

# Prolonged circulatory support with an Impella assist device in the management of cardiogenic shock associated with takotsubo syndrome, severe sepsis and acute respiratory distress syndrome

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## Abstract

Severe sepsis has been known to trigger for takotsubo syndrome which is associated with profound physical or emotional stress. Severe sepsis is also associated with sepsis-induced cardiomyopathy, a reversible myocardial depression. We report a case in which a patient with takotsubo syndrome, cardiogenic shock, severe sepsis, and adult respiratory distress syndrome was managed with an Impella Cardiac Power circulatory support device for 108 h (4.5 days) because of sustained hemodynamic compromise. To the best of our knowledge, this represents the longest reported use of the Impella Cardiac Power device for the management of cardiogenic shock in a patient with takotsubo syndrome and severe sepsis. This report also highlights the importance of considering a ventricular assist device in the management of takotsubo syndrome cardiogenic shock with severe sepsis which is unresponsive to maximal medical therapy.

## Keywords

Takotsubo cardiomyopathy, severe sepsis, Impella device

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## Introduction

Severe sepsis is a known trigger for takotsubo syndrome (TTS), also known as stress-induced cardiomyopathy.<sup>1</sup> Sepsis-induced cardiomyopathy (SIC), which was first described by Parker et al.<sup>2</sup> in 1984, is a reversible myocardial depression that can occur in patients with severe sepsis. There are many anatomical variants described in TTS. It is important to accurately distinguish between TTS and SIC in a clinically deteriorating and hemodynamically unstable patient. It is unclear whether the use of vasoactive medications for early goal-directed management of sepsis may actually be detrimental to patients with TTS by increasing the catecholamine surge, thus potentially contributing to cardiogenic shock. To manage our patient, we chose a percutaneous left ventricular assist device (Impella Cardiac Power (CP); Abiomed, Inc., Danvers, MA, USA) over the intra-aortic balloon pump (IABP). Despite being used for an extended period (4.5 days), the patient improved clinically and was without complications. To our knowledge, this represents the longest reported use of an

Impella device in a patient with stress cardiomyopathy and septic shock.

## Description of case

A 26-year-old female patient with a history of familial adenomatous polyposis and prior proctocolectomy with J-pouch underwent an elective laparotomy with ileostomy reversal. The procedure was complicated by post-operative volvulus and ischemic bowel with perforation which required emergent abdominal exploration, small bowel resection, and

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drainage of abdominal and pelvic abscesses. On admission to the intensive care unit, she was hemodynamically unstable with tachycardia to 190 beats per minute, mean arterial pressure of 65 mm Hg, central venous oxygen (SCVO<sub>2</sub>) value of 51%, and a central venous pressure of 16 cmH<sub>2</sub>O with positive fluid balance of 10 L. Escalating inotropic and vasopressor support was required with vasopressin, epinephrine, and norepinephrine infusions at maximal therapeutic doses. Arterial blood gas analysis indicated profound hypoxemia with a P/F ratio <200, acidemia with a pH of 7.18 and base excess of -5.2, and a rising serum lactate level which peaked at 21.2 mmol/L. Bilateral alveolar infiltrates were seen on chest radiograph and electrocardiogram (EKG) showed atrial flutter with variable conduction. Troponin I values were mildly elevated. Transthoracic echocardiography findings were consistent with TTS with regional wall motion abnormalities (RWMA) in the distribution of more than one coronary vessel, an akinetic left ventricular apex, compensatory hyperkinesis of the ventricle base (Supplementary Video 1), moderate tricuspid valve regurgitation, and a right ventricular systolic pressure of 60 mm Hg. The left ventricular ejection fraction (LVEF) was approximately 15%–20%. We decided against the use of an IABP device because of concerns that it would not provide adequate circulatory support in the presence of arrhythmias, sustained tachycardia, and with this degree of cardiovascular collapse. Extracorporeal membrane oxygenation (ECMO) was considered; however, the ECMO service was being utilized to capacity for other critically ill patients and transferring an extremely hemodynamic unstable patient involved too great a risk. We instead chose to insert a left ventricular assist device as it is easier to institute than ECMO, is more physiological, and is associated with fewer side effects. After the patient was transported to the cardiac catheterization laboratory, she underwent left and right heart catheterization with coronary angiogram and insertion of a Swan-Ganz pulmonary arterial catheter and an Impella CP left ventricular assist device; the initial output set at 2.8 L/min. No significant coronary obstructing lesions were found. The pulmonary arterial pressure was 43/18 mm Hg with a mean pressure of 27 mm Hg and a wedge pressure of 25 mm Hg. Once the patient was transported back to the intensive care unit, inhaled prostaglandins and a milrinone infusion were administered to reduce pulmonary arterial pressure and create a pressure gradient to increase left ventricular preload for optimal device functioning. Improved oxygenation was noted within 24 h of device placement. Despite auto-anticoagulation (international normalized ratio (INR) > 3), thrombocytopenia, and systemic heparinization to maintain an activated clotting time (ACT) of 160–180, there were no bleeding complications apart from mild hematuria which resolved spontaneously. Acute kidney injury developed as a result of acute tubular necrosis and was managed conservatively. The device remained in situ without complications for 108 h and was removed following hemodynamic improvement, with recovery of the ejection fraction

to 40% (Supplementary Video 2) and a reduction in pulmonary arterial pressure. The patient was discharged from the intensive care unit 4 weeks after admission and, on outpatient review, had returned to almost full health.

## Discussion

TTS, also known as stress-induced cardiomyopathy,<sup>1</sup> is associated with profound physical or emotional stress, is most prevalent in postmenopausal females (female-to-male ratio: 9:1), can occur in the perioperative period, and can be associated with severe complications including ventricular tachycardia (3.0%), ventricular thrombus (1.3%), and ventricular rupture (0.2%).<sup>3</sup> It is found in 1.7%–2.2% of patients presenting with acute coronary syndrome. Its clinical presentation can be life-threatening, with cardiogenic shock in up to 18% of cases.<sup>2</sup> The exact mechanism remains unclear; coronary artery vasospasm, microcirculation dysfunction, and transient obstruction of the left ventricular outflow tract have been proposed as possible underlying causes.<sup>4</sup> An excessive release of catecholamines with exaggerated sympathetic nervous system stimulation also seems to play a pivotal role in the development of stress cardiomyopathy. A 2009 retrospective cohort study, the largest cohort of TTS patients studied in Europe, reported one patient (2%) presented with an active gastrointestinal disease, ulcerative colitis.<sup>5</sup> Our patient had hereditary familial adenomatous polyposis with prior abdominal surgery complicated by bowel perforation and intra-abdominal sepsis. SIC is a reversible myocardial depression that can occur in patients with severe sepsis. Although there are distinct differences in both etiology and myocardial changes that occur between these two conditions, TTS may be an unusual presentation of septic cardiomyopathy; an accurate diagnosis will determine management and subsequent patient outcome. The diagnostic criteria for TTS remain controversial. Many diagnostic criteria have been proposed with minor differences. Among them are the 2004 Mayo Clinic Criteria, 2007 Japanese Takotsubo Cardiomyopathy Study Group, 2008 Revised Mayo Clinic Criteria, 2011 Gothenburg Criteria, 2012 Johns Hopkins Criteria, 2013 Revised Gothenburg Criteria, 2014 Takotsubo Italian Network, and the latest European Society of Cardiology Criteria 2016<sup>6</sup> which include the following seven characteristics: (1) elevated brain natriuretic peptide (BNP) in the acute phase, (2) characteristic EKG changes during the acute phase, (3) mild, transient elevation of cardiac enzymes, (4) absence of a specific coronary lesion, (5) left ventricle (LV) or right ventricle (RV) RWMA beyond a single coronary artery perfusion area with ventricular segment dysfunction, (6) transient RWMA of the LV or RV, and (7) recovery of cardiac function on imaging within 3–6 months. Most of these criteria were present in our patient. The TTS “classical pattern” typical variant describes left ventricular RWMA with apical and circumferential midventricular hypokinesia and

basal hypercontractility with the virtual apical ballooning seen at end systole.<sup>7</sup> This typical variant with apical dysfunction is present in up to 80% of cases. Other anatomical variants are atypical sparing of the apex; mid left ventricular variant which resembles the ace of spades; inverted or basal, also known as nutmeg or artichoke heart; biventricular clinical variant; and right ventricular variant.<sup>4</sup> The “circumferential pattern” of left ventricular dysfunction is characterized by symmetric wall motion abnormalities involving the mid-ventricular segments of the anterior, inferior, and lateral walls. This reversible left ventricular dysfunction which affects more than one coronary artery territory occurs in the absence of coronary artery disease. This pattern has been identified with the basal as well as mid left ventricular variants. A 2015 state-of-the-art review by Citro et al.<sup>8</sup> outlines the usefulness of echocardiography as the first-line non-invasive imaging technique to assess patients with TTS. Standard echocardiography allows for differentiation of the left ventricular patterns of RWMA and can identify any potential complications such as left ventricular outflow obstruction, reversible moderate to severe mitral regurgitation (MR), right ventricular involvement, thrombus formation, or cardiac rupture. Serial echocardiographic assessment is important in determining management, risk stratification, and follow-up of patients with TTS. Of note, a 2016 multicenter review of 424 consecutive patients enrolled in the Takotsubo Italian Network concluded that patients with right ventricular involvement are characterized by a distinct clinical profile and should undergo close clinical and echocardiographic monitoring as this cohort has a higher risk of in-hospital major adverse cardiovascular events.<sup>9</sup> Although TTS generally is associated with a good long-term prognosis, serious complications secondary to hemodynamic instability can occur. A 2014 study of 227 patients with TTS, enrolled in the Takotsubo Italian Network, identified echocardiographic findings of LVEF, reversible moderate to severe MR and E/e' ratio as independent correlates of major adverse events.<sup>10</sup> Age >75 years was also identified as an independent risk factor for a major adverse event. By identifying patients with these echocardiographic parameters early in the course of TTS, prompt institution of appropriate pharmacological treatment and adequate mechanical support may improve patient outcome.

Also, the development of TTS, believed to be secondary to an overwhelming systemic release of catecholamines and exaggerated activation of the sympathetic nervous system, is not specific to one particular disease. There are many case reports in the literature of cardiogenic shock due to TTS associated with a variety of underlying systemic diseases. In contrast, the myocardium in SIC is functionally and structurally damaged by chemical mediators including endotoxins, cytokines, and nitric oxide.<sup>1</sup> As such, in the management of cardiogenic shock from TTS and septic shock, many different circulatory support devices such as the IABP, left ventricular assist devices, and ECMO have been used, with varying degrees of success.

For all prior reported cases involving different types of Impella device, not specifically the CP device, the mean duration of support was 15 days, ranging from 2 to 36 days. A 2017 meta-analysis of three randomized controlled trials comparing Impella with IABP showed no difference in 30-day and 6-month all-cause mortality.<sup>11</sup> In total, 95 patients were randomized, and no differences in mortality or other important endpoints between the groups were found. Also, no difference was observed in LVEF between surviving IABP- and Impella-supported patients. Although the Impella has repeatedly shown to provide more hemodynamic support than the IABP, this did not translate into improved clinical outcomes. As such, American guidelines have downgraded the recommendation for usage of the IABP from Class I to IIa and European guidelines to Class III. Both American and European guidelines endorse usage of other mechanical assist devices that provide more hemodynamic support. The Surviving Sepsis Campaign recommends early goal-directed therapy (EGDT), which has become the standard of care worldwide, in the initial management of severe sepsis;<sup>12</sup> however, three recent clinical trials have demonstrated that while EGDT did not cause harm, it did not improve outcome in patients with severe sepsis when compared with usual care.<sup>13–15</sup> In our initial management of severe sepsis in this patient, EGDT with fluid resuscitation including blood transfusion and vasopressor therapy did not significantly improve hemodynamic instability. In this case, improvement of left ventricular function was associated with the insertion of the Impella device. This device can provide up to 4.0 L/min of cardiac output. Unlike the IABP, the Impella device uses continuous axial flow and consequently does not require pressure timing or electrocardiographic timing, allowing for stable output despite arrhythmias. Following clinical improvement, it was removed after 108 h without complication. To the best of our knowledge, this represents the longest reported successful use of the Impella CP device for the management of cardiogenic shock in a patient with tuberous sclerosis complex (TSC) and severe sepsis.

## Conclusion

We report the prolonged use of the Impella CP left ventricular assist device in the management of TTS with cardiogenic shock in a patient with severe sepsis and acute respiratory distress syndrome (ARDS). The Impella is an effective and minimally invasive support device that can be used successfully in some patients with hemodynamic collapse. The device should be considered for circulatory support, in the management of patients with TTS, severe sepsis, and cardiogenic shock, when ECMO is unavailable.

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### Declaration of conflicting interests

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### Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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### Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

### Supplementary material

Supplementary material for this article is available online.

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