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ORIGINAL RESEARCH

CRITICAL CARE CARDIOLOGY

Treatment Intensity for the Management of Cardiogenic Shock

Comparison Between STEMI and Non-STEMI

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ABSTRACT

BACKGROUND Cardiogenic shock is a leading cause of mortality in patients with acute myocardial infarction.

OBJECTIVES The authors sought to compare clinical characteristics, hospital trajectory, and drug and device use between patients with ST-segment elevation myocardial infarction-related cardiogenic shock (STEMI-CS) and those without (non-ST-segment elevation myocardial infarction complicated by cardiogenic shock [NSTEMI-CS]).

METHODS We analyzed data from 1,110 adult admissions with cardiogenic shock complicating acute myocardial infarction (AMI-CS) across 17 centers within Cardiogenic Shock Working Group. The primary end point was in-hospital mortality.

RESULTS Our study included 1,110 patients with AMI-CS, of which 731 (65.8%) had STEMI-CS and 379 (34.2%) had NSTEMI-CS. Most patients were male (STEMI-CS: 71.6%, NSTEMI-CS: 66.5%) and White (STEMI-CS: 53.8%, NSTEMI-CS: 64.1%). In-hospital mortality was 41% and was similar among patients with STEMI-CS and NSTEMI-CS (43% vs 39%, $P = 0.23$). Patients with out-of-hospital cardiac arrest had higher in-hospital mortality in patients with NSTEMI-CS (63% vs 36%, $P = 0.006$) as compared to patients with STEMI-CS (52% vs 41%, $P = 0.16$). Similar results were observed for in-hospital cardiac arrest in patients with STEMI-CS (63% vs 33%, $P < 0.001$) and NSTEMI-CS (60% vs 32%, $P < 0.001$). Only 27% of patients with STEMI-CS and 12% of NSTEMI-CS received both a drug and temporary mechanical circulatory support device during the first 24 hours, which increased to 78% and 61%, respectively, throughout the course of the hospitalization ($P < 0.001$ for both).

CONCLUSIONS Despite increasing use of inotropic and vasoactive support and mechanical circulatory support throughout the hospitalization, both patients with STEMI-CS and NSTEMI-CS remain at increased risk for in-hospital mortality. Randomized controls trials are needed to elucidate whether timing and sequence of escalation of support improves outcomes in patients with AMI-CS. (JACC Adv 2023;2:100314) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AMI-CS = cardiogenic shock complicating acute myocardial infarction

CA = cardiac arrest

CABG = coronary artery bypass grafting

CS = cardiogenic shock

CSWG = Cardiogenic Shock Working Group

IABP = intra-aortic balloon pump

IHCA = in-hospital cardiac arrest

MAP = mean arterial pressure

NSTEMI = non-ST-segment elevation myocardial infarction

NSTEMI-CS = non-ST-segment elevation myocardial infarction complicated by cardiogenic shock

OHCA = out-of-hospital cardiac arrest

RCT = randomized clinical trial

SBP = systolic blood pressure

SCAI = Society for Cardiovascular Angiography and Interventions

STEMI = ST-segment elevation myocardial infarction

STEMI-CS = ST-segment elevation myocardial infarction–related cardiogenic shock

tMCS = temporary mechanical circulatory support

Cardiogenic shock complicating acute myocardial infarction (AMI-CS) remains a morbid and lethal complication, occurring in 5% to 10% of acute myocardial infarction cases, and serving as the leading cause of in-hospital mortality, ranging from 35% to 50%.[1,2] Despite advances in revascularization techniques and increasing use of temporary mechanical circulatory support (tMCS) over the past 2 decades, randomized clinical trials (RCTs) have failed to identify treatment strategies that improve mortality in AMI-CS.[3-7] Data from RCTs in the contemporary era of AMI-CS management have been limited by lack of uniformity with shock definitions, focus on ST-segment elevation myocardial infarction-related cardiogenic shock (STEMI-CS) and variability of reporting of key outcome predictors among other considerations.[8-10] These trials have primarily been performed outside the United States, traditionally enrolling fewer women and lower-risk patients, thus challenging their generalizability in daily practice. Finally, there is a paucity of data on clinical characteristics, hemodynamic profiles, and outcomes in patients with non-ST-segment elevation myocardial infarction complicated by cardiogenic shock (NSTEMI-CS).[11] Hence, a better understanding of the contemporary patient population with AMI-CS is needed.

In an effort to bridge knowledge gaps, multiple retrospective and prospective national registries have been designed to help delineate AMI-CS phenotypes and inform clinical-decision making in patients presenting with AMI-CS.[12-16] The Cardiogenic Shock Working Group (CSWG) registry is a large, robust, multicenter North American registry of patients with cardiogenic shock (CS). Herein, we leveraged the CSWG registry to compare clinical characteristics, hemodynamic and metabolic phenotypes, in-hospital mortality, and elucidate drug- and device-based utilization between patients with STEMI-CS and NSTEMI-CS.

METHODS

DATA SOURCE. The CSWG registry was initiated in 2016 with 17 clinical sites across the United States contributing patient with CS data. We previously detailed definitions of database parameters and clinical outcomes, and methods for data entry and monitoring.[12] Briefly, participating sites include community and university hospitals who contribute real-world data to the registry, which includes a standardized set of data elements (patient, procedural, and outcomes) that were predefined by CSWG steering committee members with input from principal investigators at each site and collected retrospectively. Patient demographic, laboratory, and hemodynamic data were collected at a single time point as close to admission as possible, as well as across hospitalization at time points that are clinically relevant to patient with CS progression where applicable including: first vasopressor/inotrope administration, every mechanical circulatory support placement, pulmonary artery catheter placement, 24 hours after last device placement, and discharge. The diagnosis of CS was physician-adjudicated at each site and defined as a sustained episode of at least one of the following: systolic blood pressure (SBP) <90 mm Hg for at least 30 minutes, use of vasoactive agents, cardiac index <2.2 L/min/m^2 in the

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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absence of hypovolemia, determined to be secondary to cardiac dysfunction or use of a tMCS device for clinically-suspected CS. Treatment of CS was left to the discretion of the clinicians at each center and not guided by a prescribed algorithm. Quality assurance was achieved through adjudication at each site by the respective clinical coordinators and principal investigator. Values were centrally audited and screened by the CSWG research team for any discrepancies or major outliers which were resolved with the respective sites. Institutional Review Board approval was obtained by individual sites to access these de-identified data from medical records and patient consent was not required. Data abstraction and entry into the registry electronic database were performed according to the requirements from individual Institutional Review Boards, which varied from site-to-site. In all cases investigative staff members accessed medical records and removed patient identifiers. Waivers of informed consent were granted at all sites for data collected retrospectively from electronic medical records. Consent was obtained from patients for all prospective follow up data.

STUDY POPULATION. Between years 2016 and 2020, data from 1,110 adult patient hospital admissions with the diagnosis of AMI-CS were collected. CS cause was reported by each site as due to ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI) based on previously published consensus definitions. NSTEMI was defined by the presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia without evidence of ST-segment elevation. For mortality analyses, individuals with unknown mortality status at the time of hospital discharge (n = 23, 2.1%) were excluded. The same inclusion and exclusion criteria were the same for all 1,110 consecutively enrolled patients included into the registry. The first cohort of 517 patients was enrolled during the first version of the registry in which data were not available to assess changes from hospital admission over time. The second cohort of 593 patients was enrolled in the second version of the registry, using same inclusion/exclusion criteria, after additional data elements were added. Accordingly, the current analysis includes all patients with necessary data available.

DEFINING PARAMETERS FOR SCAI STAGING. The criteria for Society for Cardiovascular Angiography and Interventions (SCAI) stages have been published previously (reproduced in Supplemental Figure 1).[17] Based on the recently updated SCAI consensus document,[18] we employed the CSWG interpretation of defined SCAI stages retrospectively at the data coordinating center as follows: stage B as patients having either isolated hypoperfusion (lactate 2-5 mmol/L or alanine aminotransferase (ALT) 200-500 U/L) *or* hypotension (SBP 60-90 mm Hg or mean arterial pressure [MAP] 50-65 mm Hg) without the use of drug or device therapy. SCAI stage C patients were defined as having hypoperfusion *and* hypotension using the same criteria as for SCAI stage B or those patients who are being treated for CS with 1 drug (eg, a vasopressor or an inotrope) or 1 circulatory support device. For the purposes of this analysis, inotropes included dobutamine and milrinone. Vasopressors included norepinephrine, epinephrine, vasopressin, and phenylephrine. SCAI stage D patients were defined as having hypotension (SBP 60-90 mm Hg or MAP 50-65 mm Hg) *and* hypoperfusion (lactate 5-10 mmol/L or ALT >500 U/L) while also receiving 2 to 5 drugs or devices. Stage D also included patients on 1 drug or device with hypotension or hypoperfusion that persisted despite treatment. SCAI stage E patients were defined as having hypotension (SBP <60 mm Hg or MAP <50 mm Hg) or hypoperfusion (lactate >10 mmol/L or pH ≤7.2) or who were receiving more than 3 drugs and/or 3 devices. All patients who experienced out-of-hospital cardiac arrest (OHCA) were included in stage E.

Using this modified version of the SCAI staging approach, patients with available data within 24 hours of admission (n = 1,110) were stratified according to SCAI Stages using the first set of values acquired. This baseline SCAI stage, based on onset of CS as adjudicated by the site investigators, was then analyzed for associations with in-hospital mortality. Maximum SCAI stage reached during hospitalization using the same clinical criteria was assigned to each patient and analyzed for association with mortality. Lastly, the association between time from admission to maximum SCAI stage and in-hospital mortality was reported. For the purposes of this manuscript, *escalation* to refer to intensification of treatment strategies and *transition* or *progression* refers to upward movement between SCAI stages.

STATISTICAL ANALYSES. For all the analyses described above, continuous variables were reported as mean ± SD and categorical variables were reported as frequencies and percentages. The means of normally distributed continuous variables were compared using independent *t*-tests and medians of non-normally distributed variables were compared using Wilcoxon's test. Categorical variables were compared using chi-squared analyses. Relative comparisons were reported as odds ratio (95% CI).

TABLE 1 Baseline Demographic, Metabolic, and Hemodynamic Characteristics of the Study Population

	Total MI-CS (N = 1,110)		STEMI-CS (N = 731)		NSTEMI-CS (N = 379)		
	n (%)		n (%)		n (%)		
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	*P* Value
Demographic							
Non-survivor		449 (40.5)		305 (41.7)		144 (38.0)	0.49
Male		775 (69.8)		523 (71.6)		252 (66.5)	0.23
Race							***<0.001***
White		636 (57.3)		393 (53.8)		243 (64.1)	
Asian		53 (4.8)		38 (5.2)		15 (4.0)	
Black		42 (3.8)		22 (3.0)		20 (5.3)	
Other		23 (2.1)		15 (2.1)		8 (2.1)	
Age (y)	1,109	65.6 ± 12.5	730	63.8 ± 12.3	379	69.2 ± 12.3	***<0.001***
Weight (kg)	593	86.3 ± 22.0	349	87.0 ± 21.1	244	85.4 ± 23.3	0.10
Body mass index (kg/m^2)	588	29.4 ± 7.0	346	29.4 ± 6.6	242	29.3 ± 7.5	0.49
Medical history							
Hypertension		721 (65.0)		443 (60.6)		278 (73.4)	***<0.001***
Diabetes mellitus		482 (43.4)		280 (38.3)		202 (53.3)	***<0.001***
Atrial fibrillation/atrial flutter		125 (11.3)		66 (9.0)		59 (15.6)	***<0.001***
Chronic kidney disease (any stage)		106 (9.6)		41 (5.6)		65 (17.2)	***<0.001***
Peripheral vascular disease		86 (7.8)		43 (5.9)		43 (11.4)	***<0.001***
Chronic obstructive pulmonary disease		104 (9.4)		52 (7.1)		52 (13.7)	***<0.001***
CVA/TIA		123 (11.1)		57 (7.8)		66 (17.4)	***<0.001***
Valvular disease		80 (7.2)		36 (4.9)		44 (11.6)	***<0.001***
Percutaneous coronary intervention		297 (26.8)		201 (27.5)		96 (25.3)	0.07
Coronary artery bypass grafting		92 (8.3)		48 (6.6)		44 (11.6)	***0.003***
Implantable cardioverter defibrillator		44 (4.0)		21 (2.9)		23 (6.1)	***<0.001***
Metabolic							
Alanine aminotransferase (U/L)	858	270.6 ± 689.5	554	281.7 ± 729.6	304	250.5 ± 610.5	***<0.001***
Blood urea nitrogen (mg/dL)	1,017	28.7 ± 18.6	651	26.4 ± 17.1	366	32.9 ± 20.4	***<0.001***
Lactate (mmol/L)	703	4.7 ± 4.3	473	5.2 ± 4.5	230	3.8 ± 3.7	***<0.001***
Sodium bicarbonate (mEq/L)	819	20.2 ± 5.8	557	19.9 ± 6.1	262	20.9 ± 5.2	***<0.001***
Serum creatinine (mg/dL)	1,050	1.7 ± 1.3	683	1.7 ± 1.3	367	1.8 ± 1.3	***0.03***
pH	652	7.3 ± 0.2	463	7.3 ± 0.2	189	7.3 ± 0.1	0.11
Hemodynamic							
Left ventricular ejection fraction (%)	803	30.6 ± 16.2	492	30.0 ± 16.1	311	31.6 ± 16.3	0.20
Right atrial pressure (mm Hg)	403	14.2 ± 6.4	281	14.5 ± 6.3	122	13.6 ± 6.7	0.10
PCWP (mm Hg)	300	24.0 ± 9.2	209	23.7 ± 8.8	91	24.7 ± 10.1	0.41
Mean PAP (mm Hg)	439	29.9 ± 9.7	307	29.1 ± 9.9	132	31.7 ± 8.9	***0.001***
Cardiac output (L/min)	412	4.0 ± 2.1	296	4.0 ± 2.3	116	4.0 ± 1.7	0.83
Cardiac power output (W)	396	0.7 ± 0.4	287	0.7 ± 0.5	109	0.7 ± 0.3	0.57
Heart rate (beats/min)	1,015	91.2 ± 23.4	649	91.5 ± 24.1	366	90.7 ± 22.2	0.62
Cardiac index	415	2.0 ± 0.7	301	2.0 ± 0.7	114	2.1 ± 0.8	0.37
Mean arterial pressure (mm Hg)	1,053	81.5 ± 20.5	685	80.7 ± 21.0	368	82.8 ± 19.5	0.08
Systolic blood pressure (mm Hg)	1,002	109.6 ± 28.4	637	107.7 ± 28.3	365	113.0 ± 28.2	***0.004***
Pulmonary artery pulsatility index	80	1.7 ± 1.2	54	1.5 ± 0.9	26	2.1 ± 1.7	***0.04***

All **boldface** and italics values are statistically significant.

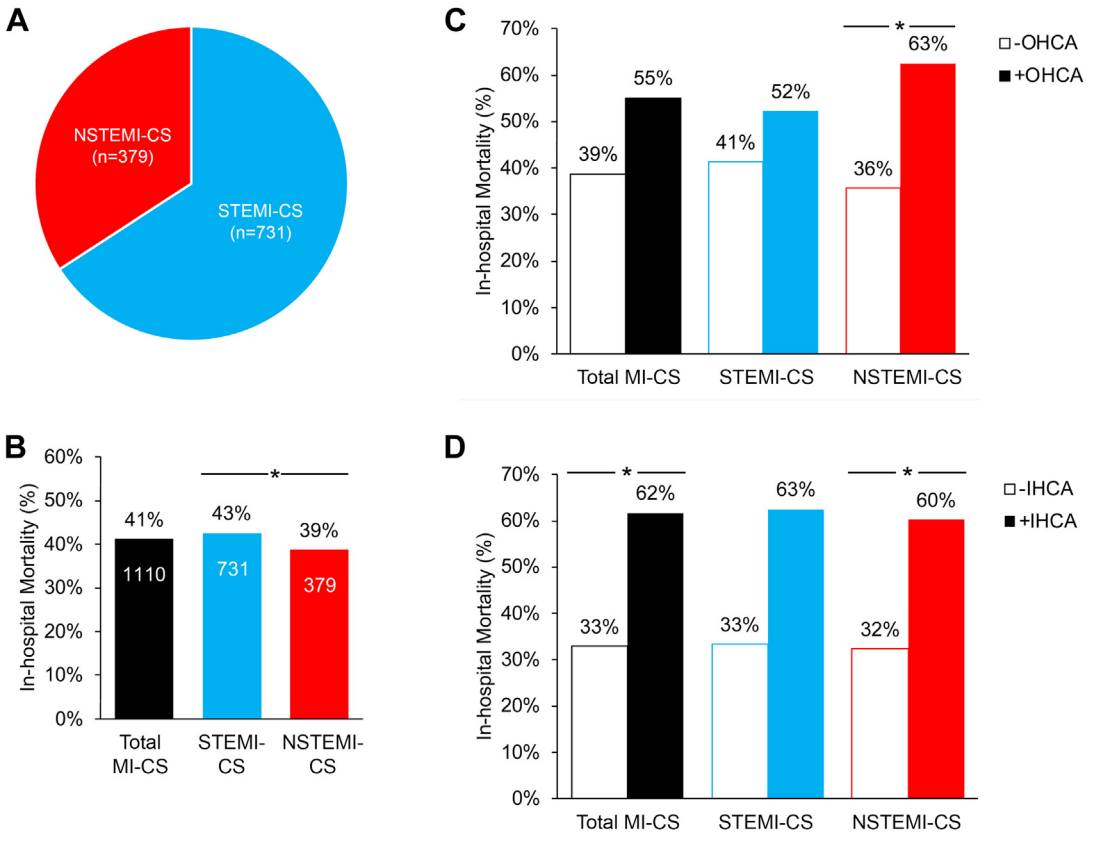
CVA = cerebrovascular accident; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; STEMI = ST-segment elevation myocardial infarction; TIA = transient ischemic attack.

Univariate logistic regressions were run to test all associations with mortality. In a secondary analysis, interaction testing was performed using a logistic regression model and multivariate logistic regressions including all significant univariate predictors of mortality were performed. Statistical significance was determined using an alpha of 0.05 for all analyses. SAS version 9.4 (SAS Institute Inc, Cary, North Carolina) was used for all data analyses.

RESULTS

BASELINE CHARACTERISTICS. Our study cohort included 1,110 patients with AMI-CS out of which 731

FIGURE 1 Distribution of Patients With Cardiogenic Shock Stratified by Etiology of Acute Myocardial Infarction and Associated In-Hospital Mortality with or without Cardiac Arrest

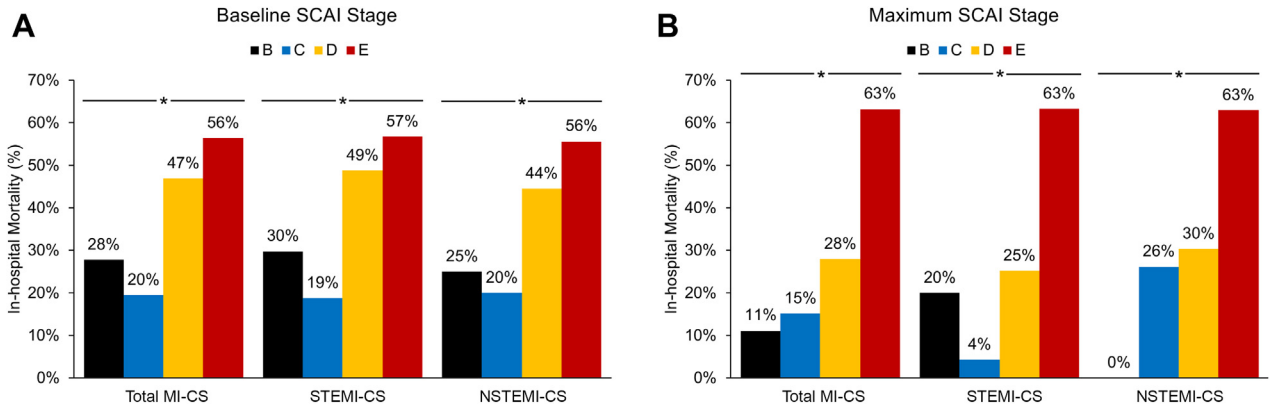


(A) Distribution of patients with cardiogenic shock stratified by etiology of acute myocardial infarction. **(B)** Unadjusted in-hospital mortality rate among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. **(C)** In-hospital mortality rate among patients with vs Without OHCA among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. **(D)** In-hospital mortality rate among patients with vs without IHCA among total MI, STEMI, and NSTEMI cohorts. IHCA = in-hospital cardiac arrest; MI-CS = cardiogenic shock complicating myocardial infarction; NSTEMI-CS = cardiogenic shock complicating non-ST-segment elevation myocardial infarction; OHCA = out-of-hospital cardiac arrest; STEMI-CS = cardiogenic shock complicating ST-segment elevation myocardial infarction.

(65.8%) had STEMI-CS and 379 (34.2%) had NSTEMI-CS. Baseline characteristics are summarized in Table 1. The majority of the patients were male (STEMI-CS: 71.6%, NSTEMI-CS: 66.5%) and White (STEMI-CS: 53.8%, NSTEMI-CS: 64.1%). Compared with patients with NSTEMI-CS, patients with STEMI-CS were younger (63.8 ± 12.3 vs 69.2 ± 12.3, $P < 0.001$). Patients with NSTEMI-CS had higher prevalence of hypertension (73.4% vs 60.6%, $P < 0.001$), diabetes (53.3% vs 38.3%, $P < 0.001$), chronic kidney disease (17.2% vs 5.6%, $P < 0.001$), peripheral vascular disease (11.4% vs 5.9%, $P < 0.001$), stroke (cerebrovascular accident or transient ischemic attack) (17.4% vs 7.8%, $P < 0.001$), and prior history of coronary artery bypass grafting (CABG) (11.6% vs 6.6%, $P = 0.003$) but had similar rates of percutaneous coronary interventions.

Compared to STEMI-CS survivors, patients with STEMI-CS who died were older (65 vs 62.7 years, $P = 0.01$), had higher prevalence of hypertension (65.9% vs 56.5%, $P = 0.02$), diabetes (46.2% vs 32.6%, $P = 0.001$), chronic kidney disease (8.9% vs 3.4%, $P = 0.002$), peripheral vascular disease (6.6% vs 5.1%, $P = 0.01$), prior history of CABG (9.2% vs 4.6%, $P = 0.049$), and lower left ventricular ejection fraction (26.5% vs 32.6%, $P < 0.001$) as shown in Supplemental Table 1A. A comparison of survivors vs non-survivors in patients with NSTEMI-CS are described in Supplemental Table 1B. Non-survivors were older (71.2 vs 67.8 years, $P = 0.005$) and had higher

FIGURE 2 Association of In-Hospital Mortality Across Baseline and Maximum SCAI Stage Among Total MI-CS, STEMI-CS, and NSTEMI-CS Patients



(A) Bar graphs illustrating the association of in-hospital mortality rate across baseline SCAI stages among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. **(B)** Bar graphs illustrating the association of in-hospital mortality rate across maximum SCAI stages among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts.
MI-CS = cardiogenic shock complicating myocardial infarction; NSTEMI-CS = cardiogenic shock complicating non-ST-segment elevation myocardial infarction; SCAI = Society for Cardiovascular Angiography and Interventions; STEMI-CS = cardiogenic shock complicating ST-segment elevation myocardial infarction.

prevalence of atrial fibrillation/flutter (21.5% vs 11.5%, $P = 0.03$).

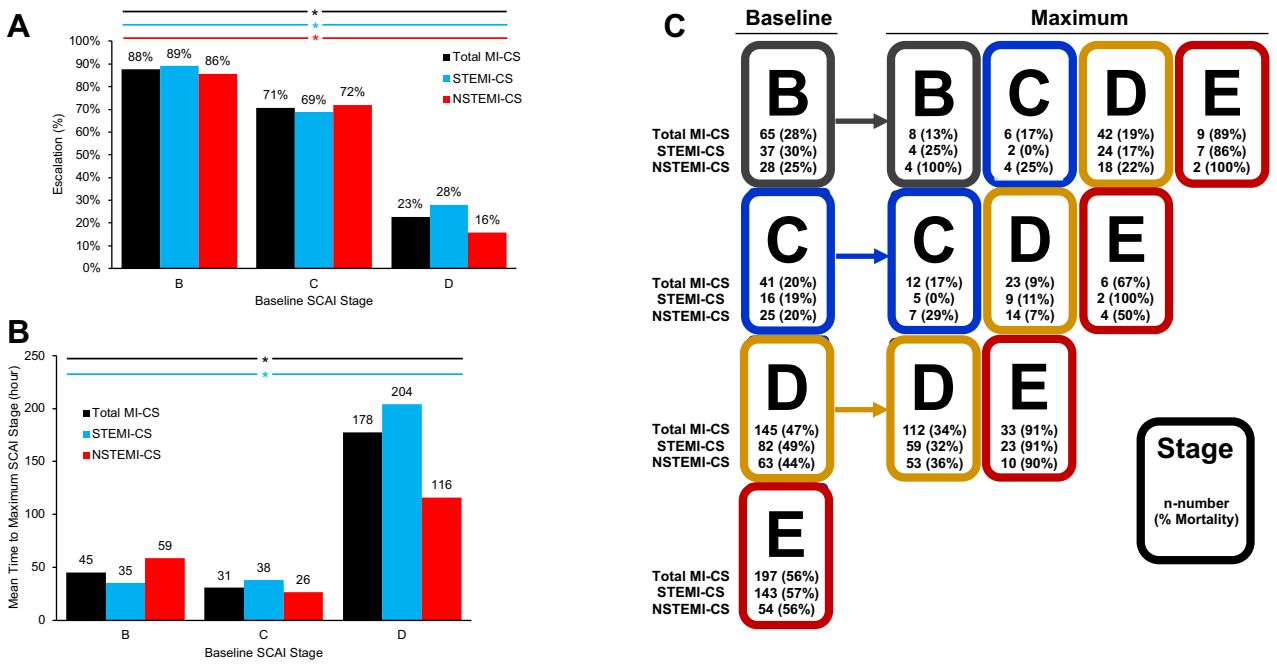
CLINICAL OUTCOMES. Overall unadjusted in-hospital mortality was 41%. Mortality was similar among patients with STEMI-CS and NSTEMI-CS (43% vs 39%, $P = 0.23$) (Figure 1B). Cardiac arrest (CA) was an effect modifier that was associated with worse prognosis. Patients with OHCA had higher in-hospital mortality (55% vs 39%, $P = 0.002$), but this was more prominently seen among patients with NSTEMI-CS (63% vs 36%, $P = 0.006$) as compared to patients with STEMI-CS (52% vs 41%, $P = 0.16$). Similar results were observed for patients with in-hospital cardiac arrest (IHCA) (62% vs 33%, $P < 0.001$) with significantly high mortality in both patients with STEMI-CS (63% vs 33%, $P < 0.001$) and NSTEMI-CS (60% vs 32%, $P < 0.001$) (Figures 1C and 1D). We also performed interaction testing using a logistic regression model of OHCA and etiology of MI (ie, STEMI-CS, NSTEMI-CS) predicting in-hospital mortality. The result turned out to be not significant for the interaction ($P = 0.12$), thereby suggesting the difference observed between the status of OHCA is consistent over etiology. We performed a similar analysis for IHCA, and noted the interaction is also not significant ($P = 0.89$).

HEMO-METABOLIC AND HEMODYNAMIC PROFILES. Laboratory markers for perfusion such as lactate levels were higher in STEMI-CS as compared to patients with NSTEMI-CS (5.2 vs 3.8 mmol/L, $P < 0.001$) (Table 1). Similarly, laboratory parameters for end-organ dysfunction such as liver dysfunction, ALT (281 vs 250.5 U/L, $P < 0.001$), and renal dysfunction, namely serum creatinine (1.8 vs 1.7 mg/dL, $P = 0.03$), were worse in patients with STEMI-CS as compared to patients with NSTEMI-CS. Non-survivors among both patients with STEMI-CS and NSTEMI-CS were noted to have higher lactate level (STEMI-CS: 6.6 vs 3.9, $P < 0.001$; NSTEMI-CS: 4.6 vs 3.2 mmol/L, $P < 0.001$), ALT levels (STEMI-CS: 377.9 vs 201.4 U/L, $P < 0.001$; NSTEMI-CS: 297.6 vs 223 U/L, $P = 0.13$), and serum creatinine (STEMI-CS: 1.9 vs 1.4, $P < 0.001$; NSTEMI-CS: 2.1 vs 1.6 mg/dL, $P < 0.001$) (Supplemental Tables 1A and 1B). Among the hemodynamic parameters in patients with STEMI-CS, non-survivors had higher right atrial pressure (16.3 vs 13.3, $P < 0.001$) and lower pulmonary artery pulsatility index (1.3 vs 1.7, $P = 0.03$).

Supplemental Tables 2 and 3 summarize the laboratory and hemodynamic parameters for patients with STEMI-CS and NSTEMI-CS at baseline and maximum SCAI stages, respectively. Lactate levels were higher in patients with SCAI stage D and E CS in both patients with STEMI-CS and NSTEMI-CS at baseline and maximum SCAI stage. At baseline, ALT was highest in stage D CS for both STEMI-CS and NSTEMI-CS whereas serum creatinine increased from stage B to stage E for STEMI-CS, but in the NSTEMI-CS cohort, it was found to be highest in stage D CS.

The in-hospital mortality rate across baseline and maximum SCAI stages for total myocardial infarction complicated by cardiogenic shock, STEMI-CS, and NSTEMI-CS is shown in Figures 2A and 2B, respectively. Notably, the SCAI C patients with STEMI were associated with the lowest mortality at baseline (19%) and at maximum (4%) across all SCAI stages.

FIGURE 3 Progression to Advanced SCAI Stages Among Total MI-CS, STEMI-CS and NSTEMI-CS Patients

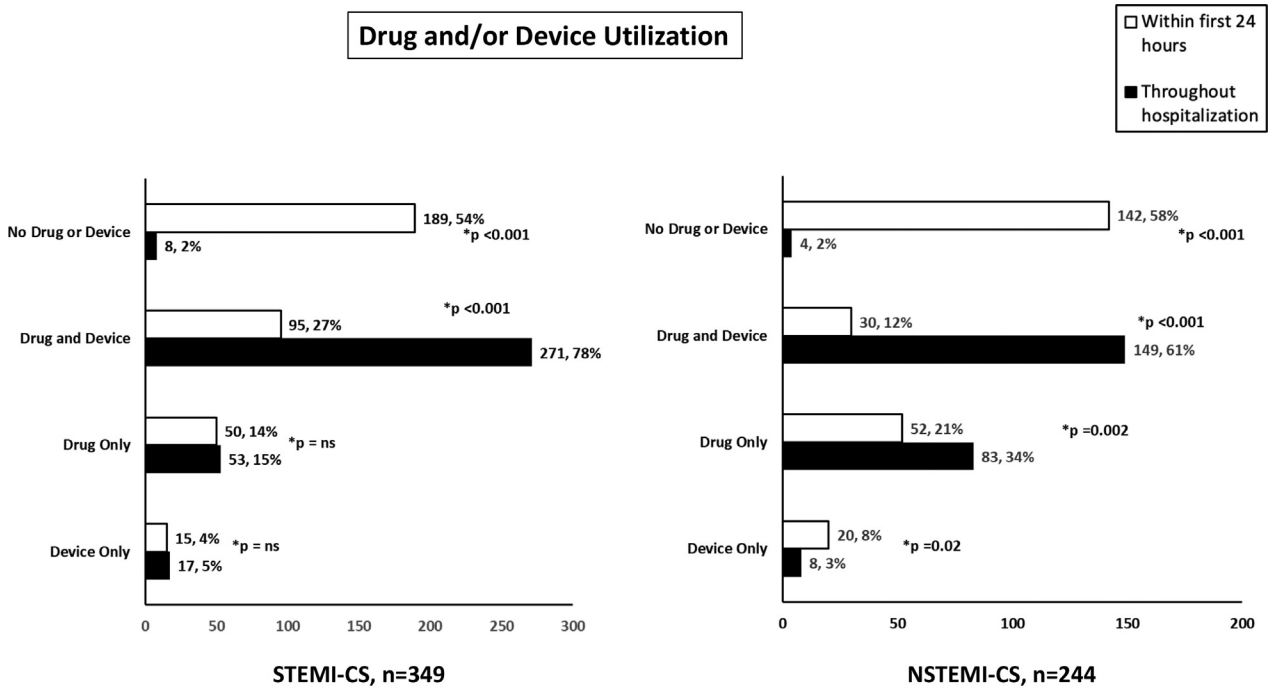


(A) Progression rate from baseline to maximum SCAI stages among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. **(B)** The mean time to progression from baseline to maximum SCAI stages among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. **(C)** Illustration showing trajectory of SCAI stages during hospitalization among total MI-CS, STEMI-CS, and NSTEMI-CS cohorts. The number of patients and percent in-hospital mortality for the maximum Society for Cardiovascular Angiography and Interventions stage achieved stratified by baseline Society for Cardiovascular Angiography and Interventions stage is shown. MI-CS = cardiogenic shock complicating myocardial infarction; NSTEMI-CS = cardiogenic shock complicating non-ST-segment elevation myocardial infarction; SCAI = Society for Cardiovascular Angiography and Interventions; STEMI-CS = cardiogenic shock complicating ST-segment elevation myocardial infarction.

PROGRESSION FROM BASELINE TO MAXIMUM SCAI SHOCK STAGE. Figures 3A and 3B summarize the overall progression of SCAI stages of patients with STEMI-CS and NSTEMI-CS patients and the average time to maximum SCAI stage during the course of the index hospitalization. Among patients with SCAI stage B CS, 89% of patients with STEMI-CS and 86% of patients with NSTEMI-CS transitioned to a higher stage with average time to maximum SCAI stage of 35 and 59 hours, respectively. Similarly, among patients presenting with stage C CS, 69% of patients with STEMI-CS and 72% of NSTEMI-CS transitioned to higher stages with average time to maximum stage of 38 and 26 hours, respectively. Among patients initially presenting in stage D CS, 28% of STEMI-CS and 16% of NSTEMI-CS progressed to stage E with average time to progression of 204 and 116 hours, respectively. The highest in-hospital mortality was seen in patients presenting with baseline SCAI stage E or those progressing to maximum SCAI stage E. Patients that presented with baseline stage D CS were noted to have higher mortality than those who transitioned to the maximum SCAI stage D (Figure 3C).

DRUG AND DEVICE UTILIZATION. The evolution of tMCS device and drug utilization based on the first 24 hours and throughout the course of the hospitalization is presented in Figure 4. Only 27% of patients with STEMI-CS and 12% of NSTEMI-CS received both a drug and tMCS device during the first 24 hours of the hospitalization, which increased to 78% and 61%, respectively, throughout the course of the hospitalization. Conversely, 54% of all patients with STEMI-CS and 58% of patients with NSTEMI-CS received neither a drug nor tMCS device within the first 24 hours, which decreased to 2% for both cohorts during the hospitalization. Vasopressors (STEMI-CS: 21%; NSTEMI-CS: 20%), followed by vasopressors and inotropes (STEMI-CS: 11%; NSTEMI-CS: 6%), were the most common drugs employed during the first 24 hours (Supplemental Figure 3A). These were also the most frequent drugs, or combinations thereof, that were employed in both cohorts during the hospitalization. Within 24 hours, the most common tMCS devices used were intra-aortic balloon pump (IABP) alone (STEMI-CS: 13%; NSTEMI-CS: 12%) and Impella alone (STEMI-CS: 12%; NSTEMI-CS: 5%)

FIGURE 4 Drug and Device Usage Distribution Within 24 Hours and Throughout Hospitalization in STEMI-CS vs Patients With NSTEMI-CS



ns = not statistically significant; NSTEMI-CS = cardiogenic shock complicating non-ST-segment elevation myocardial infarction; STEMI-CS = cardiogenic shock complicating ST-segment elevation myocardial infarction.

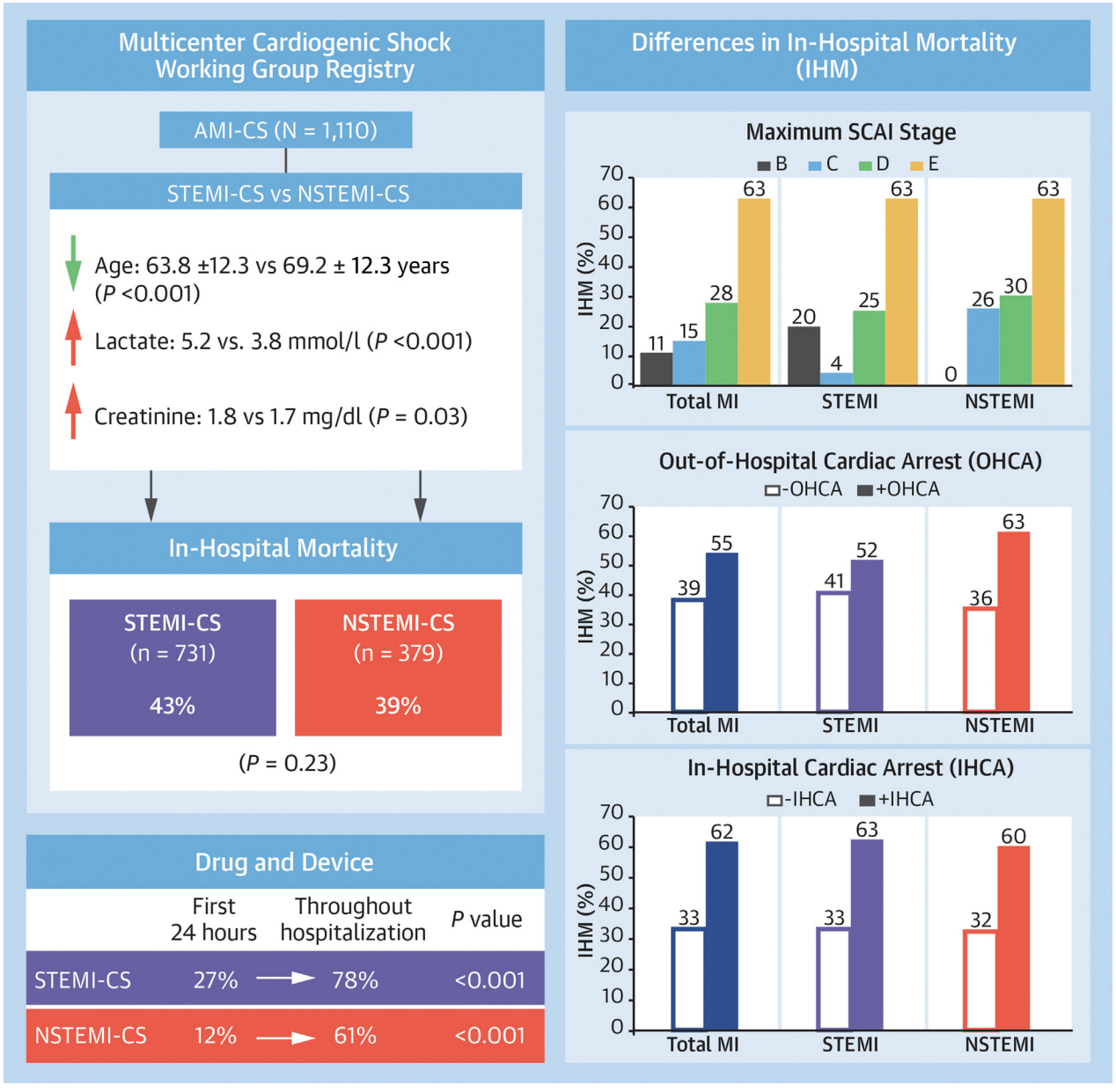
(Supplemental Figure 3B). Throughout the hospitalization, however, there was a broader distribution of device use. Among patients with STEMI-CS, 29% had IABP, 28% 2 or more devices (including VA ECMO), and 22% Impella alone. Among patients with NSTEMI-CS, 28% used IABP, 21% Impella alone, and 11% 2 or more devices (including veno-arterial extracorporeal membrane oxygenation).

DISCUSSION

To the best of our knowledge, this is one of the largest, contemporary, real-world registry-based analyses characterizing AMI-CS specifically comparing STEMI-CS and NSTEMI-CS across key clinical characteristics, hemodynamic and metabolic parameters, in-hospital mortality, as well as drug- and device-based strategies (**Central Illustration**). The main findings from this study are: first, in-hospital mortality remains high (approximately 40%-45%) across both STEMI-CS and NSTEMI-CS patients, suggesting that NSTEMI-CS patients also represent a vulnerable, high-risk cohort. Furthermore, CA, irrespective of in-hospital and out-of-hospital presentation, is an adverse effect modifier, portending significantly worse mortality in both patients with STEMI-CS and NSTEMI-CS. Second, the majority of SCAI stage B and SCAI stage C patients with STEMI-CS and NSTEMI-CS progress during their hospitalization to SCAI stage D or E; transition to a higher SCAI stage is associated with worse in-hospital outcomes as compared to those who initially presented in SCAI E. Patients withNSTEMI-CS SCAI B required a higher mean time to maximum SCAI stage as compared to patients with STEMI-CS SCAI B; highlighting potential opportunities for earlier recognition and perhaps more timely intervention in these patients. Finally, a broad distribution of drug and device exposure occurs within the first 24 hours and during the course of the hospitalization for both patients with STEMI-CS and NSTEMI-CS, which provides insights into the strategies for escalation of support. During the first 24 hours, patients with STEMI-CS were more likely to receive a drug and device, and patients with NSTEMI-CSwere more likely to receive drug only.

Our study provides an important contribution to the rapidly evolving literature, as patients with NSTEMI-CS have not been well studied in prior RCTs. Approximately 17% of patients in the SHOCK (Should

CENTRAL ILLUSTRATION **Comparison of ST-Segment-Elevation (STEMI-CS) and Non-ST-Segment-Elevation (NSTEMI-CS) Myocardial Infarction Complicated by Cardiogenic Shock**



Sinha SS, et al. JACC Adv. 2023;2(3):100314.

We sought to compare in-hospital mortality, clinical trajectories, and drug and device use between patients with ST-segment elevation myocardial infarction-related cardiogenic shock (STEMI-CS) and those without (non-ST-segment elevation myocardial infarction complicated by cardiogenic shock [NSTEMI-CS]). In-hospital mortality was similar among patients with STEMI-CS and NSTEMI-CS. Patients with out-of-hospital cardiac arrest had higher in-hospital mortality in patients with NSTEMI-CS as compared to patients with STEMI-CS. Similar results were observed for in-hospital cardiac arrest in patients with STEMI-CS and NSTEMI-CS. Only 27% of patients with STEMI-CS and 12% of NSTEMI-CS received both a drug and temporary mechanical circulatory support device during the first 24 hours, which increased to 78% and 61%, respectively, throughout the course of the hospitalization. AMI-CS = cardiogenic shock complicating acute myocardial infarction; IHM = in-hospital mortality; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; SCAI = Society for Cardiovascular Angiography and Interventions; STEMI = ST-segment elevation myocardial infarction.

We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial and 30% of patients in the IABP-SHOCK (Intra-Aortic Balloon Pump in Cardiogenic Shock) II trial presented with NSTEMI-CS.[5,19] Patients with NSTEMI-CS are often heterogeneous reflecting a spectrum of cardiovascular risk. In the The Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO)-IIb Registry, eg, patients with NSTEMI-CS had later onset of CS than patients with STEMI-CS, had more extensive coronary artery disease, and more recurrent ischemia and infarction before developing shock compared with patients with STEMI-CS.[20] The last American College of Cardiology and American Heart Association Guidelines for the management of STEMI and NSTEMI were published in 2013 and 2014, respectively, and merit a timely update.[21-24] More recently published American Heart Association/American College of Cardiology/Heart Failure Society of America (HFSA) guidelines on Heart Failure do not specifically address STEMI-CS or NSTEMI-CS.[25-27] Thus, our findings highlight that patients with NSTEMI-CS are an important high-risk cohort that merit inclusion in future clinical trials in CS to determine the optimal treatment strategies in these patients.

CA remains a very important effect modifier of CS. Indeed, both OHCA and IHCA were associated with higher in-hospital mortality in both STEMI-CS and NSTEMI-CS. OHCA was more prominently seen in the NSTEMI-CS cohort, which likely represents a heterogeneous syndrome that encompasses a broad spectrum of clinical presentations and hemo-metabolic derangements due to acute coronary syndrome not involving acute plaque rupture. Our results are consistent with prior work,[28] including that of Vallabhajosyula et al,[29] who have previously shown using National Inpatient Sample data collected from 2000 to 2017 that the combined CS and CA cohort have higher rates of multiorgan failure and in-hospital mortality as compared to CS only and CA only, respectively, in patients with STEMI-CS. Our analysis extends this work in a more contemporary cohort illustrating the impact on both STEMI-CS and now including patients with NSTEMI-CS. Matching the right therapy to the right patient at the right time in this high-risk subgroup is especially challenging given the competing risk of death due to neurologic injury.[30] Nonetheless, our data supports the burgeoning evidence that patients with STEMI and NSTEMI with both CS and CA represent a unique high-risk cohort with salient differences with respect to pathophysiology, multiorgan sequelae, and causes of death. As noted by Jentzeret al,[30] these should be analyzed separately from patients with CS without CA in future clinical trials, given confounding previously reported in subgroup analyses of IABP-SHOCK II and CULPRIT-SHOCK (Culprit Lesion Only Percutaneous Coronary Intervention Versus Multivessel Percutaneous Coronary Intervention in Cardiogenic Shock).

The present analysis also extends our prior work employing the CSWG interpretation of the revised SCAI staging classification.[31] Both STEMI-CS and NSTEMI-CS SCAI stage B (approximately 90% in both) and C (approximately 70% in both) patients transitioned to a higher SCAI stage during the course of their index hospitalization. Interestingly, patients with NSTEMI-CS SCAI B required a higher mean time to maximum SCAI stage as compared to patients with STEMI-CS SCAI B; the converse appeared to be present for patients with STEMI-CS SCAI C as compared to patients with NSTEMI-CS. When transition to SCAI E did occur, it was associated with worse outcomes then de novo presentations in SCAI E perhaps due to delay in recognition of onset of worsening or refractory hemo-metabolic shock and multiorgan failure. While these results are hypothesis-generating given that the retrospective observational dataset was not powered to adequately detect differences among these subgroups, they highlight key clinical questions that should inform future analyses. Specifically, given the dynamic nature of SCAI stages, clinicians must perform serial re-assessments to ascertain whether the maximum SCAI stage has been achieved when managing these patients with CS in the cardiac intensive care unit.

Another novel and important finding from our analysis is the detailed understanding of drug and device exposure in a contemporary real-world CS multicenter cohort. To the best of our knowledge, ours is the first detailed analysis of both drug and device utilization, both within the first 24 hours of admission as well as throughout the hospitalization for both patients with STEMI-CS and NSTEMI-CS. Within the first 24 hours of the hospitalization, it is remarkable that more than 50% of both patients with STEMI-CS and NSTEMI-CS receive neither drug nor device treatment. During this interval, patients with STEMI-CS were more likely to receive a drug and device (27% vs 12%) and patients with NSTEMI-CS were more likely to receive drug only (22% vs 15%). Perhaps not surprisingly, this distribution of drug and device use evolved significantly for both patients with STEMI-CS and NSTEMI-CS during the course of the index hospitalization. In particular, 98% of both patients with STEMI-CS and NSTEMI-CS had exposure to either a drug or device or combination thereof during the course of the hospitalization; notably, 78%

of all patients with STEMI-CS were treated with a combination of drug and device as compared to 61% of patients with NSTEMI-CS. IABP was the most common device employed in both STEMI-CS and NSTEMI-CS, both within 24 hours and throughout the course of the hospitalization.

These results are particularly noteworthy in light of the IABP-SHOCK II trial, which showed the absence of a significant effect of routine IABP on all-cause mortality at 30 days, 12 months, and at 6-year follow-up in patients with AMI-CS.[5,32] Although the routine use of IABP in Europe has diminished since the European Society of Cardiology STEMI Guidelines downgraded IABP from Class I to Class IIb in 2012 and then Class IIIb in 2017, there has been clinical inertia to adopt these recommendations in the United States.[33,34] Given that IABP still remains the most ubiquitous tMCS device used in both the United States and worldwide, future clinical trials are needed to elucidate the appropriate, select patient population, severity, and phenotype of CS that would maximally benefit from this therapy. In a similar vein, vasopressors were the most common drug exposure in STEMI-CS and NSTEMI-CS, both within 24 hours and throughout the course of the hospitalization. Interestingly, inotropes were more likely to be used in combination with vasopressors than as single agents. This finding should also be interpreted in the context of the Dobutamine Compared with Milrinone (DOREMI) trial, which did not demonstrate any significant difference between dobutamine and milrinone on a primary composite endpoint, which included all-cause, in-hospital mortality, transient ischemic attack, stroke, and cardiovascular or renal events.[6]

This multicenter cohort study has several strengths, including robust data collection of real-world patients with AMI-CS, use of invasive hemodynamics, and details regarding broad drug and device utilization throughout patients' clinical trajectories. However, there are several important limitations of this study, which should be acknowledged. First, we cannot exclude the possibility of residual confounding given the retrospective observational design of this study. In addition, the results may be influenced by local institutional clinical practices and operator expertise; no specific algorithm was prescribed to guide CS management due to the lack of randomized data and clear guidelines. Second, we were not able to capture granular information regarding temporary mechanical circulatory support and revascularization characteristics, including timing and sequence of devices and/or door to balloon time. We postulate that both type and timing of revascularization (ie, percutaneous coronary intervention vs CABG) and tMCS (ie, IABP, Impella, VA-ECMO, etc) likely serve as important mediators of in-hospital outcomes. This data have been identified as a priority for future data collection and investigation in our registry. Third, we did not use multiple imputation or other methods to account for the limited missing data as we could not confirm that the missing values were missing at random. Thus, we chose to analyze only the complete records.

CONCLUSIONS

We report one of the largest, contemporary, real-world registry-based analyses characterizing AMI-CS and specifically comparing STEMI-CS and NSTEMI-CS across key clinical characteristics, hemodynamic and metabolic parameters, in-hospital mortality, as well as drug- and device-based strategies. Despite increasing use of inotropic and vasoactive support and tMCS throughout the course of the hospitalization, both patients with STEMI-CS and NSTEMI-CS remain at increased risk for in-hospital mortality. Future RCTs are needed to elucidate whether timing and sequence of escalation of support improves outcomes in these critically ill patients.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: In-hospital mortality remains high across both patients with STEMI-CS and NSTEMI-CS, suggesting that patients with NSTEMI-CS also represent a vulnerable, high-risk cohort. CA is an adverse effect modifier for both cohorts of patients. The majority of SCAI stage B and SCAI stage C patients with STEMI-CS and NSTEMI-CS progress during their hospitalization to SCAI stage D or E; transition to a higher SCAI stage is associated with worse in-hospital outcomes as compared to those who initially presented in SCAI E. During the first 24 hours, patients with STEMI-CS were more likely to receive drug and device-based therapies whereas patients with NSTEMI-CS were more likely to receive drug therapies only, providing insights into the contemporary clinical practice of patients with AMI-CS.

TRANSLATIONAL OUTLOOK: RCTs are needed to elucidate whether timing and sequence of escalation of vasopressors, inotropes, and/or tMCS improves outcomes in patients with STEMI-CS and NSTEMI-CS, respectively.

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KEY WORDS **acute myocardial infarction, cardiogenic shock, heart failure**

APPENDIX **For supplemental tables and figures, please see the online version of this paper.**