

# Temporary Mechanical Circulatory Support for Refractory Cardiogenic Shock Before Left Ventricular Assist Device Surgery

Saraschandra Vallabhajosyula, MBBS; Shilpkumar Arora, MD, MPH; Sopan Lahewala, MD; Varun Kumar, MD; Ghanshyam P. S. Shantha, MBBS; Jacob C. Jentzer, MD; John M. Stulak, MD; Bernard J. Gersh, MBChB, DPhil; Rajiv Gulati, MD, PhD; Charanjit S. Rihal, MD; Abhiram Prasad, MD; Abhishek J. Deshmukh, MBBS

**Background**—There are limited data on the role of temporary mechanical circulatory support (MCS) devices for cardiogenic shock before left ventricular assist device (LVAD) surgery. This study sought to evaluate the trends of use and outcomes of MCS in cardiogenic shock before LVAD surgery.

*Methods and Results*—This was a retrospective cohort study from 2005 to 2014 using the National Inpatient Sample (20% stratified sample of US hospitals). This study identified admissions undergoing LVAD surgery with preoperative cardiogenic shock. Admissions for other cardiac surgery and heart transplant were excluded. Temporary MCS was identified using administrative codes. The primary outcome was hospital mortality and secondary outcomes were hospital costs and lengths of stay in admissions with and without MCS use. In this 10-year period, 9753 admissions were identified with 40.6% requiring pre-LVAD MCS. There was a temporal increase in the frequency of cardiogenic shock associated with an increase in non–intra-aortic balloon pump MCS devices. The cohort receiving MCS had greater in-hospital myocardial infarction, ventricular arrhythmias, and use of coronary angiography. On multivariable analysis, older age, myocardial infarction, and need for MCS devices were independently predictive of higher in-hospital mortality. In 696 propensity-matched pairs, use of MCS was predictive of higher in-hospital mortality (odds ratio 1.4 [95% confidence interval 1.1–1.6]; P=0.02) and higher hospital costs, but similar lengths of stay.

*Conclusions*—In patients with cardiogenic shock bridged to LVAD therapy, there was a steady increase in preoperative MCS use. Use of MCS identified patients at higher risk for in-hospital mortality and greater resource utilization. (*J Am Heart Assoc.* 2018;7: e010193. DOI: 10.1161/JAHA.118.010193.)

Key Words: cardiogenic shock • critical care • destination therapy • left ventricular assist device • mechanical circulatory support

H eart failure is a leading cause of cardiovascular mortality and morbidity that currently affects 5.7 million American adults and is projected to increase by 46% in the next 15 years.<sup>1</sup> Stage-D or end-stage heart failure constitutes <1% of the total heart failure burden, but is associated with the highest hospital costs and short-term mortality.<sup>2</sup> Patients with end-stage heart failure had 75% 1-year mortality and nearly 100% 2-year mortality despite optimal medical therapy in the landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial.<sup>3</sup> Despite the advances in the medical therapy for heart failure, these patients frequently require more advanced therapy in the form of a durable left ventricular assist device (LVAD) or orthotopic heart transplantation.<sup>2</sup> However, because of the critical shortage of donor hearts, LVAD therapy has been increasingly used in modern practice for end-stage heart failure as either destination

Received June 25, 2018; accepted October 23, 2018.

From the Department of Cardiovascular Medicine (S.V., J.C.J., B.J.G., R.G., C.S.R., A.P., A.J.D.), Division of Pulmonary and Critical Care Medicine, Department of Medicine (S.V., J.C.J.) and the Department of Cardiovascular Surgery (J.M.S.), Mayo Clinic, Rochester, MN; Division of Cardiovascular Diseases, Robert Packer Hospital/ Guthrie Clinic, Towanda, PA (S.A., V.K.); Division of Cardiovascular Diseases, Jersey City Medical Center, Jersey City, NJ (S.L.); Division of Cardiovascular Diseases, University of Iowa Carver College of Medicine, Iowa City, IA (G.P.S.S.).

A portion of these findings were presented as a poster at the American College of Cardiology Scientific Session, March 10 to 12, 2018, in Orlando, FL.

This article was handled independently by John S. Ikonomidis, MD, PhD as a guest editor. The editors had no role in the evaluation of the manuscript or in the decision about its acceptance.

Correspondence to: Abhishek J. Deshmukh, MBBS, Department of Cardiovascular Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail: deshmukh.abhishek@mayo.edu

<sup>© 2018</sup> The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

### **Clinical Perspective**

#### What Is New?

- In patients with cardiogenic shock bridged to left ventricular assist device therapy, there was a steady increase in preoperative mechanical circulatory support use.
- Use of mechanical circulatory support identified patients at higher risk for in-hospital mortality and greater resource utilization.

#### What Are the Clinical Implications?

• Careful study of risk factors and predictors of outcomes in this population is necessary to optimize clinical outcomes in this critically ill population.

therapy or bridge-to-transplant.<sup>4</sup> LVADs are used in  $\approx\!15\%$  of patients with cardiogenic shock, but the use of LVADs in patients with ongoing cardiogenic shock is associated with higher postimplant mortality as noted in the recent report from the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support).<sup>4</sup>

Despite the advances in cardiovascular medicine, patients with INTERMACS Class 1 (critical cardiogenic shock) continue to have a mortality of 35% to 45% without LVAD therapy.<sup>5</sup> In addition to optimal medical therapy with high-dose vasopressors and inotropes, these patients frequently require temporary mechanical circulatory support (MCS) devices for hemodynamic stabilization.<sup>6</sup> Historically, the intra-aortic balloon pump (IABP) was the most commonly used temporary device; however, the advent of newer devices providing more robust circulatory support has resulted in a paradigm shift in modern practice.<sup>7</sup> The role of temporary MCS has been studied extensively in cardiogenic shock in the setting of acute coronary syndromes and as an adjunct to high-risk intervention.<sup>8,9</sup> The clinical profiles and outcomes of patients with cardiogenic shock needing preoperative MCS before LVAD surgery are infrequently reported.<sup>10</sup>

This study sought to evaluate the characteristics of patients admitted with cardiogenic shock who were bridged to LVAD therapy with and without the use of temporary MCS. The primary outcome was in-hospital mortality and secondary outcomes included trends, hospital costs, and lengths of stay associated with admissions with and without the use of temporary MCS.

## Material and Methods

The data used for this study are publicly available with the Agency for Healthcare Research and Quality.<sup>11</sup> The data, analytic methods, and study materials have been made available to

other researchers for purposes of reproducing the results or replicating the procedure. Please refer to Tables 1 and 2 for detailed *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes used in this study.

## **Study Database**

The Nationwide/National Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the United States. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Quality and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.<sup>12</sup> Information regarding each discharge includes patient demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 additional secondary diagnoses, and procedural diagnoses. No institutional review board approval or informed consent was sought because of the publically available deidentified data set used in this research.

### Study Population, Variables, and Outcomes

Using the HCUP-NIS data from 2005 to 2014, a retrospective cohort of admissions including patients >18 years undergoing LVAD placement (ICM-9-CM 37.66 in the primary procedure field) were included. Since the ICD-9-CM codes were re-defined in 2005 to distinguish between permanent MCS devices (ICD-9-CM 37.66) and nonimplantable paracorporeal devices (ICD-9-CM 37.62 and 37.65), procedures performed before 2005 were excluded from this study.<sup>13</sup> Preoperative cardiogenic shock was identified using an ICD-9-CM code of 785.51 timed using the date of LVAD and date of temporary MCS insertion. Cardiogenic shock, per the ICD-9-CM classification, was defined as shock resulting from diminution of cardiac output in heart disease, shock resulting from primary failure of the heart in its pumping function, as in myocardial infarction, severe cardiomyopathy, or mechanical obstruction or compression of the heart or shock resulting from the failure of the heart to maintain adequate output. Validation studies have shown a specificity of 99.3%, a sensitivity of 59.8%, a positive predictive value of 78.8%, and a negative predictive value of 98.1% for the ICD-9-CM code 785.51 to identify cardiogenic shock.<sup>14</sup> Admissions for orthotopic heart transplants (ICD-9-CM 37.5, 37.51, or 33.6), valve repair (ICD-9-CM 35.10-35.14), valve replacement (35.20-35.28), and bypass surgery (36.1-36.2) were excluded. Short-term MCS use was defined using ICD-9-CM codes for IABP (ICD-9-CM 37.61), percutaneous MCS (Impella/TandemHeart) (ICD-9-CM 37.68), nonpercutaneous MCS (ICD-9-CM 37.60, 37.62, 37.65), extracorporeal membrane oxygenation (ECMO) (ICD-9-CM 39.65), and percutaneous cardiopulmonary support (ICD-9-CM 39.66).

Demographic characteristics (age, sex, and race), hospital characteristics (teaching status and location, bed-size, and

# Table 1. Baseline Characteristics of Patients With and Without MCS

Variable	MCS (n=3958)	No MCS (n=5795)	Overall (n=9753)	P Value
Age, y	53.3±0.5	55.9±0.4	54.0±0.3	<0.001
Female sex	23.8	24.8	24.4	0.23
Race				<0.001
White	57.0	57.5	57.3	
Nonwhite	36.5	29.4	32.3	
Missing	6.5	13.1	10.4	
Cardiac morbidity during admission				
Myocardial infarction	25.1	13.4	18.2	<0.001
Coronary angiography/percutaneous coronary intervention	23.6	15.6	18.9	<0.001
Ventricular tachycardia/fibrillation	14.4	7.2	10.1	<0.001
Pathogenesis	!			
Acute myocardial infarction	25.1	13.4	18.2	<0.001
Heart failure	94.5	93.7	94.0	0.09
Acute myocarditis	3.3	1.6	2.3	<0.001
Charlson Comorbidity Index				0.02
0–1	30.1	31.2	30.8	
≥2	69.9	68.8	69.2	
Primary expected payer				<0.00
Nonprivate insurance	51.5	55.1	53.6	1
Private insurance	48.5	44.9	45.8	
Median household income category for zip code				< 0.001
0–25th percentile	24.3	25.8	25.7	
26th-50th percentile	25.2	25.2	25.2	
51st-75th percentile	22.0	25.7	24.2	
76th–100th percentile	26.8	21.9	23.9	
Hospital bed size				0.36
Small	0.9	1.2	1.1	
Medium	9.6	10.0	9.9	
Large	89.5	88.7	89.0	
Urban location	99.6	99.8	99.8	0.10
Teaching hospital	96.4	96.8	96.6	0.35
Hospital region				<0.001
Northeast	19.4	14.6	16.5	
Midwest	18.9	23.9	21.9	
South	26.5	23.5	24.7	
West	12.1	16.6	14.8	
Weekends admission	17.9	13.9	15.5	<0.001
Obesity	10.8	12.8	12.0	0.003
Hypertension	34.7	37.9	36.6	0.002
Diabetes mellitus, type 2	24.0	28.3	26.6	<0.001
Smoking	4.6	4.4	4.5	0.61

Continued

#### Table 1. Continued

Variable	MCS (n=3958)	No MCS (n=5795)	Overall (n=9753)	P Value
Coronary artery disease	34.2	34.5	34.4	0.78
Family history of coronary artery disease	2.0	2.2	2.1	0.37
Previous myocardial infarction	8.6	11.6	10.4	<0.001
Previous percutaneous coronary intervention	7.1	6.8	6.9	0.64
Previous coronary artery bypass grafting	5.2	8.1	6.9	<0.001
Previous cardiac arrest	1.3	1.0	1.1	0.10
Atrial fibrillation	35.5	38.1	37.1	0.01
Congestive heart failure	94.5	93.7	94.0	0.09
Chronic pulmonary disease	14.2	18.5	16.8	<0.001
Pulmonary circulation disorders	0.1	0.3	0.2	0.21
Peripheral vascular disease	9.3	6.7	7.8	<0.001
Chronic renal failure	35.2	35.5	35.4	0.80
Fluid and electrolyte disorders	70.4	62.7	65.8	<0.001
Neurological disorder	6.7	6.5	6.6	0.74
Anemia	18.7	19.0	18.8	0.73
Coagulopathy	45.2	37.9	40.8	<0.001
Hematological/solid malignancy	1.3	2.0	1.7	0.007

All values represented as percentage or mean±standard error. MCS indicates mechanical circulatory support.

region) and primary payer associated with each discharge were identified from the HCUP-NIS database. The hospitals were divided into tertiles based on the annual volume of LVAD discharges. The Deyo's modification of Charlson Comorbidity Index was used to identify the burden of comorbid diseases.<sup>15</sup>

The primary outcome was in-hospital mortality in patients with and without the use of MCS for cardiogenic shock pre-LVAD surgery. Secondary outcomes included incidence and trends of MCS use in pre-LVAD surgery and the hospital costs and lengths of stay for these admissions.

#### **Statistical Analysis**

As recommended by HCUP-NIS, survey procedures using discharge weights provided with HCUP-NIS database were used to generate national estimates.<sup>16</sup> Chi-square and *t* tests were used to compare categorical and continuous variables, respectively. Linear regression was used to analyze trends over time. The inherent limitations of the HCUP-NIS database were reviewed and addressed during the statistical analysis and interpretation of these data.<sup>17</sup> Univariate analysis for trends and outcomes was performed and were represented as odds ratio with 95% confidence interval or mean $\pm$ standard error. Multivariate regression

DOI: 10.1161/JAHA.118.010193

analysis incorporating age, sex, race, myocardial infarction, coronary angiography, and/or percutaneous coronary intervention, median household income, hospital characteristics, and comorbidities was performed for in-hospital mortality using MCS as the dependent variable. For the multivariate modeling, regression analysis with purposeful selection of statistically and clinically relevant variables was conducted. Further propensity-matched cohorts were generated using 1:1 nearest neighbor matching (with 0.01 calipers and without replacement) to match patients with MCS use to those without. Propensity-matched sample has standardized differences <10% for all baseline characteristics. Two-tailed P<0.05 was considered statistically significant. All statistical analyses were performed using STATA 14.0 (StataCorp, College Station, TX).

## **Results**

In the 10-year period from 2005 to 2014, there were a total of 9753 estimated admissions for LVAD surgery that were complicated by preoperative cardiogenic shock. Temporary MCS was used in 3958 (40.6%) of these admissions. During this 10-year period there was a 4.6 times temporal increase in the incidence of cardiogenic shock pre-LVAD surgery that was associated with a 5.5 times concomitant increase in the use of temporary MCS devices (Figure 1). There was a significant increase in the

#### Table 2. Multivariate Analysis of In-Hospital Mortality\*

	Odds Ratio	95% Confidence In	95% Confidence Interval	
Parameter		Lower Limit	Upper Limit	P Value
Age	1.1	1.1	1.1	0.003
Female sex	1.0	0.9	1.3	0.67
Race		I	I	
White		Reference		
Nonwhite	0.7	0.6	0.9	0.003
Missing	2.6	1.7	4.0	< 0.001
Mechanical circulatory support	1.6	1.3	1.9	< 0.001
Cardiac morbidity during admission			1	
Myocardial infarction	1.7	1.4	2.1	< 0.001
Coronary angiography/percutaneous coronary intervention	0.6	0.5	0.8	< 0.001
Ventricular tachycardia/fibrillation	1.1	0.9	1.5	0.39
Primary expected payer				
Nonprivate		Reference		
Private	0.6	0.5	0.8	< 0.001
Median household income category for patient's zip code			1	i
0–25th percentile		Reference		
26th–50th percentile	1.7	1.3	2.2	<0.001
51st-75th percentile	1.4	1.1	1.8	0.03
75th-100th percentile	1.9	1.4	2.4	< 0.001
Hospital region	· · ·	·	· · ·	·
Northeast		Reference		
Midwest	0.5	0.2	1.3	0.17
South	0.6	0.3	1.5	0.29
West	1.3	0.5	3.5	0.55
Weekends admission	1.7	1.3	2.1	<0.001
Obesity	1.1	0.9	1.5	0.40
Hypertension	0.9	0.7	1.1	0.32
Diabetes mellitus, type 2	1.2	0.9	1.4	0.44
Previous myocardial infarction	0.7	0.5	0.9	0.01
Previous coronary artery bypass grafting	0.8	0.6	1.2	0.29
Atrial fibrillation	0.4	0.3	0.5	< 0.001
Chronic pulmonary disease	0.5	0.4	0.7	< 0.001
Peripheral vascular disease	1.5	1.1	2.0	0.01
Fluid and electrolyte disorder	1.1	0.9	1.3	0.58
Coagulopathy	2.7	2.3	3.3	< 0.001

\*All variables listed in Table 2 were used in a multivariable analysis for in-hospital mortality.

proportion of cases receiving temporary MCS, primarily because of an increase in the use of non-IABP devices (all P<0.001) (Figure 2). Baseline characteristics of patients with and without the use of temporary MCS are detailed in Table 1. End-stage heart failure was the predominant cause of cardiogenic shock without any differences between cohorts with and without MCS use (94.5% versus 93.7%; *P*=0.09). Patients receiving MCS were more likely to be younger, of nonwhite race, have acute myocardial infarction and acute myocarditis as cause, using private insurance, and had greater comorbidity burden. Greater rates of in-hospital cardiac events such as myocardial infarction, ventricular tachycardia/fibrillation, and need for coronary

angiography/percutaneous coronary intervention were noted in the patients receiving MCS. The cohort that received MCS had higher in-hospital morbidity such as acute kidney injury (69.5% versus 57.9%; P<0.001), stroke (5.9% versus 4.6%; P=0.004), and invasive mechanical ventilation (40.2% versus 36.5%; P<0.001). Trends of MCS use in patients with cardiogenic shock before LVAD surgery stratified by patient age, sex, race, and median household income for zip are shown in Figure 3A through 3D.

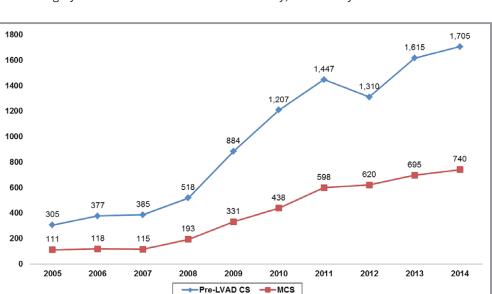
## Mortality, Lengths of Stay, and Hospital Costs

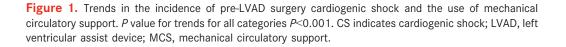
Unadjusted mortality for admissions with and without the use of MCS was 19.7% versus 14.2%; *P*<0.001. The unadjusted mortality trends over this 10-year duration are presented in Figure 4. In a multivariate model, older age, concomitant myocardial infarction, higher median household income, weekend admission, and use of temporary MCS were predictive of higher in-hospital mortality in this population (Table 2). Using propensity matching for baseline clinical and demographic variables, 696 pairs (total 1392 admissions) were generated for further analysis (Table 3). Use of MCS was predictive of higher in-hospital mortality—odds ratio 1.4 (95% confidence interval 1.1–1.6); *P*=0.02, higher hospital costs ( $2277 803\pm5199$  versus  $232 707\pm4561$ ; *P*<0.001); but similar lengths of hospital stay ( $43\pm1.2$  days versus  $40\pm1.3$  days; *P*=0.11).

# Discussion

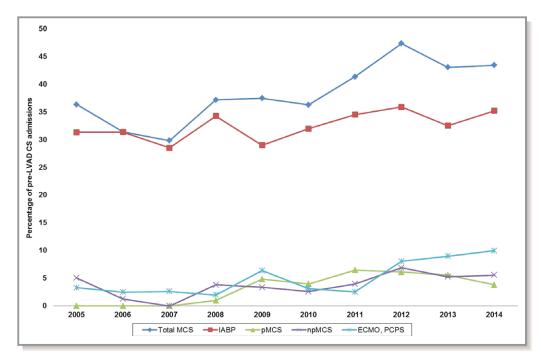
In this large nationally representative cohort of patients, this study noted a temporal increase in cardiogenic shock that previously received LVAD surgery. There was a concomitant increase in the use of temporary MCS before LVAD surgery between 2005 and 2014. Despite the IABP being the predominant device of choice, there was a steady increase in non-IABP temporary MCS. Older age, concomitant myocardial infarction, and use of MCS were independent predictors of higher in-hospital mortality. In 696 propensity-matched pairs, use of MCS was associated with higher hospital costs but no difference in length of hospital stay, suggestive of the role of higher morbidity and mortality in this population.

Consistent with the most recent INTERMACS data, this study noted a steady increase in LVAD volumes for cardiogenic shock since the approval of the continuous-flow LVADs in 2008.<sup>4</sup> As noted in the literature, end-stage cardiomyopathy was the leading cause of cardiogenic shock in patients receiving LVAD therapy in this study as compared with acute myocardial infarction or fulminant myocarditis.<sup>10,18</sup> Patients with cardiogenic shock frequently require temporary MCS to aid in hemodynamic stabilization in addition to high doses of vasoactive medications.<sup>6</sup> Prior literature has demonstrated favorable hemodynamic effects and improvement of candidacy for LVAD using percutaneous MCS before LVAD implantation.<sup>18,19</sup> This is of crucial importance since the use of emergent durable LVAD in cardiogenic shock patients is associated with unacceptably high mortality of nearly 60% to 80%.<sup>18</sup> In the background of this information, this study serves to highlight an important gap in the literature examining the role of short-term MCS in cardiogenic shock that are bridged to LVAD therapy in a large nationally representative cohort. Other international registries such as the INTERMACS and Extracorporeal Life Support Organization registries report durable MCS and ECMO, respectively, without any data on other forms of temporary MCS.





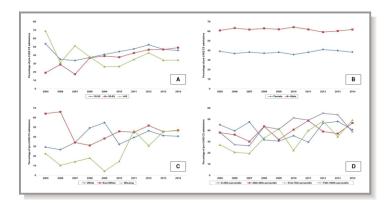
Fotal hospital admissions



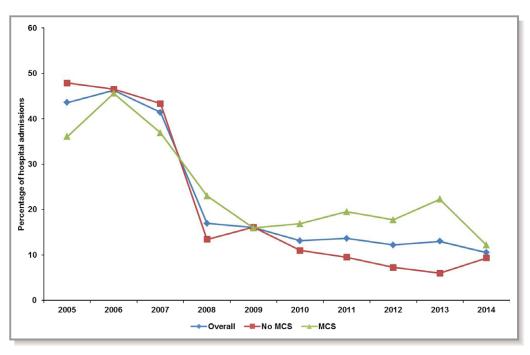
**Figure 2.** Trends in the percentage of admissions with mechanical circulatory support for pre-LVAD surgery cardiogenic shock. *P* value for trends for all categories *P*<0.001. CS indicates cardiogenic shock; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; MCS, mechanical circulatory support; npMCS, nonpercutaneous mechanical circulatory support; PCPS, percutaneous cardiopulmonary support; pMCS, percutaneous mechanical circulatory support.

There are limited contemporary data on percutaneous and nonpercutaneous MCS devices in patients with cardiogenic shock before LVAD surgery. Consistent with literature in other causes of cardiogenic shock, this study demonstrated a decrease in the use of IABP in these patients with a concomitant increase in non-IABP MCS devices.<sup>8,20</sup> Importantly, between 2012 and 2014, nearly 8% to 10% of admissions received preoperative ECMO support, which highlights a paradigm shift in care of patients with cardiogenic

shock, which is significantly higher than the use of ECMO in acute coronary syndromes.<sup>8</sup> This can be postulated to be because of greater operator comfort with ECMO technique in cardiac surgery, need for higher cardiac output (flows), and a higher incidence of biventricular failure in this population of end-stage heart failure. Conversely, this could also represent lesser elective use of IABP before LVAD surgery and limiting the use of MCS to only emergent cases.<sup>21</sup> Despite a higher overall proportion of nonprivate insurance patients, this study



**Figure 3.** Trends in the use of mechanical circulatory support stratified by age (in years) (**A**), sex (**B**), race (**C**), and median income for zip code (**D**). *P* value for trends for all categories P<0.001. CS indicates cardiogenic shock; LVAD, left ventricular assist device.



**Figure 4.** Trends of in-hospital mortality in patients with and without the use of mechanical circulatory support. *P* value for trends for all categories *P*<0.001. MCS indicates mechanical circulatory support.

noted greater use of MCS in patients with private insurance compared with those on nonprivate insurance. Prior literature from the HCUP-NIS database has alluded to the role of insurance in patient outcomes.<sup>22</sup> Given the high costs associated with care for both LVAD surgery and MCS patients, these considerations are worthy of careful evaluation in subsequent studies to ensure equitable care across the United States. Importantly, there were no differences in MCS use before LVAD surgery when hospitals were stratified by size and location. Prior data from the HCUP-NIS database have shown that the use of MCS is lesser in rural and nonacademic hospitals.<sup>23</sup> It is possible that given the differences in population and the limited centers in the United States that perform LVAD implantation, we were unable to replicate these findings. There was significant geographic variation in the use of MCS, with the highest in southern United States; however, this did not influence hospital mortality. It is pertinent to note that the time period of this study preceded the most recent guidelines on MCS use; hence the practice variability could potentially be explained by the lack of uniform consensus on the indication, duration, and type of MCS device use.<sup>7</sup>

# **Mortality Outcomes**

Despite advances in the management of cardiogenic shock of all causes, the mortality in this population has remained high at 30% to 40%.<sup>6,24</sup> In patients with cardiogenic shock, den Uil et al reported a hospital mortality of 33% to 55% depending

on the type of MCS used.<sup>10</sup> In contrast, LVAD surgery is associated with only 7% to 8% mortality across all INTERMACS classes.<sup>25</sup> In comparison, our study noted overall mortality of 20% in patients with cardiogenic shock before LVAD surgery. The results of this study are in contrast to smaller singlecenter studies that did not demonstrate any differences in outcomes in patients with and without preoperative MCS support.<sup>19,26-30</sup> This can likely be explained by the multicenter, nationally representative nature of our study and the inability to correct for the indication for temporary MCS device placement. Additionally, this study considered all forms of temporary MCS as compared with prior studies looking at specific types of MCS. It is possible that a certain portion of the IABP MCS devices used in this study were implanted electively, consistent with national practice, and the remainder of the devices were used as salvage therapy.<sup>21</sup> Importantly, given the inherent limitations of the NIS database, these results should be perceived as trends and estimates, given the inability to control for all types of confounding, and need further validation in carefully controlled prospective trials. As noted in this study, the overall mortality for patients with cardiogenic shock receiving LVAD therapy has significantly decreased over this 10-year period, with a sharp inflection point in 2008. This can be explained by multiple reasons: (1) the US Food and Drug Administration approval for continuous-flow pumps in 2008 in conjunction with improved patient-selection strategies; (2) a steady increase in non-IABP MCS devices to support cardiogenic shock since 2007, which could influence mortality in this

# Table 3. Baseline Characteristics of Propensity-Matched Patients\*

Variable	MCS (n=696)	No MCS (n=696)	P Valu
Age, y	54±0.5	54±0.5	0.92
Female sex	23.9	24.4	0.80
Race			0.58
White	56.9	59.6	
Nonwhite	36.2	34.1	
Missing	6.9	6.3	
Cardiac morbidity during admission	I	I	
Myocardial infarction	20.1	19.4	0.95
Coronary angiography/percutaneous coronary intervention	19.1	19.3	0.94
Ventricular tachycardia/fibrillation	10.8	10.3	0.79
Charlson Comorbidity Index			0.89
0	1.4	1.2	
1	30.8	30.6	
≥2	67.8	68.3	
Primary expected payer			0.96
Nonprivate insurance	53.6	53.5	
Private insurance	46.4	46.6	
Median household income category for zip code			0.91
0–25th percentile	25.3	24.4	
26th–50th percentile	25.2	25.1	
51st-75th percentile	22.6	21.4	
76th–100th percentile	25.6	27.2	
Hospital bed size			0.64
Small	1.2	1.3	
Medium	8.9	10.3	
Large	89.9	88.4	
Teaching hospital	96.6	96.3	0.77
Hospital region			0.94
Northeast	18.7	18.4	
Midwest	19.4	17.8	
South	25.9	26.0	
West	12.8	13.7	
Weekends admission	18.1	17.4	0.73
Obesity	11.6	11.2	0.80
Hypertension	35.3	35.6	0.91
Diabetes mellitus, type 2	25.0	25.0	>0.9
Smoking	4.6	4.3	0.80
Coronary artery disease	32.9	31.9	0.69
Family history of coronary artery disease	2.2	2.0	0.85
Previous myocardial infarction	9.3	8.6	0.64
Previous percutaneous coronary intervention	6.9	6.9	>0.9

Continued

#### Table 3. Continued

Variable	MCS (n=696)	No MCS (n=696)	P Value
Previous coronary artery bypass grafting	5.5	4.7	0.54
Previous cardiac arrest	1.0	1.2	0.80
Atrial fibrillation	36.8	37.6	0.74
Congestive heart failure	94.5	94.7	0.91
Chronic pulmonary disease	15.1	14.2	0.65
Pulmonary circulation disorders	0.1	0.1	>0.99
Peripheral vascular disease	8.2	8.8	0.70
Chronic renal failure	35.8	36.5	0.78
Fluid and electrolyte disorders	69.0	69.0	>0.99
Neurological disorder	6.9	6.6	0.83
Anemia	19.0	18.3	0.73
Coagulopathy	43.7	43.4	0.91
Hematological/solid malignancy	1.4	1.7	0.67

All values represented as percentage or mean±standard error. MCS indicates mechanical circulatory support.

\*All variables listed in Table 3 were used in the generation of the propensity-matched cohorts.

population; (3) improved patient selection strategies over time; and (4) the evolution and maturation of the field of critical care cardiology that could potentially have influenced the management of the acute postoperative course.<sup>31</sup>

# Limitations

This study has several limitations, some of which are inherent to the analysis of a large administrative database. There are limited data available in the NIS on the type, location, and operative and mechanistic characteristics of the LVAD, all of which are known to influence short-term outcomes.<sup>32</sup> Importantly, this study only evaluated use of temporary MCS before LVAD surgery, and therefore is unable to comment on postoperative right ventricular failure and the need for subsequent MCS.<sup>33</sup> These administrative codes cannot be used to distinguish between similar devices with improvements in technology (such as improving circulatory support with the percutaneous LVAD). This study did not evaluate patients with temporary MCS that recovered ventricular function or those who were not candidates for durable LVAD therapy and is therefore unable to comment on these important subgroups. Coding errors, misrepresentation of procedural volumes, and underreporting of comorbidities are potential limitations of using ICD-9-CM codes.<sup>34</sup> The HCUP-NIS attempts to mitigate potential errors by using internal and external quality-control measures. This study was limited to in-hospital costs and was unable to account for long-term costs of care for these patients. However, the HCUP-NIS sampling design has been widely used for research in the past and represents a large nationally representative sample for a detailed outcome analysis.<sup>34</sup>

Additionally, the incorporating of newer MCS devices in clinical care could potentially have resulted in greater use in patients over more recent years because of greater availability. Finally, because of the limitations of the HCUP-NIS database, it is not possible to ascertain whether these patients received an LVAD as destination therapy or bridge-to-transplant, which may represent 2 different populations.<sup>4</sup> Despite these limitations, this study addresses an important knowledge gap highlighting the national prevalence and trends of MCS in cardiogenic shock pre-LVAD implantation and defining the hospital outcomes including mortality, costs, and lengths of stay in this sick population.

# Conclusions

Preoperative use of temporary MCS for management of cardiogenic shock is seen in nearly 40% of all admissions for LVAD surgery, with the IABP being the most commonly used device. There has been a steady increase in non-IABP devices over this 10-year study period. Patients requiring MCS had higher inhospital mortality and hospital costs, likely reflecting higher overall severity of illness in this population. Further research on optimal patient, device, and surgical factors are required to improve clinical outcomes in this high-risk population.

# **Author Contributions**

Vallabhajosyula, Prasad, and Deshmukh were involved in study design and literature review; Vallabhajosyula, Arora,

Lahewala, Kumar, and Shantha were involved in data extraction, management, and analysis; Vallabhajosyula and Deshmukh were involved in manuscript drafting; and Jentzer, Stulak, Gersh, Gulati, Rihal, Prasad, and Deshmukh were involved in manuscript revision, intellectual revisions, and mentorship.

#### **Disclosures**

None.

#### References

- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, de Ferranti S, Despres JP, Fullerton HJ, Howard VJ, Huffman MD, Judd SE, Kissela BM, Lackland DT, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Matchar DB, McGuire DK, Mohler ER III, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Willey JZ, Woo D, Yeh RW, Turner MB. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29–e322.
- Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M, Dickinson MG, Levy P, Stough WG, Sweitzer NK, Teerlink JR, Whellan DJ, Albert NM, Krishnamani R, Rich MW, Walsh MN, Bonnell MR, Carson PE, Chan MC, Dries DL, Hernandez AF, Hershberger RE, Katz SD, Moore S, Rodgers JE, Rogers JG, Vest AR, Givertz MM. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. J Card Fail. 2015;21:519–534.
- Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med. 2001;345:1435–1443.
- Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, Miller MA, Baldwin JT, Young JB. Seventh INTERMACS annual report: 15,000 patients and counting. J Heart Lung Transplant. 2015;34:1495–1504.
- Kolte D, Khera S, Aronow WS, Mujib M, Palaniswamy C, Sule S, Jain D, Gotsis W, Ahmed A, Frishman WH, Fonarow GC. Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc.* 2014;3:e000590. DOI: 10. 1161/JAHA.113.000590.
- van Diepen S, Katz JN, Albert NM, Henry TD, Jacobs AK, Kapur NK, Kilic A, Menon V, Ohman EM, Sweitzer NK, Thiele H, Washam JB, Cohen MG. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation*. 2017;136:e232–e268.
- 7. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, Kern M, Garratt KN, Goldstein JA, Dimas V, Tu T. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. 2015;65: e7–e26.
- Agarwal S, Sud K, Martin JM, Menon V. Trends in the use of mechanical circulatory support devices in patients presenting with ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv.* 2015;8:1772–1774.
- Khera R, Cram P, Vaughan-Sarrazin M, Horwitz PA, Girotra S. Use of mechanical circulatory support in percutaneous coronary intervention in the United States. Am J Cardiol. 2016;117:10–16.
- den Uil CA, Akin S, Jewbali LS, Dos Reis Miranda D, Brugts JJ, Constantinescu AA, Kappetein AP, Caliskan K. Short-term mechanical circulatory support as a bridge to durable left ventricular assist device implantation in refractory cardiogenic shock: a systematic review and meta-analysis. *Eur J Cardiothorac Surg.* 2017;52:14–25.
- 11. HCUP-NIS. Healthcare Cost and Utilization Project (HCUP) Databases. 2018;2018.
- Introduction to the HCUP Nationwide Inpatient Sample 2009. Available at: http://www.hcup-us.ahrq.gov/db/nation/nis/NIS\_2009\_INTRODUCTION.pdf
  Accessed January 18, 2015.

- Shah N, Agarwal V, Patel N, Deshmukh A, Chothani A, Garg J, Badheka A, Martinez M, Islam N, Freudenberger R. National trends in utilization, mortality, complications, and cost of care after left ventricular assist device implantation from 2005 to 2011. Ann Thorac Surg. 2016;101:1477–1484.
- Lambert L, Blais C, Hamel D, Brown K, Rinfret S, Cartier R, Giguere M, Carroll C, Beauchamp C, Bogaty P. Evaluation of care and surveillance of cardiovascular disease: can we trust medico-administrative hospital data? *Can J Cardiol.* 2012;28:162–168.
- Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992;45: 613–619.
- 16. Project HHCaU. Nationwide Inpatient Sample Redesign Report. 2012.
- Khera R, Krumholz HM. With great power comes great responsibility: big data research from the National Inpatient Sample. *Circ Cardiovasc Qual Outcomes*. 2017;10:e003846.
- Idelchik GM, Simpson L, Civitello AB, Loyalka P, Gregoric ID, Delgado R III, Kar B. Use of the percutaneous left ventricular assist device in patients with severe refractory cardiogenic shock as a bridge to long-term left ventricular assist device implantation. J Heart Lung Transplant. 2008;27: 106–111.
- Lima B, Kale P, Gonzalez-Stawinski GV, Kuiper JJ, Carey S, Hall SA. Effectiveness and safety of the Impella 5.0 as a bridge to cardiac transplantation or durable left ventricular assist device. *Am J Cardiol.* 2016;117:1622–1628.
- Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Fuhrmann J, Bohm M, Ebelt H, Schneider S, Schuler G, Werdan K. Intraaortic balloon support for myocardial infarction with cardiogenic shock. *N Engl J Med*. 2012;367:1287–1296.
- Imamura T, Kinugawa K, Nitta D, Hatano M, Kinoshita O, Nawata K, Kyo S, Ono M. Prophylactic intra-aortic balloon pump before ventricular assist device implantation reduces perioperative medical expenses and improves postoperative clinical course in INTERMACS profile 2 patients. *Circ J*. 2015;79:1963– 1969.
- Tanenbaum JE, Alentado VJ, Miller JA, Lubelski D, Benzel EC, Mroz TE. Association between insurance status and patient safety in the lumbar spine fusion population. *Spine J.* 2017;17:338–345.
- Khera R, Cram P, Lu X, Vyas A, Gerke A, Rosenthal GE, Horwitz PA, Girotra S. Trends in the use of percutaneous ventricular assist devices: analysis of National Inpatient Sample data, 2007 through 2012. *JAMA Intern Med.* 2015;175:941–950.
- 24. Kolte D, Khera S, Dabhadkar KC, Agarwal S, Aronow WS, Timmermans R, Jain D, Cooper HA, Frishman WH, Menon V, Bhatt DL, Abbott JD, Fonarow GC, Panza JA. Trends in coronary angiography, revascularization, and outcomes of cardiogenic shock complicating non-ST-elevation myocardial infarction. *Am J Cardiol.* 2016;117:1–9.
- Stulak JM, Davis ME, Haglund N, Dunlay S, Cowger J, Shah P, Pagani FD, Aaronson KD, Maltais S. Adverse events in contemporary continuous-flow left ventricular assist devices: a multi-institutional comparison shows significant differences. J Thorac Cardiovasc Surg. 2016;151:177–189.
- Marasco SF, Lo C, Murphy D, Summerhayes R, Quayle M, Zimmet A, Bailey M. Extracorporeal life support bridge to ventricular assist device: the double bridge strategy. *Artif Organs*. 2016;40:100–106.
- Scherer M, Moritz A, Martens S. The use of extracorporeal membrane oxygenation in patients with therapy refractory cardiogenic shock as a bridge to implantable left ventricular assist device and perioperative right heart support. J Artif Organs. 2009;12:160–165.
- Schibilsky D, Haller C, Lange B, Schibilsky B, Haeberle H, Seizer P, Gawaz M, Rosenberger P, Walker T, Schlensak C. Extracorporeal life support prior to left ventricular assist device implantation leads to improvement of the patients INTERMACS levels and outcome. *PLoS One.* 2017;12: e0174262.
- Mohite PN, Zych B, Popov AF, Sabashnikov A, Saez DG, Patil NP, Amrani M, Bahrami T, DeRobertis F, Maunz O, Marczin N, Banner NR, Simon AR. CentriMag short-term ventricular assist as a bridge to solution in patients with advanced heart failure: use beyond 30 days. *Eur J Cardiothorac Surg.* 2013;44: e310–e315.
- Koudoumas D, Malliaras K, Theodoropoulos S, Kaldara E, Kapelios C, Nanas J. Long-term intra-aortic balloon pump support as bridge to left ventricular assist device implantation. J Card Surg. 2016;31:467–471.
- 31. Morrow DA, Fang JC, Fintel DJ, Granger CB, Katz JN, Kushner FG, Kuvin JT, Lopez-Sendon J, McAreavey D, Nallamothu B, Page RL II, Parrillo JE, Peterson PN, Winkelman C. Evolution of critical care cardiology: transformation of the cardiovascular intensive care unit and the emerging need for new medical staffing and training models: a scientific statement from the American Heart Association. *Circulation*. 2012;126:1408–1428.

- Maltais S, Kilic A, Nathan S, Keebler M, Emani S, Ransom J, Katz JN, Sheridan B, Brieke A, Egnaczyk G, Entwistle JW III, Adamson R, Stulak J, Uriel N, O'Connell JB, Farrar DJ, Sundareswaran KS, Gregoric I. PREVENtion of HeartMate II pump thrombosis through clinical management: the PREVENT multi-center study. J Heart Lung Transplant. 2017;36:1–12.
- Aissaoui N, Morshuis M, Schoenbrodt M, Hakim Meibodi K, Kizner L, Borgermann J, Gummert J. Temporary right ventricular mechanical circulatory

support for the management of right ventricular failure in critically ill patients. J Thorac Cardiovasc Surg. 2013;146:186–191.

34. Thakkar B, Patel A, Mohamad B, Patel NJ, Bhatt P, Bhimani R, Patel A, Arora S, Savani C, Solanki S, Sonani R, Patel S, Patel N, Deshmukh A, Mohamad T, Grines C, Cleman M, Mangi A, Forrest J, Badheka AO. Transcatheter aortic valve replacement versus surgical aortic valve replacement in patients with cirrhosis. *Catheter Cardiovasc Interv.* 2016;87:955–962.