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Original Research

Early Clinical Outcomes of Patients With Stress-Induced Cardiomyopathy Receiving Acute Mechanical Support in the US

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ABSTRACT

Background: The role of acute mechanical circulatory support (aMCS) in patients with stress-induced cardiomyopathy (SIC) complicated by cardiogenic shock (CS) is not well studied. Here, we describe the incidence and outcomes of aMCS use in SIC-CS using a large national database.

Methods: Using the Nationwide Readmissions Database from January 2016 to November 2019, we identified patients hospitalized with SIC who received isolated intra-aortic balloon pump (IABP), microaxial flow pump (Impella, Abiomed), or extracorporeal membrane oxygenation (ECMO) during the index hospitalization.

Results: A total of 902 among 94,709 hospitalizations for SIC (1.0%) required aMCS during the index hospitalization: 611 had IABP (67.7%), 189 had Impella (21.0%) and 102 had ECMO (11.3%). Patients with ECMO or Impella had higher in-hospital mortality rates than those with IABP (37.3% vs 29.1% vs 18.5%, respectively). There was an increased adjusted risk of in-hospital death with Impella (adjusted odds ratio [aOR], 1.98; 95% CI, 1.12-3.49) and ECMO (aOR, 4.15; 95% CI, 1.85-9.32) vs IABP. Impella was associated with an increased adjusted risk of 30-day readmission compared to IABP (aOR, 2.53; 95% CI, 1.16-5.51). Patients with ECMO or Impella had a higher incidence of renal replacement therapy and vascular/bleeding complications compared to those who received IABP.

Conclusions: In this nationwide analysis using an administrative database, patients who received ECMO and Impella showed higher rates of in-hospital mortality, renal replacement therapy, and vascular/bleeding complications compared to those who received IABP. Patients with more comorbidities may receive more aggressive hemodynamic support which may account for observed mortality differences. Future prospective studies with objective and universal characterization of baseline clinical and hemodynamic characteristics of patients with CS secondary to SIC are needed.

Introduction

The incidence of stress-induced cardiomyopathy (SIC) or takotsubo cardiomyopathy has increased over time.[1] SIC has a relatively good prognosis when compared to other etiologies of cardiogenic shock (CS). Nevertheless, CS has been reported in 10% to 15% of SIC cases with overall in-hospital mortality ranging between 4% to 5%.[2-5] SIC patients with CS showed a higher in-hospital mortality rate than those without CS (23.5% vs 2.3%).[4] Managing patients with CS secondary to SIC is a therapeutic dilemma. Sympathetic stimulation and marked elevation of catecholamines play a central role in this particular entity, as well as dynamic left ventricular tract obstruction resulting from hyperactive basal contractions and neurohormonal surge.[6,7] Theoretically, the use of certain inotropes in such cases could further deteriorate LVOT obstruction.[8] The use of acute mechanical circulatory support devices (aMCS) has significantly increased over the last 2 decades without clear evidence supporting better clinical outcomes in SIC-CS.[9] In the International Takotsubo Registry, in-hospital mortality of SIC-CS patients who used aMCS was lower than those who did not use in a small study which included mostly intra-aortic balloon pump (IABP) as an aMCS

Abbreviations: aMCS, acute mechanical circulatory support; AMI, acute myocardial infarction; CS, cardiogenic shock; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVOT, left ventricular outflow tract; NRD, Nationwide Readmissions Database; RRT, renal replacement therapy; SIC, stress-induced cardiomyopathy.

Keywords: cardiogenic shock; interventional heart failure; mechanical circulatory support; stress-induced cardiomyopathy.

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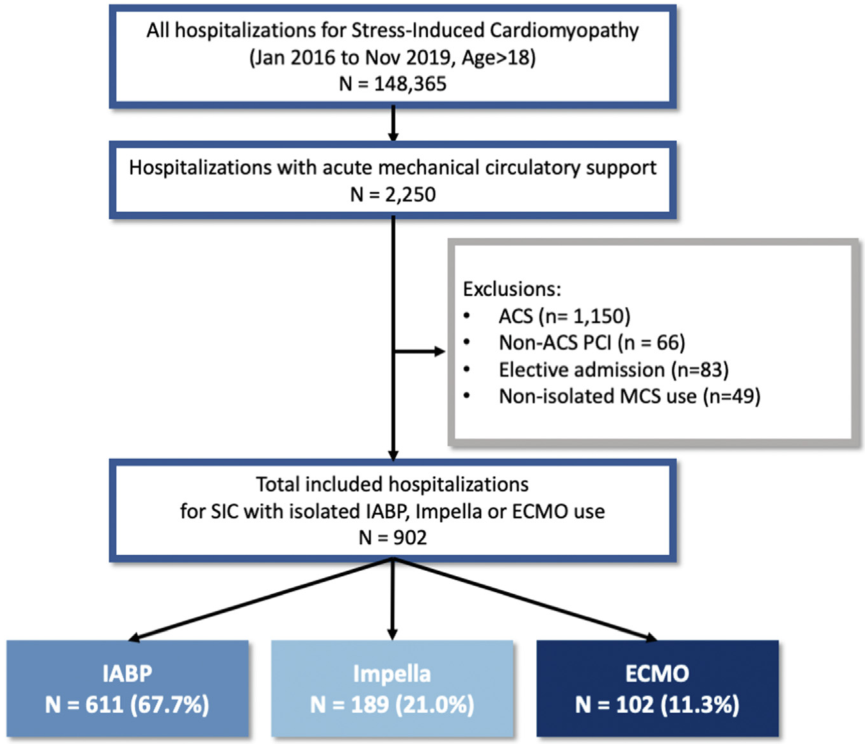


Figure 1.
Flow diagram of study population.

(12.8% vs 28.3%).[4] In the German-Italian-Spanish (GEIST) registry, the use of IABP was not associated with lower mortality rates in patients with SIC-CS.[10] Possible explanations for the inconsistent benefit of aMCS is the lack of standardized, etiology-specific risk stratification of patients presenting with CS, including those with SIC-CS. Here, we sought to describe the reported incidence, use of aMCS devices, and outcomes in patients with SIC-CS from a national administrative database.

Methods

Data source

We examined the Nationwide Readmissions Database (NRD) from 2016 to 2019 from the Agency for Healthcare Research and Quality (AHRQ), which administers the Healthcare Cost and Utilization Project (HCUP).[11] The NRD is a large administrative database including hospital discharge and readmission data from the HCUP State Inpatient Databases. Each patient record contains deidentified information on diagnoses and procedures performed during index hospitalization. Diagnoses and procedures are identified using validated International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes as described in summary statistics of NRD. This study was exempt from the Institutional Review Board as the NRD is a publicly available database with deidentified patient information.

Study design and population

Hospitalizations for SIC in patients aged >18 years who underwent utilization of aMCS during index hospitalization from January 2016 to November 2019 were extracted using ICD-10-CM codes for SIC (ICD-10-CM code I51.81) (total unweighted N = 81,237; weighted N = 148,365) (Figure 1). Patients who were discharged in December were not included to allow the completeness of data on 30-day follow-up after discharge. Patients who received IABP (ICD-10-PCS code: 5A02110, 5A02210), micro axial flow pump (Impella, Abiomed) (ICD-10-PCS code: 5A0221D, 5A0211D), or extracorporeal membrane oxygenation (ECMO) (ICD-10-PCS code: 5A1522F, 5A1522G, 5A15A2F, 5A15A2G, 5A15223) were included. Patients who had acute coronary syndrome, percutaneous coronary intervention, and the use of multiple aMCS devices during the index hospitalization were excluded.

Study outcomes

The primary outcomes were in-hospital mortality and 30-day unplanned readmission rates. The secondary outcomes were the rate of renal replacement therapy (RRT), vascular complications, postprocedural bleeding, 30-day readmission-related mortality, and 30-day readmissions for heart failure.

Statistical analyses

All statistical analyses were performed using R statistical software, version 4.2.3,[12] with its package "survey" mainly used. Discharge weight and stratum provided by NRD were used for all analyses. All the reported numbers are weighted national estimates. All analyses accounted for NRD sampling design by including hospital-year fixed effects based on hospital identification number. We compared baseline patient- and hospital-level characteristics for patients with SIC who received an IABP, Impella, or ECMO. Categorical variables are presented as frequencies and analyzed by the Rao–Scott chi-square test. Continuous variables are shown as mean with SE or median with IQR and analyzed by survey-specific ANOVA test. Survey-specific univariate and

Table 1. Patient and hospital characteristics.

Characteristics	Overall	IABP	Impella	ECMO	*P* value
Number of patients	902	611 (67.7)	189 (21.0)	102 (11.3)	
Patient characteristics					
Age, y[a]	61.1 (0.7)	62.9 (0.9)	62.5 (1.4)	47.6 (2.1)	<.001[b]
Age group					<.001[c]
<50	180 (20.0)	97 (15.9)	29 (15.4)	54 (52.9)	
50-59	172 (19.1)	119 (19.5)	41 (21.8)	12 (11.8)	
60-69	258 (28.7)	172 (28.2)	56 (29.8)	30 (29.4)	
70-79	212 (23.6)	162 (26.6)	44 (23.4)	6 (5.9)	
≥80	78 (8.7)	60 (9.8)	18 (9.6)	0 (0)	
Sex					.015
Male	213 (23.6)	133 (21.8)	39 (20.6)	41 (40.2)	
Female	689 (76.4)	478 (78.2)	150 (79.4)	61 (59.8)	
Smoking	220 (24.4)	152 (24.9)	49 (25.9)	19 (18.6)	.613
Hypertension	292 (32.4)	207 (33.9)	52 (27.5)	33 (32.4)	.526
Diabetes mellitus	210 (23.3)	151 (24.7)	41 (21.7)	18 (17.6)	.533
Dyslipidemia	300 (33.3)	220 (36.0)	64 (33.9)	16 (15.7)	.020
Family history of coronary artery disease	54 (6.0)	43 (7.0)	9 (4.8)	2 (2.0)	.276
Coronary artery disease	257 (28.5)	202 (33.1)	48 (25.4)	7 (6.9)	.153
Peripheral vascular disease	87 (9.7)	56 (9.2)	23 (12.2)	8 (7.9)	.617
History of congestive heart failure	105 (11.7)	61 (10.0)	36 (19.0)	8 (7.9)	.028
Previous stroke	62 (6.9)	49 (8.0)	12 (5.3)	1 (1.0)	.228
Chronic pulmonary disease	221 (24.5)	175 (28.6)	35 (18.6)	11 (10.8)	0.004
Pulmonary hypertension	90 (10.0)	58 (9.5)	19 (10.1)	13 (12.7)	.823
Chronic kidney disease	135 (15.0)	93 (15.2)	32 (17.0)	10 (9.9)	.546
Liver disease	83 (9.2)	54 (8.8)	14 (7.4)	15 (14.7)	.349
Anemia	240 (26.6)	164 (26.8)	49 (25.9)	27 (26.5)	.980
Atrial fibrillation	255 (28.3)	151 (24.7)	70 (37.2)	34 (33.3)	.047
Valvular heart disease	156 (17.3)	117 (19.1)	32 (17.0)	7 (6.9)	.111
Aortic valve disease	33 (3.7)	28 (4.6)	4 (2.1)	1 (1.0)	.244
Mitral valve disease	108 (12.0)	84 (13.8)	22 (11.6)	2 (2.0)	.022
Tricuspid valve disease	34 (3.8)	23 (3.8)	7 (3.7)	4 (4.0)	.992
Pulmonary valve disease	3 (0.3)	3 (0.5)	0 (0)	0 (0)	.737
Coagulopathy	283 (31.4)	151 (24.7)	69 (36.5)	63 (62.4)	<.001
Autoimmune disease	38 (4.2)	35 (5.7)	3 (1.6)	0 (0)	.047
Alcohol use disorder	50 (5.5)	34 (5.6)	9 (4.8)	7 (6.9)	.877
Drug abuse	54 (6.0)	39 (6.4)	7 (3.7)	8 (7.9)	.458
Obesity	138 (15.3)	95 (15.5)	31 (16.4)	12 (11.8)	.741
Hypothyroidism	143 (15.9)	97 (15.9)	33 (17.6)	13 (12.7)	.729
Seizure disorder	79 (8.8)	55 (9.0)	17 (9.0)	7 (6.9)	.900
Cerebrovascular disease	76 (8.4)	48 (7.9)	21 (11.1)	7 (6.9)	.501
Depression	151 (16.7)	110 (18.0)	28 (14.8)	13 (12.7)	.541
Cancer	62 (6.9)	52 (8.5)	7 (3.7)	3 (3.0)	.095
Median household income					.047
First quartile	197 (21.8)	157 (25.7)	29 (15.3)	11 (10.8)	
Second quartile	249 (27.6)	156 (25.5)	61 (32.3)	32 (31.4)	
Third quartile	267 (29.6)	187 (30.6)	48 (25.4)	32 (31.4)	
Fourth quartile	190 (21.0)	112 (18.3)	51 (27.0)	27 (26.5)	
Primary payer					.003
Medicare	467 (51.8)	339 (55.6)	104 (54.7)	24 (24.5)	
Medicaid	107 (11.9)	62 (10.2)	25 (13.2)	20 (19.6)	
Private including HMO	267 (29.6)	167 (27.4)	50 (26.3)	50 (49.0)	
Self-pay/no charge/other	61 (6.8)	42 (6.9)	11 (5.8)	8 (7.8)	
Weekend admission	274 (30.4)	202 (33.1)	43 (22.8)	29 (28.7)	.174
Cardiac arrest	76 (8.4)	49 (8.0)	12 (6.3)	15 (14.9)	.166
Length of hospital stay, d[d]	8 (4-15)	8 (5-13)	8 (3-16)	18 (10-39)	<.001
Right heart catheterization	353 (39.1)	236 (38.6)	108 (57.1)	9 (8.8)	<.001
Hospital characteristics					
Hospital teaching status					.059
Teaching	728 (81.0)	481 (78.9)	153 (81.4)	94 (93.1)	
Nonteaching	171 (19.0)	129 (21.1)	35 (18.6)	7 (6.9)	
Hospital location					.024
Rural	378 (42.0)	271 (44.4)	83 (43.9)	24 (23.8)	
Urban	522 (58.0)	339 (55.6)	106 (56.1)	77 (76.2)	
Hospital bed size					.108
Small	60 (6.7)	50 (8.2)	10 (5.3)	0 (0)	
Medium	183 (20.3)	129 (21.1)	41 (21.7)	13 (12.7)	
Large	659 (73.1)	432 (70.7)	138 (73.0)	89 (87.3)	
Disposition					.008
Home	300 (33.3)	225 (36.8)	53 (28.0)	22 (21.6)	
Facility[e]	388 (43.0)	268 (43.9)	80 (42.3)	40 (39.2)	
AMA/unknown	214 (23.7)	118 (19.3)	56 (29.6)	40 (39.2)	

Values are presented as n (%) unless otherwise indicated.

AMA, against medical advice; ECMO, extracorporeal membrane oxygenation; HMO, health maintenance organization; IABP, intra-aortic balloon pump.

[a] Values are mean (standard error). [b] Survey-specific linear regression was performed. [c] Rao–Scott χ^2 test was used for all statistical tests unless stated otherwise. [d] Values are median (IQR). [e] Facility includes skilled nursing facility, intermediate care facility, and inpatient rehabilitation facility.

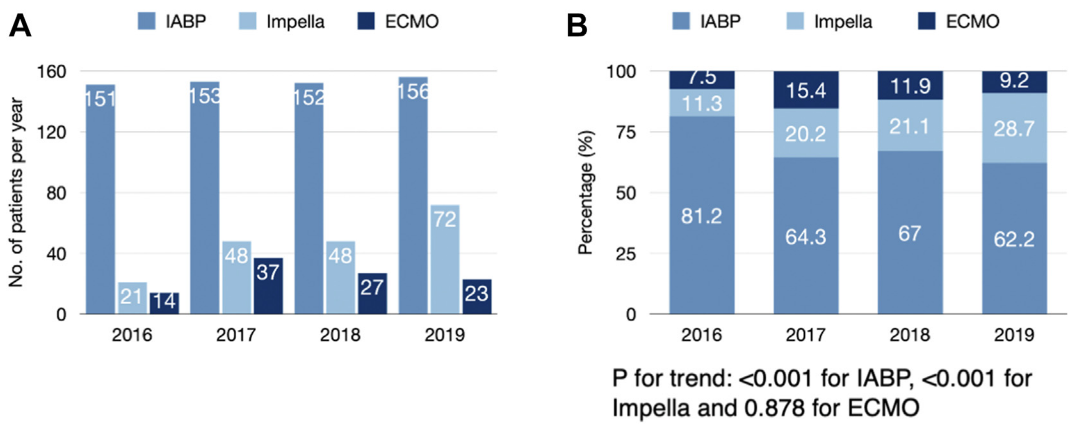


Figure 2.

Temporal trend for the number and percentage of patients per year who underwent intra-aortic balloon pump (IABP), microaxial flow pump (Impella), or extracorporeal membrane oxygenation (ECMO) for stress-induced cardiomyopathy. (**A**) The absolute number of patients per year for each device. (**B**) The percentage of patients per year for each device. The number and percentage of patients who underwent Impella increased from 2016 to 2019 (*P* for trend <.001) while the percentage of patients who underwent IABP decreased (*P* for trend <.001).

multivariable generalized linear models were used for the evaluation of the predictive value of the interventions for primary and secondary outcomes. Variables with $P < .1$ were included as initial covariates and final parsimonious models were created by backward removal, based on Akaike information criterion, while ensuring each removal did not result in >10% change in the measure of association for the primary predictor variable. Adjusted risks are shown in adjusted odds ratio (aOR), together with 95% confidence interval (CI) and *P* value. All tests were 2-sided with *P* value <.05 considered as statistically significant. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

Between 2016 and 2019, a total of 902 hospitalizations for SIC with the use of aMCS were identified and included in the final analysis: 611 patients (67.7%) received an IABP, 189 patients (21.0%) Impella and 102 (11.3%) ECMO. The mean age was 61.1 years (SE 0.7 years) and 76.4% were women (Table 1). Patients with ECMO were younger and were more likely to be male than those with IABP or Impella. From 2016 to 2019, there was a temporal increase in the absolute number of Impella use or percentage among aMCS (*P* for trend <.001) (Figure 2). There was a temporal decrease in the percentage of IABP from 2016 to 2019 (*P* for trend <.001). Right heart catheterization was more frequently used in patients with Impella compared to those with IABP or ECMO (57.1% vs 38.6% vs 8.8; $P < .001$). Hospital length of stay was the longest in patients receiving ECMO (median, 18 days; IQR, 10-39 days) compared to those with IABP (median, 8 days; IQR, 5-13 days) or with Impella (median, 8 days; IQR, 3-16 days; $P < .001$).

Patients hospitalized with SIC who received ECMO or Impella had a higher in-hospital mortality rate than those who received IABP (37.3% vs 29.1% vs 18.5% respectively; $P = .004$) (Figure 3 and Central Illustration). Thirty-day all-cause unplanned readmission rate was higher in patients with Impella use than in those with IABP use (20.1% vs 10.2%; $P = .040$; adjusted $P < .01$). There was no significant difference in 30-day readmission rates for patients with ECMO (11.1%) compared to those with IABP or Impella. After multivariable adjustment, the use of ECMO or Impella was associated with increased adjusted rate of in-hospital mortality compared to the use of IABP (aOR, 1.98; 95% CI, 1.12-3.49; $P = .019$ for patients with Impella and aOR, 4.15; 95% CI, 1.85-9.32;

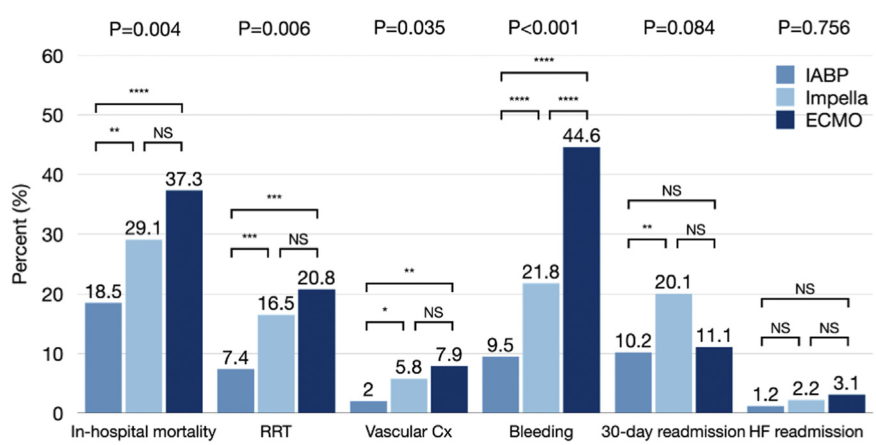
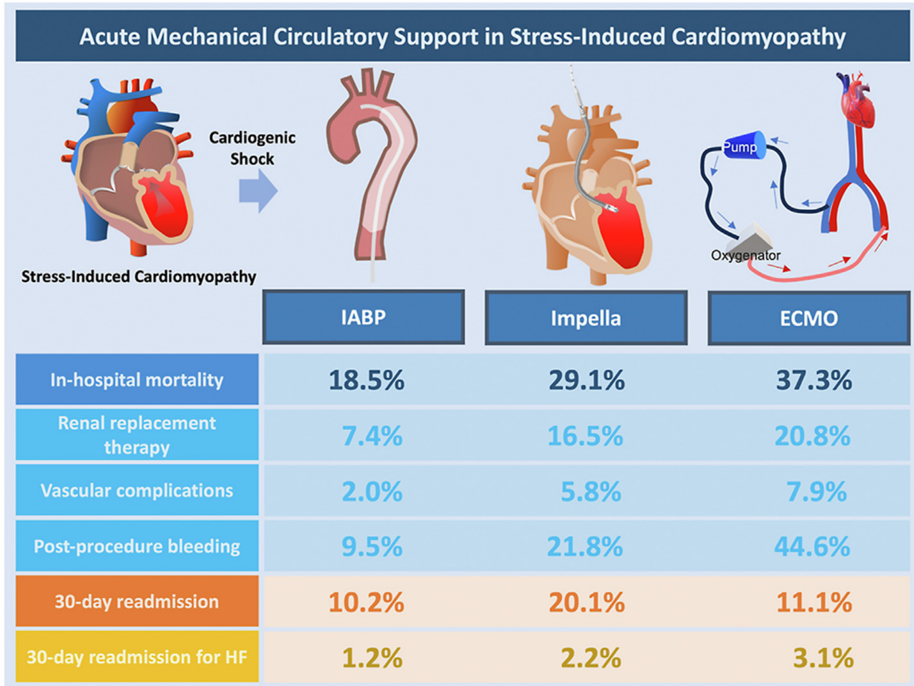


Figure 3.

In-hospital and 30-day outcomes of patients who underwent intra-aortic balloon pump (IABP), microaxial flow pump (Impella), or extracorporeal membrane oxygenation (ECMO) for stress-induced cardiomyopathy. Overall statistical significances from the Rao–Scott Chi-square test are provided at the top of the figure. Pairwise multiple comparisons are provided inside the figure with Bonferroni adjustment: NS, nonspecific; * Adjusted $P < .05$; **Adjusted $P < .01$; ***Adjusted $P < .001$; ****Adjusted $P < .0001$.



Central Illustration.
In-hospital and 30-day outcomes of patients with acute mechanical circulatory supports for cardiogenic shock from stress-induced cardiomyopathy. ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

$P < .001$ for patients with ECMO) (Figure 4, Supplemental Table S1). Patients with Impella had a greater association with the 30-day readmission compared to those with IABP (aOR, 2.53; 95% CI, 1.16-5.51; $P = .020$) (Supplemental Table S2). There was no significant interaction between age group, gender, obesity, or use of right heart catheterization for the association of MCS group and in-hospital mortality or 30-day readmission rates.

During the index hospitalization, patients receiving ECMO or Impella use had higher incidence of RRT compared to those who underwent IABP use (20.8% vs 16.5% vs 7.4%, respectively; $P = .006$). The incidence of postprocedural bleeding was the highest in patients with ECMO use (44.6%) followed by patients with Impella (21.8%) and those with IABP (9.5%) ($P < .001$). The rate of vascular complications was higher in patients with ECMO (7.9%) or in patients with Impella (5.8%) compared to those with IABP (2.0%) ($P = .035$). In the 30 days after discharge, there was no difference in the rates of readmission-related mortality or readmission for heart failure.

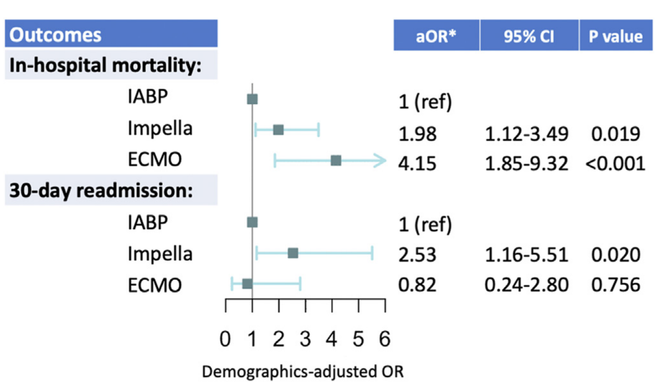


Figure 4.
Demographics-adjusted risk of microaxial flow pump (Impella) and extracorporeal membrane oxygenation (ECMO) compared with intra-aortic balloon pump (IABP) for in-hospital mortality and 30-day readmission rates in stress-induced cardiomyopathy. Adjusted odds ratio (OR) was calculated after demographic risk adjustment only with age group and cardiac arrest.

Discussion

In this large contemporary national cohort, we identified short-term aMCS use in patients with SIC complicated by CS. Here, patients who received ECMO and microaxial flow pump (Impella) had higher in-hospital mortality compared to those who received IABP. Moreover, patients who received ECMO and Impella had higher incidence of RRT and postprocedural bleeding than those with IABP. Lastly, IABP was observed to be the most used device in these patients, but the use of Impella has significantly increased over time.

CS, irrespective of its etiology, is a complex medical syndrome that begins with cardiac impairment followed by systemic hemo-metabolic derangements leading to multiorgan failure and ultimately death. Several different types of aMCS, such as IABP, Impella, or ECMO have been studied in patients with CS following acute myocardial infarction (AMI-CS) without clear benefits in hard clinical outcomes.[13-15] Furthermore, recent registry data from a large multicenter research consortium has described in detail the use of aMCS platforms in different cohorts of patients including heart failure-related cardiogenic shock.[16] However, there is no data on contemporary real-world use of aMCS, and outcomes specifically in patients with SIC-CS.

Given its complexity, dynamic nature, and increasing number of device options for patients with CS, universal and objective risk stratification is of paramount importance in order to appropriately support these patients, help inform clinical trials, shock team algorithms, and avoid reporting bias. This includes invasive hemodynamics, biomarkers of end-organ function and perfusion, and others. The Society for Coronary Angiography and Intervention (SCAI) recently proposed a staging system for CS based on expert consensus using physical, laboratory, and hemodynamic findings of patients presenting with cardiogenic shock.[17] Stages include 5 levels of severity of shock: (A) at risk for CS, (B) beginning CS, (C) classic CS, (D) deteriorating CS, (E) extremis CS.[18] Moreover, this staging system was validated in different cohorts showing a direct association between mortality and increasing SCAI stage.[19] Therefore, universal risk stratification of CS using the SCAI stage system appears to be valuable in order to approach patients presenting with CS. Although shock staging is not assessed in this administrative data, the increased in-hospital mortality in patients with ECMO and Impella is significantly higher than those with IABP in our study. Selection bias is likely partially responsible for the results reported in this analysis, where sicker patients received 1 type of device vs the other. In order to continue to expand the field of CS, it is important to understand current practice patterns in all cases of CS, including SIC, and also, to capture variables of shock severity in large national registry datasets like the NIS, NCDR, and others. Stage-specific use of MCS devices in CS would allow us to inform future studies including randomized clinical trials looking at outcomes of MCS in CS, including SIC. We suggest a stepwise approach for the use of MCS in SIC as in Figure 5 based on current available data in both SIC and CS.

Another important observation from these data is the overall increase in the use of right heart catheterization in patients who received an Impella. Conversely, the almost nonexisting use of right heart catheterization was observed in patients receiving ECMO. Analysis from the Cardiogenic Shock Working Group has demonstrated the importance and usefulness of complete hemodynamic assessment and phenotypic profiling of patients with CS and its translation into better clinical outcomes despite type of aMCS and severity of shock supporting the need for a randomized clinical trials looking at the treatment effects of right heart catheterization in patients with CS requiring aMCS.[19-21]

Importantly, the reported rate of vascular complications is concerning. It is known that vascular complications are associated with the increased risk of mortality among AMI patients.[22] Vascular complications are proportional to bore size required to deploy these devices (particularly ECMO cannulas and Impella sheath).[23] Innovation and future iterations will likely incorporate lower profile sheaths for vascular access which in conjunction with optimal operator's training and technique are bound to reduce the incidence of vascular complications. It is conceivable that the differences in in-hospital mortality and 30-day readmission rates reported may in part be driven by the increased postprocedural bleeding in patients with ECMO and Impella compared to IABP. This finding needs careful interpretation with a small number of events in total. It is noteworthy that Impella is often used in patients who are sicker and require more cardiac output support. Although baseline characteristics were not significantly different in many comorbidities and hospital characteristics, there can be a bias due to missed covariables not available in the administrative database.

The causes of CS in SIC can be attributed to several factors, including severe impairment of left ventricular systolic function, the occurrence of malignant arrhythmias, temporary mitral regurgitation, LVOT obstruction, and involvement of the right ventricle. Recent hemodynamic analysis in patients with SIC characterized that SIC is associated with severely impaired cardiac contractility, shortened systolic period, inefficient myocardial energetics, and prolonged active myocardial relaxation but unaltered diastolic passive stiffness.[24] Timely identification of complications that may result in hemodynamic instability is critical to implementing appropriate interventions that target the underlying mechanisms of CS in SIC. There is a lack of data examining the treatment of CS in patients with SIC and LVOT obstruction. However, multiple case reports have shown encouraging outcomes from the use of microaxial transvalvular axial flow, especially in cases where LVOT obstruction is pronounced.[25-27] IABP may provide a higher therapeutic benefit in patients with coexisting mitral regurgitation, which may influence outcomes in the absence of LVOT obstruction. Lastly, ECMO might be necessary in cases of complete hemodynamic collapse in SCAI stage D to E. Studies considering these different phenotypes of SIC patients are necessary to better understand which patients may benefit from different strategies. A study using a large cohort of SIC

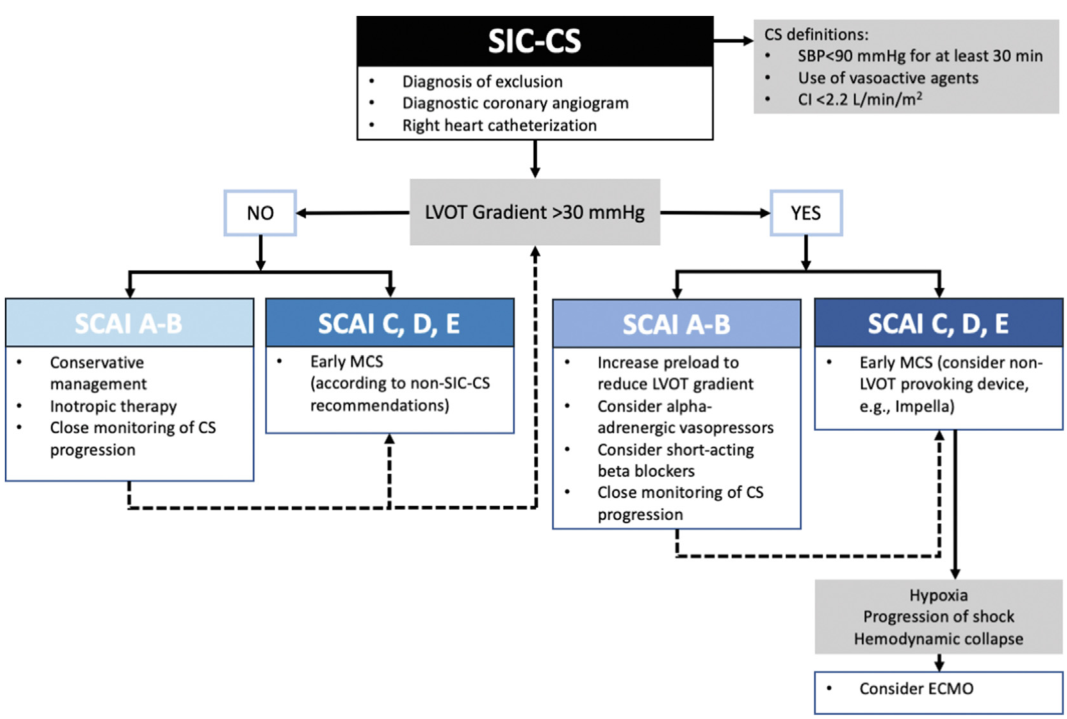


Figure 5.

Suggested algorithm for mechanical circulatory support in stress-induced cardiomyopathy cardiogenic shock. CI, cardiac index; ECMO, extracorporeal membrane oxygenation; LVOT, left ventricular outflow tract; MCS, mechanical circulatory support; SBP, systolic blood pressure; SCAI, Society for Cardiovascular Angiography & Interventions; SIC-CS, stress-induced cardiomyopathy cardiogenic shock.

from the National Inpatient Sample database identified 4 patient clusters using latent class analysis: C1 with hyperlipidemia, hypertension, and diabetes; C2 with chronic obstructive pulmonary disease, and smoking; C3 with anxiety and depression; and C4 with isolated SIC with few comorbidities.[28] C1 had the lowest in-hospital mortality (1%) whereas C2 had the highest in-hospital mortality (3.4%). Differential outcomes from different phenotypes of SIC warrant further clinical trials to identify specific patients who would get benefit from aMCS.

Study limitations

This study has limitations inherent to nonrandomized, observational cohort studies. First, the data in NRD includes a sample designed to approximate the national population, which can lead to an underrepresentation or overrepresentation of groups within the sample. However, the use of NRD to estimate national data has been validated in multiple publications.[29,30] Second, the administrative data can be subject to coding bias or missing events or variables. Especially, correct diagnosis of SIC with coding can be challenging. Nevertheless, previous studies using the administrative data and ICD-10-CM codes have shown the characteristics of SIC successfully.[31,32] Third, some important clinical characteristics including blood pressure, heart rate, echocardiographic parameters, laboratory findings, medications, class of obesity, and the severity of shock are not available in NRD. This study is intended to generate hypotheses, and future studies are required to confirm our findings with more detailed clinical information. Fourth, our 30-day outcomes do not account for out-of-hospital episodes, which may affect the accuracy of our calculated outcomes. Lastly, our study also excluded patients who underwent escalation of devices which can in turn remove sicker patients in the part of the cohort, like the IABP group.

Conclusions

In this analysis of a national administrative database, we provide new insights into the characteristics, contemporary clinical practice, and variables associated with in-hospital mortality among patients with CS secondary to SIC. Given the nature of this particular database and the absence of important clinical information such as vital signs, lactate, ejection fraction, or SCAI shock stage, adequate risk adjustment remains limited. It is possible that sicker patients received more aggressive hemodynamic support which may account for observed mortality differences. Future prospective studies with objective and universal characterization of baseline clinical and hemodynamic characteristics of patients with CS secondary to SIC are warranted in order to better define and improve treatment paradigms for unique causes of CS.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics statement and patient consent

This study used deidentified, publicly available database, making it exempted from institutional review board approval or requirement of patient consent.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the Journal of the Society for Cardiovascular Angiography & Interventions at 10.1016/j.jscai.2023.101185.

References

1. Ghadri JR, Wittstein IS, Prasad A, et al. International expert consensus document on takotsubo syndrome (Part I): Clinical Characteristics, Diagnostic Criteria, and Pathophysiology. *Eur Heart J*. 2018;39(22):2032–2046. https://doi.org/10.1093/eurheartj/ehy076
2. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. *N Engl J Med*. 2015;373(10):929–938. https://doi.org/10.1056/NEJMoa1406761
3. Lyon AR, Bossone E, Schneider B, et al. Current state of knowledge on takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail*. 2016;18(1):8–27. https://doi.org/10.1002/ejhf.424
4. Di Vece D, Citro R, Cammann VL, et al. Outcomes associated with cardiogenic shock in takotsubo syndrome. *Circulation*. 2019;139(3):413–415. https://doi.org/10.1161/CIRCULATIONAHA.118.036164
5. Mariani S, Richter J, Pappalardo F, et al. Mechanical circulatory support for takotsubo syndrome: a systematic review and meta-analysis. *Int J Cardiol*. 2020; 316:31–39. https://doi.org/10.1016/j.ijcard.2020.05.033
6. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med*. 2005;352(6):539–548. https://doi.org/10.1056/NEJMoa043046
7. Y-Hassan S, Henareh L. Plasma catecholamine levels in patients with takotsubo syndrome: implications for the pathogenesis of the disease. *Int J Cardiol*. 2015; 181:35–38. https://doi.org/10.1016/j.ijcard.2014.11.149
8. Sobczyk D. Dynamic left ventricular outflow tract obstruction: underestimated cause of hypotension and hemodynamic instability. *J Ultrason*. 2014;14(59):421–427. https://doi.org/10.15557/JoU.2014.0044
9. Napierkowski S, Banerjee U, Anderson HV, et al. Trends and impact of the use of mechanical circulatory support for cardiogenic shock secondary to takotsubo cardiomyopathy. *Am J Cardiol*. 2021;139:28–33. https://doi.org/10.1016/j.amjcard.2020.09.047
10. Santoro F, Núñez Gil IJ, Stiermaier T, et al. Impact of intra-aortic balloon counterpulsation on all-cause mortality among patients with takotsubo syndrome complicated by cardiogenic shock: results from the German-Italian-Spanish (GEIST) registry. *Eur Heart J Open*. 2023;3(1):oead003. https://doi.org/10.1093/ehjopen/oead003
11. U.S. Department of Health and Human Services. Healthcare Cost and Utilization Project (HCUP). *HCUP Nationwide Readmissions Database (NRD)*. Accessed January 1, 2022. Agency for Healthcare Research and Quality; 2016, 2017, 2018 and 2019. http://www.hcup-us.ahrq.gov/nrdoverview.jsp
12. The R Foundation. Accessed March 1, 2022. www.R-project.org
13. Schrage B, Ibrahim K, Loehn T, et al. Impella support for acute myocardial infarction complicated by cardiogenic shock. *Circulation*. 2019;139(10):1249–1258. https://doi.org/10.1161/CIRCULATIONAHA.118.036614
14. Kim Y, Shapero K, Ahn SS, Goldsweig AM, Desai N, Altin SE. Outcomes of mechanical circulatory support for acute myocardial infarction complicated by cardiogenic shock. *Catheter Cardiovasc Interv*. 2022;99(3):658–663. https://doi.org/10.1002/ccd.29834
15. Dhruva SS, Ross JS, Mortazavi BJ, et al. Use of mechanical circulatory support devices among patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA Netw Open*. 2021;4(2):e2037748. https://doi.org/10.1001/jamanetworkopen.2020.37748
16. Hernandez-Montfort J, Kanwar M, Sinha SS, et al. Clinical presentation and in-hospital trajectory of heart failure and cardiogenic shock. *JACC Heart Fail*. 2023; 11(2):176–187. https://doi.org/10.1016/j.jchf.2022.10.002
17. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: this document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv*. 2019;94(1):29–37. https://doi.org/10.1002/ccd.28329
18. Naidu SS, Baran DA, Jentzer JC, et al. SCAI SHOCK Stage Classification Expert Consensus Update: a review and Incorporation of Validation Studies: this statement was endorsed by the American College of Cardiology (ACC), American College of Emergency Physicians (ACEP), American Heart Association (AHA), European Society of Cardiology (ESC) Association for Acute Cardiovascular Care (ACVC), International Society for Heart and Lung Transplantation (ISHLT), Society of Critical Care Medicine (SCCM), and Society of Thoracic Surgeons (STS) in December 2021. *J Am Coll Cardiol*. 2022;79(9):933–946. https://doi.org/10.1016/j.jacc.2022.01.018
19. Thayer KL, Zweck E, Ayouty M, et al. Invasive hemodynamic assessment and classification of in-hospital mortality risk among patients with cardiogenic shock. *Circ Heart Fail*. 2020;13(9):e007099. https://doi.org/10.1161/CIRCHEARTFAILURE.120.007099
20. Davila CD, Esposito M, Hirst CS, et al. Right atrial pressure is associated with outcomes in patient with cardiogenic shock receiving acute mechanical

circulatory support. *Front Cardiovasc Med*. 2021;8:563853. https://doi.org/10.3389/fcvm.2021.563853

21. Garan AR, Kanwar M, Thayer KL, et al. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. *JACC Heart Fail*. 2020;8(11):903–913. https://doi.org/10.1016/j.jchf.2020.08.012
22. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. *Circulation*. 2006;114(8):774–782. https://doi.org/10.1161/CIRCULATIONAHA.106.612812
23. Davila CD, Sharma S, Krishnamoorthy P, et al. Prevalence and clinical correlates of extended mechanical support in patients undergoing high-risk percutaneous coronary intervention in current clinical practice: insights from the cVAD registry. *Cardiovasc Revasc Med*. 2020;21(3):342–347. https://doi.org/10.1016/j.carrev.2019.05.001
24. Stiermaier T, Reil JC, Sequeira V, et al. Hemodynamic assessment in takotsubo syndrome. *J Am Coll Cardiol*. 2023;81(20):1979–1991. https://doi.org/10.1016/j.jacc.2023.03.398
25. Beneduce A, Fausta Bertoldi L, Melillo F, et al. Mechanical circulatory support with Impella percutaneous ventricular assist device as a bridge to recovery in takotsubo syndrome complicated by cardiogenic shock and left ventricular outflow tract obstruction. *JACC Cardiovasc Intv*. 2019;12(4):e31–e32. https://doi.org/10.1016/j.jcin.2018.10.046
26. 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;7(1):306–310. https://doi.org/10.1002/ehf2.12546
27. Mohammedzein A, Taha A, Salwan A, Nambiar R. Impella use in cardiogenic shock due to takotsubo cardiomyopathy with left ventricular outflow tract obstruction. *JACC Case Rep*. 2019;1(2):161–165. https://doi.org/10.1016/j.jaccas.2019.06.022
28. Li P, Dai Q, Cai P, et al. Identifying different phenotypes in takotsubo cardiomyopathy by latent class analysis. *ESC Heart Fail*. 2021;8(1):555–565. https://doi.org/10.1002/ehf2.13117
29. Jang SJ, Kim LK, Sobti NK, et al. Mortality of patients with ST-segment-elevation myocardial infarction without standard modifiable risk factors among patients without known coronary artery disease: age-stratified and sex-related analysis from nationwide readmissions database 2010-2014. *Am J Prev Cardiol*. 2023;14, 100474. https://doi.org/10.1016/j.ajpc.2023.100474
30. Jang SJ, Yeo I, Feldman DN, et al. Associations between hospital length of stay, 30-day readmission, and costs in ST-segment-elevation myocardial infarction after primary percutaneous coronary intervention: A nationwide readmissions database analysis. *J Am Heart Assoc*. 2020;9(11):e015503. https://doi.org/10.1161/JAHA.119.015503
31. Jang SJ, Yeo I, Jonas C, et al. Thirty-day readmission rates after takotsubo syndrome with or without malignancy: A nationwide readmissions database analysis. *J Clin Med*. 2021;10(16). https://doi.org/10.3390/jcm10163701
32. Brinjikji W, El-Sayed AM, Salka S. In-hospital mortality among patients with takotsubo cardiomyopathy: a study of the National Inpatient Sample 2008 to 2009. *Am Heart J*. 2012;164(2):215–221. https://doi.org/10.1016/j.ahj.2012.04.010