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Invited Commentary

Reverse Takotsubo Stress Cardiomyopathy During Liver Transplantation

The Case Conference by Vannucci et al. described an interesting case of reverse Takotsubo cardiomyopathy (rTC) during orthotopic liver transplantation (OLT) and the authors should be congratulated for successfully managing such a challenging case.[1]

An OLT is a highly specialized and complicated surgery. The complex medical history, consisting of a previous liver transplant, end-stage liver disease (ESLD) complicated by hepatorenal syndrome requiring dialysis, hepatic encephalopathy, esophageal varices status postbanding, and transjugular intrahepatic portosystemic shunt complicated by thrombosis, as well as a high Model for End-Stage Liver Disease score, further increased the perioperative risk significantly in this particular patient. Thorough operative planning, including the decision to institute venovenous bypass and perform intraoperative transesophageal echocardiography (TEE) from the outset, demonstrated the foresight of the team.

Hemodynamic instability is seen commonly in all phases of OLT; however, immediately after reperfusion of the portal vein is the most challenging period. Various mechanisms play a causative role in the different phases. Losing large intraperitoneal ascitic volumes, clamping and unclamping of major vessels, reduced venous return from surgical manipulation, bleeding from coagulopathy in ESLD, splanchnic vasodilation from altered hepatic metabolism, arrhythmia from circulating unmetabolized bile acids, pulmonary hypertension, and chronic chronotropic fatigue are some important etiologies of hypotension in the prehepatic and anhepatic phases. Sudden hyperkalemia, acidosis, and release of inflammatory mediators after reperfusion take a toll on the right ventricle, causing profound right ventricular myocardial depression, systemic vasodilation, and arrhythmias, leading to hemodynamic compromise after reperfusion.[2,3] However, in this particular patient, sudden onset of hypotension and demonstration of new-onset wall motion abnormality (WMA) on TEE occurred prior to reperfusion.

Common preexisting causes of severe cardiac dysfunction in ESLD, such as cirrhotic cardiomyopathy, portopulmonary hypertension, hepatocardiac syndrome, or coronary artery disease (CAD), fortunately were ruled out in this patient by prior normal echocardiography and angiography.[4-6] The authors described new-onset WMA-basal akinesis with apical hyperkinesis and an estimated ejection fraction (EF) of 20%, which was reduced drastically from the preoperative EF of 70%. Sudden-onset WMA and reduced EF in the setting of normal coronary angiography is suggestive of stress-induced Takotsubo cardiomyopathy (TC). However, classic apical ballooning and basal hyperkinesis were absent, which prompted a clinical diagnosis of rTC in this patient.[7,8] Subsequently, the patient was managed with incremental inotropic support, and the team was able to successfully reperfuse without further worsening of cardiac function. The patient eventually was discharged home on postoperative day 25.

This article highlighted the challenges and complexities in taking care of patients with liver transplantation, especially in cases of significant hemodynamic instability. The authors made some important learning points for the liver transplant anesthesiologist. In a patient with sudden-onset WMA and reduction of EF, the differential diagnosis should be broadened to include TC and its variants.

Takotsubo cardiomyopathy and its variants are a relatively rare but potentially life-threatening phenomenon in liver transplantation during the perioperative period. It is important to have knowledge of TC and its most common variant rTC because unfamiliarity with these conditions may lead to difficulty in diagnosis. The clinical presentation of TC mimics an acute myocardial infarction. The proposed Mayo Clinic criteria for the diagnosis of TC require presence of the following 4 criteria[9]:

1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular midsegments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often but not always present.
2. Absence of obstructive CAD or angiographic evidence of acute plaque rupture.

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3. New electrocardiographic abnormalities (either ST-segment elevation and/or *t*-wave inversion) or modest elevation in cardiac troponin.
4. Absence of pheochromocytoma and myocarditis.

Reverse TC, which is the most common variant of TC, presents with basal hypokinesis and/or akinesis and apical hyperkinesis. The differences between TC and rTC are well-elucidated by Vannucci et al.[1] As mentioned in the case conference, although there are numerous case reports of TC and its variants in the perioperative period, there are very few reports with intraoperative presentation of TC, and most cases are seen in the postoperative period. The occurrence of rTC intraoperatively during liver transplantation has not been reported before.

Diagnosis of intraoperative TC is made only by intraoperative TEE and the exclusion of myocardial infarction by coronary angiography. Typically, the presence of significant CAD is evaluated in the preoperative liver transplant workup, as was in this patient. A high degree of clinical suspicion for TC and rTC in the setting of hemodynamic instability and the use of intraoperative TEE is important for appropriate diagnosis and prompt management, which is key to a favorable outcome in these high-risk patients. The authors used intraoperative TEE from the outset of this case, which was instrumental in rapid diagnosis and institution of treatment, resulting in a favorable outcome.

This case conference provokes some thoughts. Firstly, it generates the question of whether the use of TEE during OLT should be more routine, particularly in a high-risk patient. A history of esophageal varices and coagulopathy in ESLD definitely increases the risk of TEE in this patient population. However, the benefits of careful examination by expert hands can outweigh the risks. The recent position paper by the Society of Transplant Anesthesia (SATA) "suggests that TEE use in liver transplant recipients is effective and safe" and "an effective form of monitoring with a safety profile similar to that in cardiac surgery patients."[10] The SATA summary also states that TEE use can improve liver transplant outcomes in rare but life-threatening conditions, and that summarized observations showed TEE helped establish a timely diagnosis of these unanticipated life-threatening conditions in situations that are difficult to diagnose using monitors that do not provide real-time imaging.[10]

The use of TEE in liver transplants is increasing. A recent systematic review of patterns of use of TEE in liver transplantation reported on the increased use of TEE over the past 2 decades—from 11.3% of centers using it in 2003 to >90% of centers by 2018. Many centers (38%-56%) use it routinely during liver transplantation, with the remaining using it during rescue situations or in the event of specific pathology.[11] The trend of increased use of intraoperative TEE raises the important point of existing pathways and standards for TEE training for liver transplant anesthesiologists. As the authors mentioned, there are no current standards for training and certification for liver transplant anesthesiologists for intraoperative TEE. Dunkmann et al. highlighted the lack of clarity regarding the ideal training pathway. In their study, there were several different methods by which anesthesiologists acquired their TEE skills—informal methods such as self-study, continuing medical education, and on-the-job training, as well as formal training during a cardiac anesthesia fellowship.[11] The SATA supports the recommendation of the Society for Cardiovascular Anesthesiologists that all anesthesiologists who use TEE during liver transplantation complete formal training pathways that lead to certification by the National Board of Echocardiography (NBE).[10]

In 2014, Soong et al. showed that 26% of transplant anesthesiologists were advanced TEE-certified or testamurs, compared to 5.7% who were basic TEE-certified or testamurs.[12] Although a subsequent study in 2018 by Zerillo et al. did show a significant increase in the number of basic TEE-certified liver transplant anesthesiologists since 2014, there was no growth in advanced TEE-certified users or testamurs (21.7%).[13] This increase in basic TEE certification could be attributed to liver transplant anesthesiologists using the availability of the Basic Perioperative Transesophageal Echocardiography certification provided by the NBE in 2010. The overall NBE certification rate, however, remains <50%.[11] Basic NBE perioperative TEE certification requires 150 basic TEE examinations, with a combination of performed and reviewed. These numbers may be challenging to obtain, especially for liver transplant anesthesiologists in centers where the TEE numbers required for certification far exceed the number of transplants being performed at their institution. This has led to concerns, voiced by some in the survey by Zerillo et al., that the requirements of the basic TEE certification pathway discriminate against small-volume programs.[13]

Another important priority is finding the most efficient and effective method to train liver transplant anesthesiologists in the use of TEE. In the same study by Zerillo et al., 51.8% of respondents supported on-the-job training, and 51.8% supported basic TEE certification for minimum training needed for TEE use in liver transplantation. Only 7.1% thought that advanced Basic Perioperative Transesophageal Echocardiography certification was practical for the liver transplant anesthesiologist. Importantly, up to 33.1% of respondents favored the development of a specific TEE course for liver transplantation.[13]

Christensen et al. demonstrated success with a TEE simulation-based learning model for liver transplant anesthesiologists. This opens the door to the feasibility of using simulation-based learning for TEE training for liver transplant anesthesiologists in many facets—as part of a comprehensive program to aid those seeking basic TEE certification or as a stand-alone training for those unable to obtain certification and for continuing medical education.[14]

In conclusion, TC, and its variant rTC, are rare but potentially lethal phenomena that can occur intraoperatively during liver transplantation. Prompt diagnosis by intraoperative TEE is crucial for appropriate and timely management and to help result in a favorable outcome, as in the patient described here. The use of TEE in liver transplants is

increasing, raising the question about effective, practical ways for liver transplant anesthesiologists to obtain TEE training. The pathway to this training continues to have practical challenges. Future directions and opportunities may include the development of a TEE examination protocol specifically for liver transplantation and a training pathway tailored to liver transplant anesthesiologists.[11]

The authors described an educational case conference that not only reinforces the importance of considering rarer differential diagnosis when encountering hemodynamic instability in an already challenging case, but also points out that the use of important perioperative tools such as TEE can be expanded beyond the traditional scope.

Conflict of Interest

None.

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