Postoperative Elevated Resistive Indices Do Not Predict Hepatic Artery Thrombosis in Extended Criteria Donor Livers

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Abstract

Keywords

- liver transplantation
- liver transplant ultrasound
- donation after cardiac death
- hepatic macrosteatosis
- hepatic artery thrombosis
- extended criteria donors

Postoperative transplant liver ultrasounds were analyzed in standard criteria donor (SCD), extended criteria donor (ECD), and donation after cardiac death (DCD) liver allografts to determine if elevated resistive indices (RIs) are consistently present and if they are pathological. Postoperative transplant liver ultrasounds were reviewed from 115 consecutive patients. Hepatic arterial RIs were stratified based on the type of donor: DCD, macrosteatosis (>30%), or standard criteria. In all patients with elevated RI, subsequent ultrasounds were reviewed to demonstrate RI normalization. The mean RI for all 115 patients was 0.64, DCD was 0.67, macrosteatosis was 0.81, and SCD was 0.61 ($p = 0.033$). The RI on subsequent liver ultrasounds for DCD and macrosteatosis normalized without any intervention. There were no incidences of early hepatic artery thrombosis (HAT) observed in the cohort. Hepatic arterial RI in ECDs and DCDs are elevated in the immediate postoperative period but are not predictive of HAT. It represents interparenchymal graft stiffness and overall graft edema rather than an impending technical complication. The results of our study do not support the routine use of anticoagulation or routine investigation with computed tomography angiography for elevated RIs as these findings are self-limiting and normalize over a short period of time. We hope that this information helps guide the clinical management of liver transplant patients from expanded criteria donors.

Due to the global organ shortage and increasing patient need for liver donors, liver transplants are being performed with more marginal allografts.¹ Donation after cardiac death (DCD), donor liver allografts with increased levels of macrosteatosis, allografts from older donors, and other extended criteria donors (ECDs) are being used more commonly than in previous years. The use of ECD livers presents a new clinical entity.² The postoperative care of the patient who receives a liver transplant from an ECD may differ from the standard.³ What could be interpreted as a pathological finding in the standard liver transplant recipient may be a normal finding in the transplant recipient of an ECD.

Transplant liver ultrasound is an essential diagnostic tool immediately posttransplant, as hepatic artery thrombosis (HAT) can be a devastating complication leading to early graft loss.⁴ Ultrasound is routinely used to assess the patency of the arterial anastomosis in liver transplantation.⁵ Postoperative liver transplant ultrasound allows for early interrogation of vascular anastomoses, and early intervention can potentially rescue an at-risk graft.⁶ In addition to demonstrating arterial patency, the resistive index (RI) of the artery can be calculated with Doppler ultrasound. RI is calculated with the following formula: (Peak systolic velocity – End diastolic velocity)/Peak

systolic velocity.⁷ The RI increases as the diastolic flow in the hepatic artery decreases. The RI will approach 1.0 when diastolic flow is absent or near absent.⁸ Elevated hepatic artery RIs immediately following transplant may indicate downstream stenosis and impending thrombosis, or another technical error that needs immediate surgical correction.⁹ We hypothesize that RI elevations in the early postoperative period are not necessarily pathological in ECDs. We analyzed postoperative transplant liver ultrasounds from ECD to determine if elevated RIs were consistently present and if they were pathological.

Methods

Transplant liver ultrasounds were reviewed from 115 consecutive patients who underwent Doppler ultrasonography immediately after transplantation in 2014 to 2015 at the University of Maryland Medical Center. Liver transplants were evaluated with either a General Electric (GE) Logic 9 ultrasound unit using a C5-1 transducer, or a Philips Epiq 7 unit using a C6-1 or C9-2 transducer. The hepatic artery was interrogated with Doppler sonography at the level of the porta hepatis as the vessel crossed the main portal vein. Spectral waveforms of the hepatic artery were obtained in the hepatic hilum, distal to the hepatic arterial anastomosis. Multiple technically adequate sets of spectral tracings were obtained from the hepatic artery. Peak systolic and end diastolic velocities were calculated, and the RI was automatically generated. Hepatic arterial RI values were recorded and stratified based on the type of donor: DCD, ECD = macrosteatosis (>30%), hyperbilirubinemia (bilirubin greater than 10), donor age > 65, or standard criteria. In all patients with elevated RI, subsequent ultrasounds were reviewed to determine sequential normalization or persistence of elevated RIs. Mean and *p*-values were calculated based on analysis of variance (ANOVA).

Results

The mean postoperative RI for all 115 patients was 0.64. The mean RI for DCD was 0.67 (*n* = 6), for ECD (majority for macrosteatosis) was 0.81 (*n* = 15), and for standard criteria donors (SCDs) was 0.61 (*n* = 94) (*p*-value = 0.033). The RI on subsequent liver ultrasounds for DCD and macrosteatosis normalized without any intervention. There were 10 incidences of a loss of diastolic flow, associated with RI > 0.9. Those patients were initially placed on low-dose heparin and reimaged until the RI normalized. There were no incidences of early HAT observed in the cohort.

Discussion

Hepatic arterial RI in ECD and DCD donors are elevated in the immediate postoperative period but are not predictive of HAT. Elevated RI may result from intraparenchymal liver stiffness, swelling, and ischemia reperfusion induced graft edema, a transient phenomenon in liver allografts taken from DCD and expanded criteria donors (ECDs).¹⁰ This finding does not indicate a technical complication causing stenosis or

impending thrombosis. The RI elevation is typically self-limited; we do not recommend additional anticoagulation, or further diagnostic or therapeutic interventions.

There were no incidences of early HAT in the cohort. There were two incidences of late HAT. Both initial postoperative ultrasounds showed loss of diastolic flow and elevated RI; however, follow-up showed resolution of diastolic flow and normal RI. HAT occurred months later in the settings of acute sepsis.

The mean RI for macrosteatosis was higher than both DCD and standard criteria by a significant margin. The reason for this phenomenon is not manifest; however, it is hypothesized that the degree of intraparenchymal liver stiffness, swelling, or graft edema is greater in a liver with macrosteatosis than in a DCD liver. The DCD liver will usually suffer a greater degree of ischemia reperfusion injury, but that resolves more quickly than the changes encountered in macrosteatosis. It is also possible that DCD livers are chosen more selectively than brain dead donors, which would presumably decrease the incidence of posttransplant complications. A DCD allograft is more likely to be from a younger donor, with less macrosteatosis, as one would not want to take additional risk on an organ that is both DCD and potentially steatotic. After the initial ischemia reperfusion injury, the hepatic parenchymal architecture of a DCD liver may more closely resemble an SCD liver. However, the hepatic parenchymal architectural derangement of a macrosteatotic liver may be more pronounced and take longer to normalize.

Animal studies have demonstrated that macrosteatotic livers have impaired intrahepatic microcirculation, which is further exacerbated by ischemia reperfusion injury. This will also cause extrahepatic increased hepatic artery RI.¹¹ Contrast-enhanced Doppler ultrasound can visualize intrahepatic microcirculation and may be used as a tool to identify the cause of increased RI.¹² This can be of great utility in the immediate posttransplant period of an ECD liver. Identification of transient impaired intrahepatic microcirculation can lower the suspicion of extrahepatic hepatic artery stenosis or thrombosis and alleviate the need for further investigation.

In addition to contrast-enhanced ultrasound, another possible noninvasive imaging modality that may be useful is ultrasound elastography or transient elastography.¹³ Elastography can measure intraparenchymal liver stiffness.¹⁴ An assessment of a higher degree of liver stiffness posttransplant can confirm the suspicion of ischemia reperfusion injury and edema leading to increased RI. This information can be used to inform clinical decision-making, attributing the high RI to recorded intraparenchymal liver stiffness and not to technical extrahepatic arterial pathology. Liver elastography has not been studied in immediate postoperative liver transplant recipients due to technical limitations; however, it presents an area for further research.

One limitation to ultrasound based studies is that it is possible for operator-dependent variation and interpretation. However, solid organ transplant ultrasound is highly specialized and is usually performed and interpreted by sonographers and radiologists with advanced training and experience. This is the practice at our transplant center,

and all the ultrasounds in this study were performed by transplant specialized sonographers and radiologists. Studies show that ultrasound data are most reproducible when done by specialists with advanced training and experience.¹⁵ Furthermore, RI is one of the most reproducible measures since it takes the averages of multiple measurements.¹⁶ However, most of this literature is based on ultrasounds performed for kidney transplantation. There are fewer studies on adult liver transplant ultrasound reproducibility.¹⁷ We hope our study can contribute to this literature.

Conclusion

We hope that this information helps guide the clinical management of liver transplant patients from ECDs. The clinical heralds of early HAT are elevated AST, ALT, and international normalized ratio (INR), and fever. A patient who receives an ECD liver allograft may have slow recovery of graft function, and the enzymes aspartate transaminase (AST), alanine transaminase (ALT), and INR may not normalize for several days posttransplant. This can cloud the diagnosis of HAT in the early postoperative period. A patient who has an ultrasound showing elevated RIs may also have elevated AST, ALT, and INR, which would all be suspicious for HAT in a SCD allograft; however, in an ECD allograft, these findings may not be pathological. The elevated RI, AST, ALT, and INR may all be indicative of slow graft function in an ECD liver that will resolve with time. Follow-up Doppler ultrasounds are important to document normalization of RI as the clinical status improves. The results of our study do not support the routine use of anticoagulation or routine investigation with computed tomography angiography in these clinical situations.

Author Contributions

Eric Siskind contributed in writing, data collection, and data analysis. Fauzia Vandermeer contributed in writing and data analysis. Tamar Siskind contributed in data collection and data analysis. David Bruno contributed in editing. Samuel Sultan contributed in literature review. Josue Alvarez-Casas contributed in editing. Arielle Stafford contributed in data analysis. Barton Lane contributed in data analysis. John Lamattina contributed in literature review. Rolf Barth contributed in study design. Steven Hanish contributed in study design.

Disclosure

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