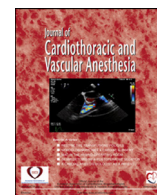


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Invited Commentary

Reverse Takotsubo Cardiomyopathy During Liver Transplantation: Expert Commentary

TAKOTSUBO CARDIOMYOPATHY (TC), otherwise known as “broken-heart syndrome,” is a condition of which most anesthesiologists are aware; however, the Case Conference by Vannucci et al.¹ points to a variation that is less familiar. Reverse Takotsubo cardiomyopathy (rTC) differs from traditional TC in that hypokinesis and/or akinesis is observed in the basilar portion of the left ventricle (LV) in contrast to the apical hypokinesis seen in the traditional form. In this case report, a patient with no prior cardiac history became acutely hypotensive and had severe depression of her LV function just prior to reperfusion during liver transplantation. Intraoperative transesophageal echocardiography (TEE) demonstrated basal akinesis and apical hyperkinesis. One might assume the patient had a traditional myocardial infarction (MI) given the high troponin scores of 478 ng/L and elevated brain natriuretic peptide of 50,000 pmol/L; however, cardiac catheterization ruled out obstructive coronary disease. With a combination of diuresis and inotropic therapy, the patient recovered to an ejection fraction of 43% at the time of discharge. It is important for anesthesiologists to become familiar with this condition so it can be recognized promptly and treated.

Pathophysiology

Takotsubo cardiomyopathy is an acute, reversible myocardial injury characterized by regional LV dysfunction. The exact mechanism is not fully understood, but it has been proposed that excessive endogenous or exogenous catecholamines present during stress states lead to microvascular dysfunction and coronary artery spasm.² The levels of catecholamines in patients with TC have been found to be up to 3 times higher than in patients presenting with acute MI, and elevated levels of norepinephrine have been found in the coronary sinus in some patients with TC. These catecholamine surges may cause direct effects on myocardium inducing arrhythmias, cellular injury, and mitochondrial dysfunction also referred to as “catecholaminergic stunning”.³ Postmenopausal women are at an increased risk due to an increased sympathetic drive and reported higher baseline

levels of anxiety, stress, and sleep disturbances. They also have higher levels of neuropeptides, such as Neuropeptide Y, which becomes activated during stress and can have a direct effect on microvascular dysfunction.⁴ Given the higher risk in this population, a lack of estrogen also has been considered a significant risk factor. Estrogen produces atrial natriuretic peptide, which is thought to be cardioprotective against the adverse effects of catecholamine surge.⁵

It is unclear why some patients have a stress response strong enough to trigger TC and others do not. General anesthesia does not appear to blunt this response. On the contrary, surgery and general anesthesia are known risk factors.³ Agarwal et al. published a systematic review of TC cases and found numerous factors in the perioperative period that may contribute to the development of this condition. They also pointed out that it is possible for volatile anesthetics to confer some cardioprotective effects.⁶ More research is needed to understand the role these agents play. This patient was on multiple vasoactive infusions prior to the event. The case report states, “...circulation was supported with...phenylephrine, vasopressin, norepinephrine to maintain mean arterial pressures greater than 65 mmHg.” Whether this patient’s event occurred due to exogenous catecholamines, endogenous catecholamines, or a combination of both, remains unknown.

Diagnosis

In the typical form, TC involves apical hypokinesis and/or akinesis and basal hyperkinesis.⁴ On echocardiography, the heart mimics the shape of a Japanese fishing pot used to trap an octopus called “takotsubo.” The presentation in this case report varied in that the patient had the reverse—apical hyperkinesis and basal akinesis. This basal type of stress cardiomyopathy, or rTC, is rare, ranging from 1%-to-23% of all TC cases.⁷ The triggering events and clinical features of rTC are similar to typical TC, and the management is similar. Diagnosis can be aided by using the International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria) or Revised Mayo criteria.⁸⁻¹⁰

When comparing patients with TC to those with a typical MI, patients with TC are more likely to be female, have a preceding

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triggering event, and have an absence of ST-segment depression.¹¹ Despite being thought of as reversible and, therefore, benign, there are substantial risks. Takotsubo cardiomyopathy can lead to LV outflow tract obstruction (LVOTO) and mitral regurgitation, given the hypercontractile basal segment of the LV. This can lead to other severe complications, including cardiogenic shock, with a 4%- to-5% in-hospital mortality.³

Making the diagnosis of TC or one of its variants can be very difficult, especially without the use of TEE. Both can result in significant troponin elevation, elevated brain natriuretic peptides, and wall motion abnormalities. One potential differentiation between the 2 pathologic processes is the specific electrocardiogram changes seen. The ST depressions are common in acute coronary syndrome but uncommon in TC. The electrocardiogram changes with TC usually involve ST elevation, *t*-wave inversion, and QT prolongation, although this is not a ubiquitous feature. The distinction between these 2 disease states can be very beneficial since the management of the 2 conditions varies.

Use of TEE in Liver Transplant

The authors have focused much of the discussion around whether TEE should be used routinely in liver transplant patients, highlighting that “. . .this complication may go unrecognized if TEE monitoring is not adopted. . .” The Society for the Advancement of Transplant Anesthesia recently released a position paper stating the benefits of TEE in liver transplant to guide real-time, rapid diagnosis and guide treatment, with a safety profile similar to cardiac surgical patients.¹² Given that the diagnosis of Takotsubo is often difficult to make, an echocardiogram may not be the panacea; however, an echocardiogram can be extremely helpful in diagnosing specific wall motion abnormalities and ongoing management. It has been noted that LVOTO and systolic anterior motion of the mitral valve can occur in 14%-to-25% of patients.⁴ This is important to recognize because inotropic agents can lead to decreased filling and increased contractility, worsening the obstruction and cardiogenic shock. LVOTO, acute coronary syndrome, and TC may all appear very similar on other routine intraoperative monitors, but can be more readily differentiated with the routine use of intraoperative TEE.

TEE also can be beneficial in diagnosing complications during venovenous bypass (VVB). VVB has been used in liver transplantation to decompress the surgical field and reduce the hemodynamic effects of inferior vena caval clamping. The use of VVB varies among leading transplant centers. Although VVB has potential benefits, complications can occur. Some of the complications that can directly affect cardiac output include hypothermia, air emboli, thrombotic emboli, infections, and bleeding.

Treatment

There are no randomized trials supporting any one specific treatment. The authors of this case report provided supportive therapy, which is the suggested approach given most patients will have a quick recovery of their cardiac function within a few weeks. Both the American College of Cardiology and the European Society of Cardiology recommend supportive care with the

management of specific complications. In severe cases, the early use of mechanical circulatory support can be considered a bridge to recovery.³ It is important to determine if there is the presence of LVOTO. In cases of LVOTO, it is important to reduce heart rate and maintain ventricular filling. If no LVOTO is present, drugs with positive inotropic action can be beneficial.

Conclusion

Reverse Takotsubo Cardiomyopathy is an acute cardiac condition that results in transient wall-motion abnormalities. Prognosis depends on prompt recognition and treatment. Anesthesiologists must remain vigilant and have a high index of suspicion if echocardiography supports the diagnosis.

Conflict of interest

None.

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