100%) |

| | | | |
|----------------|-----------|------------|------------|
| Present | 0 | 199 (100%) | 199 (100%) |
| Total | 10 (100%) | 199 (100%) | 209 (100%) |

Table 2: Comparison of DUS findings and diagnosis of portal vein thrombosis on clinical/surgical/angiographic follow-up.

Portal vein flow evaluation

All 10 patients who had absence of flow on portal vein at early postoperative DUS had thrombosis confirmed on follow-up, 1 by clinical follow-up with DUS and 9 by surgery. One patient had portal vein thrombosis on follow-up two weeks after transplantation, which could not be considered an early postoperative complication. Therefore, this patient was not included in the analysis of portal vein flow.

Based on these results, DUS had a sensitivity, specificity, positive and negative predictive value of 100% in the early postoperative diagnosis of portal thrombosis.

Hepatic veins flow evaluation

Only one patient had alteration on hepatic veins flow on DUS, which was not confirmed on follow-up. However, other three patients had hepatic veins occlusion confirmed on follow-up (angiography) without alterations at early postoperative DUS.

Outcome

We observed a total of 22 deaths in our population (10.5%). Patients who presented vascular changes at early postoperative DUS had a higher mortality than those whose DUS was normal, however this difference was not statistically significant (Table 3).

| Vascular changes by DUS | Death | | Total |
|-------------------------|------------|-------------|------------|
| | Yes | No | |
| Present | 5 (22.7%) | 17 (77.3%) | 22 (100%) |
| Absent | 17 (9.0%) | 171 (91.0%) | 189 (100%) |
| Total | 22 (10.5%) | 188 (89.5%) | 210 (100%) |
| P=0.062 | | | |

Table 3: Comparison of the presence of vascular changes on early portoperative DUS findings and mortality.

Discussion

The diagnosis of vascular complications after liver transplantation is usually achieved by DUS use in the early postoperative period. Vascular complications, which often go unnoticed during the early postoperative period, are the most important technical problem following liver transplantation [13]. The present study confirmed the findings of other papers, which observed that children and grafts from living donors have a higher risk of developing these complications, which are associated with high morbidity and decreased survival rates [14,15]. Recently, Lee et al. also found that abnormal DUS findings on postoperative days 1 and 2 was an independent risk factor for vascular complications requiring intervention [16].

The frequency of vascular complications on this study was similar to results published in literature. According to Machado et al., arterial thrombosis is the most commonly identified postoperative vascular complication, and occurs in 15-20% of children and 4-12% of adult patients [17]. Tamsel et al. described portal vein complications in 1-12.5% of liver transplantations and hepatic vein complications are seen in 0-3% [18].

Early postoperative DUS had a sensitivity of 75% and specificity of 96.6% in the diagnosis of arterial complications. Using the similar diagnostic criteria, other authors showed a sensibility between 67 and 92% and a specificity of 73-97% [12,18,19]. Despite the limitations of this retrospective study, including the operator-dependent nature of DUS and the fact that different examiners performed tests, DUS had sensitivity and specificity values, similar to the values described in the

literature. Diagnosis of arterial thrombosis by DUS had a higher positive predictive value when arterial flow was absent at both hilus and intrahepatic branches.

At our population, there were 8 false-positive and 2 false-negative results for arterial thrombosis. False-positive results has been described as common as in the present study and may be related to disproportion of the diameters of the recipient and graft vessels, kinking of the anastomoted hepatic artery, slowing of flow and small size of hepatic artery [2,12,18]. False-negative results are more important because they can delay diagnosis and treatment and may be related to thrombosis of distal parenchymal branches of the hepatic artery [18].

We observed a high sensitivity and specificity of early DUS for the diagnosis of portal vein complications after liver transplantation (91% and 100% respectively), which was also described by other authors [18,20].

Our results showed a poor correlation between DUS and follow-up data for the identification of hepatic vein complications. Hepatic vein obstruction occurs more commonly on later postoperative period (>1 week), and thus early postoperative DUS have a low sensibility to predict this complication [21,22]. In addition, DUS findings should be interpreted with caution in the immediate postoperative period because reduced hepatic vein pulsatility, which is the most important parameter for the diagnosis of hepatic vein obstruction, may be observed during this time and resolves spontaneously after a few days [20].

Conclusion

DUS is a valuable tool for screening arterial and portal thrombosis in the early postoperative period. Early detection of vascular complications by DUS can enable their immediate treatment and quick resolution, thereby reducing the mortality and improving prognosis for patients undergoing liver transplantation.

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