Characteristics of High-Performing Hospitals in Cardiogenic Shock Following Acute Myocardial Infarction

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Cardiogenic shock after acute myocardial infarction (AMI-CS) carries significant mortality despite advances in revascularization and mechanical circulatory support. We sought to identify the process-based and structural characteristics of centers with lower mortality in AMI-CS. We analyzed 16,337 AMI-CS cases across 440 centers enrolled in the National Cardiovascular Data Registry's Chest Pain-MI Registry, a retrospective cohort database, between January 1, 2015, and December 31, 2018. Centers were stratified across tertiles of risk-adjusted in-hospital mortality rate (RAMR) for comparison. Risk-adjusted multivariable logistic regression was also performed to identify hospital-level characteristics associated with decreased mortality. The median participant age was 66 (interquartile range 57 to 75) years, and 33.0% (n = 5,390) were women. The median RAMR was 33.4% (interquartile range 26.0% to 40.0%) and ranged from 26.9% to 50.2% across tertiles. Even after risk adjustment, lower-RAMR centers saw patients with fewer co-morbidities. Lower-RAMR centers performed more revascularization (92.8% vs 90.6% vs 85.9%, p <0.001) and demonstrated better adherence to associated process measures. Left ventricular assist device capability (odds ratio [OR] 0.78 [0.67 to 0.92], p = 0.002), more frequent revascularization (OR 0.93 [0.88 to 0.98], p = 0.006), and higher AMI-CS volume (OR 0.95 [0.91 to 0.99], p = 0.009) were associated with lower in-hospital mortality. However, several such characteristics were not more frequently observed at low-RAMR centers, despite potentially reflecting greater institutional experience or resources. This may reflect the heterogeneity of AMI-CS even after risk adjustment. In conclusion, low-RAMR centers do not necessarily exhibit factors associated with decreased mortality in AMI-CS, which may reflect the challenges in performing outcomes research in this complex population.
 (Am J Cardiol 2024;221:19−28)

Keywords: cardiogenic shock, critical care cardiology, myocardial infarction, risk-adjusted mortality rate

Cardiogenic shock (CS) remains a severe complication of acute myocardial infarction (AMI), carrying an in-hospital mortality of 30% to 50%.[1−3] Despite more frequent percutaneous coronary intervention (PCI) and an array of mechanical circulatory support (MCS) devices, the substantial mortality of AMI-CS nevertheless persists.[1,4−7] Adherence to process measures in other cardiology domains, such as ejection fraction assessment after AMI or initiation of guideline-directed therapy in heart failure (HF), is associated with decreased mortality.[8−12] However, AMI-CS management may vary significantly across centers, and process measures may not fully capture institutional differences affecting outcomes.[8,13] Multicenter outcomes research is further complicated by heterogeneity in clinical severity, including cardiac arrest (CA), which is associated with significantly worse mortality.[14−16] This study aimed to

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Funding: none.

See page 26 for Declaration of Competing Interest.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2024.04.002

identify hospital-level structural characteristics and process measures that affect AMI-CS outcomes at centers participating in the Chest Pain-MI Registry of the National Cardiovascular Data Registry (NCDR).

Methods

The Chest Pain-MI Registry is a national, multicenter database that collects data on patients presenting with ST-elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) or unstable angina.[17] Retrospectively collected data are entered using a standardized data collection form (DCF). All participating centers require institutional review board approval or review waiver. The Duke University institutional review board approved this analysis.

The study period included 553,173 patients at 834 centers participating in the Chest Pain-MI Registry between January 1, 2015, and December 31, 2018. Patients transferred to another institution before death or discharge were excluded. Only sites with at least 1 patient with myocardial infarction annually during the study period or at least 40 patients with AMI or 10 AMI-CS cases total since the Chest Pain-MI Registry began enrollment in 2007 were included. This cohort of 444,540 patients with AMI at 440 sites was used for calculating variables of interest such as procedural volume. Of this population, we further identified those with AMI-CS at presentation to define the final study cohort.

AMI-CS was defined using the NCDR Data Standards Workgroup criteria.[18] Briefly, CS comprised sustained (>30 minutes) hemodynamic compromise, characterized by systolic blood pressure (SBP) <90 mm Hg and/or cardiac index <2.2 L/min/m^2 because of cardiac dysfunction, and/or use of parenteral inotropic or vasopressor agents or MCS to maintain SBP >90 mm Hg or cardiac index >2.2 L/min/m^2.

Risk-adjusted mortality rate (RAMR) accounts for patient factors associated with mortality to permit a more objective comparison across populations.[19] RAMR was calculated for each participating site using the final study cohort of AM-CS:

$$RAMR = \frac{observed\ deaths}{predicted\ mortality} \times overall\ observed\ mortality\ rate$$

The overall observed mortality rate was determined from the absolute number of in-hospital deaths across all sites. Site-specific predicted mortality rates were determined using a previously described risk stratification model derived using patients enrolled in the Chest Pain-MI Registry. This model has been validated in the overall registry cohort (C-statistic = 0.877) and in the subpopulation of AMI-CS (C-statistic = 0.741).[19] The following 9 covariables at initial presentation were used for modeling: age, heart rate, SBP, CA, CS, HF, STEMI, creatinine clearance, and troponin (Tn) ratio. CA was determined by pulselessness or administration of external defibrillation or chest compressions on presentation. Tn ratio was defined as baseline Tn ÷ laboratory-specific upper limit of normal.

The collected data included baseline demographics; signs, symptoms, and laboratory values at presentation; clinical management; and in-hospital events. Revascularization was defined as either PCI or coronary artery bypass graft (CABG). MCS included intra-aortic balloon pump (IABP), temporary or durable percutaneous or surgically implanted ventricular assist device (VAD), or venoarterial extracorporeal membrane oxygenation. Specific process measures of interest were chosen from those described by the Centers for Medicare and Medicaid Services and the American College of Cardiology/American Heart Association.[20] Contraindication to catheterization was site-reported and could be because of a medical- or system-related reason or because of refusal by the patient or surrogate decision-maker. Medical management comprised nonprocedural treatment of AMI-CS with or without diagnostic catheterization. Defect-free care included prescription of aspirin, β blockers, statins, angiotensin-converting enzyme or angiotensin receptor blockers, smoking cessation counseling, and cardiac rehabilitation referral in eligible patients.

Participating sites were stratified into tertiles of low, medium, or high RAMR. The summary statistics of patient demographics and hospital characteristics were compared across tertiles. Adherence to core quality measures during hospitalization was also assessed across tertiles. Categorical variables were compared using Fisher's exact test or chi-square test when sample size was sufficient and are presented as n (%). Continuous variables were assumed to have nonparametric distributions, were compared using Kruskal-Wallis test, and are presented as median (interquartile range [IQR]).

To determine hospital and patient characteristics that affected RAMR across the entire cohort, a generalized estimating equation multivariable logistic regression model with adjustment for clustering of observations from the same hospital was constructed. The generalized estimating equation method was implemented with a compound symmetric working correlation matrix and empirical (sandwich) standard error estimates. Hospital-level covariables of interest were annual AMI-CS volume; total AMI admission volume; median time to PCI or CABG; rural versus urban location; academic hospital designation; region; hospital beds; type of hospital services available; VAD/orthotopic heart transplantation (OHT) capability; and proportions of patients who underwent angiography, revascularization, presented with CA, underwent a hypothermia protocol, presented as interfacility transfers, or received MCS. Site-specific VAD and OHT capabilities are not documented in the Chest Pain-MI Registry and were abstracted from data available from Centers for Medicare and Medicaid Services and Scientific Registry of Transplant Recipients.[21,22] Covariable co-linearity was assessed using variance inflation factors. Variance inflation factors >5 between variables was considered evidence of co-linearity. Patient covariates for risk adjustment were the same as those used to determine site-specific predicted mortality. Continuous variables were assessed for linearity and, if nonlinear, were assessed using linear splines with variable knots. The association of each variable of interest and in-hospital mortality is presented as odds ratio (OR) (95% confidence interval).

The Cochran−Armitage test for trend was used to assess temporal changes in use of PCI, CABG, medical management alone, and MCS in NSTEMI and STEMI during the study period.

Sensitivity analyses were performed excluding all patients presenting in CA from the study cohort. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina). All statistical tests were 2-sided. A $p < 0.05$ was considered statistically significant.

Results

Between January 1, 2015 and December 31, 2018, 16,337 patients presented with AMI-CS at 440 participating centers and met the inclusion criteria (Figure 1). Site-specific predicted mortality was calculated after excluding 1,059 patients (6.5%) who were missing data for any variable required for risk stratification.[19] The unadjusted overall in-hospital mortality was 38.5%, and the median RAMR was 33.4% (IQR 26.0% to 40.0%). The sites were split into tertiles of low (n = 146, RAMR 0.0% to 28.8%), medium (n = 147, RAMR 28.9% to 37.9%), and high (n = 147, RAMR 40.0% to 71.3%) RAMR. In addition to absolute in-hospital mortality (26.9% vs 39.3% vs 50.2%, p <0.001), death within 24 hours of admission (10.4% vs 16.2% vs 21.3%, p <0.001), major bleeding (26.6% vs 29.1% vs 28.7%, p = 0.008), and new dialysis requirement (3.5% vs 5.5% vs 5.0%, p <0.001) were all less frequent in lower-RAMR hospitals (Figure 2).

Patient characteristics are listed in Table 1. The median age was 66.0 years (IQR 57.0 to 75.0), and 33.0% (n = 5,390) were women. Patients at low-RAMR hospitals had fewer co-morbidities at admission, including dialysis requirement, diabetes mellitus, HF, previous CABG, and cerebrovascular disease, and had higher creatinine clearance and lower Tn ratio at clinical presentation. Markers of preadmission functional status, such as mobility, cognition, and ability to complete activities of daily living, were higher in the low-RAMR cohort. The rates of multiple process measures, particularly diagnostic catheterization (92.8% vs 90.6% vs 85.9%, p <0.001), radial access for PCI in STEMI (18.5% vs 12.5%, p <0.001), and revascularization in NSTEMI (61.0% vs 57.0% vs 47.5%, p <0.001) were more frequent at low-RAMR sites. Patients at low-RAMR sites were less likely to have a contraindication to catheterization (6.0% vs 8.0% vs 12.2%, p <0.001). MCS was less frequently used (27.9% vs 34.2% vs 33.8%, p <0.001) and more often limited to IABP (71.6% vs 64.0% vs 64.0%, p <0.001) at low-RAMR sites.

Hospital characteristics are listed in Table 2. The distribution of hospital region and location did not differ across tertiles. Low-RAMR sites were more likely to perform diagnostic catheterization (94.6% vs 93.3% vs 92.5%, p = 0.001) and revascularization procedures (80.0% vs 78.5% vs 76.4%, p = 0.001) and saw higher proportions of patients with AMI presenting with CS (3.9% vs 3.6% vs 3.0%, p <0.001). However, they were also smaller (265 vs 335 vs 336 beds, p = 0.008) and saw lower absolute volumes of AMI (191.5 vs 238.8 vs 221.8 cases, p = 0.001) and AMI-CS (6.3 vs 8.0 vs 6.0 cases, p = 0.003). There was no difference in availability of advanced HF therapies across tertiles.

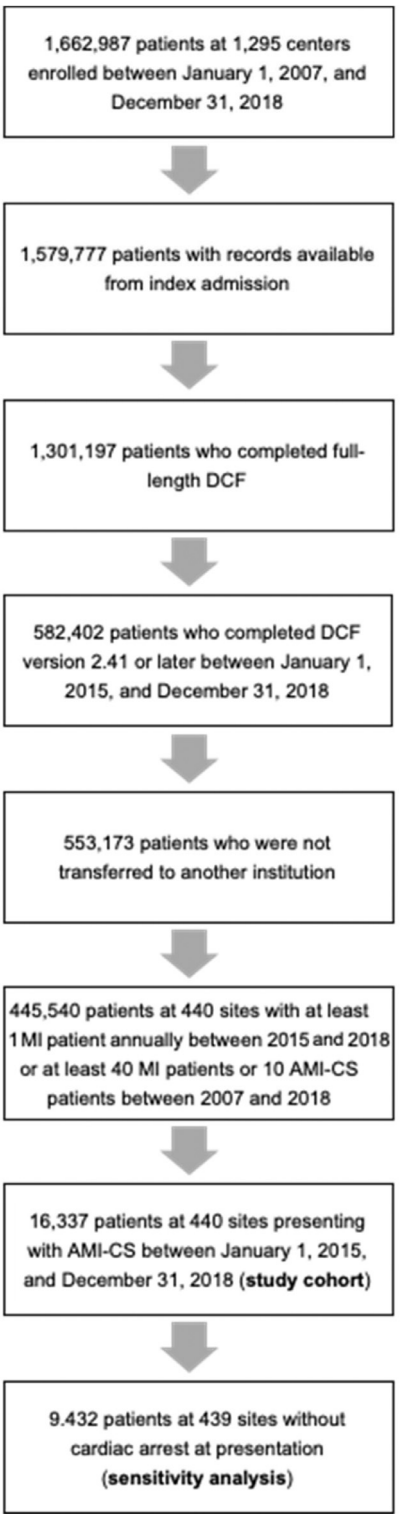

Figure 1. CONSORT diagram.

Table 3 lists the factors associated with AMI-CS mortality across the entire cohort after adjusting for patient-level covariates. In multivariable-adjusted analysis, hospital characteristics associated with lower in-hospital mortality included left ventricular assist device (LVAD) capability

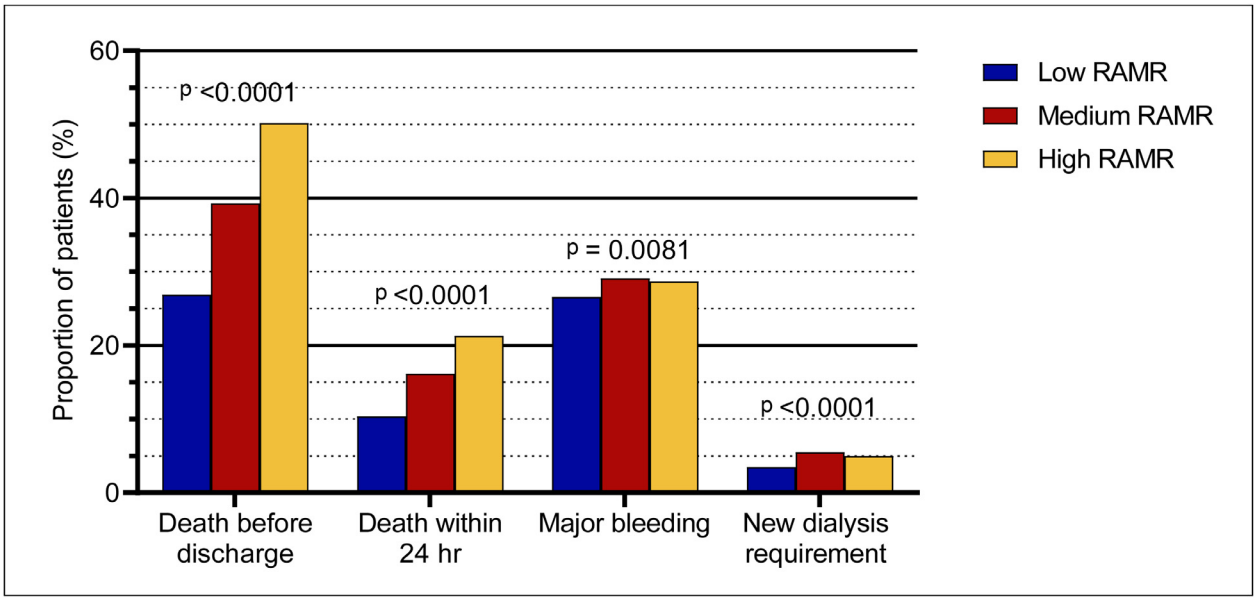

Figure 2. In-hospital outcomes and adverse events across RAMR tertiles. Proportions of all in-hospital deaths, death within 24 hours of admission, major bleeding, and new dialysis requirement are presented across low (blue), medium (red), and high (yellow) tertiles of RAMR.

(OR 0.78 [0.67 to 0.92], p = 0.002), a greater proportion of patients who underwent revascularization (OR 0.93 [0.88 to 0.98], p = 0.006), and higher annual volume of AMI-CS (OR 0.95 [0.91 to 0.99], p = 0.009). Rural hospital setting was associated with higher mortality (OR 1.16 [1.12 to 1.31], p = 0.023). The patient's SBP on arrival had the most pronounced association with mortality (OR 0.91 [0.90 to 0.93], p <0.001).

The proportion of patients with NSTEMI who underwent PCI increased from 40.5% to 53.7% during the study period (p_{trend} <0.001) (Supplementary Figure 1) and corresponded to a decrease in medical management (30.4% to 26.5%, p_{trend} <0.001). MCS was increasingly used (31.6% to 37.2%, p_{trend} <0.001) in the STEMI cohort.

Of the original cohort, 9,451 patients (57.8%) did not present with CA (see Figure 1). The median RAMR in this population was 37.6% (IQR 25.6% to 47.6%). Adverse outcomes beyond in-hospital mortality remained lower across decreasing RAMR tertiles (Supplementary Figure 2). Demographic characteristics were not meaningfully different from the overall cohort (Supplementary Table 1). Low-RAMR sites continued to demonstrate higher adherence to multiple process measures, higher proportion of CS volume (3.7% vs 3.6% vs 3.0%, p = 0.002), and more frequent revascularization (79.2% vs 79.0% vs 76.5%, p = 0.002) (Supplementary Table 2). Rural hospital setting remained associated with higher mortality (OR 1.24 [1.06 to 1.44], p = 0.008) (Supplementary Table 3). However, the rates of revascularization and annual AMI-CS volume were not associated with mortality. The association with LVAD capability (OR 0.79 [0.62 to 1.00], p = 0.049) remained significant. The rates of PCI in NSTEMI (36.9% to 50.7%, p_{trend} <0.001) and MCS in STEMI (31.2% to 39.4%, p_{trend} <0.001) increased over time as in the study cohort (Supplementary Figure 3).

Discussion

This study examined the NCDR's Chest Pain-MI Registry to identify specific hospital-level processes and characteristics associated with lower RAMR in AMI-CS. Hospitals in the lowest RAMR tertile (i.e., the highest-performing sites) demonstrated greater adherence to multiple process measures, particularly revascularization in AMI-CS. However, they were also smaller-volume centers for AMI and AMI-CS, although the proportion of CS of all-comers with AMI was larger. We identified 4 hospital characteristics associated with lower in-hospital mortality in AMI-CS: (1) more frequent revascularization, (2) higher annual volume of AMI-CS, (3) availability of LVADs, and (4) urban location. Interestingly, only the first of these was more commonly observed at low-RAMR sites. SBP and CA at presentation were inversely associated with mortality.

Previous studies have demonstrated an association between adherence to quality-of-care metrics and improved outcomes in AMI, particularly, STEMI.[8,12,23] We observed that adherence to multiple process measures in the management of AMI-CS, such as prompt aspirin administration, door-to-balloon time in STEMI, and radial access for PCI, was higher in low-RAMR centers. More frequent revascularization in NSTEMI-CS was noted over the study period across the entire cohort but specifically in low-RAMR sites. Previous multiregistry data have similarly demonstrated increased use of PCI for AMI-CS since earlier studies first demonstrated improved survival with early revascularization.[1,5,24] Interestingly, the time to revascularization in STEMI and NSTEMI was not associated with mortality, which may suggest that revascularization in AMI-CS is beneficial, irrespective of timing. Notably, patients at high-RAMR sites were more likely to have a contraindication to catheterization. Although ample data supports the benefit of revascularization, as we also

Table 1
Baseline demographics, clinical features at presentation for AMI-CS, and process measures across tertiles of RAMR

Variable	Level	Overall	Low RAMR (0-28.8%)	Medium RAMR (28.9-37.9%)	High RAMR (40.0-71.3%)	*P* value
Demographic data						
Number of patients with AMI-CS		16,337	5,332	6,153	4,852	
Age (y)*		66.0 (57.0, 75.0)	65.0 (57.0, 74.0)	66.0 (57.0, 75.0)	67.0 (58.0, 76.0)	<0.001
Female gender		5,390 (33.0%)	1,672 (31.4%)	2,035 (33.1%)	1,683 (34.7%)	0.002
BMI (kg/m^2)		27.9 (24.5, 32.1)	28.1 (24.8, 32.5)	27.8 (24.4, 32.2)	27.6 (24.4, 31.8)	0.001
Caucasian race		12,906 (79.0%)	4,305 (80.7%)	4,946 (80.4%)	3,655 (75.3%)	<0.001
Uninsured		1,712 (10.5%)	500 (9.4%)	680 (11.1%)	532 (11.0%)	<0.001
Comorbidities						
HTN		11,045 (67.6%)	3,590 (67.3%)	4,115 (66.9%)	3,340 (68.8%)	0.083
Dialysis		499 (3.1%)	138 (2.6%)	177 (2.9%)	184 (3.8%)	0.001
DM		5,444 (33.3%)	1,677 (31.5%)	2,048 (33.3%)	1,719 (35.4%)	<0.001
Prior MI		2,905 (17.8%)	907 (17.0%)	1,086 (17.7%)	912 (18.8%)	0.060
Prior HF		2,017 (124%)	572 (10.7%)	793 (12.9%)	652 (13.4%)	<0.001
Prior PCI		2,946 (18.0%)	953 (17.9%)	1,116 (18.1%)	877 (18.1%)	0.924
Prior CABG		1,330 (8.1%)	406 (7.6%)	479 (7.8%)	445 (9.2%)	0.007
CVD		1,936 (11.9%)	579 (10.9%)	760 (12.4%)	597 (12.3%)	0.024
Home functioning						
Walking	Unassisted	12,056 (73.8%)	4,168 (78.2%)	4,533 (73.7%)	3,355 (69.2%)	<0.001
	Assisted	1,167 (7.1%)	322 (6.0%)	458 (7.4%)	387 (8.0%)	
	Wheelchair/non-ambulatory	607 (3.7%)	183 (3.4%)	222 (3.6%)	202 (4.2%)	
	Unknown	2,467 (15.1%)	651 (12.2%)	919 (14.9%)	897 (18.5%)	
Cognition	Normal	12,684 (77.6%)	4,338 (81.4%)	4,783 (77.7%)	3,563 (73.4%)	<0.001
	Mildly impaired	671 (4.1%)	191 (3.6%)	259 (4.2%)	221 (4.6%)	
	Moderately or severely impaired	537 (3.3%)	132 (2.5%)	223 (3.6%)	182 (3.8%)	
	Unknown	2,409 (14.8%)	664 (12.5%)	871 (14.2%)	874 (18.0%)	
Basic ADLs	Independent	12,264 (75.1%)	4,230 (79.3%)	4,638 (75.4%)	3,396 (70.0%)	<0.001
	Partial assist >1 ADL	774 (4.7%)	240 (4.5%)	285 (4.6%)	249 (5.1%)	
	Full assist >1 ADL	618 (3.8%)	161 (3.0%)	248 (4.0%)	209 (4.3%)	
	Unknown	2,624 (16.1%)	688 (12.9%)	960 (15.6%)	976 (20.1%)	
Labs at presentation						
CrCl (ml/min/m^2)*		65.1 (45.4, 87.6)	68.8 (48.7, 91.5)	65.1 (45.1, 87.6)	61.2 (42.3, 83.0)	<0.001
Hb (g/dL)		13.6 (11.9, 15.0)	13.8 (12.2, 15.1)	13.6 (11.9, 15.0)	13.3 (11.6, 14.7)	<0.001
BNP		302.0 (90.0, 864.5)	279.0 (93.0, 802.0)	298.5 (88.0, 870.5)	342.0(92.0, 905.0)	0.075
Tn ratio*		5.5 (1.0, 66.7)	4.3 (0.7, 61.8)	6.2 (1.0, 59.2)	6.0 (1.0, 79.4)	<0.001
Signs and symptoms at presentation						
Onset to arrival (h)		1.2 (0.8, 2.4)	1.3 (0.8, 2.5)	1.3 (0.8, 2.4)	1.2 (0.8, 2.3)	0.019
HR (bpm)*		73.0 (45.0, 100.0)	74.0 (48.0, 100.0)	75.0 (45.0, 100.0)	70 (40.0, 100.0)	<0.001
SBP (mm Hg)*		95.0 (69.0, 129.0)	100.0 (73.0, 134.0)	96.0 (70.0, 129.0)	90.0 (62.0, 121.0)	<0.001
STEMI*		12,511 (76.6%)	4,191 (78.6%)	4,744 (77.1%)	3,576 (73.7%)	<0.001
HF signs*		4,791 (29.3%)	1,607 (30.1%)	1,893 (30.8%)	1,291 (26.6%)	<0.001
CA		6,886 (42.2%)	2,177 (40.8%)	2,610 (42.4%)	2,099 (43.3%)	0.046
Pre-hospital		5,743 (83.4%)	1,774 (81.5%)	2,172 (83.2%)	1,797 (85.6%)	<0.001
OSF		1,240 (18.0%)	409 (18.8%)	510 (19.5%)	321 (15.3%)	0.135
Process measures						
ASA in 24h		14,591 (93.0%)	4,909 (94.3%)	5,534 (93.6%)	4,148 (90.8%)	<0.001
Thrombolytic therapy		622 (5.0%)	186 (4.4%)	254 (5.4%)	182 (5.1%)	0.131
Diagnostic catheterization		14,695 (90.0%)	4,948 (92.8%)	5,577 (90.6%)	4,170 (85.9%)	<0.001
Contraindication to catheterization		1,405 (8.6%)	318 (6.0%)	495 (8.0%)	592 (12.2%)	<0.001
Primary PCI for STEMI		10,222 (95.5%)	3,529 (96.0%)	3,878 (95.9%)	2,815 (94.4%)	0.004
Radial access		1,634 (16.0%)	651 (18.5%)	631 (16.3%)	352 (12.5%)	<0.001
Door-to-balloon time ≤90 min (direct admits)		3,666 (92.7%)	1,341 (93.1%)	1,382 (92.9%)	943 (91.7%)	0.497
Door-to-balloon time ≤120 min (transfer-ins)		3,784 (95.6%)	1,383 (96.0%)	1,424 (95.7%)	977 (95.0%)	0.380
LVEF evaluated		14,607 (89.4%)	4,910 (92.1%)	5,484 (89.1%)	4,213 (86.8%)	<0.001
Defect-free care at discharge		7,931 (84.4%)	3,132 (85.2%)	2,980 (85.3%)	1,819 (81.6%)	<0.001

(*continued*)

Table 1 (*Continued*)

Variable	Level	Overall	Low RAMR (0-28.8%)	Medium RAMR (28.9-37.9%)	High RAMR (40.0-71.3%)	*P* value
NSTEMI intervention	PCI	1,730 (45.2%)	559 (49.0%)	657 (46.5%)	514 (40.3%)	<0.001
	CABG	377 (9.8%)	137 (12.0%)	148 (10.5%)	92 (7.2%)	
	Cath only	721 (18.8%)	213 (18.7%)	252 (17.9%)	256 (20.1%)	
	Medical management	999 (26.1%)	231 (20.3%)	355 (25.1%)	413 (32.3%)	
Hypothermia protocol		3,205 (19.6%)	979 (18.4%)	1,220 (19.8%)	1,006 (20.7%)	0.010
MCS		5,230 (32.0%)	1,486 (27.9%)	2,104 (34.2%)	1,640 (33.8%)	<0.001
MCS type	IABP	3,459 (66.1%)	1,064 (71.6%)	1,346 (64.0%)	1,049 (64.0%)	<0.001
	Impella	1,407 (26.9%)	317 (21.3%)	585 (27.8%)	505 (30.8%)	
	TandemHeart	4 (0.1%)	1 (0.1%)	2 (0.1%)	1 (0.1%)	
	ECMO	193 (3.7%)	47 (3.2%)	105 (5.0%)	41 (2.5%)	
	LVAD	28 (0.5%)	8 (0.5%)	13 (0.6%)	7 (0.4%)	
	Other	133 (2.5%)	46 (3.1%)	52 (2.5%)	35 (2.1%)	

ACE = angiotensin-converting enzyme; ADL = activity of daily living; ARB = angiotensin receptor blocker; ASA = aspirin; BMI = body mass index; BNP = brain natriuretic peptide; CA = cardiac arrest; CABG = coronary artery bypass graft; CrCl = creatinine clearance; CVD = cerebrovascular disease; DM = diabetes mellitus; ECMO = extracorporeal membrane oxygenation; Hb = hemoglobin; HF = heart failure; HR = heart rate; HTN = hypertension; IABP = intra-aortic balloon pump; LVAD = left ventricular assist device; LVEF = left ventricular ejection fraction; MCS = mechanical circulatory support; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OSF = outside facility; PCI = percutaneous coronary intervention; RAMR = risk-adjusted mortality rate; SBP = systolic blood pressure; STEMI = ST-elevation myocardial infarction; Tn = troponin.

* Variables used in calculating predicted mortality. Continuous data are presented as median (interquartile range) and compared across groups using Kruskal-Wallis test. Categorical data are presented as n (percent) and compared across groups using Fisher's exact or chi-square test where sample size allows.

CrCl was estimated in non-dialysis patients using the Cockcroft-Gault formula. BNP was available for only 5,284 patients. Tn ratio = baseline Tn ÷ laboratory-specific upper limit of normal.

observed, this may also reflect a confounder in our population because patients who cannot undergo revascularization may simply have a worse prognosis.

Greater adherence to quality measures, however, may not fully explain the better outcomes at low-mortality sites. This is especially true of benchmarks with universally high adherence, such as prompt aspirin administration (>90% across tertiles), where only incremental gains may be realized.[8,25] We, therefore, evaluated structural hospital characteristics that may be prevalent at low-RAMR centers.

The main variables identified on logistic regression, namely, higher AMI-CS volume, LVAD capability, and urban location, may reflect the advantages of greater resources and institutional and provider experiences that are to be found at larger hospitals. Similar to previous observational data, we observed an inverse association between AMI-CS volume and in-hospital mortality.[26] Centers with durable LVAD availability may have a greater array of temporary and long-term management strategies that, together, may reduce mortality. This potential benefit was observed in assessment of durable LVAD outcomes in patients with AMI enrolled in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), 66% of whom were INTERMACS profile 1 at time of implantation. Such patients demonstrated comparable outcomes to patients with an LVAD with non-AMI etiologies, despite higher acuity.[27]

We also observed lower mortality associated with urban versus rural location. Urban sites have been shown to use revascularization and MCS more aggressively in populations with higher rates of multiorgan failure.[28] Interestingly, another analysis of AMI complicated by CA demonstrated higher mortality associated with urban location.[29] However, that cohort was more critically ill and the multivariable modeling was not adjusted for certain patient-specific covariates, such as SBP and Tn ratio, which have been validated specifically for our cohort.[19] Rural hospitals are typically lower-volume centers and often serve as safety nets for their respective communities, which may relate to the observed difference in mortality.

Surprisingly, AMI-CS volume, LVAD capability, and urban location were not more common in low-RAMR centers. In fact, AMI and AMI-CS volume increased across higher RAMR tertiles, although the proportion of CS in all-comers with AMI was slightly higher in the lowest tertile. This discordance was observed despite adjusting our regression model for the same covariates used to calculate site-specific mortality and, consequently, RAMR. Moreover, in contrast to previous data, we observed that high-RAMR centers were larger.[28] Counterintuitively, low-RAMR sites, which demonstrated higher rates of revascularization and adherence to associated process measures, did not exhibit the structural characteristics typically reflective of greater institutional experience.

As previously described, the risk stratification model used to determine RAMR has been previously validated with reasonable fit in the AMI-CS population of the Chest Pain-MI Registry.[19] However, we did observe that patients at low-RAMR sites had lower rates of preexisting co-morbidities and better preadmission functional status. Critically, we also observed differing rates of contraindication to catheterization—above 10% in the highest RAMR tertile. We believe this highlights a key challenge in performing outcomes research in the AMI-CS population. Despite the strength of the stratification model used, there were likely multiple confounders affecting mortality across sites, such as preadmission co-morbidities. We also note that in the Chest Pain-MI Registry, AMI-CS was reported only based on the hemodynamic and/or supportive measures specified. Although enabling standardization across institutions, this

Table 2
Hospital characteristics across tertiles of RAMR

Variable	Level	Overall (n=440)	Low RAMR (n=146)	Medium RAMR (n=147)	High RAMR (n=147)	*P* value
Region	West	83 (18.9%)	28 (19.2%)	35 (23.8%)	20 (13.6%)	0.274
	Northeast	38 (8.6%)	13 (8.9%)	10 (6.8%)	15 (10.2%)	
	Midwest	105 (23.9%)	40 (27.4%)	32 (21.8%)	33 (22.5%)	
	South	214 (48.6%)	65 (44.5%)	70 (47.6%)	79 (53.7%)	
Capability	Cath lab only	2 (0.5%)	1 (0.7%)	0 (0%)	1 (0.7%)	0.176
	PCI only	86 (19.6%)	37 (25.3%)	22 (15.0%)	27 (18.4%)	
	PCI/CABG	352 (80.0%)	108 (74.0%)	125 (85.0%)	119 (81.0%)	
Teaching hospital	Academic	364 (82.7%)	125 (85.6%)	121 (82.3%)	118 (80.3%)	0.440
	Non-academic	70 (15.9%)	20 (13.7%)	22 (15.0%)	28 (19.1%)	
Total beds		318 (215, 493)	265 (185, 420)	335 (220, 518)	336 (234, 502)	0.008
Location	Urban	366 (83.2%)	123 (84.3%)	122 (83.0%)	121 (82.3%)	0.904
	Rural	74 (16.8%)	23 (15.8%)	25 (17.0%)	26 (17.7%)	
Advanced therapies	No LVAD/OHT	384 (87.3%)	128 (87.7%)	126 (85.7%)	130 (88.4%)	0.584
	LVAD only	21 (4.8%)	7 (4.8%)	10 (6.8%)	4 (2.7%)	
	LVAD/OHT	35 (8.0%)	11 (7.5%)	11 (7.5%)	13 (8.8%)	
Annual AMI volume		214.9 (148.0, 321.3)	191.5 (124.5, 273.8)	238.8 (169.0, 342.0)	221.8 (155.0, 341.8)	0.001
Annual AMI-CS volume		7.0 (4.6, 12.0)	6.3 (4.3, 11.5)	8.0 (5.5, 13.8)	6.0 (4.3, 10.3)	0.003
% CS volume		3.4 (2.5, 4.8)	3.9 (2.9, 5.2)	3.6 (2.6, 5.3)	3.0 (2.3, 3.9)	<0.001
% diagnostic coronary angiography		93.4 (89.9, 96.2)	94.6 (91.3, 97.0)	93.3 (89.4, 96.3)	92.5 (89.1, 95.2)	0.001
% revascularization		78.3 (72.7, 82.7)	80.0(75.2, 85.8)	78.5 (71.4, 83.7)	76.4 (72.1, 80.4)	0.001
% CA on first medical contact		3.7 (2.7, 4.8)	3.8 (2.9, 4.7)	3.8 (2.7, 5.0)	3.6 (2.7, 4.7)	0.392
% transfer-in		25.2 (9.7, 38.3)	23.2 (6.2, 35.0)	27.7 (13.8, 41.9)	22.8 (8.1, 35.7)	0.011
% hypothermia protocol		1.2(0.7, 1.9)	1.2 (0.6, 1.9)	1.3 (0.8, 1.9)	1.2 (0.7, 1.9)	0.536
% MCS		4.0 (2.2, 6.3)	3.6 (1.8, 5.9)	4.3 (2.7, 7.0)	4.0 (2.3, 6.3)	0.073
STEMI median time to PCI (min)		56.0 (48.0, 64.0)	56.0 (46.0, 64.0)	55.0 (46.5, 61.5)	58.0 (51.0, 65.0)	0.023
NSTEMI median time to PCI (hr)		18.6 (15.4, 21.3)	18.3 (14.9, 20.5)	18.5 (15.0, 21.2)	19.3 (16.0, 22.2)	0.068
Median time to CABG (hr)		76.9 (62.0, 93.1)	76.0 (60.6, 95.4)	75.4 (59.0, 90.6)	79.2 (66.5, 94.9)	0.144

Continuous data are presented as median (interquartile range) and compared across groups using Kruskal-Wallis test. Categorical data are presented as n (percent) and compared across groups using Fisher's exact or chi-square test where sample size allows.

AMI = acute myocardial infarction; CA = cardiac arrest; CABG = coronary artery bypass graft; CS = cardiogenic shock; LVAD = left ventricular assist device; MCS = mechanical circulatory support; NSTEMI = non-ST elevation myocardial infarction; OHT = orthotopic heart transplantation; PCI = percutaneous coronary intervention; RAMR = risk-adjusted mortality rate; STEMI = ST-elevation myocardial infarction.

definition comprises Society for Cardiovascular Angiography and Interventions stages B (hemodynamic instability without hypoperfusion) through E (impending/ongoing circulatory collapse).[30] The phenotype of AMI-CS, thus, likely varies significantly across individual sites and RAMR tertiles and cannot be easily captured by the current risk stratification model. This may, in part, explain why multiple hospital characteristics associated with improved in-hospital mortality were not more prevalent in low-RAMR sites and in our observation, in contrast to previous data, that high-RAMR centers were larger. For example, previous data have demonstrated greater use of MCS modalities beyond IABP at larger hospitals.[26] We similarly observed that larger (i.e., higher RAMR) hospitals used more advanced MCS more frequently. These centers may have greater practical experience in and advanced support options for AMI-CS, consequently drawing a sicker (i.e., SCAI C or greater) phenotype incompletely stratified by the NCDR definition of AMI-CS.

Presentation in CA has been shown to have a disproportionately negative effect on short- and long-term survival in AMI.[14–16,19] We observed a similar association with in-hospital mortality in AMI-CS. Sensitivity analyses excluding patients presenting in CA did not significantly change our key findings, specifically patient- and hospital-level differences across RAMR tertiles. Interestingly, the mortality benefit associated with revascularization, LVAD availability, and AMI-CS volume was lost after excluding patients with CA. This may be because of the smaller sample size compared with the overall cohort. It may also suggest differences in the relative benefits of these hospital characteristics for AMI-CS with versus without CA. Previous studies have described marked improvement in in-hospital mortality and a strong associated survival benefit with successful PCI versus no revascularization in AMI-CS with CA.[31,32] Given the significant mortality of CA in AMI-CS, these patients may stand to benefit the most from the expertise and capabilities available at shock centers.

This study is limited primarily by the observational nature of the Chest Pain-MI Registry. Each year, data collected from approximately 10% of participating sites are audited to ensure accuracy, with mean agreement >88% during the study period.[33] Although reassuringly accurate, the data are, however, limited to only that collected in the DCF. This eliminated a larger potential study cohort and limited the start of the study period to 2015. Additional potential variables of interest, such as postdischarge outcomes or rates of culprit-only versus total revascularization at presentation, could not be studied. Finally, as discussed, despite stratification of centers into RAMR tertiles using a

Table 3
Multivariable association of RAMR in AMI-CS

Variable	OR (95% CI)	*P* value (individual)	*P* value (global)
SBP (per 5-mmHg increase if ≤90 mmHg)	0.91 (0.90, 0.93)	<0.001	<0.001
SBP (per 5-mmHg increase if >90 mmHg)	0.96 (0.95, 0.96)	<0.001	
LVAD only (vs. no LVAD/OHT)	0.78 (0.67, 0.92)	0.002	0.007
LVAD/OHT (vs. no LVAD/OHT)	0.85 (0.70, 1.04)	0.110	
% CA (per 1% increase if ≤3%)	0.87 (0.74, 1.02)	0.090	0.026
% CA (per 1% increase if >3% but ≤6%)	1.09 (1.03, 1.16)	0.004	
% CA (per 1% increase if >6%)	0.87 (0.78, 0.96)	0.006	
Hospital bed size per 50-bed increase (if ≤350 beds)	1.05 (1.02, 1.09)	0.004	0.011
Hospital bed size per 50-bed increase (if >350 beds)	1.00 (1.00, 1.00)	0.124	
% undergoing revascularization (per 5% increase)	0.93 (0.88, 0.98)	0.006	-
Annual AMI volume (per 50 increase)	1.03 (1.01, 1.05)	0.007	-
Annual AMI-CS volume (per 5 increase)	0.95 (0.91, 0.99)	0.009	-
Rural (vs. urban)	1.16 (1.02, 1.31)	0.023	-
% MCS (per 1% increase)	1.02 (1.00, 1.03)	0.062	-
% diagnostic catheterization (per 1% increase)	1.06 (0.97, 1.15)	0.181	-
Northeast (vs. West)	1.01 (0.85, 1.21)	0.907	0.682
Midwest (vs. West)	1.02 (0.90, 1.16)	0.744	
South (vs. West)	1.07 (0.95, 1.21)	0.270	
% hypothermia protocol (per 1% increase)	1.03 (0.98, 1.09)	0.259	-
Median time to CABG (per 5-hr increase)	1.01 (1.00, 1.02)	0.302	-
PCI only (vs. catheterization lab only)	1.30 (0.38, 4.42)	0.674	0.680
CABG (vs. catheterization lab only)	1.22 (0.36, 4.13)	0.753	
NSTEMI median time to PCI (per 1-hr increase)	1.00 (0.98, 1.01)	0.520	-
STEMI median time to PCI (per 10-min increase)	1.01 (0.95, 1.07)	0.712	-
% transfer-in (per 5% increase)	1.00 (0.98, 1.02)	0.730	-
Academic (vs. nonacademic)	1.00 (0.88, 1.13)	0.955	-

Multivariable logistic regression was performed to identify hospital factors associated with RAMR for AMI-CS after adjusting for patient covariates used to calculate predicted mortality.

AMI = acute myocardial infarction; CA = cardiac arrest; CABG = coronary artery bypass graft; CI = confidence interval; CS = cardiogenic shock; LVAD = left ventricular assist device; MCS = mechanical circulatory support; NSTEMI = non-ST elevation myocardial infarction; OHT = orthotopic heart transplantation; OR = odds ratio; PCI = percutaneous coronary intervention; RAMR = risk-adjusted mortality rate; STEMI = ST-elevation myocardial infarction.

validated model, significant variability among patient characteristics persisted. These, in addition to various in-hospital variables of shock severity not adequately captured by the DCF, impose important limitations to the use of RAMR alone in attempting to define a high-performing shock center.

In conclusion, we stratified the participating centers in the Chest Pain-MI Registry by RAMR to attempt to better characterize high-performing centers in the care of AMI-CS. We observed excellent adherence to multiple process measures, particularly more frequent revascularization, at low-RAMR sites. Patient characteristics, however, likely remain highly deterministic of outcomes even after risk adjustment. In addition, several hospital-level factors also predicted mortality. These observed effects likely reflect institutional expertise and capability for increasingly complex therapeutic and supportive modalities, especially for AMI-CS presenting with CA. Our findings also highlight the difficulty in capturing the heterogeneity and variable severity of AMI-CS and the consequent challenge in adequately defining the high-performing shock center despite using a high-quality national database. From a health policy standpoint, further assessment is an important and necessary endeavor. Future research will benefit from collection of and adjustment for additional patient-level variables to better stratify hospital performance across the spectrum of AMI-CS.

Declaration of competing interest

Dr. Bhatt discloses the following relationships - Advisory Board: Angiowave, Bayer, Boehringer Ingelheim, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, High Enroll, Janssen, Level Ex, McKinsey, Medscape Cardiology, Merck, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, Stasys; Board of Directors: American Heart Association New York City, Angiowave (stock options), Bristol-Meyers Squibb (stock), DRS.LINQ (stock options), High Enroll (stock); Consultant: Broadview Ventures, GlaxoSmithKline, Hims, SFJ, Youngene; Data Monitoring Committees: Acesion Pharma, Assistance Publique-Hôpitaux de Paris, Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (Chair, PEITHO trial), Cleveland Clinic, Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo; for the ABILITY-DM trial, funded by Concept Medical; for ALLAY-HF, funded by Alleviant Medical), Novartis, Population Health Research Institute; Rutgers University (for the NIH-funded MINT trial); Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Chair, ACC Accrediation Oversight Committee), Arnold

and Porter law firm (work related to Sanofi/Bristol-Meyers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering committees), CSL Behring (AHA lecture), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), K2P (Co-Chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Oakstone CME (Course Director, Comprehensive Review of Interventional Cardiology), Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national coleader, funded by Bayer), WebMD (CME steering committees), Wiley (steering committee); Other: Clinical Cardiology (Deputy Editor); Patent: Sotagliflozin (named on a patent for sotagliflozin assigned to Brigham and Women's Hospital who assigned to Lexicon; neither I nor Brigham and Women's Hospital receive any income from this patent); Research Funding: Abbott, Acesion Pharma, Afimmune, Aker Biomarine, Alnylam, Amarin, Amgen, AstraZeneca, Bayer, Beren, Boehringer Ingelheim, Boston Scientific, Bristol-Meyers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CinCor, Cleerly, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix, Janssen, Javelin, Lexicon, Lilly, Medtronic, Merck, Moderna, MyoKardia, NirvaMed, Novartis, Novo Nordisk, Otsuka, Owkin, Pfizer, PhaseBio, PLx Pharma, Recardio, Regeneron, Reid Hoffman Foundation, Roche, Sanofi, Stasys, Synaptic, The Medicines Company, Youngene, 89Bio; Royalties: Elsevier (Editor, Braunwald's Heart Disease); Site Co-Investigator: Abbott, Biotronik, Boston Scientific, CSI, Endotronix, St. Jude Medical (now Abbott), Philips, SpectraWAVE, Svelte, Vascular Solutions; Trustee: American College of Cardiology; Unfunded Research: FlowCo. oooo Dr. Fonarow reports consulting for Abbott, Amgen, AstraZeneca, Bayer, Cytokinetics, Edwards, Janssen, Medtronic, Merck, and Novartis. Dr. Grodin reports consulting for Alnylam, Eidos, Sarepta, and Pfizer. Dr. Khera is a coinventor of US Pending Patent Applications. 63/177,117 and 63/346,610, unrelated to the present study; also a founder of Evidence2Health and Ensight-AI; received support from the National Heart, Lung, and Blood Institute of the National Institutes of Health (R01HL167858 and K23HL153775) and the Doris Duke Charitable Foundation (2,022,060); and receives research support from Bristol-Myers Squibb, Novo Nordisk, and BridgeBio, through Yale. The remaining authors have no competing interests to declare.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2024.04.002.

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