

Frailty Among Older Adults With Acute Myocardial Infarction and Outcomes From Percutaneous Coronary Interventions

Abdulla A. Damluji, MD, MPH; Jin Huang, PhD, MS; Karen Bandeen-Roche, PhD; Daniel E. Forman, MD; Gary Gerstenblith, MD; Mauro Moscucci, MD, MBA; Jon R. Resar, MD; Ravi Varadhan, PhD; Jeremy D. Walston, MD; Jodi B. Segal, MD, MPH

Background—Frailty is a predictor of adverse outcomes after acute myocardial infarction (AMI).

Methods and Results—We estimated the prevalence of frailty among adults age \geq 75 years admitted with AMI and examined the relationship between frailty, interventions, and mortality. We used the Premier Healthcare Database to identify older adults with primary diagnoses of AMI. We classified individuals as frail or not using the validated Claims-based Frailty Index. We described patients' characteristics and receipt of percutaneous coronary intervention stratified by frailty status. The primary outcome was hospital mortality. From 2000 to 2016, we identified 469 390 encounters for older patients admitted with AMI. The median age was 82 years, 53% were women, and 75% were white. The prevalence of frailty was 19%. Frail patients were less likely to receive percutaneous coronary intervention than nonfrail (15% versus 33%, *P*<0.001) and much less likely to receive coronary artery bypass surgery (1% versus 9%, *P*<0.001). There were far fewer interventions in individuals over age 85 years. Frailty was associated with higher mortality during AMI admission (unadjusted odds ratio [OR] 1.43, Cl 1.39–1.46). While there was a differential benefit of the interventions because of frailty, frail patients had reduced hospital mortality with percutaneous coronary intervention (frail: OR 0.59, Cl 0.55–0.63; nonfrail: OR 0.49, Cl 0.47–0.50, *P* for interaction <0.001) and with coronary artery bypass surgery (frail: OR 0.77, Cl 0.65–0.93; nonfrail: OR 0.74, Cl 0.71–0.77, *P* for interaction <0.001) relative to no intervention.

Conclusions—In the United States, frailty is common among older patients admitted with AMI. While these vulnerable patients are at an increased risk for mortality, judicial use of revascularization with percutaneous coronary intervention in frail older patients still confers immediate survival benefit. (*J Am Heart Assoc.* 2019;8:e013686. DOI: 10.1161/JAHA.119.013686.)

Key Words: administrative claims • cardiovascular disease • elderly • frailty • myocardial infarction

I n the United States, the older patient population is expanding rapidly, particularly among those >75 years of age.¹ There were 19 million aged 75 years or older in 2012, representing 6% of the total population, and these estimates are projected to increase to 46 million in 2050, representing 11.5% of the population.² This population is particularly susceptible to cardiovascular disease and its complications.³ While outcomes have improved markedly over the past decades, the care for older adults with cardiovascular disease is often complicated by the presence of geriatric syndromes including multimorbidity, polypharmacy, functional decline, falls, and frailty.³

Frailty is highly prevalent among older adults with cardiovascular disease.⁴ It is a state of increased vulnerability to stressors, with limited reserves to stabilize declines across multiple physiologic systems,⁵ and is therefore of particular

From the Inova Center of Outcomes Research, Inova Heart and Vascular Institute, Falls Church, VA (A.A.D.); Divisions of Cardiology (A.A.D., G.G., J.R.R.) and Geriatric Medicine and Gerontology (J.H., K.B.-R., J.D.W.), Johns Hopkins University, Baltimore, MD; Departments of Biostatistics (K.B.-R., R.V.) and Health Policy and Management (J.B.S.), Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Geriatric Cardiology Section, University of Pittsburgh, PA (D.E.F.); Geriatric Research, Education, and Clinical Center, VA Pittsburgh Healthcare System, Pittsburgh, PA (D.E.F.); University of Michigan Health System, Ann Arbor, MI (M.M.); Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland (J.B.S.).

This work was presented at the American Heart Association's Scientific Sessions, November 10 to 14, 2018, in Chicago, IL and as a moderated oral presentation at the American College of Cardiology's Scientific Sessions, March 16 to 18, 2019, in New Orleans, LA. The study was also part of a symposium and an oral presentation at the International Conference on Frailty and Sarcopenia Research, February 20 to 22, 2019, in Miami Beach, FL.

Correspondence to: Abdulla A. Damluji, MD, MPH, Johns Hopkins University, 2024 East Monument Street, Suite 2-700, Baltimore, MD 21205; Inova Center of Outcomes Research, 3300 Gallows Rd, Suite I4900, Falls Church, VA 22042. E-mail: abdulla.damluji@jhu.edu and Jodi B. Segal, MD, MPH, Johns Hopkins University School of Medicine, Room 644, 624 North Broadway, Baltimore, MD 21205. E-mail: jsegal@jhmi.edu

Received June 25, 2019; accepted August 7, 2019.

^{© 2019} The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Clinical Perspective

What Is New?

- The prevalence of frailty during first observed acute myocardial infarction admission was 19%; it was much higher in patients who were not treated with percutaneous coronary intervention (PCI) or coronary artery bypass surgery, and this prevalence has increased over the past decades paralleled by the higher survival in older populations with acute myocardial infarction.
- Frail older patients were less likely to receive revascularization with PCI or coronary artery bypass surgery, and had a higher in-hospital mortality rate, referral to hospice, and discharge to rehabilitation centers, as compared with nonfrail patients.
- Frailty modified the relationship between PCI and in-hospital mortality, but PCI in frail older patients was still associated with improvement in survival.

What Are the Clinical Implications?

- Frailty assessment adds important clinical perspective to the treatment paradigm for older adults admitted with acute myocardial infarction.
- While this patient group is at an increased risk for hospital mortality and cardiovascular complications during their first observed acute myocardial infarction hospitalization, use of revascularization with PCI in frail older patients is still associated with survival benefit.

importance when an older adult experiences a severe stress, such as an acute myocardial infarction (AMI). A few small studies have estimated the prevalence of frailty in older patients with severe coronary artery disease,^{6–10} but national estimates of frailty in older patients specifically with AMI are rare. To facilitate the study of frailty from epidemiologic and population health perspectives, Segal and colleagues developed and validated a Claims-based Frailty Index (CFI)^{11,12} that approximates the widely used Fried physical frailty phenotype,^{13–15} which relies on measures that are often not available from clinical encounters.

Most importantly, the best treatment for older adults, and in particular for frail older adults, with AMI remains unclear. The extents to which suboptimal outcomes in frail older adults are primarily attributable to the acute stressor (ie, AMI) or because of the underuse or overuse of procedures aimed to reestablish coronary perfusion are not known. In this study, we aimed to quantify the prevalence of frailty among older patients with AMI in the United States and to examine the influence of frailty on hospital mortality in a large populationbased study. Finally, we aimed to understand whether frailty is responsible for heterogeneity in outcomes from percutaneous coronary intervention (PCI) during the AMI admission.

Methods

Data

This study utilized the Premier Healthcare Database (Premier, Inc, Charlotte, NC) that is populated with detailed patient-level information from >750 hospitals in the United States. It contains information from >717 million hospital encounters, which is ≈ 1 in 5 discharges in the United States. Data available for this study include demographic characteristics, disease status, as well as billed services in a de-identified patient daily service record. Each patient enrolled in this database has a unique identifier, which allows tracking of individual patients across inpatient and hospital-based outpatient settings within the same hospital system. The data that support the findings of this study will not be made available to other researchers because of restrictions in the data use agreement between Premier Inc and Johns Hopkins Medicine. Informed consent to perform this study was waived and this study was approved by the Institutional Review Board at Johns Hopkins University.

Population

The study population included patients aged 75 years or older who were admitted to the hospital with AMI between July 2000 and January 2016 in the United States. Patients were excluded if they died in the Emergency Department before hospital admission. AMI was defined a priori as the primary admission diagnosis using *International Classification of Diseases, Ninth and Tenth Revisions* (*ICD-9* and *ICD-10*) *Clinical Modification codes* (*ICD-9*: 410; *ICD-*121).^{16–20}

Claims-Based Frailty Index

Segal and colleagues previously developed and validated the CFI.^{11,12} Briefly, diagnoses considered reflective of the underlying domains of the physical frailty phenotype were identified and a model was optimized against the measured Fried frailty phenotype. We used the CFI to identify frailty among individuals in this cohort using data from inpatient and outpatient encounters in the 6 months before each patient's index AMI admission. Each variable from these encounters was coded as present or absent and then multiplied by the beta-coefficient, obtained from the original regression, to get a continuous score (Table 1).¹¹ Similar to the methods used in the development and the validation of the CFI, we used a probability cutoff of 0.20 to classify individuals admitted with AMI as frail versus nonfrail. It should be noted that the CFI was developed and validated against a performance-based test, the Fried frailty phenotype, and as such we use the term "physical frailty" interchangeably with "frailty" identified by the CFI throughout this article.

Table 1. Claims-Based Frailty Index Variables

Variables
Admission in past 6 mo
Age
Arthritis (any type)
Charlson comorbidity index (>0, 0)
Cognitive impairment
Congestive heart failure
Chronic skin ulcer
Depression
Falls
Gout
Impaired mobility
Male sex
Musculoskeletal problems
Mycoses
Paranoia
Parkinson disease
Pneumonia
Skin and soft tissue infection
Stroke
Urinary tract infection
White race

Study Outcome

Our primary outcome was in-hospital mortality, defined as death occurring after admission and before hospital discharge.

Comorbidities and Procedures

All comorbid conditions were defined in accordance with the Elixhauser Comorbidity Software, which was developed as part of the Healthcare Cost and Utilization Project by the Agency for Healthcare Research and Quality.^{21,22} For each patient, we selected the first admission for AMI observed in the data. For this analysis, readmissions for AMI after this index admission were excluded. In a similar fashion, patients who received PCI or coronary artery bypass surgery (CABG) during their index admission for AMI were identified.

Statistical Analysis

We first aggregated data across all years and used descriptive statistics to describe the cohort participants' baseline demographics, cardiovascular and noncardiovascular comorbidities, and use of cardiovascular procedures stratified by frailty status. We then characterized the cohort stratified by cardiovascular procedure (PCI, CABG, and medical therapy alone). Given the infrequent use of CABG in the frail population, individuals treated with CABG were excluded from further analyses. Differences between groups were tested using t tests and χ^2 tests, as appropriate. To describe secular trends, we plotted the prevalence of frailty, the prevalence of use of PCI, and the in-hospital mortality rate within the cohort by calendar year. We then calculated the odds of in-hospital mortality by frailty status to examine the influence of frailty on hospital outcome during AMI admission, inclusive of patients receiving any therapies. To understand whether frailty simply recapitulates age, we also examined the influence of frailty on hospital mortality adjusting for age, as age strongly determines the CFI score.

For a crude odds ratio (OR), we calculated the odds of inhospital mortality for those receiving PCI and those not receiving PCI, separately for frail and nonfrail cohort members. We then used multivariable logistic regression to evaluate the influence of PCI on hospital mortality during index AMI admission, controlling for possible confounders, in separate models for the frail and nonfrail cohort members. In the frail model, the covariates that contributed to the CFI were excluded from the model. The multivariable model included pulmonary circulatory disorder, valvular heart disease, peripheral vascular disease, paralysis, stroke or transient ischemic attack, chronic lung disease, diabetes mellitus with and without complications, hypothyroidism, renal failure, liver disorder, ulcer, lymphoma, tumors, or metastasis, weight loss, electrolyte and fluid disorder, iron deficiency anemia, alcoholism, drug overdose, psychiatric disorder, and year of admission. These stratified analyses were repeated using forward and backward logistic regression to help identify a parsimonious model.

To examine effect measure modification, we fit a multivariable logistic regression model that included frailty interacting with PCI. To understand the influence of PCI on hospital mortality among frail older patients alone, the mortality rate was calculated by treatment status (PCI versus no-PCI) adjusting for confounders (see model above). Finally, to understand the influence of PCI by age, we plotted the mortality rate of those who were treated with versus without PCI by age during their index AMI admission. All statistical analyses were performed using STATA version 15 MP (Stata-Corp, College Station, TX). We considered a P value of <0.05 as significant and all tests were 2-sided.

Results

From 2000 to 2016, we identified 469 390 encounters for patients \geq 75 years admitted with AMI (Table 2). The average

 Table 2.
 Demographic Characteristics in Older Adults With AMI by Baseline Frailty Status in Premier Healthcare Database From

 2000 to 2016

Variable*	Total (n=469 390)	Frail [†] (n=89 820)	Nonfrail (n=379 570)
Demographic characteristics			
Age, y, mean	82.3 (75.0–89.0)	85.9 (78.0–89.0)	81.5 (75.0–89.0)
Male, %	46.8 (46.6–46.6)	33.4 (33.0–33.7)	50.0 (49.8–50.1)
White ethnicity, %	75.1 (75.0–75.3)	48.9 (48.5–49.1)	81.3 (81.2–81.5)
Cardiovascular comorbidities			
Congestive heart failure, %	9.16 (9.08–9.24)	28.4 (28.0–28.7)	4.62 (4.55–4.68)
Valvular heart disease, %	4.00 (3.94–4.05)	10.9 (10.7–11.1)	2.36 (2.30–2.41)
Pulmonary circulation disorder, %	1.29 (1.25–1.31)	3.76 (3.63–3.88)	0.70 (6.73–7.27)
Peripheral vascular disease, %	17.5 (17.4–17.6)	22.1 (21.8–22.3)	16.5 (16.3–16.6)
Noncardiovascular comorbidities	· · · ·	· · · ·	
Paraplegia, %	2.89 (2.83–2.93)	4.79 (4.65–4.93)	2.43 (2.38–2.48)
Neurologic disorder, %	11.1 (10.9–11.1)	18.6 (18.4–18.9)	9.25 (9.15–9.34)
Chronic lung disease, %	25.4 (25.3–25.5)	31.3 (30.9–31.6)	24.0 (23.9–24.2)
Diabetes mellitus, %	30.7 (30.5–30.9)	35.9 (35.6–36.3)	29.5 (29.3–29.6)
Diabetes mellitus with complications, %	6.95 (6.89–7.02)	10.1 (9.92–10.3)	6.19 (6.11–6.26)
Hypothyroidism, %	17.4 (17.3–17.5)	22.8 (22.5–23.1)	16.1 (16.0–16.3)
Renal failure, %	23.9 (23.7–24.0)	34.9 (34.6–35.3)	21.3 (21.1–21.4)
Liver disease, %	0.85 (0.82–0.88)	1.12 (1.05–1.19)	0.79 (0.79–0.81)
Peptic ulcer disease, %	0.11 (0.10-0.12)	0.14 (0.10–0.17)	0.10 (0.10-0.11)
AIDS, %	0.01 (0.00-0.01)	0.01 (0.00-0.02)	0.01 (0.00-0.01)
Lymphoma, %	0.77 (0.74–0.79)	1.10 (1.03–1.17)	0.69 (0.66–0.72)
Metastasis, %	1.33 (1.30–1.36)	1.81 (1.72–1.90)	1.22 (1.12–1.25)
Tumor, %	3.12 (3.07–3.17)	4.59 (4.45–4.72)	2.77 (2.71–2.82)
Arthritis, %	3.14 (3.08–3.18)	4.58 (4.44–4.72)	2.79 (2.74–2.84)
Coagulopathy, %	6.64 (6.56–6.67)	7.93 (7.77–8.11)	6.33 (6.25–6.41)
Obesity, %	6.84 (6.76–6.91)	6.53 (6.36–6.66)	6.91 (6.82–6.98)
Weight loss, %	4.64 (4.58–4.70)	8.44 (8.25–8.62)	3.74 (3.68–3.80)
Electrolyte disorder, %	31.1 (30.9–31.1)	47.1 (46.7–47.3)	27.3 (27.1–27.4)
Blood loss, %	2.33 (2.28–2.36)	3.84 (3.71–3.96)	1.97 (1.92–2.01)
Iron deficiency anemia, %	27.2 (27.0–27.3)	42.8 (42.4–43.1)	23.5 (23.3–23.6)
Alcohol intoxication, %	1.05 (1.02–1.08)	0.77 (0.70–0.82)	1.12 (0.11–0.15)
Drug abuse, %	0.21 (0.20-0.22)	0.33 (0.29–0.36)	0.19 (0.17–0.20)
Psychiatric disorder, %	2.37 (2.32–2.41)	4.38 (4.24–4.51)	1.89 (1.85–1.93)
Depression, %	8.65 (8.56–8.73)	15.9 (15.7–16.1)	6.92 (6.84–0.70)
Cardiovascular procedures			'
Diagnostic coronary angiography, %	50.8 (50.6–50.9)	26.7 (26.4–26.9)	56.5 (56.3–56.6)
PCI, %	29.8 (29.6–29.9)	15.4 (15.1–15.6)	33.2 (33.0–33.3)
CABG, %	7.33 (7.25–7.40)	1.40 (1.32–1.48)	8.73 (8.64–8.82)
Hospital outcomes			
In-hospital mortality, %	10.3 (10.2–10.4)	13.2 (13.0–13.4)	9.63 (9.53–9.72)
Discharged home, %	41.9 (41.8–42.1)	28.2 (27.9–28.5)	45.2 (45.1–45.3)

Continued

Table 2. Continued

Variable*	Total (n=469 390)	Frail [†] (n=89 820)	Nonfrail (n=379 570)
Discharged to hospice, %	3.00 (2.94–3.04)	5.77 (5.62–5.92)	2.34 (2.29–2.39)
Discharged to rehabilitation, %	20.9 (20.7–21.0)	29.7 (29.3–29.9)	18.8 (18.6–18.9)

AIDS indicates acquired immune deficiency syndrome; AMI, acute myocardial infarction; CABG, coronary artery bypass surgery; PCI, percutaneous coronary intervention. *AII estimates were presented with 95% CI.

[†]Frailty was defined according to the claims-based frailty index derived from inpatient and outpatient data from 6 months before the AMI admission.

age of this cohort was 82 years; 53% were women and were 75% were white. Among the total cohort, the prevalence of frailty was 19%. Frail patients were older, more likely to be women and ethnic minority members, and had more cardiovascular and noncardiovascular comorbidities. While the prevalence of frailty increased in the early years, it remained relatively stable in the later years (Figure 1). Relative to nonfrail older adults, frail older patients with AMI were more likely to die during the index AMI admission. In the entire cohort, frailty increased hospital mortality by 43% (Frailty odds ratio [OR] 1.43, 95% Cl 1.39-1.46). When this estimate was adjusted for age, frailty remained a significant predictor of hospital mortality (OR 1.16, 95% CI 1.13-1.19). When adjusting for cardiovascular and noncardiovascular comorbidities, frailty remained associated with mortality (OR 1.25, 95% CI 1.22-1.28).

In this cohort of older adults admitted with AMI, the overall mortality rate was 10.3%, and it was higher in the frail than nonfrail patients (Frail: 13.2% versus Nonfrail: 9.6%, P<0.001). When evaluating the secular trends over the 17-year study period, the rate of utilization of PCI increased in the early years of the study and this was paralleled by a consistent decline in the overall in-hospital mortality rates. Patients treated with PCI were younger and their comorbidity burden

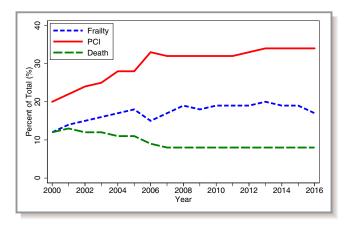


Figure 1. Secular trends in frailty, PCI, and hospital mortality in the Premier Healthcare Database from 2000 to 2016. The denominator is total patients aged \geq 75 years with first acute myocardial infarction. PCI indicates percutaneous coronary intervention.

was less than that of non-PCI-treated patients (Table 3). Across all years, PCI-treated patients had lower in-hospital mortality (PCI versus non-PCI: 6% versus 12%, P<0.001).

Frail patients were less likely to receive percutaneous revascularization with PCI than nonfrail patients (15% versus 33%, P<0.001) and much less likely to receive surgical revascularization with CABG (frail 1% versus nonfrail 9%, P<0.001) during the AMI admission. The prevalence of frailty in PCI-treated patients was 9.9% and 23.1% in patients without intervention. The rate of utilization of PCI during index AMI admission was significantly higher in nonfrail older adults at all ages, but the utilization of PCI in even nonfrail older adults decreased dramatically in patients over 85 years of age (Figure 2).

In an unadjusted model including the whole cohort, the use of PCI was associated with >51% reduction in hospital mortality (OR 0.49, 95% CI 0.47-0.50). Frail older adults benefited from PCI with a mortality reduction of 41% (OR 0.59, 95% CI 0.55-0.0.63), although nonfrail patients experienced improvement in survival after PCI, 51% (OR 0.49, 95% CI 0.47-0.50) compared with patients managed medically. Similarly, frail older adults benefited from CABG with a mortality reduction of 23% (95% CI 7-35%), although nonfrail patients experienced a greater improvement in survival after PCI, 26% (95% CI 23-29%), compared with the medical management group. In the multivariable analysis, adjusting for cardiovascular and noncardiovascular comorbidities, nonfrail older adults treated with PCI had lower hospital mortality (OR 0.58, 95% CI 0.56–0.60) than frail adults, although they too are associated with substantial survival benefit (OR 0.67, 95% CI 0.63-0.71). The interaction between PCI and frailty was significant (P-value for interaction <0.001), supporting a differential benefit in the frail and nonfrail patient populations; the absolute mortality difference was 1.3%. Among frail older patients, the adjusted mortality was lower among those who received PCI than those who received medical management alone (Figure 3). This association with survival was consistent across all older age groups (Figure 4).

Discussion

This is the largest study to examine the prevalence and impact of frailty in older adults aged \geq 75 years admitted with

Table 3. Demographic Characteristics in Older Adults With AMI by Their Treatment Status in Premier Healthcare Database From2000 to 2016

Variable*	Total (n=469 827)	PCI (n=140 089)	Non-PCI (n=329 738
Demographic characteristics			
Age, y, mean	82.3 (75.0–89.0)	80.9 (75.0–89.0)	82.9 (75.0–89.0)
Male, %	46.8 (46.6–46.6)	51.0 (50.7–51.3)	45.0 (44.8–45.1)
White ethnicity, %	75.1 (75.0–75.3)	76.1 (75.9–76.3)	74.7 (74.5–74.8)
Frailty [†] , %	19.1 (19.0–19.2)	9.89 (9.73–10.0)	23.1 (22.9–23.2)
Cardiovascular comorbidities			
Congestive heart failure, %	9.16 (9.08–9.24)	4.58 (4.47-4.69)	11.1 (11.0–11.2)
Valvular heart disease, %	4.00 (3.94–4.05)	2.21 (2.13–2.28)	4.76 (4.69–4.83)
Pulmonary circulation disorder, %	1.29 (1.25–1.31)	0.68 (6.37–7.24)	1.54 (1.50–1.58)
Peripheral vascular disease, %	17.5 (17.4–17.6)	15.9 (15.7–16.1)	18.2 (18.0–18.3)
Noncardiovascular comorbidities	;		
Paraplegia, %	2.89 (2.83–2.93)	1.61 (1.54–1.67)	3.43 (3.36–3.49)
Neurologic disorder, %	11.1 (10.9–11.1)	6.72 (6.58–6.85)	12.9 (12.7–13.0)
Chronic lung disease, %	25.4 (25.3–25.5)	20.8 (20.5–20.9)	27.4 (27.2–27.5)
Diabetes mellitus, %	30.7 (30.5–30.9)	29.0 (28.7–29.2)	31.5 (31.2–31.6)
Diabetes mellitus with complications, %	6.95 (6.89–7.02)	5.38 (5.26-5.49)	7.62 (7.52–7.70)
Hypothyroidism, %	17.4 (17.3–17.5)	15.8 (15.5–15.9)	18.1 (17.9–18.2)
Renal failure, %	23.9 (23.7–24.0)	18.5 (18.2–18.6)	26.2 (26.0–26.3)
Liver disease, %	0.85 (0.82–0.88)	0.66 (0.62–0.71)	0.93 (0.90-0.96)
Peptic ulcer disease, %	0.11 (0.10–0.12)	0.10 (0.10-0.12)	0.11 (0.08–0.11)
AIDS, %	0.01 (0.00-0.01)	0.01 (0.00-0.01)	0.01 (0.00-0.01)
Lymphoma, %	0.77 (0.74–0.79)	0.59 (5.52–6.63)	0.85 (8.16-8.79)
Metastasis, %	1.33 (1.30–1.36)	0.78 (0.73–0.82)	1.57 (1.52–1.61)
Tumor, %	3.12 (3.07–3.17)	2.46 (2.37–2.54)	3.40 (3.33–3.46)
Arthritis, %	3.14 (3.08–3.18)	3.03 (2.94–3.12)	3.18 (3.12–3.24)
Coagulopathy, %	6.64 (6.56–6.67)	5.09 (4.97–5.20)	7.30 (7.20–7.38)
Obesity, %	6.84 (6.76–6.91)	7.84 (7.69–7.98)	6.41 (6.32–6.49)
Weight loss, %	4.64 (4.58–4.70)	2.66 (2.57–2.74)	5.49 (5.41–5.56)
Electrolyte disorder, %	31.1 (30.9–31.1)	21.3 (21.0–21.4)	35.2 (35.0–35.3)
Blood loss, %	2.33 (2.28–2.36)	1.66 (1.59–1.73)	2.61 (2.55–2.66)
Iron deficiency anemia, %	27.2 (27.0–27.3)	21.0 (20.8–21.2)	29.8 (29.6–29.9)
Alcohol intoxication, %	1.05 (1.02–1.08)	0.93 (0.88–0.98)	1.11 (1.06–1.14)
Drug abuse, %	0.21 (0.20-0.22)	0.18 (0.15–0.20)	0.23 (0.21–0.24)
Psychiatric disorder, %	2.37 (2.32–2.41)	1.62 (1.55–1.68)	2.69 (2.63–2.74)
Depression, %	8.65 (8.56-8.73)	6.40 (6.27–6.53)	9.61 (9.50–9.70)
Diagnostic coronary angiography, %	50.8 (50.6–50.9)	100	31.9 (31.7–32.0)
Hospital outcomes	· · · ·		
In-hospital mortality, %	10.3 (10.2–10.4)	6.22 (6.09–6.34)	12.1 (11.9–12.1)
Discharged home, %	41.9 (41.8–42.1)	64.7 (64.4–64.9)	32.3 (32.1–32.4)
Discharged to hospice, %	3.00 (2.94–3.04)	0.77 (0.72–0.82)	3.94 (3.87–4.01)
Discharged to rehabilitation, %	20.9 (20.7–21.0)	12.4 (12.2–12.5)	24.5 (24.3–24.6)

AIDS indicates acquired immune deficiency syndrome; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention.

*All estimates are presented with 95% Cl.

[†]Frailty was defined according to the claims-based frailty index derived from inpatient and outpatient data from 6 months before the AMI admission.

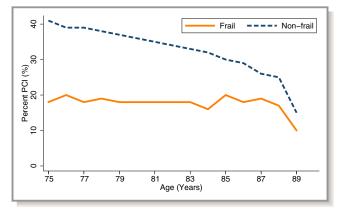


Figure 2. PCI use in older patients by frailty status during acute myocardial infarction. PCI use in older patients by frailty status during first observed acute myocardial infarction in the Premier Healthcare Database. The denominator is total patients aged \geq 75 years with first observed acute myocardial infarction. PCI indicates percutaneous coronary intervention.

AMI in the United States. We found that the prevalence of frailty in older adults during an AMI hospitalization is 19%. During these admissions, frail older patients were less likely to receive PCI or CABG as a treatment for AMI, as compared with nonfrail adults. When we examined secular trends over the 17-year period of the study, the rate of PCI utilization increased and morality decreased, even though the prevalence of the physical frailty syndrome increased. Frail older adults experienced higher hospital mortality during their AMI admission and were more likely to be discharged to rehabilitation or hospice care. Throughout the study period, PCI was associated with survival in frail older patients, although this association was stronger in nonfrail patients.

The prevalence of frailty during AMI or severe multivessel disease was studied previously, but the estimates were

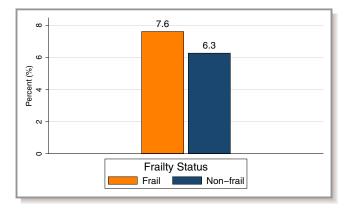


Figure 3. Hospital mortality by frailty status in patients treated with PCI. Hospital mortality by frailty status in older patients treated with PCI during first observed AMI in the Premier Healthcare Database. AMI indicates acute myocardial infarction; PCI, percutaneous coronary intervention.

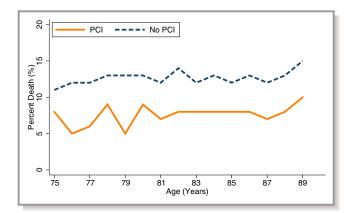


Figure 4. Mortality rate by PCI. Mortality rate by PCI among frail older adults with acute myocardial infarction. PCI indicates percutaneous coronary intervention.

variable.⁴ This may be because of the lack of uniformity in the tools used to identify physical frailty phenotype in the setting of AMI and small study sizes. Afilalo and colleagues summarized this body of evidence in a seminal review.⁴ Purser et al reported that the prevalence of frailty in patients with multivessel coronary disease is 27%; this study measured frailty as the Fried phenotype and included only 309 patients.⁸ In a study from the Mayo Clinic of 629 patients undergoing PCI, the prevalence of the Fried phenotype frailty was 19%,¹⁰ identical to the point prevalence we observed in this study.

When physicians encounter patients with physical frailty or multisystem degeneration in clinical practice, a less aggressive approach to therapy is usually selected. In a study of 307 patients aged 75 years or older with non-ST-segmentelevation myocardial infarction, coronary angiography was attempted in only 15.4% and revascularization was performed in only 6.7% of the frail older patients.⁷ In the study described above, of the 309 patients aged 70 years or older with multivessel coronary disease or left main involvement who underwent cardiac catheterization, only 45.6% and 8.8% of the patients deemed frail in accordance with the Fried phenotype received PCI and CABG, respectively.8 Our study complements these findings as it adds national estimates from a large sample of older patients with AMI. In almost 90 000 frail patients, we found that PCI was attempted in only 16% and CABG was utilized in only 1.4% of the sample. These results may suggest that clinicians try to avoid exposing older patients to invasive procedures because of their increased risk for complications. Recommendations regarding use of PCI in frail older adults in the context of AMI are not based on clinical trial evidence; thus good clinical judgment was advised in the position statement from the American Heart Association Council on Clinical Cardiology. 23,24

Several prior studies reported that frailty increased the risk for hospital mortality in the setting of multivessel coronary disease and PCI.^{7,8} We addressed whether baseline frailty

modified the relationship between PCI and in-hospital mortality. In our study, frail older patients experienced substantial improvement in survival, even though that benefit was less than that experienced by nonfrail older patients. It is also plausible that there is underlying "selection bias" in which PCI is given to those patients with lesser degrees of frailty, which results in the no-PCI group having higher proportions of patients with frailty burden. These results emphasize that PCI in frail patients was associated with survival after development of AMI. While clinical trial data are needed in this growing population of older patients, revascularization should not reflexively be withheld solely because of the presence of frailty.²⁵ Frailty status assessment should be integrated in the assessment of older patients being considered for invasive cardiovascular procedures to allow for informed, shared decision-making about revascularization.

We acknowledge several limitations in this work. First, we identified diagnoses based on ICD-9 and ICD-10 administrative codes. Diagnoses that are not directly tied to reimbursement may be "undercoded," as may be the case with the elements of the CFI. Despite this limitation, many healthcare settings are increasingly adept at using their claims and electronic health record data in real-time to inform patient care; and in this regard the CFI may be a valuable resource for identification of frail older adults at risk of adverse health events and higher utilization of healthcare resources during their AMI admission. Second, risk scores to predict hospital mortality after AMI were not used in this analysis because existing risk scores (eg, NCDR CathPCI Risk Score System) include some variables that were used to define the CFI (eg, age, heart failure, stroke, etc).²⁶ Third, CFI is an imperfect surrogate for Gold standard criteria, but CFI is an important tool to study frailty from a population level when the measurement of underling domains is not available. While the adjustments utilized in our study were comprehensive, residual confounding may still exist. Furthermore, Premier Healthcare Database contains inpatient and outpatient data for patients followed within the same hospital system (ie, this analysis included only patients who sought care in the same hospital system of their AMI admission). Patients without data from outpatient visits preceding their index AMI admission, because of receipt of care at other institutions, were necessarily omitted from the cohort. However, we have no reasons to believe they would have been more or less frail than the included patients. Additionally, a recent study that used a Hospital Frailty Risk Score derived from ICD-10 diagnostic codes for patients 75 years or older admitted to the National Health Service in England reported prevalence estimates similar to those of our study.²⁷ Finally, frailty by itself can be a spectrum that ranges from mild to severe form. In this study, the effect of PCI on this severity spectrum cannot be ascertained.

This study has several important strengths. First, this is the largest population-based study to examine the prevalence of frailty in adults admitted with AMI by the treatment they received in "real world" clinical practice. Second, the CFI for identification of frailty used claims data that are fairly ubiquitous; this may allow for other population-based studies of frailty in different contexts within cardiovascular medicine. Third, our study used data on frailty status collected from inpatient and outpatient visits 6 months before the AMI admission. This is especially important because we were able to measure frailty status before the acute stressor and this probably represents the individual at their baseline. Fourth, inhospital mortality should/could be a therapeutic "target" in very old patients >85 years of age, which in contrast could be an understandable target in patients aged 75 to 85 years. This is especially important because the World Health Organization reported that coronary heart disease deaths will increase by 120% to 137% during the next 2 decades, and a person aged 80 years can expect about 9 remaining years of life.²⁸ Finally, this analysis is the first to examine frailty as an effect measure modifier in the association between PCI and hospital mortality. This analysis will expand the field by focusing on the integration of frailty assessment during AMI and appropriate choice of therapies for the frail older adult group.

Future research efforts should focus on studying how frailty may be mitigated in the setting of AMI (ie, physical strengthening and rehabilitation programs, nutritional support) and directing even more appropriate treatments for AMI to target this vulnerable patient group (ie, shorter dual antiplatelet therapy to reduce the risk of bleeding, type of stents [drug-eluting versus bare metal], and blood pressure and cholesterol targets as secondary prevention goals). While improvement in hospital mortality is an important hard clinical outcome after PCI, quality of life measures and survival after discharge should be integrated into future research on PCI in frail older adults. Finally, validation of simple bed-side measures of frailty (eg, essential frailty toolset, gait speed) during AMI and identification of novel biomarkers to reflect frailty status are essential to advance the field of frailty and multisystem degeneration in the setting of acute cardiovascular illness. 15,29

Conclusion

In this large study, we report that the prevalence of physical frailty syndrome in adults aged \geq 75 years during first observed AMI admission was 19%; frailty was much more prevalent among patients who were not treated with PCI or CABG. While overall survival after AMI has improved over the past 2 decades, partly because of increased utilization of early revascularization, the prevalence of frailty has

increased as the age of patients admitted with AMI is also rising. As shown in smaller studies, frail older patients are less likely to receive revascularization therapies with PCI or CABG and have higher in-hospital mortality rates. Frailty acts as an effect measure modifier in the relationship between PCI and in-hospital mortality, but PCI in frail older adults was still associated with survival as compared with medically treated patients. Frailty assessment should be considered in the treatment paradigm for older adults admitted with AMI, and clinicians should recognize that frail patients may benefit from intervention.

Acknowledgments

This work is part of a PhD thesis for Dr Damluji at the Johns Hopkins University's Graduate Training Program in Clinical Investigation. The authors would like to acknowledge the Jane and Stanley F. Rodbell family for their generous research support to improve outcomes for older Americans living with cardiovascular disease.

Sources of Funding

Dr Damluji receives research funding from the Pepper Scholars Program of the Johns Hopkins University Claude D. Pepper Older Americans Independence Center (OAIC) funded by the National Institute on Aging (NIA) P30-AG021334. This study was also funded in part by a research grant from the Jane and Stanley F. Rodbell family in support of Geriatric Cardiology research at Sinai Hospital of Baltimore. Drs Bandeen-Roche and Walston are co-principal investigators of the OAIC; Drs Bandeen-Roche, Walston, and Gerstenblith are supported by funding from NIA P30-AG021334. Dr Segal is supported by funding from NIA 5K24-AG049036.

Disclosures

Dr Moscucci received book royalties from Wolters Kluwer Lippincott Williams & Wilkins and has stock ownership in Gilead Sciences, Inc. The remaining authors have no disclosures to report.

References

- Damluji AA, Ramireddy A, Otalvaro L, Forman DE. Secondary cardiovascular prevention in older adults: an evidence based review. J Geriatr Cardiol. 2015;12:459–464.
- Ortman J, Velkoff VA, Hogan H. An aging nation: the older population in the United States. *Current Population Reports*. 2014;P25–P1140.
- Damluji AA, Ramireddy A, Forman DE. Management and care of older cardiac patients. In: Vasan RS, Sawyer DB, eds. *Encyclopedia of Cardiovascular Research and Medicine*. Oxford: Elsevier; 2018:245–265.
- Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, Popma JJ, Ferrucci L, Forman DE. Frailty assessment in the cardiovascular care of older adults. J Am Coll Cardiol. 2014;63:747–762.
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381:752–762.

- ORIGINAL RESEARCH
- Gharacholou SM, Roger VL, Lennon RJ, Rihal CS, Sloan JA, Spertus JA, Singh M. Comparison of frail patients versus nonfrail patients >/=65 years of age undergoing percutaneous coronary intervention. *Am J Cardiol.* 2012;109:1569–1575.
- Ekerstad N, Swahn E, Janzon M, Alfredsson J, Lofmark R, Lindenberger M, Carlsson P. Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. *Circulation*. 2011;124:2397–2404.
- Purser JL, Kuchibhatla MN, Fillenbaum GG, Harding T, Peterson ED, Alexander KP. Identifying frailty in hospitalized older adults with significant coronary artery disease. J Am Geriatr Soc. 2006;54:1674–1681.
- McNulty EJ, Ng W, Spertus JA, Zaroff JG, Yeh RW, Ren XM, Lundstrom RJ. Surgical candidacy and selection biases in nonemergent left main stenting: implications for observational studies. *JACC Cardiovasc Interv.* 2011;4:1020– 1027.
- Singh M, Rihal CS, Lennon RJ, Spertus JA, Nair KS, Roger VL. Influence of frailty and health status on outcomes in patients with coronary disease undergoing percutaneous revascularization. *Circ Cardiovasc Qual Outcomes*. 2011;4:496– 502.
- Segal JB, Chang HY, Du Y, Walston JD, Carlson MC, Varadhan R. Development of a claims-based frailty indicator anchored to a well-established frailty phenotype. *Med Care*. 2017;55:716–722.
- Segal JB, Huang J, Roth DL, Varadhan R. External validation of the claims-based frailty index in the National Health and Aging Trends Study cohort. *Am J Epidemiol.* 2017;186:745–747.
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research G. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146–M156.
- Frisoli A Jr, Ingham SJ, Paes AT, Tinoco E, Greco A, Zanata N, Pintarelli V, Elber I, Borges J, Camargo Carvalho AC. Frailty predictors and outcomes among older patients with cardiovascular disease: data from Fragicor. *Arch Gerontol Geriatr.* 2015;61:1–7.
- 15. Afilalo J, Lauck S, Kim DH, Lefevre T, Piazza N, Lachapelle K, Martucci G, Lamy A, Labinaz M, Peterson MD, Arora RC, Noiseux N, Rassi A, Palacios IF, Genereux P, Lindman BR, Asgar AW, Kim CA, Trnkus A, Morais JA, Langlois Y, Rudski LG, Morin JF, Popma JJ, Webb JG, Perrault LP. Frailty in older adults undergoing aortic valve replacement: the FRAILTY-AVR Study. J Am Coll Cardiol. 2017;70:689–700.
- Yaghi S, Pilot M, Song C, Blum CA, Yakhkind A, Silver B, Furie KL, Elkind MS, Sherzai D, Sherzai AZ. Ischemic stroke risk after acute coronary syndrome. J Am Heart Assoc. 2016;5:e002590. DOI: 10.1161/JAHA.115.002590.
- McFalls EO, Larsen G, Johnson GR, Apple FS, Goldman S, Arai A, Nallamothu BK, Jesse R, Holmstrom ST, Sinnott PL. Outcomes of hospitalized patients with non-acute coronary syndrome and elevated cardiac troponin level. *Am J Med.* 2011;124:630–635.
- Manemann SM, Gerber Y, Chamberlain AM, Dunlay SM, Bell MR, Jaffe AS, Weston SA, Killian JM, Kors J, Roger VL. Acute coronary syndromes in the community. *Mayo Clin Proc.* 2015;90:597–605.
- Herzog CA, Littrell K, Arko C, Frederick PD, Blaney M. Clinical characteristics of dialysis patients with acute myocardial infarction in the United States: a collaborative project of the United States Renal Data System and the National Registry of Myocardial Infarction. *Circulation*. 2007;116:1465–1472.
- 20. Desai JR, Vazquez-Benitez G, Xu Z, Schroeder EB, Karter AJ, Steiner JF, Nichols GA, Reynolds K, Xu S, Newton K, Pathak RD, Waitzfelder B, Lafata JE, Butler MG, Kirchner HL, Thomas A, O'Connor PJ; Group S-DS. Who must we target now to minimize future cardiovascular events and total mortality?: lessons from the surveillance, prevention and management of diabetes mellitus (SUPREME-DM) cohort study. *Circ Cardiovasc Qual Outcomes*. 2015;8:508–516.
- Definitions of comorbidities. 2018. Available at: https://www.hcup-us.ahrq. gov/toolssoftware/comorbidity/Table2-FY2010-V3_5.pdf. Accessed August 22, 2019.
- Elixhauser comorbidity software. 2018. Available at: https://www.hcup-us. ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp#references. Accessed August 22, 2019.
- 23. Alexander KP, Newby LK, Cannon CP, Armstrong PW, Gibler WB, Rich MW, Van de Werf F, White HD, Weaver WD, Naylor MD, Gore JM, Krumholz HM, Ohman EM; American Heart Association Council on Clinical Cardiology; Society of Geriatric Cardiology. Acute coronary care in the elderly, part I: non-ST-segment-elevation acute coronary syndromes: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation*. 2007;115:2549–2569.
- Alexander KP, Newby LK, Armstrong PW, Cannon CP, Gibler WB, Rich MW, Van de Werf F, White HD, Weaver WD, Naylor MD, Gore JM, Krumholz HM, Ohman EM; American Heart Association Council on Clinical Cardiology; Society of Geriatric

Cardiology. Acute coronary care in the elderly, part II: ST-segment-elevation myocardial infarction: a scientific statement for healthcare professionals from the American Heart Association Council on Clinical Cardiology: in collaboration with the Society of Geriatric Cardiology. *Circulation*. 2007;115:2570–2589.

- 25. Tegn N, Abdelnoor M, Aaberge L, Endresen K, Smith P, Aakhus S, Gjertsen E, Dahl-Hofseth O, Ranhoff AH, Gullestad L, Bendz B; After Eighty study i. Invasive versus conservative strategy in patients aged 80 years or older with non-ST-elevation myocardial infarction or unstable angina pectoris (After Eighty study): an open-label randomised controlled trial. *Lancet.* 2016;387:1057–1065.
- Peterson ED, Dai D, DeLong ER, Brennan JM, Singh M, Rao SV, Shaw RE, Roe MT, Ho KK, Klein LW, Krone RJ, Weintraub WS, Brindis RG, Rumsfeld JS, Spertus JA; Participants NR. Contemporary mortality risk prediction for

percutaneous coronary intervention: results from 588,398 procedures in the National Cardiovascular Data Registry. *J Am Coll Cardiol.* 2010;55:1923–1932.

- 27. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, Arora S, Street A, Parker S, Roberts HC, Bardsley M, Conroy S. 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;391:1775–1782.
- Mackay J, Mensah G, Mendis S, Greenland K. The Atlas of Heart Disease and Stroke. Geneva: World Health Organization; 2004.
- Afilalo J, Forman DE. Gait speed assessment in transcatheter aortic valve replacement: a step in the right direction. *Circ Cardiovasc Interv.* 2017;10: e005746.