JACC: ADVANCES © 2024 THE AUTHORS. PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION. THIS IS AN OPEN ACCESS ARTICLE UNDER THE CC BY LICENSE (http://creativecommons.org/licenses/by/4.0/).

ORIGINAL RESEARCH

Association Between Frailty and Management and Outcomes of Acute Myocardial Infarction Complicated by Cardiogenic Shock

Yasser Jamil, MD,^{a,*} Dae Yong Park, MD,^{b,*} Sunil V. Rao, MD,^c Yousif Ahmad, MD, PhD,^d Nikhil V. Sikand, MD,^d Hayden B. Bosworth, PhD,^{e,f,g} Theresa Coles, PhD,^g Abdulla A. Damluji, MD, PhD,^{h,i} Michael G. Nanna, MD, MHS,^d Marc D. Samsky, MD^d

ABSTRACT

BACKGROUND Cardiogenic shock (CS) in the setting of acute myocardial infarction (AMI) is associated with high morbidity and mortality. Frailty is a common comorbidity in patients with cardiovascular disease and is also associated with adverse outcomes. The impact of preexisting frailty at the time of CS diagnosis following AMI has not been studied.

OBJECTIVES The purpose of this study was to examine the prevalence of frailty in patients admitted with AMI complicated by CS (AMI-CS) hospitalizations and its associations with in-hospital outcomes.

METHODS We retrospectively analyzed the National Inpatient Sample from 2016 to 2020 and identified all hospitalizations for AMI-CS. We classified them into frail and nonfrail groups according to the hospital frailty risk score cut-off of 5 and compared in-hospital outcomes.

RESULTS A total of 283,700 hospitalizations for AMI-CS were identified. Most (70.8%) occurred in the frail. Those with frailty had higher odds of in-hospital mortality (adjusted OR [aOR]: 2.17, 95% CI: 2.07 to 2.26, P < 0.001), do-not-resuscitate status, and discharge to a skilled nursing facility compared with those without frailty. They also had higher odds of in-hospital adverse events, including intracranial hemorrhage, gastrointestinal hemorrhage, acute kidney injury, and delirium. Importantly, AMI-CS hospitalizations in the frail had lower odds of coronary revascularization (aOR: 0.55, 95% CI: 0.53-0.58, P < 0.001) or mechanical circulatory support (aOR: 0.89, 95% CI: 0.85-0.93, P < 0.001). Lastly, hospitalizations for AMI-CS showed an overall increase from 53,210 in 2016 to 57,065 in 2020 (P trend <0.001), with this trend driven by a rise in the frail.

CONCLUSIONS A high proportion of hospitalizations for AMI-CS had concomitant frailty. Hospitalizations with AMI-CS and frailty had higher rates of in-hospital morbidity and mortality compared to those without frailty. (JACC Adv 2024;3:100949) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

From the ^aDepartment of Medicine, Yale School of Medicine, New Haven, Connecticut, USA; ^bDepartment of Medicine, Cook County Health, Chicago, Illinois, USA; ^cGrossman School of Medicine, New York University Langone Health System, New York University, New York, New York, USA; ^dSection of Cardiovascular Medicine, Yale School of Medicine, New Haven, Connecticut, USA; ^eDivision of General Internal Medicine, Department of Medicine, Duke University, Durham, North Carolina, USA; ^fDepartment of Psychiatry and Behavioral Health Sciences, Duke University School of Nursing, Durham, North Carolina, USA; ^gDepartment of Population Health Sciences, Duke University School of Medicine, Durham, North Carolina, USA; ^hJohns Hopkins University School of Medicine, Baltimore, Maryland, USA; and the ⁱInova Center of Outcomes Research, Falls Church, Virginia, USA. *Drs Jamil and Park have contributed equally to this paper.

ABBREVIATIONS AND ACRONYMS

2

AMI = acute myocardial infarction

AMI-CS = acute myocardial infarction with cardiogenic shock

CABG = coronary artery bypass graft

CS = cardiogenic shock

CVD = cardiovascular disease

MCS = mechanical circulatory support

NSTEMI = non-ST-segment elevation myocardial infarction

GoL = quality of life

STEMI = ST-segment elevation myocardial infarction

railty is an age-related syndrome characterized by a reduced physiologic reserve and increased vulnerability to external and internal stressors.¹ It is associated with poor health outcomes, increased mortality, morbidity, and a reduced quality of life (QoL).2,3 Increased attention has been given to the bidirectional association between frailty and cardiovascular diseases (CVD) and its correlation with a heightened risk of cardiovascular events.⁴ Frailty increases the risk of adverse cardiovascular outcomes; conversely, CVD increases the risk of being frail. This bidirectional association has been seen in patients with acute myocardial infarction (AMI) and several other cardiovascular conditions.5-8

However, frailty is not well characterized in patients with cardiogenic shock (CS), which is a highly lethal condition that can develop after AMI and is independently associated with poor outcomes.⁹

CS is the leading cause of death in patients with AMI and is associated with multimorbidity, reduced QoL, and physical disability.⁹ In the broader general population of patients with AMI, frail individuals are more likely to undergo conservative management, with lower utilization of revascularization therapies and advanced hemodynamic support.^{10,11} However, the prevalence of frailty in this vulnerable population and clinical characteristics of frail patients with AMI complicated by CS (AMI-CS) have not been characterized. Furthermore, the relationship between frailty and clinical outcomes among the highest-risk subset of individuals suffering from CS as a complication of AMI remains unknown. Therefore, we sought to define the prevalence of frailty in patients admitted to AMI-CS hospitalizations and examine its associations with in-hospital outcomes.

METHODS

DATA SOURCE. We retrospectively analyzed the National Inpatient Sample, the largest all-payer inpatient care database in the United States, developed for the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality.¹² When weights are applied to the 20% of participating hospitals across 49 participating states, each year of HCUP contains data on

approximately 35 million hospitalizations, which can be used to identify, track, and analyze health care utilization, access, costs, quality, and outcomes. The database has been devised to account for more than 97% of admissions occurring nationally. The HCUP is devoid of state, hospital, and patient identifiers to guarantee patient confidentiality, and since all hospital encounters are strictly deidentified, our study was exempt from the purview of our institutional review board. HCUP is open to the public and can be accessed through its public website.¹² This study was exempt from ethics approval as publicly available deidentified data from the National Inpatient Sample were used.

STUDY POPULATION AND COVARIATES. We collected all hospitalizations for AMI-CS in either primary or secondary diagnoses from the HCUP years 2016 to 2020. We then excluded hospitalizations under 18 years old and entries containing missing data on demographics, hospital characteristics, primary payer, median income,¹² day of hospitalization, inhospital mortality, and length of hospital stay (LOS). After the application of inclusion and exclusion criteria, we extracted data on demographics (sex, age, race), hospital characteristics (region, bed size, urban location), primary payer, median income, and day of hospitalization (weekday, weekend), all of which are present in the original databases. In each hospitalization, we examined the presence of many comorbidities, as shown in Table 1. Using International Classification of Diseases-10th Revision Clinical Modification (ICD-10-CM) codes (Supplemental Table 1), we calculated hospital frailty risk score (HFRS), a validated measure of clinical frailty, for each hospitalization. In short, HFRS is derived by awarding each prespecified ICD-10-CM code with a different number of points and then aggregating all the points awarded.¹³ We defined the presence of frailty as having an HFRS of at least 5, consistent with the definition used by many previous studies.¹⁴⁻¹⁶ AMI-CS hospitalizations were grouped into those with and without frailty. Clinical presentation was classified into ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI). All the comorbidities and procedural data used in our study were established on the basis of ICD-10-CM and International Classification of Diseases-10th Revision, Procedural Coding System

Manuscript received July 31, 2023; revised manuscript received November 27, 2023, accepted January 23, 2024.

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.

Obesity

Heart failure

Previous PCI

Previous CABG

Previous stroke

Liver cirrhosis

Malnutrition

Dementia

HFRS

COPD

Previous pacemaker

Pulmonary hypertension

Chronic kidney disease

End-stage renal disease

History of malignancy

Deficiency anemia

Major depression

Atrial fibrillation

Valvular heart disease

Peripheral artery disease

Chronic ischemic heart disease

3

Complicated by Cardiogenic Shock Hospitalizations With and Without Frailty							
	Frailty (+)	Frailty (–)	P Value				
Number of hospitalizations	200,970	82,800					
Male	63.0	65.6	< 0.001				
Age, y	69.5 ± 12.6	$\textbf{66.2} \pm \textbf{12.6}$	< 0.001				
Race ^a			<0.001				
White	71.1	74.6					
Black	10.9	7.8					
Hispanic	9.7	8.9					
Asian	4.0	3.8					
AI/AN	0.7	0.7					
Other	3.6	4.3					
Comorbidities ^b							
Smoking	37.0	43.5	< 0.001				
Hypertension	17.0	33.9	< 0.001				
Diabetes mellitus	45.4	36.9	< 0.001				
Hyperlipidemia	47.8	57.8	< 0.001				

16.3

70.0

14.6

33.9

13.2

10.3

1.1

7.5

10.4

2.3

22.0

10.9

40.0

9.1

2.9

73

58

11.6

7.8

0.6

9.3

16.5

50.9

10.0

24.3

11.4

82

1.3

6.5

5.8

1.9

16.7

6.5

12.0

3.0

1.5

71

26

36

1.1

0.4

2.6

0.660

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

0.104

< 0.001

< 0.001

0.003

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

0 4 9 5

< 0.001

< 0.001

< 0.001

< 0.001

< 0.001

TABLE 1 Baseline Characteristics of Acute Myocardial Infarction
Complicated by Cardiogenic Shock Hospitalizations With and
Without Frailty

database is provided by the Healthcare Cost and Utilization Project partner organizations, and the protocol whereby race was determined is not specifically mentioned but rather left to the discretion of the data source. ^bThe variables used to define the comorbidities are shown in Supplemental Table 2. ^cThe variables used to derive HFRS are shown in Supplemental Table 1.

 ${\sf AI/AN} = {\sf American \ Indian/Alaska \ Native; \ {\sf CABG} = {\sf coronary \ artery \ bypass \ graft;}$ $\mathsf{COPD} \ = \ \mathsf{chronic} \ \ \mathsf{obstructive} \ \ \mathsf{pulmonary} \ \ \mathsf{disease}; \ \ \mathsf{CS} \ = \ \ \mathsf{cardiogenic} \ \ \mathsf{shock};$ HFRS = Hospital Frailty Risk Score; NSTEMI = non-ST-segment elevation myocardial infarction: PCI = percutaneous coronary intervention: STEMI = STsegment elevation myocardial infarction.

codes, respectively. These codes can be found in Supplemental Table 2.

STUDY OUTCOMES. The primary outcome of interest was in-hospital mortality. Secondary outcomes included do-not-resuscitate status (DNR), palliative care consult, discharge to a skilled nursing facility, coronary revascularization, use of mechanical circulatory support (MCS), intracranial hemorrhage, gastrointestinal hemorrhage, acute kidney injury (AKI), delirium, LOS, and total hospital cost. Coronary revascularization was defined as having undergone percutaneous coronary intervention or coronary artery bypass graft. Percutaneous coronary intervention was defined as the implantation of a drug-eluting stent, bare-metal stent, or balloon angioplasty.

Mechanical circulatory support was defined as using an intra-aortic balloon pump, percutaneous left ventricular assist device, durable left ventricular assist device, or extracorporeal membranous oxygenation. Total hospital cost was calculated by multiplying the total hospital charge with the cost-to-charge ratios from separate files obtained via HCUP.¹⁷

STATISTICAL ANALYSIS. In all statistical analyses, we applied weights of hospital-level discharge to produce results representative of national estimates. We compared categorical and continuous covariates in the baseline characteristics using the chi-square

	Frailty (+)	Frailty (–)	P Value
Hospital characteristics			
Hospital region			< 0.001
Northwest	15.8	17.6	
Midwest	21.6	19.6	
South	40.6	42.1	
West	21.9	20.7	
Hospital bed-size			0.020
Small	14.1	14.4	
Medium	27.9	28.8	
Large	58.0	56.8	
Urban location			< 0.001
Rural	4.3	5.5	
Urban nonteaching	18.2	20.1	
Urban teaching	77.5	74.4	
Primary payer			< 0.001
Medicare	66.2	53.6	
Medicaid	9.2	9.8	
Private insurance	18.0	27.2	
Self-pay	3.6	5.7	
No charge	0.3	0.3	
Others	2.7	3.3	
Median income			0.615
Quartile 1	30.1	29.6	
Quartile 2	26.9	27.1	
Quartile 3	23.8	24.1	
Quartile 4	19.2	19.3	
Clinical presentation			< 0.001
STEMI	43.2	62.2	
NSTEMI	56.8	37.8	
Day of hospitalization			0.963
Weekday	73.2	73.2	
Weekend	26.8	26.8	

Continued in the next column

test and the Student's t test, respectively. We examined the trend of the number of hospitalizations from 2016 to 2020 using the Jonckheere-Terpstra test. When selecting covariates to adjust statistical models, we first examined all baseline characteristics in a correlation matrix to ensure that no 2 covariates were highly correlated, as defined by a Pearson correlation coefficient >0.80. Secondly, we investigated for multicollinearity using variance inflation factor and tolerance, whose cut-offs were 3 and 0.1, respectively. Thirdly, we ran collinearity diagnostics for an eigensystem analysis of covariance to doublecheck the absence of multicollinearity. After addressing multicollinearity, we used stepwise selection on a multivariable logistic regression model to select covariates to adjust when comparing AMI-CS with frailty vs without frailty. The model with covariates that produced the least Akaike information criterion was selected. The following 21 covariates were selected: age, sex, race, smoking, diabetes mellitus, hyperlipidemia, obesity, heart failure, chronic ischemic heart disease, atrial fibrillation, peripheral artery disease, previous coronary artery bypass graft, previous stroke, pulmonary hypertension, end-stage renal disease, liver cirrhosis, deficiency anemia, malnutrition, dementia, major depression, and STEMI.

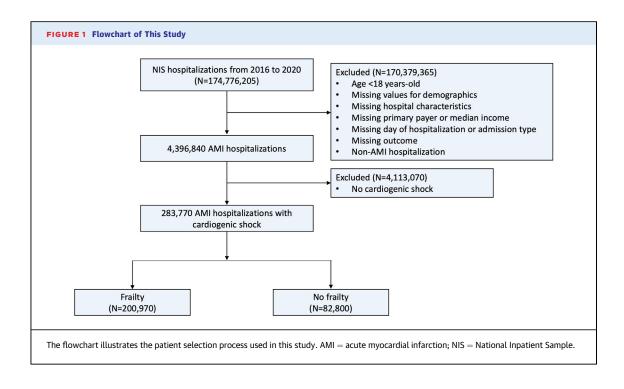
To compare primary and secondary outcomes, which were binary, we used both simple and multivariable logistic regression to produce crude odds ratios and adjusted ORs (aORs) with respective 95% CI. We utilized linear regression when comparing continuous secondary outcomes. We conducted a sensitivity analysis in which we included AMI-CS managed with either revascularization or MCS. We also performed 2 subgroup analyses: one stratified to younger (age <65 years) and older (age ≥ 65 years) adults, and one stratified to STEMI and NSTEMI. Moreover, after stratifying into frail and nonfrail groups, we looked at the impact of revascularization, MCS, or either one of them on the in-hospital outcomes of AMI-CS using the same analytical methodology. Finally, to examine the correlation of frailty score with in-hospital outcomes, the same multivariable logistic regression models were used to calculate the log-odds of each of the in-hospital outcomes, which were then graphed against the frailty score using cubic splines with smoothing parameter set at 0.7. Afterward, simple linear regression was used to assess for linear trends. All tests were 2-sided, and P values <0.05 were considered significant. Data curation and all statistical analyses were conducted using SAS, version 9.4 (SAS Institute). Production of figures were assisted by R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 4,396,840 AMI hospitalizations were identified, of which 283,770 (6.5%) also had CS (Figure 1). Among the AMI-CS hospitalizations, 200,970 (70.8%) occurred in the frail, while 82,800 (29.2%) occurred in those without frailty. The frail group was slightly older than the nonfrail group (age 69.5 years vs 66.2 years, P < 0.001) and had a higher proportion of individuals identified as of black race and Hispanic ethnicity (Table 1). In the frail group, the proportions of diabetes mellitus, heart failure, atrial fibrillation, previous stroke, chronic obstructive pulmonary disease, chronic kidney disease, deficiency anemia, malnutrition, and dementia were significantly higher. However, the proportions of smoking, hypertension, and hyperlipidemia were lower (Table 1). The majority of the frail group presented with NSTEMI (56.8%), in contrast to STEMI being the major clinical presentation for the nonfrail group (62.2%). The overall number of hospitalizations for AMI-CS increased from 53,210 in 2016 to 57,065 in 2020 (P trend <0.001) (Figure 2). This increasing trend was mediated by an increasing number of AMI-CS hospitalizations in the frail (P trend <0.001), in contrast to the decreasing number of AMI-CS hospitalizations in the nonfrail (*P* trend < 0.001).

AMI-CS hospitalizations with frailty had significantly higher unadjusted rates of in-hospital mortality (40.0% vs 24.5%, *P* < 0.001) compared with those without frailty (Table 2). The odds of in-hospital mortality were significantly higher even after adjusting for confounders (aOR: 2.17, 95% CI: 2.07-2.26, P < 0.001). The frail group had higher odds of having DNR status or receiving a palliative care consult (Central Illustration). They also had higher odds of disposition to a skilled nursing facility, intracranial hemorrhage, gastrointestinal hemorrhage, AKI, and delirium. However, they had lower odds of undergoing coronary revascularization or receiving MCS. The LOS in the frail group was significantly higher (adjusted mean difference 3.91 days, 95% CI: 3.71-4.10, P < 0.001) and more expensive (adjusted mean difference \$17,705, 95% CI: 16,629-18,781, *P* < 0.001).

Sensitivity analysis of AMI-CS managed with either revascularization or mechanical circulatory support showed similar results of increased in-hospital mortality, ICH, gastrointestinal bleed, and longer length of stay (Supplemental Table 3). Subgroup analyses stratified by younger (n = 104,025) and older adults



(n = 179,745) revealed similar results in both AMI-CS hospitalizations occurring in ages <65 years and \geq 65 years (Supplemental Table 4). The results were largely similar in another subgroup analysis stratified to STEMI and NSTEMI, except for the similar rates of MCS use regardless of frailty in STEMI hospitalizations (Supplemental Table 5). Revascularization was associated with lower odds of in-hospital mortality in frail and nonfrail groups. However, MCS was associated with lower odds of in-hospital mortality only in the frail group (aOR: 0.91, 95% CI: 0.87-0.96, P < 0.001). (Supplemental Table 6). Spline

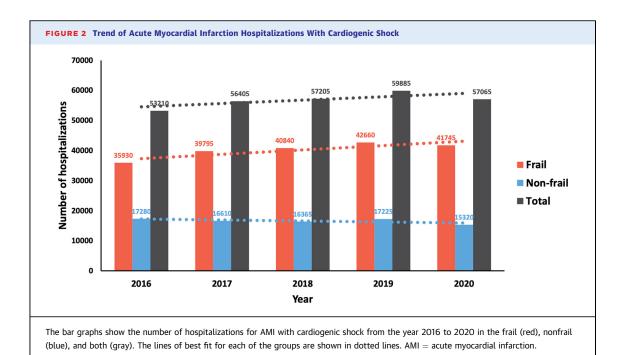


TABLE 2 Comparison of Outcomes in Acute Myocardial Infarction Complicated by Cardiogenic Shock With and Without Frailty						
Outcome	Frailty (+)	Frailty (–)	Crude OR (95% CI)	P Value	Adjusted OR (95% CI) ^a	P Value
In-hospital mortality	40.0	24.5	2.06 (1.98-2.15)	< 0.001	2.17 (2.07-2.26)	< 0.001
Do not resuscitate	29.7	13.6	2.70 (2.57-2.84)	< 0.001	2.36 (2.24-2.49)	< 0.001
Palliative care consult	21.1	8.8	2.79 (2.62-2.96)	< 0.001	2.40 (2.25-2.56)	< 0.001
Skilled nursing facility	26.1	10.7	2.94 (2.78-3.10)	< 0.001	2.23 (2.10-2.35)	< 0.001
Revascularization	47.4	68.8	0.41 (0.39-0.43)	< 0.001	0.55 (0.53-0.58)	< 0.001
MCS	34.0	42.1	0.71 (0.68-0.74)	< 0.001	0.89 (0.85-0.93)	< 0.001
Intracranial hemorrhage	1.7	0.3	5.35 (4.06-7.04)	< 0.001	5.73 (4.31-7.61)	< 0.001
Gastrointestinal hemorrhage	8.5	2.4	3.88 (3.49-4.32)	< 0.001	3.64 (3.26-4.08)	< 0.001
Acute kidney injury	71.4	19.8	10.11 (9.67-10.57)	< 0.001	11.06 (10.55-11.59)	< 0.001
Delirium	5.6	0.4	14.80 (11.58-18.90)	< 0.001	13.20 (10.32-16.87)	< 0.001
Length of stay, days	11.0 ± 12.3	$\textbf{3.5}\pm\textbf{3.6}$	5.27 (5.07-5.47) ^b	< 0.001	3.91 (3.71-4.10) ^c	< 0.001
Total hospital cost, \$	$58,\!075\pm 66,\!153$	$\textbf{38,290} \pm \textbf{37,921}$	19,785 (18,712-20,859) ^b	<0.001	17,705 (16,629-18,781) [∈]	< 0.001

Values are % or mean ± SD unless otherwise indicated. ^aAdjusted for age, sex, race, smoking, diabetes mellitus, hyperlipidemia, obesity, heart failure, chronic ischemic heart disease, atrial fibrillation, peripheral artery disease, previous CABG, previous stroke, pulmonary hypertension, end-stage renal disease, liver cirrhosis, deficiency anemia, malnutrition, dementia, major depression, and ST-segment elevation myocardial infarction. ^bCrude mean difference with a 95% CI. ^cAdjusted mean difference with a 95% CI. CABG = coronary artery bypass graft; MCS = mechanical circulatory support.

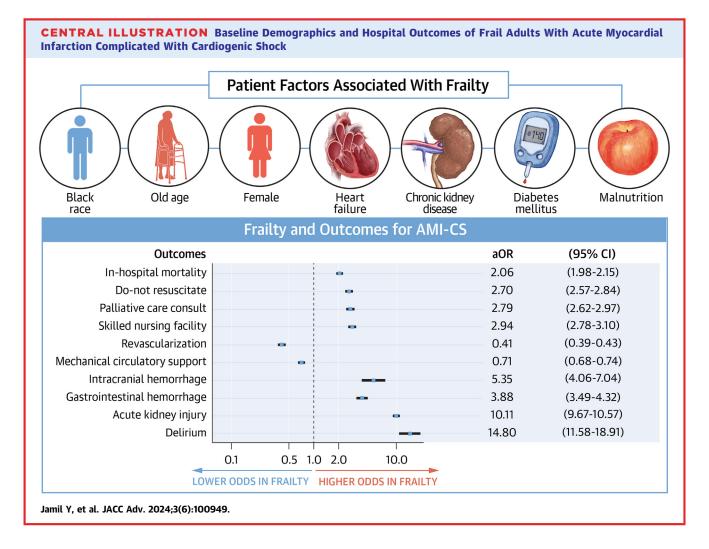
curves showed a positive correlation between HFRS and log-odds of in-hospital mortality, DNR status, palliative consult, discharge to a skilled nursing facility, AKI, and delirium (Figure 3). On the other hand, a negative correlation was seen between HFRS, log odds of revascularization, and MCS. All the linear trends were significant.

DISCUSSION

This nationally representative study assessed the association between frailty, clinical management, and clinical outcomes in AMI-CS hospitalizations. First, the prevalence of frailty in AMI-CS hospitalization is high, with nearly three-quarters being frail. Second, frailty during AMI-CS hospitalization was associated with higher rates of mortality and in-hospital complications such as bleeding, delirium, and longer LOS than those with nonfrail status. Third, frailty in AMI-CS was associated with a lower likelihood of coronary artery revascularization and temporary MCS devices. Lastly, among the frail group, those who underwent coronary revascularization experienced lower inhospital mortality. However, mortality benefit from MCS was observed specifically in the frail group and not the nonfrail.

Our findings suggest that frailty is more prevalent in adults hospitalized with AMI-CS than in other cardiovascular conditions. Up to 70% of AMI-CS hospitalizations had frailty, which could be attributed to the combined burden of 2 acute CVD diagnoses (AMI and CS). Furthermore, on the opposite end, the reduced overall reserve in frail individuals makes them more susceptible to CS following AMI.¹⁸⁻²¹ Previous studies reported varying rates of frailty in CVD. For example, frailty prevalence in patients with acute CVD has been reported to range from 24 to 86%, varying according to the underlying CVD process.^{6,22-} ²⁵ The variability in the reported rates can be attributed to multiple factors, such as the lack of standardized diagnosis, assessment tools for frailty, and the differences in underlying CVD severity.⁴ Furthermore, our study revealed that hospitalizations for AMI-CS with concomitant frailty were associated with a 40% in-hospital mortality rate. Similar to the current study, previous registries, such as the LONGEVO-SCA (Impact of Frailty and Other Geriatric Syndromes on the Management and Vital Prognosis of the Elderly with Acute Coronary Syndrome without ST Segment Elevation) registry and TRILOGY ACS (Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes) trial, demonstrated up to 40% in-hospital mortality rates in patients with ACS who were considered frail.^{23,26,27} The high mortality rates among frail adults may be attributed to a higher number of comorbidities and higher rates of sarcopenia, reduced physiological reserve, and diminished rehabilitation potential.28 However, it remains unknown if interventions that directly target frailty can improve outcomes in AMI-CS complicated by frailty.

This study showed that frailty was associated with negative outcomes across age groups (>65 vs <65 years), emphasizing that the adverse effects of frailty in those with AMI-CS extend across the aging spectrum. This finding across age groups is noteworthy because some may assume that frailty is exclusively observed in older adults, whereas



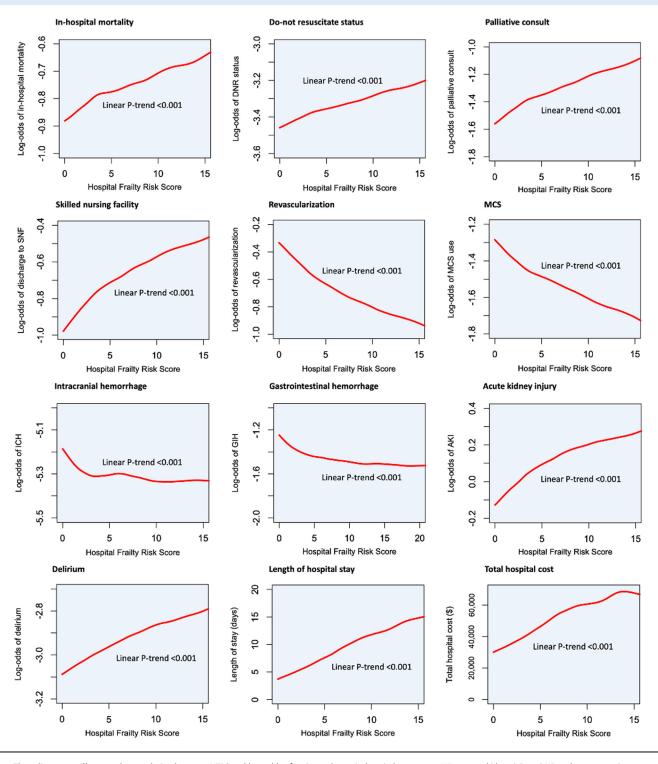
younger adults are also susceptible to frailty. Most studies reporting frailty, however, include adults above 65 years of age and sometimes even higher, limiting the generalizability of the evidence in the frail younger population.²⁹

In terms of treatment strategies, this study revealed that frailty during AMI-CS hospitalization was associated with a lower likelihood of receiving coronary artery revascularization (47.4% vs 68.6%, P < 0.001) or MCS (34.0% vs 42.1%, P < 0.001). Consistent with prior research, the CONCORDANCE and ACTION registries demonstrated that older adults with frailty and AMI-CS had a lower likelihood of receiving invasive cardiac care (ie, percutaneous coronary intervention), as low as 6%.^{20,30-32} Interestingly, in the current study, among the frail group, those who underwent coronary artery revascularization had lower hospital mortality compared to those who did not (aOR: 0.44, 95% CI: 0.42-0.46, P < 0.001). Other studies similarly demonstrated benefit, a 21% reduction in mortality rates among those who received revascularization.³³⁻³⁶ Regarding MCS, it is unsurprising that frail adults are managed more conservatively. Although it is uncertain whether MCS can decrease long-term mortality rates as well as reverse frailty, this study noted a hospital mortality benefit in the frail group who had MCS (aOR: 0.91, 95% CI: 0.87-0.96, P < 0.001), which was not seen in the nonfrail group. Most landmark trials have excluded frail adults, such as in the EURO-SHOCK, or failed to measure and/or report frailty with their interventions.³⁷ Therefore, the precise impact of given therapies on frail populations remains unclear.

STUDY LIMITATIONS. There are several limitations to this study. This is a retrospective analysis, which is prone to bias and confounders. The data used in the study is based on an administrative dataset, which has inherent limitations. The HFRS is based on ICD codes, which may result in inaccurate coding and

7





The spline curves illustrate the correlation between HFRS and log-odds of various adverse in-hospital outcomes. AKI = acute kidney injury; DNR = do not resuscitate; GIH = gastrointestinal hemorrhage; ICH = intracranial hemorrhage; MCS = mechanical circulatory support; SNF = skilled nursing facility.

inaccuracies in the diagnosis of frailty.^{13,38} Patients with CS are historically not reported in cardiovascular quality improvement registries, and markers of frailty are also not reported. Therefore, national datasets such as the HCUP provide a unique opportunity to complete these analyses. Although the frailty score utilized in this study, known as the HFRS, has been validated and demonstrated a reasonable degree of overlap with the Fried and Rockwood Frailty Index and shows consistent correlations with frailty indices in other studies.^{13,39} While HFRS has shown validation in acute illness across various patient subsets, establishing associations with factors such as level of independence, functional impairment, QoL, mortality, length of stay, and hospital admission, it is important to note that several other essential elements, such as polypharmacy, mobility, sarcopenia, and hand grip strength, are not accounted for in the score.^{13,40} A notable gap exists in standardized frailty assessment during acute cardiovascular illness, which may not accurately represent a patient's true frailty level, particularly in cases of critical illnesses like CS, and the timing for evaluating and diagnosing frailty remains elusive. We were only able to assess in-hospital mortality and do not have data on longerterm outcomes that may be relevant, particularly for younger frail individuals. Finally, shared decisionmaking between clinicians and patients was not captured, potentially leading to selection bias as to whether patients who underwent conservative management did so due to their frailty, multimorbidity, ineligibility, or patient preferences.

CONCLUSIONS

In this nationally representative sample of hospitalizations for AMI-CS, frailty was common and had increased from 2016 to 2020. The presence of frailty was associated with less revascularization and MCS use. Interventions that directly target frailty should be studied to explore their benefit during AMI-CS hospitalizations. **ACKNOWLEDGMENTS** Data included in this study can be found on the public website of the Healthcare Cost and Utilization Project.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Ahmad is a consultant for Cardiovascular Systems Inc and Shockwave and serves on the Medical Advisory Board of Boston Scientific, Dr Bosworth has received research funding through his institution from BeBetter Therapeutics, Boehringer Ingelheim, Esperion, Improved Patient Outcomes, Merck, NHLBI, Novo Nordisk, Otsuka, Sanofi, Veterans Aministration, Elton John Foundation, Hilton foundation, Pfizer; and provides consulting services for Abbott, Esperion, Imatar, Novartis, Sanofi, Vidya, Walmart, and Webmed. He was also on the board of directors of Preventric Diagnostics. Dr Coles has received research support from Merck and consulting with Regenxbio. Dr Damluji has received research funding from the Pepper Scholars Program of the Johns Hopkins University Claude D. Pepper Older Americans Independence Center funded by the National Institute on Aging P30-AG021334 and receives mentored patient-oriented research career development award from the National Heart, Lung, and Blood Institute K23-HL153771-01. Dr Nanna has received research support from the American College of Cardiology Foundation supported by the George F. and Ann Harris Bellows Foundation, the Patient-Centered Outcomes Research Institute (PCORI), the Yale Claude D. Pepper Older Americans Independence Center (P30AG021342), and the National Institute on Aging/National Institutes of Health from R03AG074067 (GEMSSTAR award). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Marc D. Samsky, Yale New Haven Hospital, 20 York Street, New Haven, Connecticut 06510, USA. E-mail: marc. samsky@yale.edu.

PERSPECTIVES

COMPETENCY IN PATIENT CARE: AMI-CS is associated with high morbidity and mortality. Frailty is a common comorbidity present during hospitalization for AMI-CS and is associated with less revascularization and MCS use.

TRANSLATIONAL OUTLOOK IMPLICATIONS: When presented with AMI-CS, frailty is associated with worse outcomes. Future research targeting frailty during hospitalization for AMI-CS is needed.

REFERENCES

1. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56(3):M146–M156. https://doi.org/10.1093/gerona/56.3.m146

2. Cesari M, Prince M, Thiyagarajan JA, et al. Frailty: an emerging public health priority. *J Am Med Dir Assoc*. 2016;17(3):188-192. https://doi. org/10.1016/j.jamda.2015.12.016

3. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*.

2013;381(9868):752-762. https://doi.org/10. 1016/s0140-6736(12)62167-9

4. Ijaz N, Buta B, Xue QL, et al. Interventions for frailty among older adults with cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol. 2022;79(5):482-503. https://doi.org/10. 1016/j.jacc.2021.11.029

5. Yang X, Lupón J, Vidán MT, et al. Impact of frailty on mortality and hospitalization in chronic heart failure: a systematic review and meta-

analysis. J Am Heart Assoc. 2018;7(23):e008251. https://doi.org/10.1161/jaha.117.008251

6. Marengoni A, Zucchelli A, Vetrano DL, et al. Heart failure, frailty, and pre-frailty: a systematic review and meta-analysis of observational studies. *Int J Cardiol*. 2020;316:161-171. https://doi.org/10. 1016/j.ijcard.2020.04.043

7. Xu W, Cai Y, Liu H, Fan L, Wu C. Frailty as a predictor of all-cause mortality and readmission in older patients with acute coronary syndrome : a

systematic review and meta-analysis. *Wien Klin Wochenschr*. 2020;132(11-12):301-309. https:// doi.org/10.1007/s00508-020-01650-9

8. Zhang S, Meng H, Chen Q, et al. Is frailty a prognostic factor for adverse outcomes in older patients with acute coronary syndrome? *Aging Clin Exp Res.* 2020;32(8):1435-1442. https://doi.org/10.1007/s40520-019-01311-6

9. Samsky MD, Morrow DA, Proudfoot AG, Hochman JS, Thiele H, Rao SV. Cardiogenic shock after acute myocardial infarction: a review. JAMA. 2021;326(18):1840-1850. https://doi.org/10. 1001/jama.2021.18323

10. Lisiak M, Uchmanowicz I, Wontor R. Frailty and quality of life in elderly patients with acute coronary syndrome. *Clin Interv Aging*. 2016;11:553-562. https://doi.org/10.2147/cia.S99842

11. Uchmanowicz I, Lisiak M, Wleklik M, Gurowiec P, Kałużna-Oleksy M. The relationship between fraiłty syndrome and quality of life in older patients following acute coronary syndrome. *Clin Interv Aging*. 2019;14:805–816. https://doi. org/10.2147/cia.S204121

 HCUP Databases. Healthcare cost and utilization project (HCUP). Agency for healthcare research and quality. Accessed November 28, 2022. https:// www.hcup-us.ahrg.gov/nisoverview.jsp

13. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet.* 2018;391(10132): 1775-1782. https://doi.org/10.1016/s0140-6736(18)30668-8

14. McAlister FA, Savu A, Ezekowitz JA, Armstrong PW, Kaul P. The hospital frailty risk score in patients with heart failure is strongly associated with outcomes but less so with pharmacotherapy. J Intern Med. 2020;287(3):322-332. https://doi.org/10.1111/joim.13002

15. Orlandi M, Dover DC, Sandhu RK, Hawkins NM, Kaul P, McAlister FA. The introduction of direct oral anticoagulants has not resolved treatment gaps for frail patients with nonvalvular atrial fibrillation. *Can J Cardiol.* 2022;38(1):77-84. https://doi.org/10.1016/j.cjca.2021.09.021

16. Rottler M, Ocskay K, Sipos Z, et al. Clinical Frailty Scale (CFS) indicated frailty is associated with increased in-hospital and 30-day mortality in COVID-19 patients: a systematic review and metaanalysis. Ann Intensive Care. 2022;12(1):17. https:// doi.org/10.1186/s13613-021-00977-4

17. Cost-to-charge ratio for inpatient files. Healthcare cost and utilization project (HCUP). Agency for healthcare research and quality. Accessed November 28, 2022. https://www.hcupus.ahrq.qov/db/ccr/ip-ccr/ip-ccr.jsp

18. Kang YP, Chen LY, Zhu JJ, Liu WX, Ma CS. Association of frailty with in-hospital outcomes in elderly patients with heart failure. *World J Clin Cases.* 2021;9(36):11208-11219. https://doi.org/ 10.12998/wjcc.v9.i36.11208

19. Hosseini F, Pitcher I, Kang M, et al. Abstract 11087: impact of frailty on short-term and long-term outcomes among St-elevation myocardial infarction patients receiving primary percutaneous coronary intervention. *Circulation*. 2022;146(SuppL1):A11087.https://doi.org/10.1161/ circ.146.suppL1.11087

20. Patel A, Goodman SG, Yan AT, et al. Frailty and outcomes after myocardial infarction: insights from the CONCORDANCE registry. *J Am Heart Assoc.* 2018;7(18):e009859. https://doi.org/10. 1161/JAHA.118.009859

21. Volle K, Delmas C, Ferrières J, et al. Prevalence and prognosis impact of frailty among older adults in cardiac intensive care units. *CJC Open*. 2021;3(8):1010–1018. https://doi.org/10.1016/j. cjco.2021.03.009

22. Marinus N, Vigorito C, Giallauria F, et al. Frailty is highly prevalent in specific cardiovascular diseases and females, but significantly worsens prognosis in all affected patients: a systematic review. Ageing Res Rev. 2021;66:101233. https:// doi.org/10.1016/j.arr.2020.101233

23. White HD, Westerhout CM, Alexander KP, et al. Frailty is associated with worse outcomes in non-ST-segment elevation acute coronary syndromes: insights from the targeted platelet Inhibition to clarify the optimal strategy to medically manage acute coronary syndromes (TRILOGY ACS) trial. *Eur Heart J Acute Cardiovasc Care.* 2016;5(3): 231-242.

24. Reeves GR, Whellan DJ, Patel MJ, et al. Comparison of frequency of frailty and severely impaired physical function in patients \geq 60 years hospitalized with acute decompensated heart failure versus chronic stable heart failure with reduced and preserved left ventricular ejection fraction. *Am J Cardiol.* 2016;117(12):1953–1958.

25. Denfeld QE, Winters-Stone K, Mudd JO, Gelow JM, Kurdi S, Lee CS. The prevalence of frailty in heart failure: a systematic review and meta-analysis. *Int J Cardiol.* 2017;236:283-289. https://doi.org/10.1016/j.ijcard.2017.01.153

26. Rodríguez-Queraltó O, Formiga F, López-Palop R, et al. FRAIL scale also predicts long-term outcomes in older patients with acute coronary syndromes. J Am Med Dir Assoc. 2020;21(5): 683-687.e1. https://doi.org/10.1016/j.jamda. 2019.10.007

27. Venkatason P, Zubairi YZ, Wan Ahmad WA, et al. In-hospital mortality of cardiogenic shock complicating ST-elevation myocardial infarction in Malaysia: a retrospective analysis of the Malaysian National Cardiovascular Database (NCVD) registry. *BMJ Open*. 2019;9(5):e025734. https://doi.org/ 10.1136/bmjopen-2018-025734

28. Damluji AA, Alfaraidhy M, AlHajri N, et al. Sarcopenia and cardiovascular diseases. *Circulation*. 2023;147(20):1534-1553. https://doi.org/10. 1161/circulationaha.123.064071

29. Spiers GF, Kunonga TP, Hall A, et al. Measuring frailty in younger populations: a rapid review of evidence. *BMJ Open.* 2021;11(3):e047051. https://doi.org/10.1136/bmjopen-2020-047051

30. Ekerstad N, Swahn E, Janzon M, et al. Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. *Circulation*. 2011;124(22):2397-2404. https://doi.org/10.1161/ CIRCULATIONAHA.111.025452 **31.** Rubens M, Ramamoorthy V, Saxena A, et al. Management and outcomes of ST-segment elevation myocardial infarction in hospitalized frail patients in the United States. *Am J Cardiol.* 2022;175:1-7. https://doi.org/10.1016/j.amjcard. 2022.04.006

32. Dodson JA, Hochman JS, Roe MT, et al. The association of frailty with in-hospital bleeding among older adults with acute myocardial infarction: insights from the ACTION registry. *J Am Coll Cardiol Intv.* 2018;11(22):2287-2296. https://doi. org/10.1016/j.jcin.2018.08.028

33. Damluji AA, Bandeen-Roche K, Berkower C, et al. Percutaneous coronary intervention in older patients with ST-segment elevation myocardial infarction and cardiogenic shock. *J Am Coll Cardiol*. 2019;73(15):1890-1900. https://doi.org/10.1016/ j.jacc.2019.01.055

34. Dzavik V, Sleeper LA, Cocke TP, et al. Early revascularization is associated with improved survival in elderly patients with acute myocardial infarction complicated by cardiogenic shock: a report from the SHOCK Trial Registry. Eur Heart J. 2003;24(9):828-837. https://doi.org/10.1016/ s0195-668x(02)00844-8

35. Borovac JA, Mohamed MO, Kontopantelis E, et al. Frailty among patients with acute ST-elevation myocardial infarction in the United States: the impact of the primary percutaneous coronary intervention on in-hospital outcomes. *J Invasive Cardiol.* 2022;34(1):E55–e64.

36. Webb JG, Sanborn TA, Sleeper LA, et al. Percutaneous coronary intervention for cardiogenic shock in the SHOCK Trial Registry. *Am Heart* J. 2001;141(6):964–970. https://doi.org/10.1067/ mhj.2001.115294

37. Banning AS, Adriaenssens T, Berry C, et al. Veno-arterial extracorporeal membrane oxygenation (ECMO) in patients with cardiogenic shock: rationale and design of the randomised, multicentre, open-label EURO SHOCK trial. *Euro Intervention.* 2021;16(15):e1227-e1236. https:// doi.org/10.4244/eij-d-20-01076

38. Rumalla K, Schmidt MH, Bowers CA. Letter to the editor. Limitations of the hospital frailty risk score in metastatic spinal column tumor surgery. *J Neurosurg Spine*. 2022;38(3):412-414. https://doi.org/10.3171/2022.9.Spine22990

39. Turcotte LA, Heckman G, Rockwood K, et al. External validation of the hospital frailty risk score among hospitalised home care clients in Canada: a retrospective cohort study. *Age Ageing*. 2023;52(2):afac334. https://doi.org/10.1093/ ageing/afac334

40. Eckart A, Hauser SI, Haubitz S, et al. Validation of the hospital frailty risk score in a tertiary care hospital in Switzerland: results of a prospective, observational study. *BMJ Open.* 2019;9(1): e026923. https://doi.org/10.1136/bmjopen-2018-026923

KEY WORDS acute myocardial infarction, cardiogenic shock, frailty

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