CLINICAL VIGNETTE

Impella Use as Bridge-to-Recovery for Takotsubo Syndrome Complicated by Left Ventricular Outflow Tract Obstruction

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Background

Takotsubo Syndrome, or stress-induced cardiomyopathy (SIC), is a nonischemic cardiomyopathy that mainly affects postmenopausal women. It is often preceded by a physical or emotional stressor and involves transient systolic dysfunction of the left ventricle (LV) not associated with coronary artery plaque rupture. The exact mechanism behind the disease remains unclear, but is postulated and widely accepted to involve sympathetic overdrive. Increased catecholamines and catecholamine metabolites induce coronary spasm or direct myocardial injury, leading to the hallmark apical ballooning phenomenon of the LV.

Treatment of SIC is mainly supportive but guided by the clinical presentation and hemodynamic status. Although historically thought to be a benign disease with low mortality, more recent studies have reported 10% of SIC patients develop cardiogenic shock (CS), leading to poor outcomes.[1-4] Given the theoretical role that catecholamines play in driving SIC, the use of mechanical circulatory support (MCS) has risen in favor over the use of catecholaminergic inotropes for treatment of SIC-induced CS.[5]

The use of MCS in SIC has not been well-studied. Extracorporeal membrane oxygenation (ECMO) or intra-aortic balloon pump (IABP) were generally included as the MCS of choice. Impella (Abiomed, Danvers, Massachusetts), a catheter-based microaxial flow pump left ventricular assist device, is increasingly used for the management of cardiogenic shock, but not as widely used for management of SIC-induced cardiogenic shock as ECMO or IABP. The utility of Impella use in this setting is poorly understood. Other than a recent retrospective analysis, only a few case reports have been published regarding its use as management for SIC-induced CS.[6] We present a patient with SIC complicated by CS that was successfully managed with Impella support.

Case Presentation

A 75-year-old woman with history of migraine and unspecified heart murmur presented to the emergency department with crushing, substernal, exertional chest pain radiating to her left shoulder which started two hours prior. She had associated shortness of breath and dizziness that resolved in the emergency department. ECG revealed mild ST elevations in the inferior and lateral leads (II, III, and aVF; V4-V6) and troponin elevation to 3.01 ng/mL. Bedside echocardiogram revealed anterior wall motion abnormalities along with a mild pericardial effusion. The patient became hypotensive to the 70s/40s while in the emergency department and was started on a dopamine infusion for circulatory support. She was emergently transported to the cardiac catheter lab.

Coronary angiogram revealed moderate to severe proximal right coronary artery disease, mild non-obstructive coronary artery disease elsewhere, but "no obvious acute coronary syndrome/type 1 myocardial infarction culprit lesions." Subsequent left ventriculography revealed severely reduced left ventricular systolic function with an ejection fraction of 25%, basal hyperkinesis, and apical ballooning consistent with SIC. Left heart catheterization revealed a significant intra-cavitary left ventricular (LV) gradient (around 40-50 mmHg), later confirmed by intra-operative echocardiography which also showed severe left ventricular outflow tract obstruction and severe mitral regurgitation.

While in the lab, the patient remained hypotensive, and circulatory support was switched from dopamine to phenylephrine infusion. Near the end of the procedure, the patient continued to require maximum doses of phenylephrine for circulatory support and developed worsening hypoxia secondary to flash pulmonary edema, confirmed with chest radiographs. At this time, a decision was made to place an Impella via right femoral arterial access for hemodynamic support and LV unloading. The patient was also intubated for mechanical ventilatory support in the setting of her acute hypoxic respiratory failure and transferred to the Cardiac Care Unit (CCU) for further care.

The patient remained hemodynamically stable and Impella flow settings and phenylephrine infusion rates were gradually decreased over 48 hours. We removed the Impella and stopped the phenylephrine infusion 48 hours after admission, transitioning her to an oral regimen to optimize diastolic filling and for continued afterload support. Echocardiography on hospital day two showed an improved ejection fraction to 42.5% with continued mild LV diastolic dysfunction consistent with SIC. The patient was extubated 72 hours after intubation and quickly weaned to room air. She also complained of migraine headaches. After communicating with her neurologist, we deferred giving naratriptan, her abortive drug of choice, to avoid a theoretical sympathetic surge and risk worsening her cardiomyopathy. Six days after Impella removal, the patient was ambulating, tolerating her medications, oxygenating well on room air, and was

subsequently discharged home with close cardiology and neurology follow-up.

Discussion

Stress-induced Cardiomyopathy Etiology

As a post-menopausal woman, our patient's demographics are consistent with features of patients diagnosed with SIC. However, her event was not preceded by an intense emotional or physical stressor. A possible etiology for our patient's disease may have been her triptan usage, which she used to abort migraine headaches, on an as-needed basis for the past few years. Only a few case reports of triptan-induced cardiomyopathy exist,[7,8] and there was no clear correlation between the patient's last triptan use and onset of SIC, so we would hesitate to classify this as triptan-induced cardiomyopathy.

Acute Coronary Syndrome vs Stress-induced Cardiomyopathy Presentation

SIC often presents similarly to acute coronary syndrome (ACS), making it a difficult diagnosis on initial presentation. As with our patient, SIC often presents with chest pain, dyspnea, ST-segment elevations on ECG, elevated troponin, and wall-motion abnormalities on echocardiography. Although our patient had right proximal coronary artery disease on coronary angiography, it was unlikely to have contributed to her presentation given the location of wall motion abnormalities. While it has been speculated that acute coronary plaque rupture can trigger SIC, it is unlikely that this occurred in our patient, and her presentation was more likely due solely to SIC pathophysiology.[9]

Treatment of SIC is generally supportive, but hemodynamic support should be given if patients are in cardiogenic shock. Early distinctions between SIC and ACS may help dictate which vasoactive medications to use, as inotropes such as dobutamine have been found to induce SIC, and catecholamines should be avoided altogether given the role they play in the pathophysiology of SIC. The development of LV outflow tract obstruction, while not unique to SIC, would require afterload support, slowing the heart rate, and optimizing preload, which was done for our patient with phenylephrine (later midodrine) and a beta-blocker. Finally, the use of mechanical circulatory support (MCS) is appropriate in cases of severe cardiogenic shock.

Impella vs IABP vs ECMO in the Setting of LVOT Obstruction

In the setting of LVOT obstruction, where afterload support is crucial to minimizing the obstruction, reduction of LV afterload by IABP, a device which inflates during diastole and deflates during systole, may worsen the LVOT obstruction and subsequently decrease forward flow. ECMO, while providing adequate afterload support and ensuring systemic perfusion, markedly elevates left ventricular end diastolic pressure (LVEDP) by delivering perfusion in a retrograde fashion and increasing afterload, which may not be favorable in SIC, where LVEDP has been shown to be a predictor of worse outcomes.[10] Compared to the aforementioned therapies, Impella for circulatory support has potential advantages when LVOT obstruction is present, with ability to offload the LV without reducing afterload or increasing LVEDP. A recent multicenter retrospective analysis reported Impella was a viable treatment option for cardiogenic shock in the setting of SIC. Several case reports of Impella use in this setting have also been published.[6,11,12] According to Napp et. al's analysis, patients were supported by Impella for an average of 1.9 days, and 13 of 16 patients survived with significant LVEF recovery at discharge, both features shared with our patient. Comparative, prospective studies of Impella, IABP, and ECMO use is warranted for management of cardiogenic shock in the setting of SIC.

REFERENCES

1. **Almendro-Delia M, Núñez-Gil IJ, Lobo M, Andrés M, Vedia O, Sionis A, Martin-García A, Cruz Aguilera M, Pereyra E, Martín de Miguel I, Linares Vicente JA, Corbí-Pascual M, Bosch X, Fabregat Andrés O, Sánchez Grande Flecha A, Pérez-Castellanos A, Pais JL, De Mora Martín M, Escudier Villa JM, Martín Asenjo R, Guillen Marzo M, Rueda Sobella F, Aceña Á, García Acuña JM, García-Rubira JC; RETAKO Investigators**. Short- and Long-Term Prognostic Relevance of Cardiogenic Shock in Takotsubo Syndrome: Results From the RETAKO Registry. *JACC Heart Fail*. 2018 Nov;6(11):928-936. doi: 10.1016/j.jchf.2018.05.015. Epub 2018 Oct 10. PMID: 30316938.
2. **Bybee KA, Kara T, Prasad A, Lerman A, Barsness GW, Wright RS, Rihal CS**. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med*. 2004 Dec 7;141(11):858-65. doi: 10.7326/0003-4819-141-11-200412070-00010. PMID: 15583228.
3. **Stiermaier T, Eitel C, Desch S, Fuernau G, Schuler G, Thiele H, Eitel I**. Incidence, determinants and prognostic relevance of cardiogenic shock in patients with Takotsubo cardiomyopathy. *Eur Heart J Acute Cardiovasc Care*. 2016 Oct;5(6):489-496. doi: 10.1177/2048872615612456. Epub 2015 Oct 16. PMID: 26474843.
4. **Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, Yoshiyama M, Miyazaki S, Haze K, Ogawa H, Honda T, Hase M, Kai R, Morii I; Angina Pectoris-Myocardial Infarction Investigations in Japan**. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol*. 2001 Jul;38(1):11-8. doi: 10.1016/s0735-1097(01)01316-x. PMID: 11451258.
5. **Mariani S, Richter J, Pappalardo F, Bělohlávek J, Lorusso R, Schmitto JD, Bauersachs J, Napp LC**. Mechanical circulatory support for Takotsubo syndrome: a systematic review and meta-analysis. *Int J Cardiol*. 2020

Oct 1;316:31-39. doi: 10.1016/j.ijcard.2020.05.033. Epub 2020 May 28. PMID: 32473281.

6. **Napp LC, Westenfeld R, Møller JE, Pappalardo F, Ibrahim K, Bonello L, Wilkins C, Pershad A, Mannino SF, Schreiber TL, Hall PA, Medjamia AM, Haurand JM, Sieweke JT, Schäfer A, Grines CL, Burkhoff D, Moses JW, Ohman EM, O'Neill WW, Kapur NK, Bauersachs J**. Impella Mechanical Circulatory Support for Takotsubo Syndrome With Shock: A Retrospective Multicenter Analysis. *Cardiovasc Revasc Med*. 2022 Jul;40:113-119. doi: 10.1016/j.carrev.2021.11.018. Epub 2021 Nov 19. PMID: 34916157.
7. **Chohan A**. Sumatriptan-induced Takotsubo cardiomyopathy. *J Am Coll Cardiol*. 2023 Mar;81(8 Suppl):3498.
8. **Somers-Edgar TJ, Shah J, Kueh A, Kasargod Prabhakar C**. Triptan-induced takotsubo syndrome: a case report. *Eur Heart J Case Rep*. 2023 May 3;7(8):ytad221. doi: 10.1093/ehjcr/ytad221. PMID: 37575544; PMCID: PMC10413313.
9. **Sharkey SW, Kalra A, Henry TD, Smith TD, Pink VR, Lesser JR, Garberich RF, Maron MS, Maron BJ**. Coexistence of acute takotsubo syndrome and acute coronary syndrome. *Catheter Cardiovasc Interv*. 2020 Oct 1;96(4):825-829. doi: 10.1002/ccd.28595. Epub 2019 Nov 6. PMID: 31696663.
10. **Del Buono MG, Montone RA, Meucci MC, La Vecchia G, Camilli M, Giraldi L, Pedicino D, Trani C, Sanna T, Galiuto L, Niccoli G, Crea F**. Left ventricular end-diastolic pressure predicts in-hospital outcomes in takotsubo syndrome. *Eur Heart J Acute Cardiovasc Care*. 2021 Aug 24;10(6):661-667. doi: 10.1093/ehjacc/zuab028. PMID: 34195806.
11. **Attisano T, Silverio A, Prota C, Briguori C, Galasso G, Citro R**. Impella in Takotsubo syndrome complicated by left ventricular outflow tract obstruction and severe mitral regurgitation. *ESC Heart Fail*. 2020 Feb;7(1):306-310. doi: 10.1002/ehf2.12546. Epub 2020 Jan 3. PMID: 31898420; PMCID: PMC7083498.
12. **Nishikawa R, Nagano N, Kokubu N, Hashimoto K, Nakata J, Kishiue N, Takahashi R, Otomo S, Tsuchihashi K, Yano T**. Favorable Effects of Impella on Takotsubo Syndrome Complicated with Cardiogenic Shock. *Int Heart J*. 2021 Nov 30;62(6):1430-1435. doi: 10.1536/ihj.21-299. Epub 2021 Nov 17. PMID: 34789645.