Utilization and Outcomes of Temporary Mechanical Circulatory Support Devices in Cardiogenic Shock

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Cardiogenic shock (CS) is associated with high morbidity and mortality despite recent advances in the temporary mechanical circulatory support (MCS) devices. The current utilization and outcomes of these MCS devices with or without vasopressors compared with conventional medical therapy (no-MCS) in CS remain poorly described. The study population was extracted from the 2014 Nationwide Readmissions Database using International Classification of Diseases, Ninth Revision, Clinical Modification codes for CS, temporary MCS devices, and vasopressor infusion. Study end points included in-hospital all-cause mortality, length of index hospital stay (LOS), the likelihood of receiving invasive treatment, postprocedural bleeding, vascular complications, total hospitalization charges, and discharge disposition. A total of 59,148 discharges with a diagnosis of CS were identified (age 67 years; 38.5% female). Temporary MCS devices were utilized in 22.7%. The use of these devices was associated with lower in-hospital all-cause mortality (33.0% vs 39.7%, p <0.01), increased likelihood of invasive therapy (75.7% vs 26.3%, p <0.01), and increased likelihood of being discharged home (24.8% vs 20.6%, p <0.01). However, the MCS group had longer LOS (16.9 vs 12.1 days, p <0.01), higher vascular complications (2.6% vs 1.4%, p <0.01), bleeding (31.2% vs 16.8%, p <0.01), and total hospitalization charges ($374,574 vs $182,045, p <0.01). In conclusion, the use of the temporary MCS devices for the treatment of CS was associated with lower mortality, increased the likelihood of receiving invasive treatment and the likelihood of being discharged home. However, it was associated with higher in-hospital complications, LOS, and hospitalization charges. **(Am J Cardiol 2019;124:505−510)**

Cardiogenic shock (CS) is a state of organ dysfunction secondary to low cardiac output as a result of ventricular failure with an estimated in-hospital mortality of 40% to 50%.[1] Acute myocardial infarction (AMI) is responsible for 80% of CS.[2,3] The incidence of post-AMI CS in the United States increased between 2003 and 2010 from 6.3% to 10.1%.[4] Some studies have shown that early and complete coronary revascularization post-MI CS might improve mortality and outcomes[5,6]; however, the role temporary mechanical circulatory support (MCS) devices is less clear because either the clinical trials have failed to show improved mortality (as in case of intra-aortic balloon pump [IABP]) or due to the lack of outcomes data (as in case of extracorporeal membrane oxygenation [ECMO] and percutaneous ventricular assist devices (PVAD) including Impella and Tandem Heart). Furthermore, there are no robust data supporting the use of vasoactive drugs in CS.[7−13] We sought to conduct this real-world analysis to provide insight into the contemporary treatment of CS, utilization of the temporary MCS devices, the associated outcomes, and cost in the United States.

Methods

The Nationwide Readmissions Data (NRD) is one of the largest collections of deidentified longitudinal hospital care data in the United States, that supports various types of analyses with safeguards to protect the privacy of individual patients, physicians, and hospitals. It contains more than a hundred clinical and nonclinical variables for each hospital stay, including a verified patient linkage number for linking hospital visits for the same patient across hospitals, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes for principal and secondary procedures and diagnoses (including comorbidities and complications), age, gender, length of stay (LOS), and others.[14]

The ICD-9-CM codes were used to search discharges with a diagnosis of CS as a principal or secondary diagnosis, co-morbidities, temporary MCS devices (including IABP, ECMO, percutaneous, and nonpercutaneous devices), vasopressor infusion, in-hospital postprocedural complications, and outcomes of interest (Table 1). The NRD excludes discharges from patients with missing age, missing linkage numbers or from hospitals with more than 50% of their discharges excluded because of these criteria, as patients treated at these hospitals may not be reliably tracked over time.

Co-morbid conditions were identified by the ICD-9-CM codes used in the Medicare and Medicaid diagnosis-related

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See page 509 for disclosure information.

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Table 1
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes used to define discharges, co-morbidities, and in-hospital complications from the Nationwide Readmission Data (NRD) database

Diagnosis	ICD-9-CM Codes
Cardiogenic shock	'78551', '99801'
Acute myocardial infarction	'410.xx'
Subendocardial acute myocardial infarction	'410.7x'
Transmural acute myocardial infarction	'410.xx' except '410.7x'
Mechanical circulatory support devices	'3760' to '3762', '3765','3766','3768', '3965','3966'
Intra-aortic balloon pump	'3761'
Extracorporeal membrane oxygenation	'3965'
Impella/tandem heart	'3768'
Nonpercutaneous mechanical circulatory support devices	'3760', '3762', '3765'
Vasopressor infusion	'0017'
Invasive treatment	'3722', '3723', '8850', '8853' to '8857', 'V4582', '0066', '0059', '3601' to '3607'
Percutaneous coronary intervention	'V4582', '0066', '0065', '3601' to '3607'
Bleeding	'9981', '99811','99812', '9900' to '9909', '2851'
Vascular complications	'900.xx' to '904.xx', 'e8700' to 'e8709', '9992', '9982', '99779' and Dissection '44329' and Fistula '4470' to '4472' and Retroperitoneal bleed '86804' and VC requiring surgery '3931','3932','3941', '3949','3951' to '3953', '3956' to '3959', '3979'
Smoker	'v1582','3051', '30510', '30511','30512', '30513', '98984', '8694'
Coronary artery disease	'4140', '41400' to '41407', '4142', '4143', '4144', '4148', '4149', '412', 'v4582', 'v4581'
Peripheral vascular disease	'440.0' to '440.9' and '441' to '442.9 and '443.1' to '443.9' and '3925', 'v434', '7854', '4471', '5571', '5579'
Hyperlipidemia	'2720' to '2729'
Diabetes mellitus	'249.xx', '250.xx', '3572', '7902.0-9','v4584','v5391', 'v6546')
Hypertension	'401.x', '402.xx', '403.xx', '404.xx', '405.xx', '4372', '36211'
Chronic kidney disease	'v420', 'v451', 'v4511', 'v4512', 'v560', 'v561', 'v562', 'v5631', 'v5632', 'v568', '3995', '5498', '582.xx', '583.xx', '585.x','586' to '589.xx','59000', '59001'
Chronic obstructive pulmonary disease	'490' to '492', and '496'
Heart failure (systolic and diastolic)	'428.xx','40291', '40211', '40201', '39891'
Systolic heart failure	'4282.x', '4284.x'
Atrial fibrillation	'42731'
Atrial flutter	'42732'
Long-term anticoagulation	'V5861'

groups and in the co-morbidity indices. The Patient Safety Indicators (version 4.4, March 2012, which are groups of ICD-9-CM codes used to monitor preventable adverse events during hospitalization) and postprocedural complications codes were used to identify in-hospital complications (Table 1).[15–18] All Healthcare Cost and Utilization Project (HCUP) recommendations and best practices to use the HCUP databases highlighted by Khera et al were followed.[19]

The primary outcomes included in-hospital all-cause mortality, LOS, the likelihood of receiving invasive treatment for suspected ischemic etiology of the CS, postprocedural bleeding, vascular complications (VC), total hospitalization charges, and discharge disposition. The NRD 2014 reports all-cause in-hospital deaths, mean LOS, total hospitalization charges, and discharge disposition for each discharge. The total charges represent how much the hospital billed for the service but not necessarily the actual cost or the amount the hospital actually received. The actual cost was calculated by multiplying the total charges by the cost/charge ratio based on the NRD recommendations.[20] The discharge-to-home excluded discharges to skilled facilities, nursing homes, discharge against medical advice, home health care, in-hospital death or unknown destination.[21] Invasive treatment included left heart catheterization and/or coronary angiogram with/without percutaneous coronary intervention (PCI). PCI included percutaneous coronary angioplasty, insertion of bare metal and/or drug-eluting metal stent. Bleeding included postprocedural bleeding or anemia, or blood or blood product transfusion. VC included accidental puncture or injury of blood vessel or retroperitoneum, or arteriovenous fistula formation.

Statistical Analysis System (SAS) software 9.4 (TS1M4, SAS Institute Inc, Cary, North Carolina) was used for the statistical analysis which was performed on the unweighted (i.e., actual) number of discharges. Pearson Chi-square of Independence test was used to compare categorical variables of the baseline characteristics and outcomes, while the unpaired-sample t Test was used to compare continuous variables. The univariable and multivariable logistic regression models were used to identify predictors of in-hospital all-cause mortality in MCS group by calculating adjusted odds ratios (OR) and 95% confidence intervals (95% CI) for each baseline characteristics and common co-morbidities.[22,23] A 2-tailed p value of <0.05 was used for statistical significance.

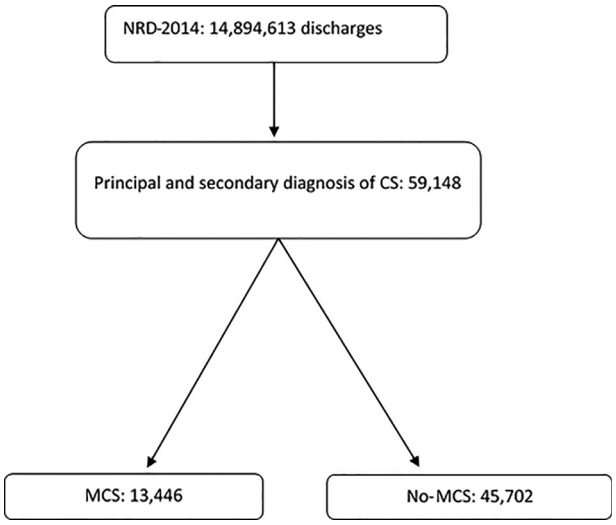

Figure 1. Flow chart demonstrating the extraction of the study population.

Results

In the 2014 NRD database, there were 14.9 million unweighted (actual number) and 36 million weighted (the national estimate which roughly equals 2.2 times actual number) discharges.[14] A total of 59,148 unweighted discharges with either principal or secondary diagnosis of CS were identified (Figure 1); the mean age was 67 years and 38.5% were female. Seventy-four percent of the hospitals were tertiary teaching hospitals, the rest were rural non-teaching hospitals. Of the total CS cohort, 43.4% had a diagnosis of AMI, CS was the principal diagnosis in 0.5%. CS complicated 6.4% of total AMIs in the 2014 NRD database. Temporary MCS devices were utilized in 22.7% of all CS patients. IABP, ECMO, PVAD, and a combination of more than 1 device were used in 83.2%, 8.2%, 10.6%, and 11.5% of MCS group, respectively. The baseline characteristics are shown in (Table 2).

The temporary MCS group was associated with significantly lower in-hospital all-cause mortality (33.0% vs 39.7%, p <0.01, OR 0.75, 95% CI 0.72 to 0.78), was more likely to be treated invasively (75.7% vs 26.3%, p <0.01, OR 8.74, 95% CI 8.36 to 9.14), and was more likely to be discharged home (24.8% vs 20.6%, p <0.01, OR 1.27, 95% CI 1.21 to 1.33). However, the MCS group had longer LOS (16.9 vs 12.1 days, p <0.01), higher VC (2.6% vs 1.4%, p <0.01, OR 1.88, 95% CI 1.65 to 2.14), bleeding (31.2% vs 16.8%, p <0.01, OR 2.24, 95% CI 2.15 to 2.35), and total ($374,574 vs $182,045, p <0.01) and actual ($96,405 vs $46,475, p <0.01) hospital charges (Table 3). Both groups were comparable in terms of 30-day readmission rates (21.1% vs 21.7%, OR 0.97 95% CI 0.91 to 1.03, p = 0.27). Similar results were observed when analysis was performed on AMI associated CS subgroup.

In the subgroup analysis, 68.2% of the total cohort was treated with neither vasopressors nor MCS, 9.0% were treated with vasopressors only, 20.3% were treated with MCS only, and 2.4% were treated with both vasopressors and MCS. The concomitant use of vasopressors with or without MCS was associated with increased mortality (Figure 2). The mortality rates associated with different MCS device types were 30% with IABP, 45% with PVAD, and 50% with ECMO (all p <0.01).

In multivariable logistic regression, AMI, VC, chronic kidney disease, and peripheral vascular disease were associated with increased mortality in MCS group, while invasive treatment and long-term anticoagulation were associated with lower mortality (Supplemental Table 1). MCS device use was a predictor of increased LOS, higher total charges, and increased discharge-to-home.

Table 2
Demographics, baseline characteristics and co-morbidities of cardiogenic shock treated with and without mechanical circulatory support (MCS) devices

	MCS (N = 13,446)	No-MCS (N = 45,702)	p Value
Mean age (years)	64.2	67.8	<0.01
Female	30.9%	40.7%	<0.01
Diagnosis of AMI during hospitalization	66.8%	36.5%	<0.01
Acute myocardial infarction as principal diagnosis	54.3%	20.2%	<0.01
Hypertension	63.2%	62.4%	0.11
Diabetes mellitus	43.8%	39.4%	<0.01
Hyperlipidemia	48.4%	39.3%	<0.01
Chronic kidney disease	28.8%	37.0%	<0.01
Heart failure (systolic or diastolic)	65.2%	61.4%	<0.01
Systolic heart failure	39.4%	31.6%	<0.01
Chronic coronary artery disease	73.6%	50.7%	<0.01
Atrial fibrillation	30.5%	35.6%	<0.01
Atrial flutter	7.3%	7.1%	0.40
Long-term anticoagulation	5.0%	8.0%	<0.01
Smoker	17.2%	13.1%	<0.01
Peripheral vascular disease	14.9%	14.7%	0.60
Chronic obstructive pulmonary disease	15.1%	20.5%	<0.01

Discussion

This study shows that in patients with CS, the use of temporary MCS was associated with lower in-hospital all-cause mortality, increased likelihood of invasive treatment, and improved rate of discharge-to-home from the hospital. However, MCS use was associated with longer LOS, VC, bleeding, and total hospitalization charges, and similar 30-day readmission rates. It also shows 68% of CS were neither treated with vasopressor nor MCS devices, possibly because there is no CS treatment with proven benefit, 26% of the hospitals were small rural, and CS was a principal diagnosis in 0.5% only which might indicate that the diagnosis was overlooked and subsequently undertreated.

There are a number of potential mechanisms by which the use of temporary MCS devices reduces mortality in CS as shown in this study. The use of MCS reduces left ventricular filling pressures, wall stress, and increases coronary perfusion which might potentially reduce microvascular injury, infarct size, and myocardial cell death especially when utilized early in the course of the

Table 3
Comparison of the study outcomes between cardiogenic shock treated with mechanical circulatory support (MCS) versus no-MCS devices

Outcome/Group	MCS	No-MCS	OR	95% CI	p Value
All-cause mortality	33.0%	39.7%	0.75	0.72-0.78	<0.01
Mean length of stay (days ± SD)	16.9 (21.3)	12.1 (15.6)	-	-	<0.01
Bleeding	31.2%	16.8%	2.24	2.15-2.35	<0.01
Received invasive treatment	75.7%	26.3%	8.74	8.74-9.14	<0.01
Vascular complications	2.6%	1.4%	1.88	1.65-2.14	<0.01
Discharge to home	24.8%	20.6%	1.27	1.21-1.33	<0.01
Total charges	$374,574	$182,045	-	-	<0.01
Actual charges	$96,405	$46,475	-	-	<0.01

OR = odds ratio; SD = standard deviation; 95% CI = 95% confidence interval.

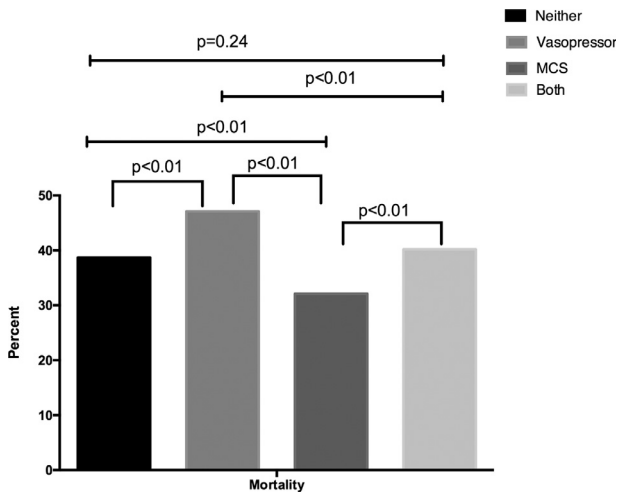

Figure 2. In-hospital all-cause mortality of cardiogenic shock treated with: neither vasopressors or mechanical circulatory support (MCS), vasopressors only, MCS only and both vasopressors and MCS.

CS.[24,25] MCS use is known to enable complete coronary revascularization more frequently which is also associated with greater improvement in myocardial function.[26] Furthermore, the large size of the study ensured appropriate power to address the clinical utility of MCS use in CS. AMI, VC, chronic kidney disease, and peripheral vascular disease were all predictors of increased mortality in the MCS group, while early invasive treatment was a predictor of lower mortality.

CS causes mortality by several mechanisms including hemodynamic deterioration, metabolic disruption, systemic inflammation, and consequently multiorgan failure. Although the use of MCS addresses the perfusion and hemodynamic deterioration, it may not address the metabolic, inflammatory, and late-stage organ failure consequences. This fact might have confounded the conflicting results of the previous studies of MCS use in CS.[7] The complications associated with the use of these devices might also have attenuated the potential benefits. In addition, the most unstable CS patients had been excluded from many trials.[7,12] When the most critically ill CS patients, including postcardiac arrest, were included in the randomized studies, there was no clear signal of a benefit from these devices.[9] Furthermore, most previous studies were underpowered to show a mortality reduction.[7,24] It is worthwhile mentioning that device-specific mortality rates in this study for IABP, PVAD, and ECMO were 30%, 45%, and 50%, respectively. This likely reflects selection bias, sicker patients were more likely to be treated with PVAD or ECMO.

Although vasopressor use in CS treatment is cited in the practice guidelines, it is not supported by robust evidence from clinical trials and is associated with increased myocardial oxygen demand and arrhythmias.[11–13] Moreover, previous studies suggested that vasopressor use increased mortality in both septic and CS.[27,28] The present study shows that vasopressor use, with/without MCS was associated with increased mortality, with the highest mortality observed in vasopressor-only treated CS subgroup, and concurrent use with MCS abolished the mortality benefit seen in the MCS-only treated subgroup. It is unclear whether this association represents a cause-effect relation or selection bias (i.e., sicker patients did not receive MCS).

The cost of the MCS devices and the associated complications, and the longer LOS are factors that could have contributed to the higher hospitalization cost. The average actual cost of ST-elevation AMI complicated by CS was around 46,000$ which is close to the no-MCS group of this study.[4] However, the use of MCS was associated with almost double the cost. This high cost highlights an important issue of whether or not MCS devices would be a cost-effective intervention. The cost-effectiveness should include quantity and quality measures of life gained by certain intervention, that is quality-adjusted life year. Previous data had suggested that certain MCS devices could be cost-effective in the long-term.[29] Although this study shows increased in-hospital cost, it also shows that MCS-treated patients are more likely to be discharged to home and that likely correlates with better functional status and quality of life in the long-term.

Compared with current literature, this study has a large sample size and represents a real-world practice and outcomes of CS in the United States. It supports current guidelines for utilizing MCS devices in CS. It shows that the national estimate of MCS utilization in CS treatment was 22.7% which could indicate that these devices are underutilized and CS is undertreated. The study also highlights a possible detrimental effect and increased death with vasopressor use in CS settings.

This study has several limitations. It is a retrospective; heterogeneity is an unavoidable factor because the CS population represents a very diverse population with variable illness severity and co-morbidities. Some of the ICD-9-CM codes are not specific to one vasopressor or MCS device, access, or time of insertion (i.e., early vs late, before, or after PCI). The IABP (which provides the least circulatory support)[7] was the most common MCS device used in this study, which might have confounded the results. The use of other MCS devices (PVAD and ECMO) has increased in recent years, however, randomized comparisons of MCS devices have not shown a differential benefit.[9,30,31] The time and completeness of coronary revascularization could not be determined. Finally, longer-term outcomes could not be assessed.

In conclusion, the use of MCS devices for the treatment of CS was associated with lower in-hospital mortality and higher discharge-to-home despite the increased complications, LOS, and cost, and similar 30-day readmission rate. Isolated vasopressors infusion or concomitant with MCS, was associated with increased mortality.

Disclosures

All authors have no conflict of interest, financial disclosure or relationship with industry.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.05.032.

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