Mechanical circulatory support for refractory cardiogenic shock in Takotsubo syndrome: a case report and review of the literature

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Abstract

Takotsubo syndrome (TTS) complicated by refractory cardiogenic shock is a challenging clinical problem, as treatment with inotropic agents and/or vasopressors is contraindicated. We illustrate this by a patient presenting with chest pain and shortness of breath caused by TTS complicated by cardiogenic shock requiring mechanical circulatory support (MCS). The patient received central extracorporeal life support with a cannula in the left atrium (preload reduction of left ventricle) and the return cannula in the ascending aorta (neutral on afterload). Treatment with MCS was complicated by a cardiac tamponade. Left ventricular function recovered after 24 h, and the patient was doing well at the outpatient clinic 7 weeks after discharge. In addition, we reviewed the literature (PubMed search) reporting on MCS in patients with TTS. Including our patient, 17 cases of TTS induced cardiogenic shock receiving MCS have been reported. Age of the patients ranged from 16 years to 74 years, and 71% of the patients were female. Extracorporeal life support was the most used type of MCS (82% of the cases). Two patients died, and complications of MCS were rare (one case of leg ischaemia). Theoretically, MCS devices that reduce pre-load and are neutral on afterload are preferable. However, no specific type of MCS can be recommended as randomized trials are lacking. In conclusion, our case and the available literature suggests that MCS in TTS induced refractory cardiogenic shock is an immediate and feasible lifesaving treatment.

Keywords

Takotsubo syndrome • Cardiogenic shock • Mechanical circulatory support • Extracorporeal life support • Case report

Learning points

• Takotsubo syndrome (TTS) complicated by cardiogenic shock is a challenging clinical problem, as treatment with inotropic agents and/or vasopressors is contraindicated.
• Mechanical circulatory support for TTS-induced cardiogenic shock is a reasonable treatment option and has acceptable outcomes.

Introduction

Takotsubo syndrome (TTS) is an acute and usually reversible heart failure syndrome with an estimated prevalence of 1–2% in patients suspected of an acute coronary syndrome. Several diagnostic criteria have been proposed, and we support the criteria suggested by the Heart Failure Association of the European Society of Cardiology. Takotsubo syndrome is characterized by regional wall abnormalities of the myocardium (no culprit of atherosclerotic coronary artery disease), frequently preceded by a stressful trigger (emotional or physical). The classical pattern of regional wall abnormalities is apical.
and circumferential mid-ventricular hypokinesia and basal hypercontractility; however, anatomical variants exist. In the classical pattern, end-systolic the left ventricle resembles a Takotsubo, which is a Japanese word for an octopus trap with a narrow neck and globular lower portion. Excessive catecholamine release caused by the stressful trigger are believed to play a crucial role in the pathophysiology of TTS. Complications that can occur include mitral regurgitation, arrhythmias, thrombus formation, pericardial effusion, ventricular wall rupture, cardiogenic shock, and death. Treatment of refractory cardiogenic shock in TTS is particularly challenging, as catecholamines are contraindicated and mechanical circulatory support (MCS) may be the only option left. We present here such a patient and review the literature reporting on the treatment of TTS with MCS.

**Patient information**
A 67-year-old woman discovered that there had been a burglary in her daughter’s house. Immediately she developed severe chest pain combined with shortness of breath and her husband called the emergency services. Her medical history consisted of type 2 diabetes mellitus controlled by oral drugs and chronic obstructive pulmonary disease (COPD). During transport to the hospital, an electrocardiogram (ECG) was taken, and ST-elevation myocardial infarction was suspected.

**Physical examination**
On arrival at the catheterization laboratory, the patient was in severe distress, heart rate was 107 b.p.m., and blood pressure was 88/64 mmHg. Central capillary refill time was 6 s. Cardiac and pulmonary auscultation revealed no abnormalities.

**Diagnostic assessment**
An ECG (Figure 1) was obtained showing sinus rhythm of 108 b.p.m.; intermediate heart axis and normal conduction times; 1 mm concave ST-segment elevations in leads V4 through V6; 1 mm PT-a segment depression in lead II, to a lesser extent also in leads aVF, V5, and V6; and PT-a segment elevation in lead AVR. The differential diagnosis included pericarditis, acute coronary syndrome, or TTS. It was decided to continue with a coronary angiogram to exclude or treat significant obstructive coronary artery disease. Coronary angiography did not show obstructive coronary artery disease, and a left ventriculogram (Figure 2A and B, see Supplementary material online, Video S1) showed apical and mid-ventricular akinesia and basal hypercontractility supporting a diagnosis of TTS.

**Interventions**
Already shortly after arrival at the catheterization laboratory, it was concluded that the patient was in shock and a fluid challenge was initiated. During diagnostic evaluation at the catheterization laboratory, the patient received 2 L of sodium chloride (0.9%) for 45 min. In addition, phenylephrine (0.05 mg/minute) was added; however, the patient continued to deteriorate due to cardiogenic shock. The cardiothoracic surgeon was consulted to perform emergency implantation of central extracorporeal life support (ECLS). To relieve the left ventricle, a cannula was inserted in the left atrium, and a return cannula was inserted in the ascending aorta (output 3.8 L/min). The haemodynamic parameters stabilized, and the patient was transferred to the intensive care unit (ICU).

**Follow-up and outcomes**
About 24 h later, the patient deteriorated. A high central venous pressure together with collapse of the right atrium on transoesophageal echocardiography (TOE) led to the diagnosis of cardiac tamponade as a bleeding complication of ECLS. A repeat sternotomy was performed, and once the tamponade was relieved, direct visual inspection as well as TOE (see Supplementary material online, Video S2) demonstrated that the left ventricular function was completely recovered and no regional wall abnormalities were present. The patient was successfully weaned from the ECLS in the same session. The further course of the patient on the ICU was complicated by atrial fibrillation, prolonged mechanical ventilation due to COPD exacerbation and a delirium. The patient was discharged from the hospital 30 days after admission. Seven weeks after discharge the patient was seen in the outpatient clinic and was doing well.

**Discussion**
Cardiogenic shock caused by TTS, as was the case in the patient we reported here, is a difficult entity to treat. In retrospect, the initial treatment with an aggressive fluid challenge and phenylephrine seems inappropriate. It is, however, important to keep in mind that a final diagnosis had not yet been made, and the patient was in shock (‘dry and cold’). At first, after 1 L of sodium chloride (0.9%), the patient was responsive to this treatment. Therefore, it was decided to...
continue fluid infusion until a final diagnosis had been made. Phenylephrine was added when the shock was progressive, which we believe was a reasonable choice as it is a vasopressor primarily affecting the peripheral vasculature. In hindsight, it would have been more appropriate to discontinue the fluid challenge after 0.5–1 L of sodium chloride (0.9%) and start an inotropic agent and/or vasopressor when the patient further deteriorated in shock. Yet, given the final diagnosis of TTS, there was no perfect treatment strategy to follow. Inotropic agents and/or vasopressors (e.g. dobutamine, dopamine, norepinephrine, epinephrine, and milrinone) are considered contraindicated in TTS as they might worsen the clinical situation and prognosis by further activation of catecholamine-related pathways. Mechanical circulatory support might be the only remaining viable treatment option, which led to the decision of treatment by ECLS in our patient.

**Mechanical circulatory support**

The choice for the type of MCS in cardiogenic shock depends on several factors, including institutional availability and experience. Evidence is lacking to recommend a specific type. An intra-aortic
balloon pump (IABP) has been used during cardiogenic shock in TTS. However, haemodynamic support by an IABP is usually inadequate, and the results of the IABP-SHOCK II trial, although a different patient category than patients with TTS, do not provide evidence for the use of an IABP. Femoral venoarterial ECLS has several theoretical advantages: quick and relatively easy insertion, circulatory support up to >4.5 L/min (depending on the cannula size) and extracorporeal membrane oxygenation improves tissue oxygenation in case of pulmonary oedema. However, afterload reduction in TTS is desirable and femoral venoarterial ECLS may, in the contrary, increase afterload. In theory, central MCS would therefore be preferable, being neutral on afterload. However, there are no randomized trials comparing the outcome of these devices in cardiogenic shock, let alone in TTS-induced cardiogenic shock. We chose central ECLS with venous return from the left atrium and a return cannula in the ascending aorta, because this creates reduction of preload, is neutral on afterload, and provides adequate haemodynamic support.

**Systematic review of the literature**

To gain insight in the use of MCS for TTS-induced cardiogenic shock, we performed a PubMed search (Figure 3) using the following search terms: (Takotsubo) AND (Extracorporeal Circulation or Heart-Assist Devices). Including our patient, 17 cases of TTS-induced cardiogenic shock requiring MCS have been reported in the literature (Table 1). The age of the patients ranged from 16 years to 74 years, and 71% of the patients were female.

ECLS was the most used type of MCS (82% of the cases). In-hospital survival was 88%, and the two deaths were not related to the device or TTS but were considered to result from traumatic brain injury. Although there might be a publication bias, complications were rare in the reported cases. In one patient, femoral venoarterial ECLS was complicated by leg ischaemia, which resolved without permanent injury. In our case, MCS was complicated by...
cardiac tamponade. Bleeding complications occur frequently in patients with MCS and is related to the use of anticoagulation.

**Conclusion**

Inotropic agents and/or vaspressors are contraindicated in TTS-induced refractory cardiogenic shock, making MCS a reasonable treatment option in this situation, and this has acceptable outcomes. Devices that reduce pre-load and do not increase afterload are preferable on theoretical grounds. Prospectively designed studies with sufficient number of patients are needed to further investigate the role of MCS in TTS-induced refractory cardiogenic shock.

**Supplementary material**

Supplementary material is available at European Heart Journal - Case Reports online.

**Consent**

Informed consent was obtained from this patient for publication of this case history and associated images in line with COPE recommendations.

**Conflict of interest:** none declared.

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