BMC Cardiovascular Disorders

RESEARCH

Open Access

Risk of acute ischemic stroke with early versus late initiation of mechanical circulatory support in hospitalizations with acute myocardial infarction complicated by cardiogenic shock: a propensity-matched analysis

Rui Yan[2,1], Jie Yang[2,3,4], Bo Shi[1,2], Congyan Ye[1,2], Shizhe Fu[1,2], Kairu Wang[1,2], Ru Yan[2,3,4], Shaobin Jia[2,3,4,5,6*], Xueping Ma[2,3,4,5,6*] and Guangzhi Cong[2,3,4*]

Abstract

Background Mechanical circulatory support (MCS) devices have been widely used for managing acute myocardial infarction complicated by cardiogenic shock (AMI-CS). However, their use additionally elevates acute ischemic stroke (AIS) risk. There is insufficient data on the risk of AIS associated with early versus late initiation of MCS in AMI-CS cases. Therefore, this study aimed to assess the timing of MCS initiation associated with the risk of AIS in hospitalizations with AMI-CS.

Methods A retrospective data analysis of the National Inpatient Sample (January 2016–December 2020) identified AMI-CS hospitalizations: categorized into early MCS initiation (< 48 h) and late MCS initiation (> 48 h). The primary outcome was AIS; the secondary outcomes included in-hospital mortality, acute kidney injury (AKI), cardiac arrest, major bleeding, and blood transfusion. The outcomes were compared using logistic multivariate regression and 1:1 propensity score matching analyses between the groups.

Results Among 78,405 weighted hospitalizations with AMI-CS receiving MCS, 82.77% ($n = 64,895$) and 17.23% ($n = 13,510$) underwent early and late MCS initiation, respectively. Hospitalizations with late MCS initiation had higher risks of AIS (adjusted odds ratio [aOR], 1.46; 95%confidence interval [CI], 1.19–1.79; $p < 0.001$), AKI (aOR, 1.41; 95%CI, 1.27–1.55; $p < 0.001$), and major bleeding (aOR, 1.12; 95%CI, 1.01–1.23; $p = 0.028$). After propensity score matching, late

Jie Yang, Ru Yan, Shaobin Jia, Xueping Ma and Guangzhi Cong these authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

*Correspondence:
Shaobin Jia
jsbxn@163.com
Xueping Ma
maxueping4033@126.com
Guangzhi Cong
schatz1898@gmail.com
Full list of author information is available at the end of the article

MCS initiation remained associated with increased risks of AIS (aOR, 1.39; 95%CI, 1.08–1.78; $p=0.010$), AKI (aOR, 1.37; 95%CI, 1.23–1.53; $p<0.001$), and major bleeding (aOR, 1.14; 95%CI, 1.02–1.28; $p=0.027$).

Conclusions Late initiation of MCS was associated with increased risks of AIS, AKI, and major bleeding.

Keywords Acute ischemic stroke, Acute myocardial infarction, Cardiogenic shock, Mechanical circulatory support, Propensity score matching

Background

Cardiogenic shock (CS) remains the most common cause of death in hospitalizations with acute myocardial infarction (AMI) [1, 2]. Despite using early revascularization, in-hospital mortality due to AMI complicated by CS (AMI-CS) remains continually high, with rates ranging between 38 and 50% [3–5]. Supportive medical therapies, such as inotropes, have failed to improve outcomes in this setting. Therefore, percutaneous mechanical circulatory support (MCS) devices including intra-aortic balloon pumps (IABPs); extracorporeal membrane oxygenation (ECMO); and percutaneous ventricular assist devices, such as Impella and TandemHeart, are frequently utilized to improve cardiac output and blood supply to the essential organs [6]. However, MCS use is linked to high rates of stroke, increasing the risk of both mortality and disability [7–10].

Stroke is one of the leading complications following MCS placement [11, 12]. According to several studies, the incidence of stroke associated with these technologies falls between 3 and 14% [7, 13–16]. Regarding the mechanisms underlying this increased risk of stroke, many versions of research share concerns, implicating MCS devices for disrupting atheromatous plaques on the aorta wall and acting as a thrombogenic nidus, which could result in embolism into the cerebral vasculature [12]. Other device-specific mechanisms of stroke associated with IABPs include air embolism due to ruptured balloons and IABP malposition, which could obstruct the major arteries and cause cerebral ischemia [17]. Regarding the other MCS devices (Impella, TandemHeart, and ECMO), shear-mediated platelet fragmentation has the potential to induce an inflammatory and coagulopathic milieu. This could ultimately result in microthrombi production and pump thrombosis [18].

The timing of MCS initiation may impact the incidence rate of stroke. However, the impact of the timing of initiation of these devices on stroke in hospitalizations with AMI-CS remains mostly unknown. A deeper comprehension about how the timing of MCS implantation could impact neurologic events among hospitalizations with AMI-CS may lead to improved clinical management. Therefore, our analysis aimed to investigate trends surrounding the use of MCS devices and assess the relationship between acute ischemic stroke (AIS) and the timing of MCS initiation during hospitalization in hospitalizations with AMI-CS.

Methods

Study design and patient population

The National Inpatient Sample (NIS) database was sponsored by the Agency for Healthcare Research and Quality (Healthcare Cost and Utilization Project). It is the largest publicly available all-payer inpatient care database in the United States, including over 7 million unweighted hospitalizations annually and over 100 clinical and non-clinical data elements. When weighted, the NIS database is estimated to include more than 35 million hospitalizations nationally. The discharge weight variable from the Healthcare Cost and Utilization Project could be used to determine the national estimate [19]. Inpatient diagnoses and procedures were coded by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) and Procedure Coding System (ICD-10-PCS) (Table S1), and Elixhauser Comorbidity Software Refined for ICD-10-CM, provided by the Healthcare Cost and Utilization Project, was used to identify comorbidities (Table S2). The NIS database has been previously validated to be possibly used for characterizing the prevalence and consequences of cardiovascular disease [20, 21].

Since the NIS contains deidentified patient information and is accessible to the public, there was no requirement for consent to participate and it was deemed exempt from the Institutional Review Board approval requirement.

The NIS data from 2016 to 2020 was retrospectively reviewed to identify hospitalizations admitted with AMI in the primary diagnosis field (ICD-10-CM I21.x) and a secondary diagnosis of CS (ICD-10-CM R57.0) The accuracy of ICD-10 codes to identify AMI and CS has been previously validated with high specificity and sensitivity [22–24]. We identified the use of MCS devices (IABP, Impella, and ECMO) using the ICD-10-PCS codes (Table S1). Hospitalizations aged < 18 years at hospital admission; receiving no MCS or receiving MCS before admission; and with missing data (age, sex, race, payer, income quartile, year, hospital region, teaching status, bed size, and died) were excluded (Fig. 1). We divided the hospitalizations into the two groups according to whether the MCS was started earlier (< 48 h) or later (> 48 h). The

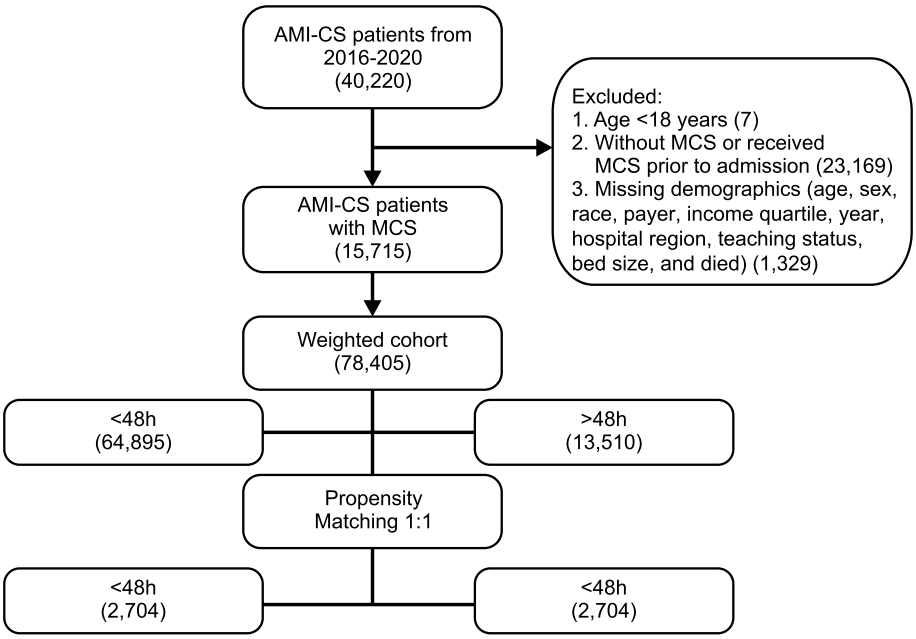

Fig. 1 Flowchart of patient selection. AMI-CS, acute myocardial infarction complicated by cardiogenic shock; MCS, mechanical circulatory support

primary endpoint was an AIS during hospitalization. The secondary endpoints included inhospital mortality, acute kidney injury (AKI), cardiac arrest, major bleeding, and blood transfusion. Additionally, we investigated trends in the use of MCS devices and in the incidence of AIS from 2016 to 2020.

Statistical analysis

Continuous data were expressed as mean ± SD or median with its interquartile range if the normal distribution was not satisfied. Categorical variables are expressed as numbers and percentages for demographics, clinical features, and study outcomes. As advised by the Healthcare Cost and Utilization Project for the use of the NIS data set, discharge weights were applied to the national estimates. The impact of the timing of MCS on in-hospital outcomes was assessed using multivariable logistic regression; data are presented as adjusted odds ratio (aOR) with a 95%confidence interval (CI). The variables included in the model were age, sex, race, hypertension, diabetes mellitus, congestive heart failure, smoking, atrial fibrillation, ventricular tachycardia, prior percutaneous coronary intervention (PCI), prior myocardial infarction, and prior coronary artery bypass grafting (CABG). Dyslipidemia; coagulopathy; liver disease; fluid and electrolyte disorder; other neurological disorders; pulmonary circulation disorders; valvular disease; chronic anticoagulation; chronic antiplatelet; thrombolysis; vasopressor use; and coronary angiography, CABG, and PCI were also among the variables included in the model. Differences between continuous variables were evaluated using the Mann–Whitney U test, while differences between categorical variables were assessed using the $\chi 2$ test; the corresponding aOR and 95%CI are presented as forest plots. Propensity score matching (PSM) was applied to balance between confounders across hospitalizations with early and late initiation of MCS via multivariable logistic regression by including the above baseline variables. A 1:1 matching procedure without replacement (greedy-matching method) was used for matching, with a caliper width equal to 0.02 of the standard deviation of the logit of the propensity score. Standardized mean differences (SMD) for all baseline variables were calculated to evaluate the balance of baseline characteristics between before and after matching. A baseline variable was considered well-balanced when the SMD was less than 0.10. To obtain a balanced distribution of all the covariates in the PSM cohort, if any baseline features did not satisfy the balanced distribution, a second adjustment ("double adjustment") was performed to eliminate any residual confounding deviations after PSM [25]. The R statistical software package (http://www.R-project.org; The R Foundation) and EmpowerStats (http://www.empowerstats.com; X&Y Solutions, Inc., Boston, MA, USA) were used for all analyses. A two-sided P value < 0.05 was considered statistically significant for all comparisons.

Results

Population characteristics

From January 2016 to December 2020, there were weighted data for 78,405 hospitalizations with AMI-CS undergoing MCS. Among this cohort, 82.77% ($n=$ 64,895) underwent early initiation of MCS within 48 h, whereas 17.23% ($n=$ 13,510) underwent late initiation of MCS after 48 h (Fig. 1). Hospitalizations receiving late initiation of MCS were older (67.85 years vs. 66.14 years, $p<$ 0.001) and female (32.68% vs. 29.95%, $p=$ 0.007). Race, income quartile, hospital region, and teaching status were evenly distributed in both arms.

A comparison between the comorbidity profiles in our cohort found that hospitalizations with early device placement exhibited a statistically significant increase in family history of coronary artery disease, smoking, and drug abuse (all, $p<$ 0.050). In contrast, hospitalizations with late device placement had a statistically significant increase in atrial fibrillation, congestive heart failure, valvular disease, chronic pulmonary disease, pulmonary circulation disorder, diabetes mellitus, hypertension, chronic renal failure, and peripheral vascular disease (all, $p<$ 0.050). Overall, the hospitalizations with late initiation MCS had a higher burden of Elixhauser comorbidities (comorbidity index >4, 50.74% vs. 31.97%, $p<$ 0.001). The hospitalizations with early MCS initiation were more likely to have undergone coronary angiography (58.17% vs. 54.55%, $p=$ 0.019) or PCI (65.62% vs. 42.49%, $p<$ 0.001), while those with late MCS initiation were more likely to have undergone CABG (44.82% vs. 17.80%, $p<$ 0.001). The hospitalizations in the early group were more likely to have received IABP (72.99% vs. 69.84%, $p=$ 0.003), while those in the late group were more likely to have received Impella (30.68% vs. 29.69%, $p=$ 0.445) and ECMO (8.25% vs. 5.15%, $p=$ 0.001) (Table 1). With the nonrandomized design and imbalanced baseline in mind, PSM produced a cohort of 2704 hospitalizations with AMI-CS with early MCS initiation and 2704 hospitalizations with late MCS initiation. Matching eliminated almost all significant differences in demographics, payment source, hospital characteristics, clinical characteristics, and comorbidity prevalence between the two cohorts (Table S3 and Figure S1).

Temporal trends in MCS utilization and stroke incidence

From 2016 to 2020, the use of IABP decreased from 35.89% to 30.21%, whereas Impella use increased from 8.49% to 15.27%, and ECMO use increased from 2.05% to 2.90% (Figure S2). The incidence of AIS in hospitalizations with AMI-CS receiving MCS remained stable over the study period: 3.55% in 2016 and 4.54% in 2020 (P trend =0.277) (Figure S3).

In-hospital outcomes

Compared with hospitalizations with early MCS initiation, hospitalizations with late MCS initiation were associated with statistically significant increases in AIS (5.74% vs. 3.60%; aOR, 1.46; 95%CI, 1.19–1.79; $p<$ 0.001), AKI (61.73% vs. 50.40%; aOR, 1.41; 95%CI, 1.27–1.55; $p<$ 0.001), and major bleeding (43.19%2 vs. 9.72%; aOR, 1.12; 95%CI, 1.01–1.23; $p=$ 0.028). There were no significant differences between the groups in terms of incident in-hospital mortality, cardiac arrest, and blood transfusion ($p>$ 0.05) (Table 2 and Fig. 2). PSM analysis revealed that the hospitalizations with late MCS initiation remained associated with an increased risk of AIS (5.70% vs. 4.14%; aOR, 1.39; 95%CI, 1.08–1.78; $p=$ 0.010), AKI (61.69% vs. 53.55%; aOR, 1.37; 95%CI, 1.23–1.53; $p<$ 0.001), and major bleeding (43.27% vs. 38.50%; aOR, 1.14; 95%CI, 1.02–1.28; $p=$ 0.027) (Table 3 and Fig. 3). Furthermore, subgroup analysis revealed that an AMI-CS hospitalization with late MCS was consistently associated with a high AIS risk among all subgroups (Fig. 4).

Discussion

In this nationwide retrospective cohort study of MCS use for AMI-CS, we evaluated the impact of the timing of initiation of MCS on in-hospital outcomes. The main findings were: First, during the study period, the use of Impella and ECMO increased, whereas the use of IABP decreased with the passage of time. Second, occurrence of AIS was significantly higher in hospitalizations who received MCS 48 h after admission compared with in those who received it within 48 h. Third, late initiation of MCS was also associated with an increased risk of AKI and major bleeding.

Barssoum et al.'s [26] study assessing the effects of mechanical support on non-AMI-CS reported results different from the results of our study. As opposed to this study, we chose the cohort undergoing hospitalization based on acute AMI codes. In our study, we found that from 2016 to 2020, the use of IABP declined, whereas the use of Impella and ECMO increased over time, which is consistent with the findings of previous reports that demonstrated a shift toward use of novel MCS devices [27, 28]. We further identified that the incidence of AIS in hospitalizations with AMI-CS with MCS remained stable over the study period.

In our analysis, the incidence of AIS was higher in the late initiation group, both using multivariable logistic regression and PSM analysis. This positive effect was evident in all subgroups considered and after adjustments. This can be explained in various ways. First, we observed increased prevalence of classic risk factors for atherosclerosis in the group of late MCS initiation as this group

Table 1 Baseline and hospital characteristics before propensity score matching (weighted)

Variables[a]	< 48 h *n* = 64,895	> 48 h *n* = 13,510	*P*-value
Age	66.14 (65.78,66.50)	67.85 (67.34,68.36)	< 0.001
Sex			0.007
Male	70.05 (69.08,71.01)	67.32 (65.58,69.01)	
Female	29.95 (28.99,30.92)	32.68 (30.99,34.42)	
Race			0.758
White	74.04 (72.48,75.54)	73.50 (68.94,77.61)	
Black	8.24 (7.44,9.12)	8.96 (7.39,10.82)	
Hispanic	9.06 (8.15,10.07)	9.36 (7.67,11.38)	
Other	8.65 (8.12,9.21)	8.18 (6.67,9.99)	
Payer			0.002
Medicare/Medicaid	64.20 (63.19,65.19)	68.39 (64.96,71.64)	
Private insurance	27.13 (26.19,28.09)	21.98 (20.36,23.70)	
Self-pay	5.35 (4.85,5.91)	3.77 (2.96,4.81)	
No charge/Other	3.32 (2.90,3.80)	5.85 (2.78,11.87)	
Income Quartile			0.902
0 to 25	28.89 (27.61,30.19)	28.09 (23.78,32.84)	
26 to 50	27.02 (25.98,28.09)	26.50 (24.54,28.55)	
51 to 75	24.35 (22.53,26.27)	25.02 (22.99,27.16)	
76 to 100	19.74 (18.11,21.48)	20.39 (18.16,22.82)	
Hospital region			0.210
Northeast	22.80 (18.16,28.21)	25.20 (15.66,37.94)	
Midwest	22.15 (20.53,23.86)	18.80 (15.75,22.29)	
South	40.17 (37.42,42.98)	42.15 (35.73,48.85)	
West	14.88 (13.71,16.13)	13.84 (11.52,16.55)	
Teaching status			0.565
Rural	7.83 (7.14,8.58)	7.07 (5.74,8.68)	
Urban nonteaching	77.93 (76.27,79.51)	78.65 (74.85,82.01)	
Urban teaching	14.24 (13.16,15.39)	14.29 (11.92,17.03)	
Bed size			< 0.001
Small	13.21 (12.02,14.49)	10.62 (8.77,12.82)	
Medium	28.23 (26.16,30.40)	24.17 (20.40,28.38)	
Large	58.56 (55.65,61.42)	65.21 (59.50,70.51)	
Prior MI	11.67 (10.67,12.76)	13.10 (10.91,15.65)	0.120
Prior PCI	12.02 (10.99,13.13)	10.66 (8.83,12.81)	0.117
Prior CABG	5.92 (5.37,6.51)	7.88 (6.46,9.59)	0.001
Prior CVA	5.00 (4.44,5.63)	5.81 (4.70,7.16)	0.137
Prior PPM or ICD	1.23 (1.04,1.45)	1.92 (1.40,2.63)	0.007
Smoking	42.08 (40.55,43.64)	36.57 (33.19,40.08)	< 0.001
Alcohol abuse	4.28 (3.66,5.01)	3.77 (2.96,4.81)	0.328
Drug abuse	3.52 (2.94,4.22)	2.33 (1.75,3.10)	0.009
Obesity	16.87 (15.60,18.21)	18.84 (15.85,22.25)	0.086
Family history of CAD	9.42 (8.47,10.45)	6.70 (5.42,8.26)	< 0.001
Known CAD	6.69 (6.08,7.35)	8.99 (7.41,10.87)	< 0.001
Dyslipidaemia	54.82 (53.06,56.57)	56.25 (50.05,62.27)	0.571
Carotid artery disease	1.77 (1.53,2.05)	4.55 (3.62,5.70)	< 0.001
Atrial fibrillation	23.77 (22.07,25.55)	32.94 (29.83,36.20)	< 0.001
Ventricular fibrillation	21.74 (20.97,22.52)	12.88 (10.74,15.37)	< 0.001
Ventricular tachycardia	25.36 (24.45,26.28)	23.43 (21.48,25.50)	0.086
Congestive heart failure	18.68 (17.50,19.93)	23.43 (19.69,27.63)	0.002

Table 1 (continued)

Variables[a]	< 48 h *n* = 64,895	> 48 h *n* = 13,510	*P*-value
Chronic pulmonary disease	16.98 (15.70,18.34)	21.98 (18.55,25.85)	< 0.001
Pulmonary circulation disorder	7.85 (7.27,8.48)	14.51 (12.14,17.25)	< 0.001
Coagulopathy	18.99 (17.60,20.46)	27.68 (25.24,30.27)	< 0.001
Diabetes mellitus	39.92 (38.88,40.97)	48.56 (41.16,56.02)	0.015
Hypertension	53.44 (51.75,55.12)	59.88 (53.07,66.33)	0.025
Hypothyroidism	9.18 (8.32,10.11)	9.73 (8.05,11.73)	0.470
Liver disease	18.50 (17.53,19.51)	19.25 (17.72,20.87)	0.359
Fluid and electrolyte disorder	58.22 (57.25,59.18)	65.88 (62.74,68.88)	< 0.001
Other neurological disorder	21.57 (20.75,22.42)	19.84 (18.25,21.52)	0.047
Peripheral vascular disease	11.79 (11.13,12.48)	15.91 (13.33,18.89)	< 0.001
Chronic renal failure	22.41 (21.11,23.76)	38.19 (34.61,41.91)	< 0.001
Valvular disease	15.12 (14.28,16.00)	27.17 (24.97,29.48)	< 0.001
Rheumatoid arthritis. collagen vascular disease	1.79 (1.54,2.07)	2.11 (1.57,2.84)	0.280
Intracardiac thrombus	1.59 (1.11,2.27)	1.96 (1.44,2.67)	0.359
Elixhauser comorbidities			< 0.001
0	4.61 (3.82,5.54)	0.63 (0.38,1.03)	
1–4	63.43 (62.20,64.63)	48.63 (42.92,54.38)	
> 4	31.97 (30.21,33.78)	50.74 (45.09,56.37)	
Chronic anticoagulation	4.26 (3.83,4.74)	5.59 (4.50,6.92)	0.006
Chronic antiplatelet	5.23 (4.72,5.79)	5.51 (4.43,6.85)	0.594
Vasopressor use	13.19 (11.32,15.31)	11.44 (9.41,13.84)	0.367
CABG	17.80 (16.93,18.70)	44.82 (40.93,48.77)	< 0.001
PCI	65.62 (64.27,66.95)	42.49 (38.33,46.75)	< 0.001
Thrombolysis	1.31 (1.10,1.55)	0.89 (0.58,1.36)	0.079
Coronary angiography	58.17 (55.24,61.05)	54.55 (52.53,56.55)	0.019
Invasive hemodynamic monitoring	26.94 (24.30,29.76)	26.87 (24.47,29.41)	0.975
MCS			
IABP	72.99 (71.78,74.18)	69.84 (68.03,71.59)	0.003
Impella	29.69 (28.62,30.78)	30.68 (28.06,33.44)	0.445
ECMO	5.15 (4.60,5.75)	8.25 (6.90,9.85)	< 0.001

CAD coronary artery disease, *CABG* coronary artery bypass grafting, *ECMO* extracorporeal membrane oxygenation, *IABP* intra-aortic balloon pump, *MI* myocardial infarction, *PCI* percutaneous coronary intervention, *CVA* cardiovascular accident, *PPM* permanent pacemaker, *ICD* implantable cardioverter defibrillator, *MCS* mechanical circulatory support

[a] Values are percentage or median (interquartile range)

Table 2 Comparison between in-hospital outcomes in the overall cohort

In-hospital outcomes[a]	< 48 h *n* = 64,895	> 48 h *n* = 13,510	*P*-value
Acute ischemic stroke	3.60 (3.22,4.02)	5.74 (4.33,7.56)	0.008
In-hospital mortality	31.12 (30.13,32.13)	28.05 (23.75,32.80)	0.170
Acute kidney injury	50.40 (48.95,51.85)	61.73 (59.11,64.28)	< 0.001
Cardiac arrest	12.86 (12.12,13.64)	11.32 (9.40,13.59)	0.147
Major bleeding	29.72 (27.72,31.80)	43.19 (40.66,45.76)	< 0.001
Transfusion	10.60 (9.83,11.42)	15.14 (12.63,18.04)	0.001

[a] Values are percentage or median (interquartile range)

included more hospitalizations who were older, were female, and had comorbidities such as diabetes mellitus, hypertension, and atrial fibrillation [29]. However, the risk of AIS remained higher in the late group after adjustment for these confounding variables. Second, previous studies have reported that different MCS devices could carry varying risks of stroke. Hospitalizations receiving IABP had a low risk of stroke. The randomized SHOCK II trial showed that the rate of hospitalizations with AMI-CS was 0.7% [15], while the rate of individuals receiving Impella was 3.6% [7]. Compared with IABP and Impella devices, although ECMO is advised in hospitalizations with profound CS, it is associated with a significantly

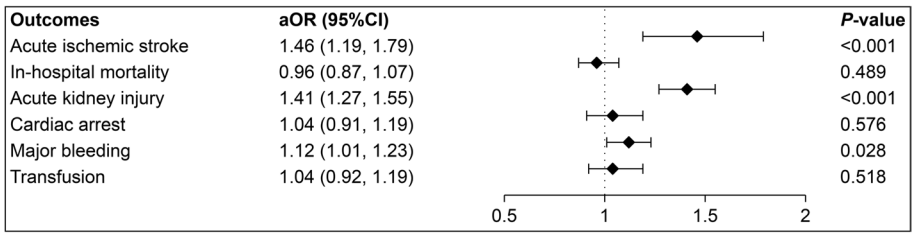

Fig. 2 Forest plot of multivariable regression analysis to predict in-hospital outcomes in overall hospitalizations. CI, confidence interval; aOR, adjusted odds ratio

Table 3 Comparison between in-hospital outcomes in the matched cohort

In-hospital outcomes[a]	< 48 h *n* = 2,704	> 48 h *n* = 2,704	*P*-value
Acute ischemic stroke	112 (4.14%)	154 (5.70%)	0.008
In-hospital mortality	759 (28.07%)	760 (28.11%)	0.976
Acute kidney injury	1448 (53.55%)	1668 (61.69%)	< 0.001
Cardiac arrest	310 (11.46%)	306 (11.32%)	0.864
Major bleeding	1041 (38.50%)	1170 (43.27%)	< 0.001
Transfusion	358 (13.24%)	408 (15.09%)	0.051

[a] Values are expressed as n (%)

increased risk for stroke [7]. The incidence of ischemic stroke in hospitalizations undergoing ECMO varies from 4.2% to 15.0% [13, 30]. Veno-arterial (VA)-ECMO is frequently used as a femoral venous to femoral arterial circuit. It may increase the risk of stroke by necessitating systemic anticoagulation, encouraging aortic root or left ventricle thrombosis, elevating systemic inflammation, or inducing systemic hemolysis [12, 31]. Additionally, North–South syndrome is a frequent complication of VA-ECMO with which patient's blood has low oxygen content being expelled from the left heart due to insufficient lung function or ventilator assistance. Competition for deoxygenated blood from normal circulation results from the ECMO cannula's retrograde input of oxygenated blood from the femoral artery. It causes significant bilateral cerebral hypoxia [32]. In this study, we found that IABP was more used within 48 h, whereas Impella and ECMO were more used after 48 h, increasing the risk of stroke. Third, PCI was the most common revascularization strategy in both patient types [1]. However, we found that more hospitalizations with late MCS initiation compared with those with early MCS underwent CABG therapy. In hospitalizations with CS, CABG can raise the risk of hypoperfusion and embolize atheromatic plaques from the ascending aorta during surgery, which can increase the risk of stroke [33, 34].

Fourth, MCS can lead to coagulation-related complications, including device-related thrombosis and thromboembolic phenomena. Supraphysiological shear stress exposure of blood cellular and protein constituents traveling through these devices is central in this MCS-related coagulopathy. Shear-mediated platelet activation can stimulate coagulopathy and inflammation, which can result in thrombosis [35]. In addition, these devices also degrade von Willebrand Factor multimers [36]. Anticoagulation with unfractionated heparin is the standard of care for preventing thromboembolic complications while on most types of MCS. Heparin-induced thrombocytopenia is thought to occur between 0.1% and 5.0% of the time and can result in venous and arterial thromboembolism [37]. The presence of an endovascular device may increase this risk to a further extent. In our study, the hospitalizations with late initiation of MCS had a higher prevalence of coagulopathy. The resulting thrombocytopenia and acquired coagulopathy could increase the risk of strokes.

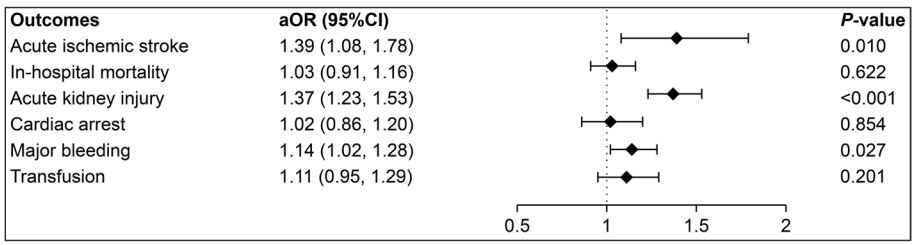

Fig. 3 Forest plot of multivariable regression analysis to predict in-hospital outcomes in propensity score–matched hospitalizations. CI, confidence interval; aOR, adjusted odds ratio

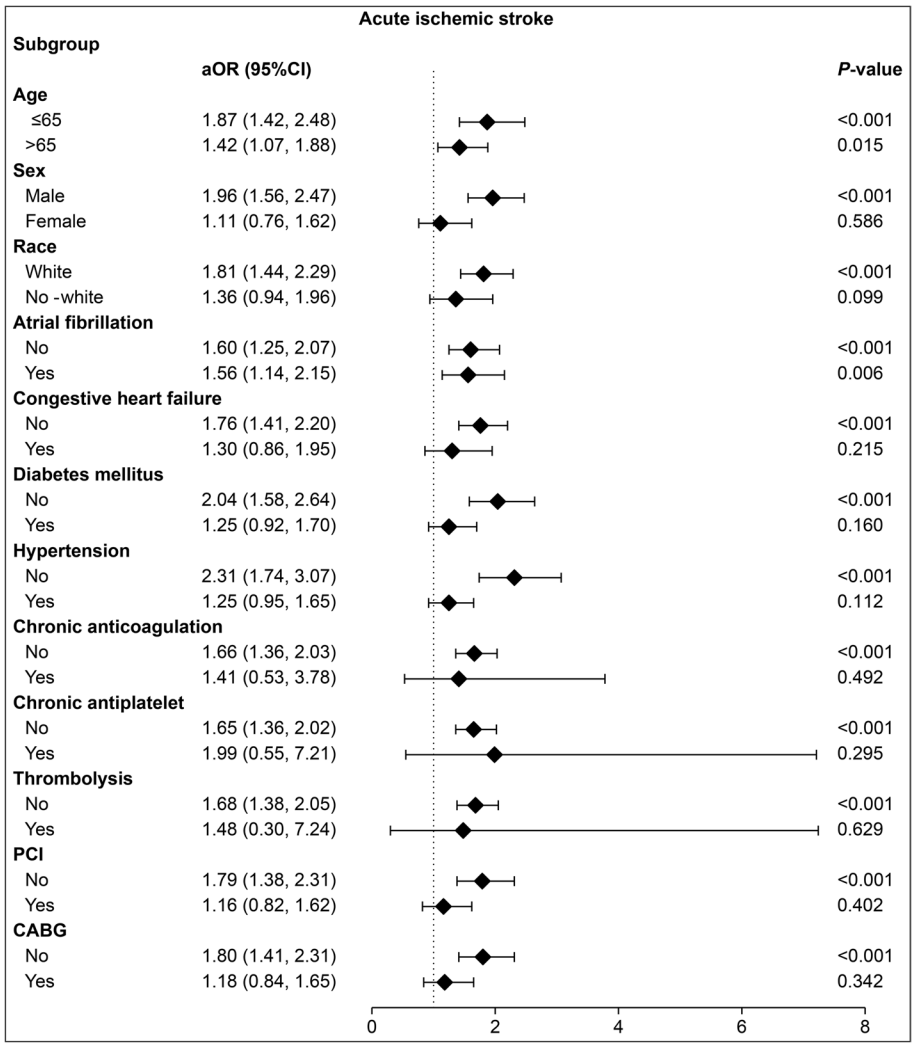

Fig. 4 Subgroup analyses of acute ischemic stroke for AMI-CS with early and late MCS. aOR, adjusted odds ratio; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention

This analysis further found that the late initiation group had a higher incidence of AKI and major bleeding. This can be explained by the fact that the late group included older hospitalizations with more comorbidities; the impact persisted even after adjustment for baseline characteristics. On the other hand, the late group had higher utilization of Impella and ECMO. However, Impella and ECMO were associated with more bleeding and more AKI [38].

The present study has some limitations. First, identifying the specific causes of early versus late MCS initiation was impossible. The patient condition (the severity of CS and response to initial treatment), logistics (staff and equipment availability), and institutional or provider preferences could have influenced the timing of MCS initiation. Second, we could not ascertain the actual CS onset, preventing us from determining the time from CS onset to MCS initiation, which could have been different from the time from admission to MCS initiation. In addition, a key limitation is the inability to establish temporal relationships between AIS and MCS in the NIS database, potentially affecting causal interpretation. Third, the administrative database lacked clinical details, such as biochemistry analyses, medications, and imaging data. In addition, since this is an observational study using retrospective data, selection bias and unmeasured confounding factors could not have been avoided; other possible sources of bias including coding errors and underreporting of secondary diagnoses might have existed. Nevertheless, numerous internal and external validations have been performed on the NIS. Moreover, to ensure the NIS database's internal validity, yearly evaluations of data quality were carried out [39].

Despite these limitations, the NIS is a large and reliable database containing hospitalized patient data from over 4,000 hospitals in over 30 states in the United States, which can be applied to the entire American population. Moreover, our study provides the largest contemporary evaluation of the association between MCS initiation delays and higher AIS rates in a large-scale national study. Further, using contemporary databases, we extensively analyzed trends in the use of multiple MCS devices including IABP, Impella, and ECMO. Furthermore, robust analyses were performed before and after PSM; and subgroup analysis was also performed.

Conclusion

Among hospitalizations with AMI-CS, late initiation of MCS significantly increased the risk of AIS. It was also associated with increased risks of AKI and major bleeding. Our study suggested that early initiation of MCS in hospitalizations with AMI-CS could reduce the risk of AIS and other complications. Further studies are needed to decipher the optimal timing of MCS initiation to improve outcomes in this critically ill population.

Abbreviations

MCS	Mechanical circulatory support
CS	Cardiogenic shock
AMI-CS	Acute myocardial infarction complicated by cardiogenic shock
AIS	Acute ischemic stroke
AKI	Acute kidney injury
aOR	Adjusted odds ratio
CI	Confidence interval
IABP	Intra-aortic balloon pump
ECMO	Extracorporeal membrane oxygenation
NIS	National Inpatient Sample
ICD-10-CM/PCS	International Classification of Diseases, Tenth Revision, Clinical Modification/ Procedure Coding System
PCI	Percutaneous coronary intervention
CABG	Coronary artery bypass grafting
PSM	Propensity score matching
SMD	Standardized mean differences

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04810-9.

Supplementary Material 1

Acknowledgements

Not applicable.

Clinical trial number

Not applicable.

Authors' contributions

G. C., X.M., and S.J.: contribution to study design, critical revision of the manuscript, and final approval of the version to be published. R. Y. and J.Y.: contribution to data analysis and interpretation, and the writing of the manuscript. B.S., C.Y., S.F., and K.W.: contribution to critical revision of the manuscript for important intellectual content. R.Y.: data visualization. All authors contributed to the article and approved the submitted version.

Funding

This work was supported by the Central Government Guided Local Science and Technology Project [grant number 2022 FRD05046]; the Natural Science Foundation of Ningxia Province [grant numbers 2018 AAC02015]; Natural Science Foundation of Ningxia Province [grant number 2022 AAC03479]; Natural Science Foundation of Ningxia Province [grant number 2023 AAC02071]; and National Natural Science Foundation of China [grant number 82260086:82060057].

Data availability

The dataset used and analysed in the current study is a publicly available dataset (National Inpatient Sample), part of the Healthcare Cost and Utilization Project from the United States, and can be accessed at the following link: https://hcup-us.ahrq.gov/nisoverview.jsp.

Declarations

Ethics approval and consent to participate

Not applicable. This article does not contain any studies with human participants or animals performed by any of the authors. Additionally, this observational study used identified publicly available data, hence there was no requirement for consent to participate and it was deemed exempt by the Internal Review Board (IRB) of General Hospital of Ningxia Medical University. So, there is no need to grant permission in the Ethics approval and consent to participate section. All methods are carried out following relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]School of Clinical Medicine, Ningxia Medical University, Yinchuan, Ningxia, China. [2]Institute of Medical Sciences, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, China. [3]Institute of Cardiovascular Medicine, General Hospital of Ningxia Medical University, Ningxia, China. [4]Department of Cardiology, General Hospital of Ningxia Medical University, Ningxia Medical University, Ningxia, China. [5]National Health Commission Key Laboratory of Metabolic Cardiovascular Diseases Research, Ningxia Medical University, Ningxia, China. [6]Ningxia Key Laboratory of Vascular Injury and Repair Research, Ningxia Medical University, Ningxia, China.

Received: 21 December 2024 Accepted: 30 April 2025
Published online: 17 May 2025

References

1. Henry TD, Tomey MI, Tamis-Holland JE, Thiele H, Rao SV, Menon V, et al. Invasive management of acute myocardial infarction complicated by cardiogenic shock: a scientific statement from the american heart association. Circulation. 2021;143(15):e815–29.
2. Tehrani BN, Truesdell AG, Psotka MA, Rosner C, Singh R, Sinha SS, et al. A standardized and comprehensive approach to the management of cardiogenic shock. JACC Heart Fail. 2020;8(11):879–91.
3. Lawler PR, Berg DD, Park JG, Katz JN, Baird-Zars VM, Barsness GW, et al. The range of cardiogenic shock survival by clinical stage: data from the critical care cardiology trials network registry. Crit Care Med. 2021;49(8):1293–302.
4. Hyun DY, Han X, Oh S, Ahn JH, Lee SH, Cho KH, et al. Long-term clinical outcomes in patients with acute myocardial infarction complicated by cardiogenic shock according to the application and initiation time of extracorporeal membrane oxygenation in South Korea. Cardiol J. 2023;30(5):713–24.

5. Mebazaa A, Combes A, van Diepen S, Hollinger A, Katz JN, Landoni G, et al. Management of cardiogenic shock complicating myocardial infarction. Intensive Care Med. 2018;44(6):760–73.
6. Schrage B, Ibrahim K, Loehn T, Werner N, Sinning JM, Pappalardo F, et al. Impella support for acute myocardial infarction complicated by cardiogenic shock. Circulation. 2019;139(10):1249–58.
7. Ouweneel DM, de Brabander J, Karami M, Sjauw KD, Engstrom AE, Vis MM, et al. Real-life use of left ventricular circulatory support with Impella in cardiogenic shock after acute myocardial infarction: 12 years AMC experience. Eur Heart J Acute Cardiovasc Care. 2019;8(4):338–49.
8. Huang M, Ong BH, Hoo AEE, Gao F, Chao VTT, Lim CH, et al. Prognostic factors for survival after extracorporeal membrane oxygenation for cardiogenic shock. ASAIO J. 2020;66(2):141–5.
9. Sjauw KD, Engstrom AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, et al. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009;30(4):459–68.
10. Amin AP, Spertus JA, Curtis JP, Desai N, Masoudi FA, Bach RG, et al. The evolving landscape of impella use in the united states among patients undergoing percutaneous coronary intervention with mechanical circulatory support. Circulation. 2020;141(4):273–84.
11. Saeed D, Loforte A, Morshuis M, Schibilsky D, Zimpfer D, Riebandt J, et al. Stroke complications in patients requiring durable mechanical circulatory support systems after extracorporeal life support. ASAIO J. 2023;69(2):145–50.
12. Bae DJ, Willey JZ, Ibeh C, Yuzefpolskaya M, Colombo PC. Stroke and mechanical circulatory support in adults. Curr Cardiol Rep. 2023;25(12):1665–75.
13. Cheng R, Hachamovitch R, Kittleson M, Patel J, Arabia F, Moriguchi J, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. Ann Thorac Surg. 2014;97(2):610–6.
14. Gaudard P, Mourad M, Eliet J, Zeroual N, Culas G, Rouviere P, et al. Management and outcome of patients supported with Impella 5.0 for refractory cardiogenic shock. Crit Care. 2015;19:363.
15. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med. 2012;367(14):1287–96.
16. Pahuja M, Chehab O, Ranka S, Mishra T, Ando T, Yassin AS, et al. Incidence and clinical outcomes of stroke in ST-elevation myocardial infarction and cardiogenic shock. Catheter Cardiovasc Interv. 2021;97(2):217–25.
17. Russo MJ, Jeevanandam V, Stepney J, Merlo A, Johnson EM, Malyala R, et al. Intra-aortic balloon pump inserted through the subclavian artery: a minimally invasive approach to mechanical support in the ambulatory end-stage heart failure patient. J Thorac Cardiovasc Surg. 2012;144(4):951–5.
18. Roka-Moiia Y, Li M, Ivich A, Muslmani S, Kern KB, Slepian MJ. Impella 5.5 Versus Centrimag: A Head-to-Head Comparison of Device Hemocompatibility. ASAIO J. 2020;66(10):1142–51.
19. Healthcare Cost And Utilization Project (HCUP). Introduction to the HCUP National Inpatient Sample (NIS) 2019. 2021. https://www.hcup-us.ahrq.gov/db/nation/nis/NISIntroduction2019.
20. Osman M, Syed M, Patibandla S, Sulaiman S, Kheiri B, Shah MK, et al. Fifteen-year trends in incidence of cardiogenic shock hospitalization and in-hospital mortality in the United States. J Am Heart Assoc. 2021;10(15):e021061.
21. Alkhouli M, Alqahtani F, Tarabishy A, Sandhu G, Rihal CS. Incidence, predictors, and outcomes of acute ischemic stroke following percutaneous coronary intervention. JACC Cardiovasc Interv. 2019;12(15):1497–506.
22. Coloma PM, Valkhoff VE, Mazzaglia G, Nielsson MS, Pedersen L, Molokhia M, et al. Identification of acute myocardial infarction from electronic healthcare records using different disease coding systems: a validation study in three European countries. BMJ Open. 2013;3(6):e002862.
23. Nakai M, Iwanaga Y, Sumita Y, Kanaoka K, Kawakami R, Ishii M, et al. Validation of acute myocardial infarction and heart failure diagnoses in hospitalized patients with the nationwide claim-based JROAD-DPC database. Circ Rep. 2021;3(3):131–6.
24. Lauridsen MD, Gammelager H, Schmidt M, Nielsen H, Christiansen CF. Positive predictive value of International Classification of Diseases, 10th revision, diagnosis codes for cardiogenic, hypovolemic, and septic shock in the Danish National Patient Registry. BMC Med Res Methodol. 2015;15:23.
25. Nguyen TL, Collins GS, Spence J, Daures JP, Devereaux PJ, Landais P, et al. Double-adjustment in propensity score matching analysis: choosing a threshold for considering residual imbalance. BMC Med Res Methodol. 2017;17(1):78.
26. Barssoum K, Patel HP, Abdelmaseih R, Hassib M, Victor V, Mohamed A, et al. Characteristics and outcomes of early vs late initiation of mechanical circulatory support in non-acute myocardial infarction related cardiogenic shock: an analysis of the national inpatient sample database. Curr Probl Cardiol. 2023;48(5):101584.
27. Schrage B, Becher PM, Gossling A, Savarese G, Dabboura S, Yan I, et al. Temporal trends in incidence, causes, use of mechanical circulatory support and mortality in cardiogenic shock. ESC Heart Fail. 2021;8(2):1295–303.
28. Nishimoto Y, Inohara T, Kohsaka S, Sakakura K, Kawai T, Kikuchi A, et al. Changing trends in mechanical circulatory support use and outcomes in patients undergoing percutaneous coronary interventions for acute coronary syndrome complicated with cardiogenic shock: insights from a nationwide registry in Japan. J Am Heart Assoc. 2023;12(23):e031838.
29. Essa H, Hill AM, Lip GYH. Atrial fibrillation and stroke. Card Electrophysiol Clin. 2021;13(1):243–55.
30. Iacobelli R, Fletcher-Sandersjoo A, Lindblad C, Keselman B, Thelin EP, Broman LM. Predictors of brain infarction in adult patients on extracorporeal membrane oxygenation: an observational cohort study. Sci Rep. 2021;11(1):3809.
31. Lorusso R, Gelsomino S, Parise O, Di Mauro M, Barili F, Geskes G, et al. Neurologic injury in adults supported with veno-venous extracorporeal membrane oxygenation for respiratory failure: findings from the extracorporeal life support organization database. Crit Care Med. 2017;45(8):1389–97.
32. Cai J, Abudou H, Chen Y, Wang H, Wang Y, Li W, et al. The effects of ECMO on neurological function recovery of critical patients: a double-edged sword. Front Med (Lausanne). 2023;10:1117214.
33. Astrom A, Soderstrom L, Mooe T. Risk of ischemic stroke after acute myocardial infarction in patients undergoing coronary artery bypass graft surgery. Sci Rep. 2020;10(1):3831.
34. Palmerini T, Savini C, Di Eusanio M. Risks of stroke after coronary artery bypass graft - recent insights and perspectives. Interv Cardiol. 2014;9(2):77–83.
35. Roka-Moiia Y, Miller-Gutierrez S, Palomares DE, Italiano JE, Sheriff J, Bluestein D, et al. Platelet dysfunction during mechanical circulatory support: elevated shear stress promotes downregulation of alpha(IIb)beta(3) and GPIb via microparticle shedding decreasing platelet aggregability. Arterioscler Thromb Vasc Biol. 2021;41(4):1319–36.
36. Badimon JJ, Santos-Gallego CG. Modulatory role of pulsatility on von willebrand factor: implications for mechanical circulatory support-associated bleeding. J Am Coll Cardiol. 2018;71(19):2119–21.
37. Arepally GM, Padmanabhan A. Heparin-induced thrombocytopenia: a focus on thrombosis. Arterioscler Thromb Vasc Biol. 2021;41(1):141–52.
38. Yeo I, Axman R, Lu DY, Feldman DN, Cheung JW, Minutello RM, et al. Impella versus intra-aortic balloon pump in patients with cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation: an observational study. J Am Heart Assoc. 2024;13(3):e032607.
39. Goodney PP, Beck AW, Nagle J, Welch HG, Zwolak RM. National trends in lower extremity bypass surgery, endovascular interventions, and major amputations. J Vasc Surg. 2009;50(1):54–60.

Publisher's Note