Relation of Frailty to Outcomes in Patients With Acute Coronary Syndromes

Chun Shing Kwok, MBBS, MSc, BSc[a,b], Gina Lundberg, MD[c], Hussam Al-Faleh, MD[d], Alex Sirker, MB BChir, PhD[e], Harriette G.C. Van Spall, MD, MPH[f,g], Erin D. Michos, MD[h], Muhammad Rashid, MBBS[a], Mohamed Mohamed, MBBCh[a,b], Rodrigo Bagur, MD PhD[a], and Mamas A. Mamas, BM BCh, DPhil[a,b,*]

This study examines a national cohort of patients with a diagnosis of acute coronary syndrome (ACS) for the prevalence of frailty, temporal changes over time, and its association with treatments and clinical outcomes. The National Inpatient Sample database was used to identify US adults with a diagnosis of ACS between 2004 and 2014. Frailty risk was determined using a validated Hospital Frailty Risk Score based on ICD-9 codes using the cutoffs <5, 5 to 15, and >15 for low- (LRS), intermediate- (IRS), and high-risk (HRS) frailty scores, respectively. Logistic regression assessed associations of frailty with clinical outcomes, adjusted for patient co-morbidities and hospital characteristics. From 7,398,572 hospital admissions with ACS between 2004 and 2014, 86.5% of patients had LRS, 13.4% had an IRS, and 0.1% had an HRS. From 2004 to 2014, the prevalence of IRS and HRS patients increased from 8.1% to 18.2% and 0.03% to 0.18%, respectively (p <0.001 for both). The proportion of patients treated with percutaneous coronary intervention was greatest among patients with lowest frailty risk scores (LRS 42.9%, IRS 21.0%, and HRS 14.6%). Comparing HRS to LRS, there was a significant increase in bleeding complications (odds ratio [OR] 2.34, 95% confidence interval [CI] 2.03 to 2.69), vascular complications (OR 2.08, 95% CI 1.79 to 2.41), in-hospital stroke (OR 7.84, 95% CI 6.93 to 8.86), and in-hospital death (OR 2.57, 95% CI 2.18 to 3.04). Risk of frailty is common among patients with ACS, is increasing in prevalence, and is associated with differential management strategies, and outcomes during hospitalization. Increased awareness could facilitate frailty-tailored care to minimize the risk of adverse outcomes. **(Am J Cardiol 2019;124:1002−1011)**

Frailty is defined as an age-related decline in the resilience to stressors caused by deterioration in multiple physiological systems.[1] Although the phenotype was described by Fried et al[2] nearly 20 years ago, there is growing interest in frailty as a prognostic factor in cardiovascular medicine due to the ageing population.[3]

Previous studies have evaluated the prevalence and prognostic impact of frailty in elderly patients with acute coronary syndrome (ACS).[4−14] These studies have shown that frailty is associated with an increased risk of death, cardiovascular events,[4,5,7,8,10,11] and major bleeding.[6,9] However, these studies have several limitations. First, the vast majority of these studies have fewer than 400 patients, and may be underpowered to detect rare events like death and complications in ACS. Second, these studies generally include elderly patients using age cutoffs[4−11] that may exclude patients who are frail but younger than the age cutoffs. For example, there is emerging evidence to suggest that some younger patients, especially those with chronic disease or critical illness, may also be considered frail.[15,16] Third, ACS can be managed either medically or invasively and the influence of how frailty may impact on ACS management and how this has changed over time is not well understood. In addition to adverse events and mortality, other important outcomes such as cost have never been considered in the care of frail patients. Fourth, single-center studies reflect local population case mix and management protocols that may not be applicable nationally or internationally. To date there have been no national analyses of frailty in the setting of a broad ACS population.

In this study, we use the Hospital Frailty Risk Score (HFRS) to evaluate frailty in a national cohort of over 7 million patients with ACS in the United States to study temporal trends in frailty, differences in management strategies and the association between frailty and clinical and health economic outcomes.

[a]Keele Cardiovascular Research Group, Keele University, Stoke-on-Trent, United Kingdom; [b]Department of Cardiology, Royal Stoke University Hospital, Stoke-on-Trent, United Kingdom; [c]Emory Women's Heart Center, Emory University School of Medicine, Atlanta, Georgia; [d]Department of Cardiology and Cardiovascular Surgery, Security Forces Hospital, Riyadh, Saudi Arabia; [e]Department of Cardiology, University College Hospital, London, United Kingdom; [f]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [g]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada; and [h]Ciccarone Center for Prevention of Heart Disease, Johns Hopkins University, Baltimore, Maryland. Manuscript received April 25, 2019; revised manuscript received and accepted July 2, 2019.

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*Corresponding author: Tel: +44 (0)1782 671654.

E-mail address: mamasmamas1@yahoo.co.uk (M.A. Mamas).

Methods

A retrospective cohort study was undertaken on national United States hospital data from the National Inpatient Sample (NIS), the largest all-payer inpatient health care database, produced by the Agency for Healthcare Research and Quality (AHRQ). In this study, data from 2004 to 2014 were used, encompassing information from 7 to 8 million hospital discharges per year.[17] This dataset contains patient demographic variables, AHRQ co-morbidity measures, hospital variables, ICD-9 diagnostic codes (15 between 2004 and 2008, 25 between 2009 and 2013, and 30 in 2014), as well as 15 procedure codes.

All patients aged 18 years or over with a primary diagnosis of ACS between January 2004 and December 2014 were included. ACS was defined by the composite of the ICD-9 diagnostic codes for ST-segment elevation myocardial infarction (STEMI; 4100*, 4102*, 4103*, 4104*, 4105*, 4106*, 4108*, 4109*), non-STEMI (NSTEMI; 4107*), and unstable angina (4111).

Frailty was defined by the Hospital Frailty Score as previously described.[16] Although the score was previously derived from ICD-10 codes, only ICD-9 codes were available in the 2004 to 2014 NIS dataset. Our mapping of the codes from ICD-10 to ICD-9, along with the weights applied for each variable, is shown in Supplementary Table 1.

Data were collected on patient demographics, which included age, gender, ethnicity, elective admission, weekend admission, and median household income defined by ZIP code. The AHRQ co-morbidities measures were defined by the Elixhauser co-morbidity software.[18] They included alcohol misuse, hypertension, diabetes, obesity, congestive heart failure, peripheral vascular disease, chronic lung disease, renal failure, liver disease, rheumatoid arthritis/collagen vascular disease, peptic ulcer disease, tumor, lymphoma, paralysis, and acquired immune deficiency syndrome. Additionally, ICD-9 diagnostic codes were used to define smoking (V1582, 3051), hypercholesterolemia (2720/2724), coronary artery disease (41400/41407), previous myocardial infarction (412), previous percutaneous coronary intervention (PCI; V4582), previous coronary artery bypass graft (CABG) surgery (V4581), atrial fibrillation (42731), previous stroke (V1254 438*), dementia (290* 2941* 2942* 2948 3310/3312 33182 797), and cardiogenic shock (78551). Leukemia was defined by Clinical Classification Software code 39. Hospital characteristics including urban versus rural designation and number of beds per hospital were also collected. Finally, the Charlson co-morbidity index, derived according to previous published methods, was used as a measure of co-morbidity.[19] Left ventricular assist device and intra-aortic balloon pump use was defined by the ICD-9 procedural codes 376* and 9744. The management of patients was defined by receipt of coronary angiogram (procedural codes 8853 8854 8855 8856 3722 3723), thrombolysis (procedural code 9910), PCI (procedural code 0066 3606 3607), and current CABG (procedural code 361* 362 3631 3632 369*).

The main outcomes of interest were bleeding complications (diagnostic codes 5789 4590 56881 4329 431*, procedure codes 990*), vascular complications (diagnostic codes 900/904 9982 447 86804 9997, procedural code 3931 3941 3949 3952 3953 3956/3959 3979 990*), in-hospital stroke/transient ischemic attack (TIA; diagnostic codes 99700/99703 4300/4379), length of stay, cost of admission, and in-hospital death. Direct costs were determined by multiplying the charge-to-cost ratio by the total charge.

Statistical analysis was performed using Stata v14.0 (College Station, Texas). Sample sizes were estimated by applying the discharge weight and using Stata's survey estimation command. In addition to analyzing the HFRS as a continuous variable, we also divided the frailty score into 3 groups: low risk (HFRS <5), intermediate risk (HFRS 5 to 15), and high risk (HFRS >15) as defined by Gilbert et al.[20] A histogram was used to examine the distribution of nonzero frailty scores. The percentage of patients in each frailty score group was plotted graphically according to year of ACS admission and also by whether the patient had a diagnosis of NSTEMI/unstable angina or STEMI. Further trend analysis was performed to consider the year of ACS and type of management (medical with no angiogram or thrombolysis, medical with angiogram, thrombolysis, PCI, and CABG) as well as frailty status. Descriptive statistics for baseline characteristics and outcomes are presented by the frailty group. For continuous variables, the mean and standard deviation were determined, whereas for categorical variables, percentages were determined. Adjusted logistic regressions were performed to examine the associations between HFRS group membership and adverse outcomes after ACS, with the reference group being the low HFRS group. A combined intermediate and high risk of frailty score was used because of the low prevalence of patients with high risk of frailty score. Adjusted models included all variables above which included patient demographics, co-morbidities, hospital characteristics, and care received. A sensitivity analysis was performed considering a diagnosis of NSTEMI/unstable angina and STEMI separately. A further analysis was performed considering the receipt of PCI as the reference group and the association of other management strategies on adverse outcomes, stratified by frailty groups.

Results

There were a total of 7,398,572 hospitalizations for patients with ACS after excluding cases with missing data for age, gender, and in-hospital death (Figure 1). Using the previously published HFRS cutoffs,[16] there were 86.5%, 13.4%, and 0.1% in the low-risk (<5; LRS), intermediate-risk (5 to 15; IRS), and high-risk (>15; HRS) groups, respectively. A histogram of the nonzero values of HFRS is shown in Supplementary Figure 1. There were 4,942,346 patients with a diagnosis of NSTEMI or unstable angina (66.8%) and 2,450,922 with a diagnosis of STEMI (33.2%). The breakdowns of the prevalence of the markers of frailty that define the HFRS in the study cohort are shown in Supplementary Table 2.

Evaluation of the trends in frailty over time suggests that the annual prevalence of HRS and IRS among patients increased from 8.1% to 18.2% for IRS and from 0.03% to 0.18% between 2004 and 2014 (Figure 2; p trend <0.001 for both). Over time, among patients with NSTEMI or unstable

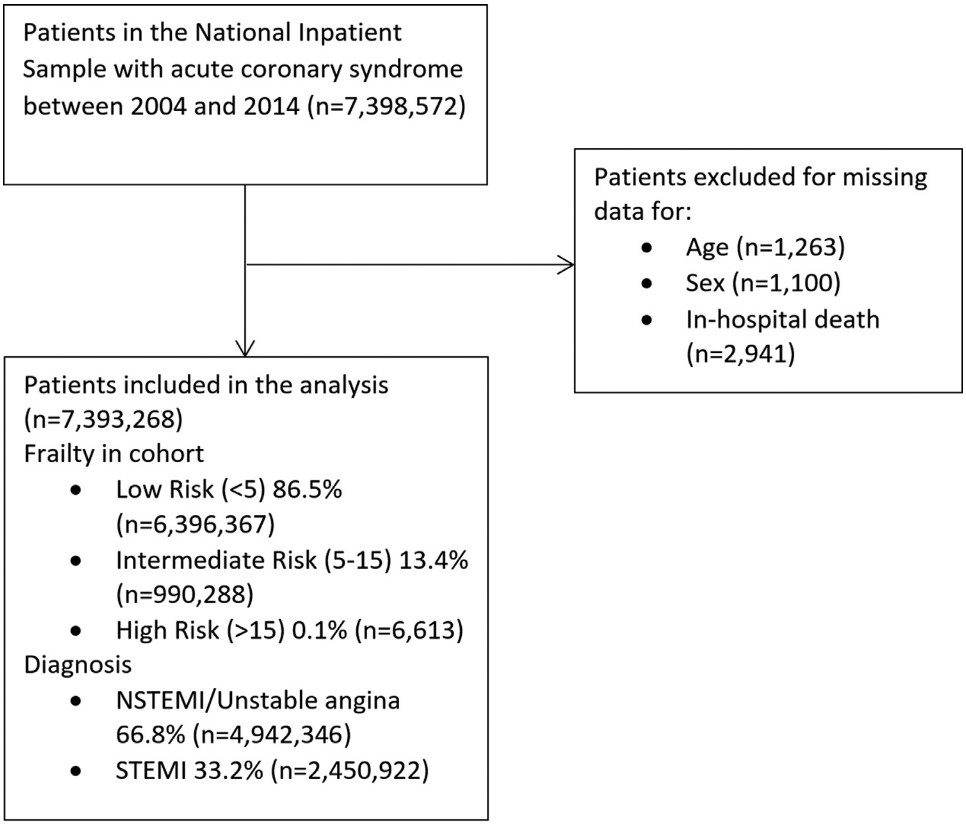


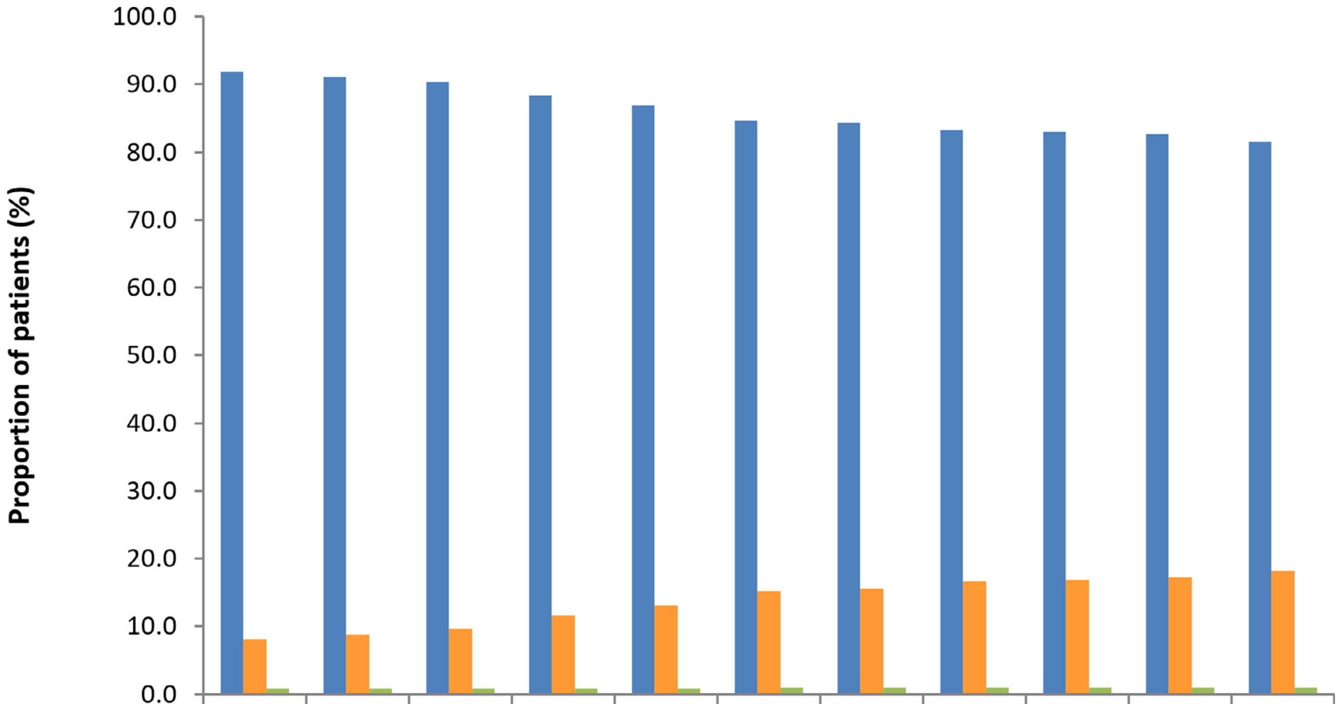
Figure 1. Flow diagram of patient inclusion.

angina patients with IRS increased from 8.4% to 19.6%, whereas those with HRS increased from 0.03% to 0.20%. Similar increases were observed for patients with STEMI, which was 7.7% to 14.7% with IRS and 0.02% to 0.12% with HRS.

The characteristics and outcomes of patients according to frailty status are shown in Table 1 (complete table in Supplementary Table 3). Patients with IRS or HRS of frailty were older, and the mean age was 75 and 80 years, respectively (compared with 66 years old in low risk of frailty group). There were also a greater proportion of female patients in the IRS (48.5%) and HRS (47.5%) compared with the LRS (39.0%) group. There was also a greater proportion of patients receiving Medicare and having higher frailty (LRS 53.3%, IRS 77.4%, and HRS 84.6%). Those with higher HFRS had greater prevalence of congestive heart failure (LRS 0.5%, IRS 2.7%, and HRS 4.5%), atrial fibrillation (LRS 14.3%, IRS 26.2%, and HRS 30.5%), previous stroke (LRS 4.8%, IRS 11.2%, and HRS 19.3%), peripheral vascular disorders (LRS 9.7%, IRS 15.7%, and HRS 15.7%), chronic lung disease (LRS 19.4%, IRS 27.5%, and HRS 20.6%), renal failure (LRS 11.5%, IRS 43.2%, and HRS 50.9%), liver failure (LRS 1.0%, IRS 2.1%, and HRS 1.9%), and dementia (LRS 3.5%, IRS 18.6%, and HRS 60.3%).

In terms of management, 34.2% of patients were medically managed without coronary angiogram, 23.3% were medically treated after coronary angiogram, 0.4% were treated with thrombolysis, 39.9% were treated with PCI, and 2.2% were treated with CABG. Examining trends over time between 2004 and 2014, the proportion of patients treated with PCI increased from 31.6% to 46.0%. Overall, the proportion of patients treated with PCI was greatest among patients with lowest frailty risk scores (LRS 42.9%, IRS 21.0%, and HRS 14.6%) and medical management without coronary angiography was most frequent among patients with higher frailty risk scores (LRS 31.0%, IRS 54.8%, and HRS 70.9%). Temporal trends among patients with LRS between 2004 and 2014 revealed a decrease in the use of thrombolysis (1.1% to 0.1%) and medical management with no angiogram (40.8% to 22.8%; Figure 3). PCI usage increased in all 3 groups with increases also seen in the LRS, IRS, and HRS groups (LRS 33.4% to 50.3%, IRS 12.2% to 26.8%, and HRS 2.5% to 19.1%; Figure 3). Medical management without coronary angiogram decreased over time in all groups but showed the greatest decrease among IRS and HRS patients (IRS 71.1% to 44.4%, HRS 95.0% to 57.8%). Between 2004 and 2014, use of CABG remained similar in the LRS group (2.2% to 2.3%), whereas there was an increase in the IRS group (IRS 1.3% to 3.8%).

In-hospital adverse outcomes, including bleeding complications, vascular complications, in-hospital stroke/TIA, and in-hospital death, occurred in 7.2%, 6.6%, 4.1%, and 5.5% of patients, respectively, for year 2004 to 2014 combined. As shown in Figure 4, these complications increased with increasing frailty risk score (bleeding complications: LRS 5.5%, IRS 18.1%, HRS 21.3%; vascular complications: LRS 5.2%, IRS 15.7%, HRS 18.1%; in-hospital stroke/TIA: LRS 3.2%, IRS 9.9%, HRS 35.5%; and in-hospital death:



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Low	91.8	91.1	90.3	88.4	86.9	84.7	84.3	83.2	82.9	82.6	81.6
Intermediate	8.1	8.9	9.7	11.6	13.0	15.2	15.5	16.7	16.9	17.3	18.2
High	0.03	0.03	0.02	0.04	0.04	0.12	0.13	0.16	0.15	0.14	0.18

Year

Figure 2. Trends in frailty risk over time.

LRS 3.7%, IRS 16.9%, HRS 14.9%). The length of stay and cost also increased with greater HFRS (4.1 days, 8.8 days, and 11.5 days for low risk, intermediate risk, and high risk and cost of $16,159 for low-risk, $26,133 for intermediate-risk, and $29,988 for high-risk frailty status).

The rates of in-hospital complications and death according to management and frailty risk are shown in Table 2. For all outcomes, patients with IRS and HRS had worse outcomes than those with LRS. For LRS patients, mortality rates were 7.4%, 2.5%, and 1.8% for patients managed medically without coronary angiogram, medically with coronary angiogram, and PCI, respectively (Figure 5). Rates of death were much higher for patients with HRS that were 15.0, 12.1, and 16.9%, respectively (Figure 5). In-hospital mortality was consistently lower in the cohort managed with PCI compared with those managed noninvasively for LRS but patients managed medically with angiogram had lower risk in the HRS group compared with PCI (Figure 5).

The association of frailty on the odds of adverse outcomes adjusted for baseline factors is shown in Table 3. Compared with LRS, patients with IRS had twofold increase odds of bleeding complications, vascular complications, and in-hospital stroke/TIA and fourfold increase in odds of in-hospital death. For HRS, the odds were twofold increase for bleeding complications and vascular complications but much higher (eightfold) increase in odds for in-hospital stroke and threefold increase in in-hospital death.

Discussion

Our study is the first to describe the prevalence and associated clinical outcomes of frailty in ACS using a US nationwide cohort of over 7 million patients. We demonstrate that risk of frailty is common in patients presenting with ACS and has increased over time; as the rate of IRS patients have more than doubled from 8.1% to 18.2% of patients with ACS (representing 990,288 patients) and HRS patients have significantly increased from 0.03% to 0.18% (representing 6,613 patients), respectively. Second, we show that revascularization by PCI occurs in 40% of patients overall, but is offered less frequently to those with high frailty risk scores. Rates vary from just below one-half of patients (42.9%) with LRS to less than 1/5 of patients (14.6%) with HRS; more than 2/3 of patients (70.9%) with high frailty risk scores are medically managed without angiogram. Third, we show that treatment with PCI is associated a mortality benefit among patients with LRS but for HRS, management with PCI was associated with greater mortality compared with medical management without angiogram.

Table 1
Characteristics of patients according to frailty risk*

Variable	Degree of risk		
	Low (n = 6,396,367)	Intermediate (n = 990,288)	High (n = 6,613)
Age (year)	66±14	75±13	80±11
Female	39.0%	48.5%	47.5%
Diagnosis			
Unstable angina pectoralis	6.5%	1.4%	0.8%
NSTEMI	59.5%	71.4%	77.8%
STEMI	34.1%	27.2%	21.4%
Primary expected payer			
Medicare	53.3%	77.4%	84.6%
Medicaid	6.4%	5.2%	4.3%
Private insurance	30.3%	12.8%	8.1%
Self-pay	6.4%	2.7%	1.7%
Other	3.0%	1.7%	1.2%
Smoker	35.5%	22.4%	14.6%
Alcohol abuse	2.7%	3.5%	3.3%
Hypercholesterolemia	55.9%	41.0%	39.0%
Hypertension	66.2%	67.3%	69.6%
Diabetes mellitus	32.8%	40.7%	36.6%
Obesity	11.9%	10.6%	7.8%
Congestive heart failure	0.5%	2.7%	4.5%
Coronary artery disease	74.2%	61.8%	56.1%
Previous myocardial infarction	10.3%	9.6%	8.5%
Previous percutaneous coronary intervention	11.7%	8.1%	5.0%
Previous coronary artery bypass graft surgery	7.4%	7.6%	6.6%
Atrial fibrillation	14.3%	26.2%	30.5%
Previous stroke	4.8%	11.2%	19.3%
Peripheral vascular disorders	9.7%	15.7%	15.7%
Chronic lung disease	19.4%	27.5%	20.6%
Renal failure	11.5%	43.2%	50.9%
Liver disease	1.0%	2.1%	1.9%
Dementia	3.5%	18.6%	60.3%
Charlson comorbidity index	1.2±1.4	2.5±1.7	3.8±1.8
Outcomes			
Bleeding complication	5.5%	18.1%	21.3%
Vascular complication	5.2%	15.7%	18.1%
In-hospital stroke/transient ischemic attack	3.2%	9.9%	35.5%
In-hospital death	3.7%	16.9%	14.9%
Length of stay during index	4.1±4.5	8.8±9.4	11.5±12.4
Cost of index	$16,159±14,982	$26,133±31,980	$29,988±37,083

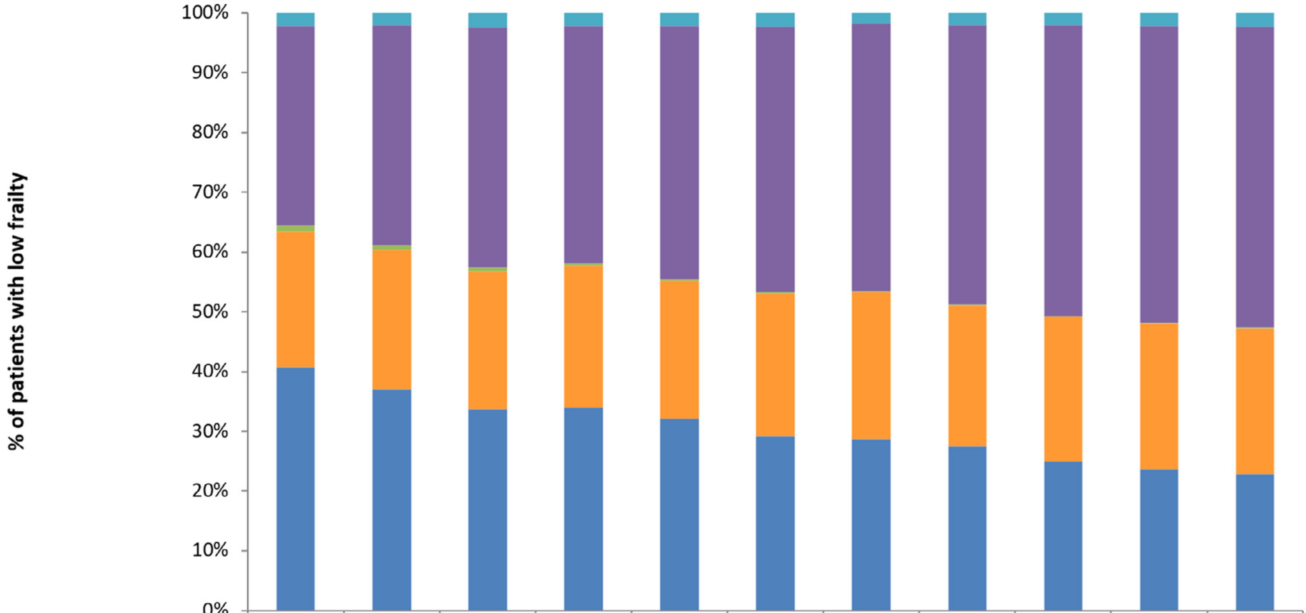
CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

Hypertension was defined by the AHRQ co-morbidity measure for ICD-9-CM code for hypertension (combined uncomplicated and complicated). Hyperlipidemia defined by ICD-9 codes 272.0 (pure hypercholesterolemia), 272.1 (pure hyperglyceridemia), 272.2 (mixed hyperlipidemia), 272.3 (hyperchylomicronemia), and 272.4 (other and unspecified hyperlipidemia).

* Full table is shown in Supplementary Table 3.

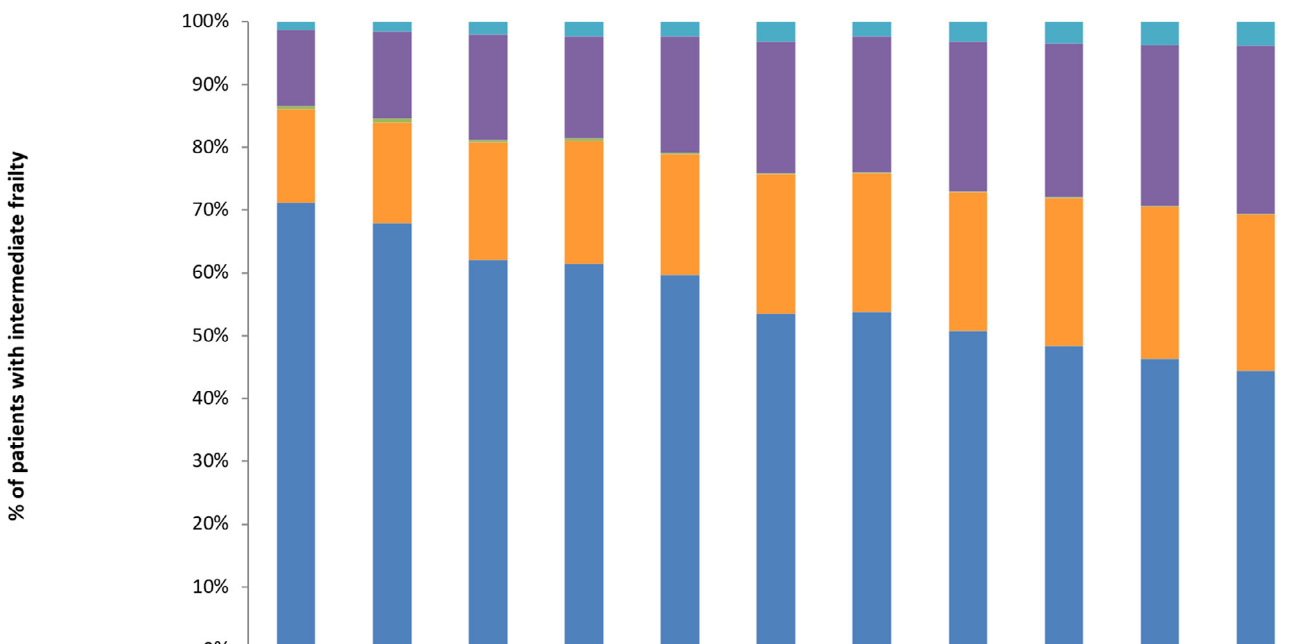
Several studies have examined frailty in ACS patients but our study is the first to consider it in a national cohort. The largest study to date of 129,330 acute myocardial infarction patients aged ≥65 years between 2015 and 2016 from 775 hospitals in the ACTION registry reported rates of frailty of 16.4%. Another study by Singh et al[21] reported that 18.6% were frail and 47.4% were of intermediate frailty among patients aged ≥65 years who underwent PCI. Frailty rates do vary considerably in other studies as has been reported to be as low as 4.7%[6] and as high as 48.5%.[3] We have added to the literature by studying frailty and outcomes in a cohort monitored over a decade that is nonselective and we demonstrate that patients presenting with ACS are increasingly frail. Furthermore, trend analysis in the present study demonstrates the differences in care received, as more than half of patients with low frailty are now revascularized with PCI and less than 1/4 are medically managed without an angiogram, whereas in the high frailty risk group more than half are medically managed without an angiogram and <1 in 5 are revascularized with PCI. This suggests that there may be differences in patient care associated with varying levels of frailty.

Our findings suggest that frail patients have worse in-hospital outcomes. After adjusting for confounders, intermediate- and high-risk frailty patients have twofold to fourfold increases in the risk of bleeding complications, vascular complications, and in-hospital death and high risk of frailty in particular was associated with in-hospital stroke/TIA (nearly eightfold increase in odds). Similarly, in-hospital mortality has been reported by Ekerstad et al[4]



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
CABG	2.2	2.0	2.4	2.2	2.2	2.2	1.8	2.0	2.0	2.2	2.3
PCI	33.4	36.8	40.2	39.7	42.4	44.5	44.7	46.8	48.7	49.7	50.3
Thrombolysis	1.1	0.8	0.6	0.4	0.3	0.2	0.2	0.1	0.1	0.1	0.1
Medical with angiogram	22.6	23.4	23.1	23.7	23.1	23.9	24.6	23.6	24.2	24.4	24.5
Medical no angiogram	40.8	37.0	33.7	33.9	32.1	29.2	28.7	27.5	25.0	23.7	22.8

Year



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
CABG	1.3	1.5	2.1	2.3	2.3	3.2	2.3	3.2	3.5	3.7	3.8
PCI	12.2	13.9	16.8	16.4	18.6	21.0	21.7	23.8	24.4	25.6	26.8
Thrombolysis	0.5	0.6	0.4	0.3	0.2	0.1	0.2	0.2	0.1	0.1	0.2
Medical with angiogram	14.9	16.1	18.7	19.6	19.2	22.3	22.0	22.0	23.7	24.3	24.9
Medical no angiogram	71.1	67.9	62.1	61.4	59.7	53.5	53.8	50.8	48.3	46.3	44.4

Year

Figure 3. Trends in management of acute coronary syndrome by frailty.

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
CABG	2.5	2.3	0.0	0.0	0.0	3.2	0.6	3.4	0.5	0.0	4.0
PCI	2.5	0.0	8.3	4.0	6.8	10.3	17.5	13.3	16.2	22.6	19.1
Thrombolysis	0.0	0.0	0.0	0.0	0.0	0.6	0.6	1.5	0.0	0.0	0.0
Medical with angiogram	0.0	2.3	5.6	4.0	10.2	9.6	13.0	12.3	12.4	15.3	19.1
Medical no angiogram	95.0	95.3	86.1	92.0	83.1	76.3	68.2	69.5	70.8	62.1	57.8

Figure 3. Continued

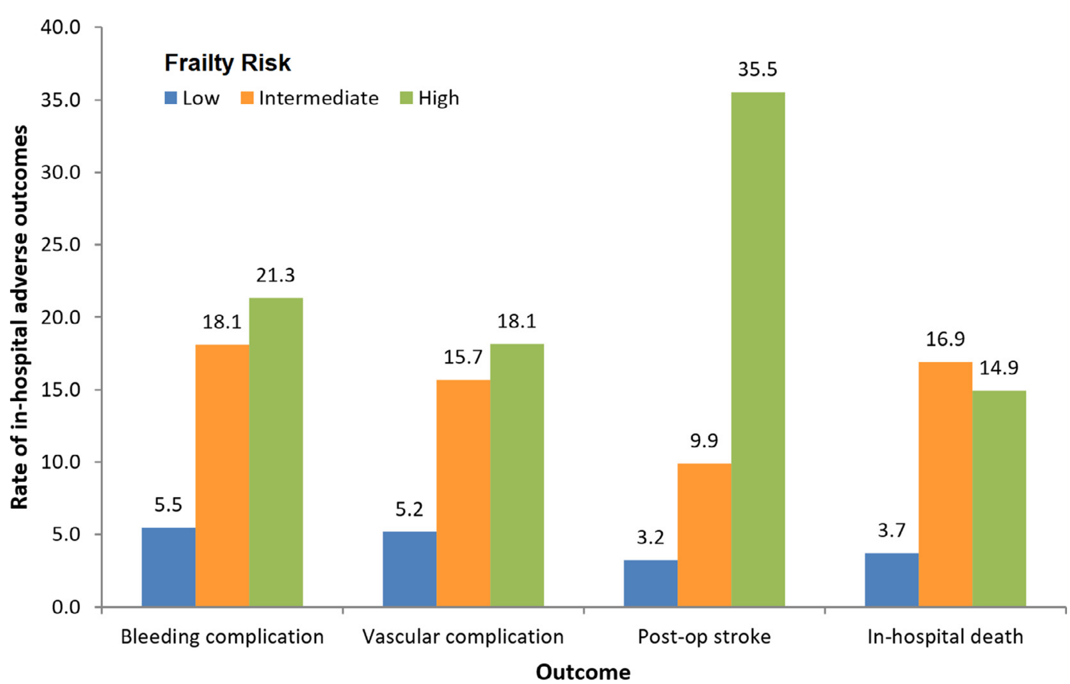


Figure 4. In-hospital adverse outcomes according to frailty risk.

Table 2
In-hospital outcomes by frailty risk and management

Outcome	Frailty risk	Medical no angiogram	Medical with angiogram	Thrombolysis	PCI	CABG
Bleeding complication	Low	6.8%	7.7%	4.6%	2.6%	19.5%
	Intermediate	17.2%	20.5%	24.6%	16.9%	26.2%
	High	20.7%	26.7%	40.0%	19.5%	20.0%
Vascular complication	Low	5.8%	7.5%	3.1%	2.8%	20.7%
	Intermediate	14.4%	19.0%	19.9%	14.3%	26.1%
	High	17.2%	23.0%	40.0%	17.4%	24.0%
In-hospital stroke/TIA	Low	4.0%	4.4%	3.2%	1.8%	6.5%
	Intermediate	9.4%	11.8%	18.5%	8.7%	13.9%
	High	33.7%	41.8%	40.0%	38.5%	40.0%
In-hospital death	Low	7.4%	2.5%	6.4%	1.8%	3.7%
	Intermediate	19.5%	11.2%	31.1%	16.5%	12.0%
	High	15.0%	12.1%	40.0%	16.9%	12.0%

CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

who reported a 4.6-fold increase in odds of in-hospital mortality. The study by Dodson et al suggests a 1.3- to 1.4-fold increase in bleeding complications,[6] whereas the study by Alonso Salinas et al[9] suggests that frailty was associated with a 2.7-fold increase in hazards of 30-day major bleeding. In contrast, the large post hoc analysis of the TRILOGY ACS trial of NSTEMI patients found no association between frailty and bleeding but a hazard ratio of 1.76 for 30-month cardiovascular death, myocardial infarction, or stroke and a hazard ratio of 1.98 for 30-month all-cause mortality while comparing frail versus nonfrail patients.[7] A further study by Alonso Salinas et al[11] of 285 patients from 3 Spanish hospitals suggests that frailty was an independent predictor with a threefold risk of mortality and of the composite of mortality and reinfarction. They also found that complete revascularization was associated with reduced risk of death or reinfarction[11] but they did not consider how frailty influences the benefit of complete revascularization. It is clear that regardless of which method of frailty assessment and population studied, patients with frailty are at a disadvantage in terms of outcomes compared with nonfrail patients.

The in-hospital death rates among patients in the intermediate- and high-risk frailty groups treated medically without angiogram and PCI raises questions about the optimal management for frail patients with ACS. Our results show that there was slightly lower mortality from PCI (16.5% vs 19.5%) compared with medical management without angiogram in intermediate risk frailty patients. In high frailty risk patients, there was greater risk of mortality among patients with PCI compared with medical management without angiogram (16.9% vs 15.0%). Among patients with both

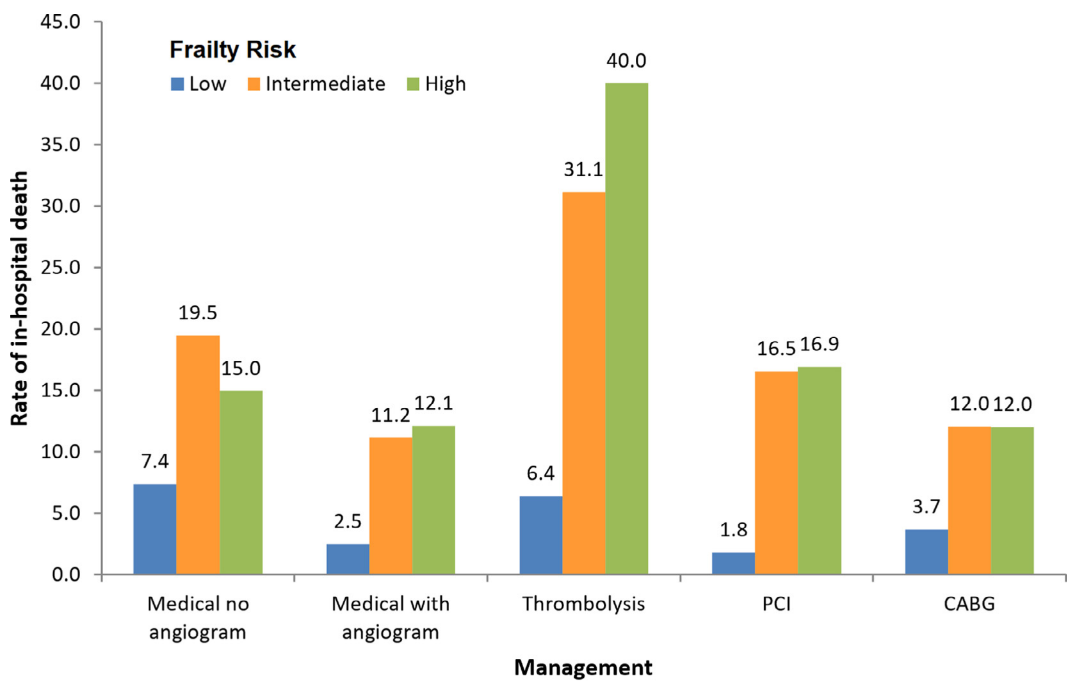


Figure 5. In-hospital death by frailty risk and management.

Table 3
Frailty risk as a predictors of in-hospital adverse outcomes

Outcome	Frailty risk	Odds ratio* (95% CI)	p Value
Bleeding complication	Intermediate vs low risk	2.40 (2.36-2.44)	<0.001
	High vs low risk	2.34 (2.03-2.69)	<0.001
	Incremental increase	1.19 (1.18-1.19)	<0.001
Vascular complication	Intermediate vs low risk	2.17 (2.13-2.20)	<0.001
	High vs low risk	2.08 (1.79-2.41)	<0.001
	Incremental increase	1.16 (1.16-1.16)	<0.001
In-hospital stroke/TIA	Intermediate vs low risk	1.99 (1.95-2.03)	<0.001
	High vs low risk	7.84 (6.93-8.86)	<0.001
	Incremental increase	1.15 (1.15-1.15)	<0.001
In-hospital death	Intermediate vs low risk	3.73 (3.66-3.80)	<0.001
	High vs low risk	2.57 (2.18-3.04)	<0.001
	Incremental increase	1.25 (1.25-1.26)	<0.001

* Odds ratios are adjusted for patient demographics, patient co-morbidities, and hospital characteristics, as further described in the "Methods" section.

intermediate and high frailty risks those who have the lowest mortality have medical management after angiogram (11.2% and 12.1% for intermediate and high risk, respectively). The recent position paper from the Acute Cardiovascular Care Association suggests that frailty is clearly associated with poor outcome and therefore must be taken into account when assessing the balance of benefit when considering any contingent intervention.[22] However, the HFRS appears to be too complex to implement at the bedside and future work should consider whether a simplified version of the assessment can provide a similar level of predictive value. It remains unknown the predictive value of clinical judgment compared with frailty assessment in identifying high-risk patients and how these judgments affect the care received by patients. As this analysis is derived from hospital discharge code level data, we are not certain that any of the patients frail or not frail were appropriately or inappropriately managed. It is further possible that patients who undergo coronary angiograms, PCI, and CABG are already highly selected and despite this they still do less well.

Our study has several limitations. First, the NIS is constructed in a way that patients may appear more than once and it is not possible to determine the extent of the patient appearing more than once. Second, only ICD-9 codes were available so we had to map the codes from ICD-10 to ICD-9. However, there is evidence that ICD-9 and ICD-10 administrative data in recording clinical conditions are similar.[23] Third, there is the potential for residual confounding and we cannot prove causality in our associations between frailty and outcome. Most importantly, treating physicians may have exerted a certain degree of reluctance to perform invasive procedures such as PCI in frail patients who were admitted to the hospital, so that patients in our "high frailty risk" group may have been biased toward a more critical clinical situation and, hence, higher mortality and complication risk. However, the opposite may be true that better frail patients may also undergo investigations but it is not possible to be certain of decision making on an individual patient level in this cohort. Therefore, it may not be entirely accurate that frailty is independently associated with observed outcomes and there may be circumstances where shared decision making cannot be exemplified by the retrospective nature of the database. Fourth, the NIS lacks information on angiographic findings, PCI approaches and periprocedural medications which may influence patient outcomes. Fifth, although there are other measures of frailty, we were only able to assess the HFRS. The strength of the Hospital Frailty Index is that it has been validated against both the Rockwood and Fried scores. Finally, we cannot exclude the possibility of coding errors which may be driven by financial incentives which could result in underreporting of secondary and co-morbid diagnoses in this large administrative database.

In conclusion, we have demonstrated that risk of frailty is an important prognostic marker of clinical outcomes in patients with ACS. We show that the prevalence of intermediate or high frailty risk patients has increased over time particularly in the patients with NSTEMI/unstable angina cohort. Frail patients are less likely to receive PCI and are more likely to be managed medically without coronary angiogram. Unlike low risk of frailty patients where PCI is associated with reduced risk for all adverse outcomes, patients with high risk of frailty that are managed with PCI have worse mortality compared with those managed medically without an angiogram. These results suggest that risk of frailty is common and should be considered as part of the risk assessment and clinical decision-making process of patients with ACS in order to provide tailored care.

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Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.07.003.

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