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The Association of Frailty with In-hospital Bleeding among Older Adults with Acute Myocardial Infarction: Insights from the ACTION Registry®

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Abstract

Background: Our aim was to determine whether frailty, a common syndrome in older adults, was associated with increased bleeding risk in the setting of acute myocardial infarction (AMI).

Methods: We examined frailty among AMI patients age ≥65 treated at 775 U.S. hospitals participating in the ACTION Registry® from 1/2015 – 12/2016. Frailty was classified based on impairments in 3 domains: walking (unassisted, assisted, wheelchair/non-ambulatory), cognition (normal, mildly impaired, moderately/severely impaired), and ADLs. Impairment in each domain was scored as 0, 1, or 2, and we then created a summary variable consisting of 3 categories: 0 (fit/well), 1–2 (vulnerable/mild frailty), and 3–6 (moderate to severe frailty). Multivariable logistic regression was used to examine the independent association between frailty and bleeding.

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Disclosures:

Dr. Fonarow reports serving as Consultant to Bayer and Janssen, and is a member of the ACC NCDR ACTION Registry Research and Publications Committee.

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Results: Among 129,330 AMI patients, 16.4% had any frailty. Frail patients were older, more often female, and were less likely to undergo cardiac catheterization. Major bleeding increased across categories of frailty (fit/well: 6.5%; vulnerable/mild frailty: 9.4%; moderate to severe frailty: 9.9%, P<0.001). Among patients who underwent catheterization, both frailty categories were independently associated with bleeding risk compared with the non-frail group (vulnerable/mild frailty: adjusted OR 1.33, 95% CI 1.23–1.44; moderate to severe frailty: adjusted OR 1.40, 95% CI 1.24–1.58). Among patients managed conservatively, there was no association of frailty with bleeding (vulnerable/mild frailty: adjusted OR 1.01, 95% CI 0.86–1.19; moderate to severe frailty: adjusted OR 0.96, 95% CI 0.81–1.14).

Conclusions: Frail patients had lower use of cardiac catheterization and higher risk of major bleeding (when catheterization was performed) than non-frail patients, making attention to clinical strategies to avoid bleeding imperative in this population.

Condensed Abstract

We used the ACTION registry, which began collecting frailty data in 2015, to investigate whether frailty was associated with increased bleeding risk in the setting of acute myocardial infarction (AMI) in older adults (age ≥65). We found that among 129,330 patients, increasing frailty was associated with major bleeding overall, and in the subgroup of patients undergoing cardiac catheterization (but not in those managed conservatively). These findings persisted after multivariable adjustment, which underscore that frailty should be considered as an independent risk factor for bleeding in older adult AMI patients managed invasively.

Keywords

Myocardial infarction; older adults; bleeding; geriatric

INTRODUCTION:

With the aging of the population in developed countries, there has been a fundamental shift among patients with acute myocardial infarction (AMI); the typical patient with AMI is now older, with more comorbidities, than 20 years ago.[1] Simultaneously, older adults with AMI are being treated more aggressively; for example, in the past two decades there has been a tenfold increase in the use of coronary revascularization procedures among the “oldest old”,[2] and recent registry data demonstrate that over half of patients undergoing percutaneous coronary intervention (PCI) in the United States (U.S.) are ≥65 years of age.[3] Concomitant to the growth in PCI among older adults, there has been an increase in the proportion who receive either dual antiplatelet therapy (DAPT) or “triple therapy” (DAPT plus oral anticoagulant) at hospital discharge.[4,5] While these therapies confer benefit, older adults are also at highest risk of treatment-related major bleeding, which has both immediate consequences (e.g. prolonged hospitalization) as well as long-term adverse outcomes including increased risk of mortality.[6,7] In practice it can be challenging to predict risk for these events in older adults at the time of AMI, as age alone is a relatively crude measure.

The frailty syndrome is generally defined as a state of increased physiologic vulnerability to stressors common among older adults and reflects physiologic rather than chronologic age.

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To date, several small cohort studies have found that the frailty syndrome is associated with in-hospital major bleeding among AMI patients.[8–10] Frailty may confer bleeding risk for several reasons, including underlying biologic vulnerability (e.g. poor vascular integrity or altered hemostatic factors) as well as treatment-related issues (e.g. overdosing of anticoagulants). While small cohort studies have measured frailty in the setting of AMI, historically most large cardiovascular registries have failed to capture it, and therefore confirming prior findings from smaller cohorts has remained challenging.

In response to this gap in knowledge, in 2015 the National Cardiovascular Data Registry® (NCDR) Acute Coronary Treatment and Intervention Outcomes Network Registry® (ACTION Registry) database began collecting information on frailty elements among U.S. patients hospitalized with AMI. With two years of data now collected, this registry provides an opportunity to investigate the prevalence of frailty and its association with in-hospital major bleeding among older adults. We hypothesized that a frailty scale (based on walking, cognition, and activities of daily living) would be independently associated with in-hospital major bleeding, after adjusting for potential confounders.

METHODS

Data sources:

Details of the ACTION Registry have been described previously.[11] Briefly, the ACTION Registry is an ongoing voluntary quality improvement initiative sponsored by the American College of Cardiology and American Heart Association. Data for patients hospitalized with non–ST-segment elevation myocardial infarction (NSTEMI) or STEMI are submitted by participating U.S. medical centers, and include presentation characteristics, comorbidities, therapies administered, and in-hospital complications. Definitions for the data elements of the registry are available at: https://www.ncdr.com/webncdr/action/home/datacollection. The ACTION Registry includes data abstraction training, data quality thresholds for inclusion, site data quality feedback reports, independent auditing, and data validation. Auditing of data has demonstrated chart review agreement of >93% of collected variables.[12] At participating sites, registry participation was approved by an institutional review board.

Study population:

The initial population included 144,354 AMI patients aged ≥65 years between January 1, 2015 and December 31, 2016 from 778 ACTION Registry hospitals. Patients were sequentially excluded if they had missing data for any of the 3 frailty status elements (n=632) or unknown frailty was marked in the data collection form (DCF) (n=14,392) (“unknown” was a distinct field in the DCF that could be marked by sites, while “missing” denoted that no fields were marked). After these exclusions, the final study population consisted of 129,330 AMI patients from 775 hospitals. For the in-hospital major bleeding analyses, we further excluded those transferred out of an ACTION Registry hospital (n=6,736) and patients who had missing components to determine the major bleeding outcome (n=755), which left with an analysis population of 121,839 patients from 772 hospitals.

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Definitions:

Our primary outcome was in-hospital major bleeding based on the ACTION Registry definition,[13] including: absolute hemoglobin decrease ≥4 g/dL (baseline to nadir), intracranial hemorrhage, documented or suspected retroperitoneal bleed, any blood transfusion with baseline hemoglobin ≥9 g/dL, or any transfusion with hemoglobin <9 g/dL and a suspected bleeding event. Major bleeding following CABG was excluded due to the different context of this procedure.

The three variables constituting our frailty score were: (a) walking (0=unassisted; 1=assisted; and 2=wheelchair/non-ambulatory), (b) cognition (0=normal; 1=mildly impaired; and 2=moderately/severely impaired), and (c) basic activities of daily living (ADLs) which included bathing, eating, dressing, and toileting (0=independent in all ADLs; 1=partial assistance ≥1 ADL; and 2=full assistance ≥1 ADL). We conceptualized these deficits as distinct and additive based on the model by Rockwood et al. from the Canadian Study on Health and Aging, which incorporates measures of cognitive and functional performance to describe various degrees of frailty (14). We created a score for each patient by summing across three frailty variables, where the range of the score is from 0 to 6 (Table 1). For ease of interpretation, we then collapsed this score into a summary variable consisting of 3 categories: 0 (fit/well [no frailty present]), 1–2 (vulnerable/mild frailty), and 3–6 (moderate to severe frailty).

Covariates were reported based on standard formatting in prior ACTION Registry publications. For the variable of excess anticoagulant dosing, we based our criteria on prior definitions in the literature. Excess dosing for unfractionated heparin (UFH) was defined as an initial bolus dose >60 units/kg (max 4,000 units) or initial infusion >12 units/kg/h (max 1,000 units/h).[14] Excess dosing for low molecular weight heparin (LMWH) was defined as enoxaparin total daily dose that exceeded the recommended daily dose by more than 10mg over a total daily dose of 2 mg/kg for patients with creatinine clearance ≥30mL/min, or more than 10mg over 1 mg/kg for patients with creatinine clearance <30mL/min or on dialysis.[15] Excess dosing for glycoprotein IIb/IIIa inhibitor (GP IIb/IIIa) was defined as failure to appropriately reduce doses for creatinine clearance. For eptifibatide, full dose infusion was defined as 2μg/kg per minute, with reduced dose of 1μg/kg per minute for patients with creatinine clearance <50mL/min and/or dialysis patients. For tirofiban, full dose infusion was defined as 0.1μg/kg per minute, with reduced dose of 0.05μg/kg per minute for patients with creatinine clearance <30mL/min and/or dialysis patients.[14] The patient's recorded body weight was used for all calculations. Creatinine clearance was estimated using the Cockcroft-Gault equation from age, gender, creatinine, and weight.

Statistical analysis:

To explore the relationship between baseline variables (i.e., baseline patient characteristics, in-hospital treatment patterns, in-hospital major bleeding, and access site among patients with a suspected bleeding event) and the 3 frailty categories, Chi-square and Kruskal-Wallis tests were used to compare categorical and continuous variables, respectively. Categorical variables were reported as percentages and continuous variables were reported as mean ± standard deviation (SD). We further analyzed the rate of in-hospital bleeding stratified by

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frailty categories among the following relevant clinically subgroups of patients: 1) managed with cardiac catheterization vs. without catheterization; 2) AMI type (STEMI vs. NSTEMI); 3) sex; 4) excess dosing vs. no excess dosing for heparin; and 5) excess dosing vs. no excess dosing for GP IIb/IIIa.

To assess the relationship between in-hospital bleeding and frailty categories, logistic generalized estimating equations (GEE) regression was used, with an exchangeable working correlation matrix to account for within-hospital clustering of the outcome. This approach produces estimates that are similar to those from logistic regression with variances that are adjusted for the correlation of outcomes within a hospital.[16] Covariates included in the models are based on the previously validated and published ACTION Registry in-hospital bleeding:[13] age, sex, race, weight, AMI type, heart failure (HF), cardiogenic shock and cardiac arrest on first medical contact, heart rate and systolic blood pressure at presentation, medical history (hypertension, diabetes mellitus, prior peripheral arterial disease, current/recent smoker, dyslipidemia, prior myocardial infarction, prior PCI, prior coronary artery bypass grafting, prior HF, prior stroke, prior atrial fibrillation, history of cancer), laboratory results (initial hemoglobin and initial serum creatinine), and home medications (aspirin, clopidogrel, warfarin, beta blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, aldosterone blocking agent, statin, non-statin lipid-lowering agent). Furthermore, the association between in-hospital bleeding and frailty status was explored across subgroups (catheterization status, AMI type, sex) using logistic GEE regression and interaction between frailty status and each subgroup was tested. Adjusted odds ratios (ORs), 95% confidence intervals (CIs) for in-hospital major bleeding by frailty categories, where non-frail patients were set as the reference group.

The percentage of missing data was low, less than 2% for most variables. For modeling, missing values of the continuous covariates were imputed to the AMI type and sex-specific median of the non-missing values. For categorical variables, missing values were imputed to the most frequent group.

A p-value of <0.05 was considered significant for all analyses. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

RESULTS

Baseline characteristics

The majority (83.6%) of patients had a frailty score of 0 (fit/well), while 11.1% had a score of 1–2 (vulnerable/mild frailty) and 5.3% had a score of 3–6 (moderate to severe frailty). Distribution of each frailty impairment is shown in the Appendix. Age, comorbidities, and acuity of presentation (cardiogenic shock, heart failure) increased with frailty severity, while weight decreased with frailty (Table 2). Patients with frailty were more likely to be female and to present with NSTEMI than STEMI ($P<0.001$) and were less likely to undergo diagnostic catheterization (fit/well: 91.1%; vulnerable/mild frailty: 72.1%; moderate to severe frailty: 46.6%, $P<0.001$). In the overall study population, most patients with STEMI underwent primary PCI, but fewer than half of NSTEMI patients underwent in-hospital PCI. Frail patients were less likely to undergo primary PCI in STEMI (fit/well: 91.6%;

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vulnerable/mild frailty: 88.8%; moderate to severe frailty: 78.2%, P<.001) or in-hospital PCI in NSTEMI (fit/well: 51.7%; vulnerable/mild frailty: 36.1%; moderate to severe frailty: 19.8%; P<0.001). Frailty was also associated with significantly lower rates of radial artery access for PCI.

Bleeding outcomes

Overall, in-hospital major bleeding occurred in 7.0% of the population (8,505 patients). The rate of major bleeding was higher among those with frailty (fit/well: 6.5%; vulnerable/mild frailty: 9.4%; moderate to severe frailty: 9.9%, P<0.001). This pattern was noted among patients undergoing cardiac catheterization (fit/well: 6.4%; vulnerable/mild frailty: 10.3%; moderate to severe frailty: 13.6%, P<0.001), but not among those managed conservatively (fit/well: 7.4%; vulnerable/mild frailty: 7.0%; moderate or severe frailty: 6.7%, P=0.38) (Figure 1). Among AMI subgroups, the overall rate of in-hospital major bleeding was higher among patients with STEMI (9.5%) than among those with NSTEMI (5.7%), and higher among females (8.4%) compared with males (6.0%).

Among patients who underwent cardiac catheterization where a suspected bleeding event was reported, 30.7% of bleeding events were related to access site. This proportion was relatively consistent across categories of frailty (fit/well: 30.3%; vulnerable/mild frailty: 33.2%; moderate or severe frailty: 31.6%, P=0.36). Slightly fewer than half (48.1%) of all bleeding events involved a transfusion.

Among patients who received unfractionated heparin (UFH) or low-molecular weight heparin (LMWH) (81% of sample), excessive dosing occurred in 52.3% of patients, and was slightly less common with increasing frailty (fit/well: 52.6%; vulnerable/mild frailty: 51.6%; moderate to severe frailty: 49.5%, P<0.001) (Table 2). In-hospital major bleeding rates were higher with excessive dosing of UFH or LMWH compared with no excessive dosing (8.1% vs. 6.2%, P<0.001) (Table 3). Among patients who received GP IIb/IIIa inhibitor (16% of sample), excessive dosing occurred in 12.1% of patients, and was considerably more common with increasing frailty (fit/well: 10.9%; vulnerable/mild frailty: 22.3%; moderate to severe frailty: 26.7%, P<0.001) (Table 2). Similar to the pattern seen with excessive UFH or LMWH, patients receiving excess GP IIb/IIIa doses were more likely to experience major bleeding compared with those with no excess dosing (18.5% vs. 10.0%, P<0.001) (Table 3).

Multivariable results

After adjusting for known bleeding risk factors from the ACTION Registry in-hospital major bleeding model,[13] we found that the presence of frailty was associated with increased bleeding overall among patients with vulnerable/mild frailty (OR 1.23 [95% CI 1.15–1.33]) but not with moderate to severe frailty (OR 1.09 [95% CI 0.98–1.20]) when compared with non-frail patients (Figure 2). Among patients who underwent catheterization, both frailty categories were independently associated with increased bleeding risk (vulnerable/mild frailty vs. fit/well: OR 1.33 [95% CI 1.23–1.44]; moderate to severe frailty vs. fit/well: OR 1.40 [95% CI 1.24–1.58]). There was no association between increased bleeding and frailty among patients managed conservatively (vulnerable/mild frailty vs. fit/well: OR 1.01 [95% CI 0.86–1.19]; moderate to severe frailty vs. fit/well: OR 0.96 [95% CI 0.81–1.14]). The

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interaction between frailty and catheterization status was statistically significant (P<0.001). Conversely, among the subgroups of AMI type (STEMI and NSTEMI) and sex (female and male), there were similar directional associations between bleeding and frailty status (P for interaction [AMI type]=0.64; P for interaction [sex]=0.51) (Figure 2).

DISCUSSION

This is the first large U.S. registry study investigating the association between frailty and in-hospital major bleeding in the setting of AMI. The presence of frailty increased bleeding risk by more than 50%, and this finding remained significant after adjustment for baseline characteristics. However, increased bleeding risk was observed only in frail patients who underwent catheterization, and not those treated with conservative (medical) management. These observations underscore that frailty is an important additional risk factor among older adults with AMI managed with an invasive strategy, confirming prior reports from several smaller cohorts.[8,17]

Prior studies have documented that major bleeding among patients hospitalized for AMI carries a range of adverse consequences including stent thrombosis, ischemic events, and both short- and long-term mortality.[6,7,18] For example, an analysis from the ACUITY trial demonstrated that patients with major bleeding during hospitalization experienced a six-fold risk of death within 30 days, which persisted after multivariable adjustment.[18] Patients with major bleeding may require cessation of antithrombotic therapy, and may experience hypovolemia as well as adverse effects from transfusion, all of which may place them at increased risk from these hazards.[18,19] Major bleeding has other downstream consequences such as prolonged hospitalization and diagnostic testing which can burden patients and increase health care costs. In this context, frailty is associated with an increased risk of bleeding that can be used to help clinicians and patients make informed decisions about therapy. While the expected benefits of intervention and the need for immediate decision-making in the setting of STEMI may limit the utility of bleeding risk assessment, understanding the impact of frailty on bleeding risk may assist with decisions among selected patients with NSTEMI, wherein the benefits of early, rapid intervention are often less clear. Notably, patients with NSTEMI represented the majority (77%) of frail patients in our sample.

Frailty may mediate bleeding through a number of mechanisms including inflammation, hemostatic changes (alterations in coagulation factors and/or platelet reactivity), variable pharmacokinetics and inappropriate medication dosing (due to low muscle mass), and vascular fragility.[10,20,21] The lack of a linear increase between severity of frailty (from vulnerable/mild frailty to moderate to severe frailty) and bleeding risk could represent a threshold effect. A different assessment of frailty might provide more stratification by degrees, or the majority of information may be conveyed by the mere presence of frailty. While the frailty syndrome is not modifiable in the acute setting, our findings suggest that there are several opportunities to mitigate bleeding risk among frail AMI patients undergoing an invasive strategy. Paradoxically, despite being at higher bleeding risk, frail patients were less likely to receive strategies known to reduce bleeding. For example, only one in four (26%) frail patients in our sample received radial access, despite several

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randomized trials demonstrating that radial access significantly lowers bleeding risk – including a 2016 meta-analysis of 22,843 participants demonstrating an odds ratio (major bleeding) of 0.53 for radial vs. femoral access (95% CI 0.42 to 0.65).[22] Among older adults, an analysis of patients age ≥80 in the London Heart Attack Group found that radial access was associated with a considerably reduced bleeding risk (odds ratio 0.20, 95% CI 0.10–0.77).[23] While radial access was used in only 19% of patients in the London cohort, the randomized After Eighty Study (which enrolled exclusively patients age ≥80 with NSTEMI or unstable angina) achieved 90% radial access in patients randomized to an invasive approach, and reported a bleeding rate of 1.7%.[24] In our sample, while patient specific factors (e.g. arteries that are small, calcified, or tortuous, all of which are common among older adults) may have prohibited radial access in selected frail patients (although this knowledge is beyond the scope of our dataset), it appears feasible based on other cohorts that higher rates of radial access are possible.

Another important finding is that half of patients (both frail and non-frail) received an excess initial heparin or LMWH bolus, and 12% received excess GP IIb/IIIa inhibitor. Excess dosing of anticoagulants among AMI patients has been reported in prior studies and associated with increased bleeding risk.[25,26] While overdosing based on weight-based thresholds is common in obese individuals, overdosing smaller and frail patients may be especially likely to increase the adverse sequelae of adjustable anticoagulant medications.[27] This finding therefore represents a potential opportunity to modulate bleeding risk through appropriate medication administration, for example through electronic health record decision support systems.

Several limitations should be considered when interpreting our results. First, we based our frailty assessment on available elements (walking, cognition, ADLs) that differ from prior classification schemes using physical measurements,[8,9,28] although we believe there is firm theoretical grounding of our construct based on the Rockwood conceptualization of frailty.[29] Second, we likely underestimated the prevalence of frailty given our reliance on chart documentation of elements included in our frailty score, as well as the potential for survival bias (if patients with the greatest degree of frailty died early in-hospital without documented frailty status). Studies that have formally measured frailty criteria in hospitalized older adults have generally found higher prevalences.[8,30] For example, Sanchis et al. performed a frailty assessment on 342 patients age ≥65 hospitalized with acute coronary syndrome and found a prevalence of 34%, using the criteria defined by Fried et al.[30] However, we believe these limitations are balanced by the benefit of investigating frailty on a scale which, to our knowledge, has not been done in prior large registry studies. In future cohorts, frailty assessments that include gait speed, grip strength, or balance – either individually or as composite instruments (e.g. Timed Up and Go, Short Physical Performance Battery) – could prospectively measure actual physical performance.[31–33] A third limitation is that details of clinical decision making (e.g. reasons for invasive versus conservative management) are unknown, which is an inherent limitation of any large registry study. Fourth, our bleeding definition was based on registry data included severe witnessed bleeding events, transfusion events (excluding anemia on admission), and drop in hemoglobin values. However, this bleeding definition has been used in prior ACTION registry publications[13,34] and we believe it represents true bleeding events given the thresholds chosen. In addition, we excluded

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transfusions related to CABG given their different clinical context. Finally, although we attempted to address in-hospital bleeding and frailty by adjusting for a broad range of patient-level clinical factors, the possibility of confounding by unmeasured covariates remains.

In conclusion, in a large U.S. sample of AMI patients age ≥65, approximately one in six patients were frail. After adjustment for potential confounders, frailty was associated with a 30–40% higher risk of bleeding among patients submitted for cardiac catheterization but not among those managed conservatively. These findings highlight the conundrum with invasive management strategies in frail AMI patients. Awareness of vulnerability and greater utilization of evidence-based strategies to reduce bleeding, including radial access and properly dose-adjusted anticoagulant therapies, may mitigate some bleeding events. When applicable, estimation of bleeding risk in frail patients prior to invasive care may facilitate clinical decision-making and the informed consent process.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIAITONS AND ACRONYMS

AMI	acute myocardial infarction
PCI	percutaneous coronary intervention
ADL	activities of daily living
CABG	coronary artery bypass graft
DAPT	dual antiplatelet therapy
NSTEMI	non–ST-segment elevation myocardial infarction
STEMI	ST-segment elevation myocardial infarction
GEE	generalized estimating equations
DCF	data collection form
UFH	unfractionated heparin
LMWH	low molecular weight heparin

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HF	heart failure

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PERSPECTIVES

WHAT IS KNOWN?

Older adults with acute myocardial infarction (AMI) are at increased risk for in-hospital bleeding compared with younger patients.

WHAT IS NEW?

In a large U.S. registry of AMI patients age ≥65, we found that frailty (based on a composite score of impairments in walking, cognition, or activities of daily living) was an independent risk factor for bleeding after adjusting for known predictors in the ACTION Registry bleeding model.

WHAT IS NEXT?

Formal evaluation of frailty in older adults with AMI may assist with informed decision making about the risks and benefits of invasive therapies.

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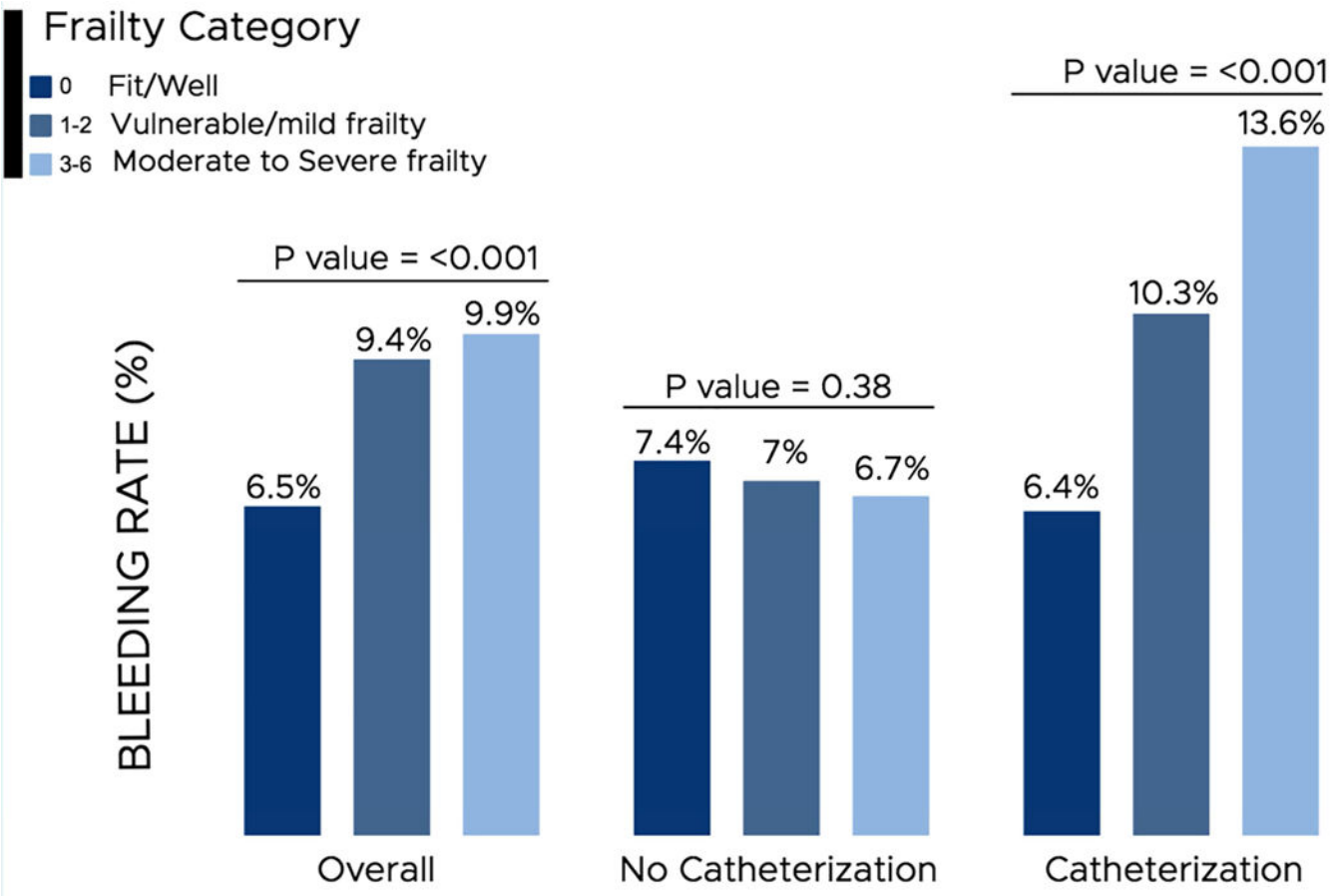

Figure 1. Observed in-hospital major bleeding rates by frailty categories.

Overall, the presence of frailty was associated with significantly increased bleeding rates. Bleeding occurred in 9.4% of patients classified with vulnerable/mild frailty, and in 9.9% of patients with moderate to severe frailty (versus 6.5% of patients with no frailty). Among subgroups, this pattern persisted among patients undergoing cardiac catheterization, but not those managed conservatively.

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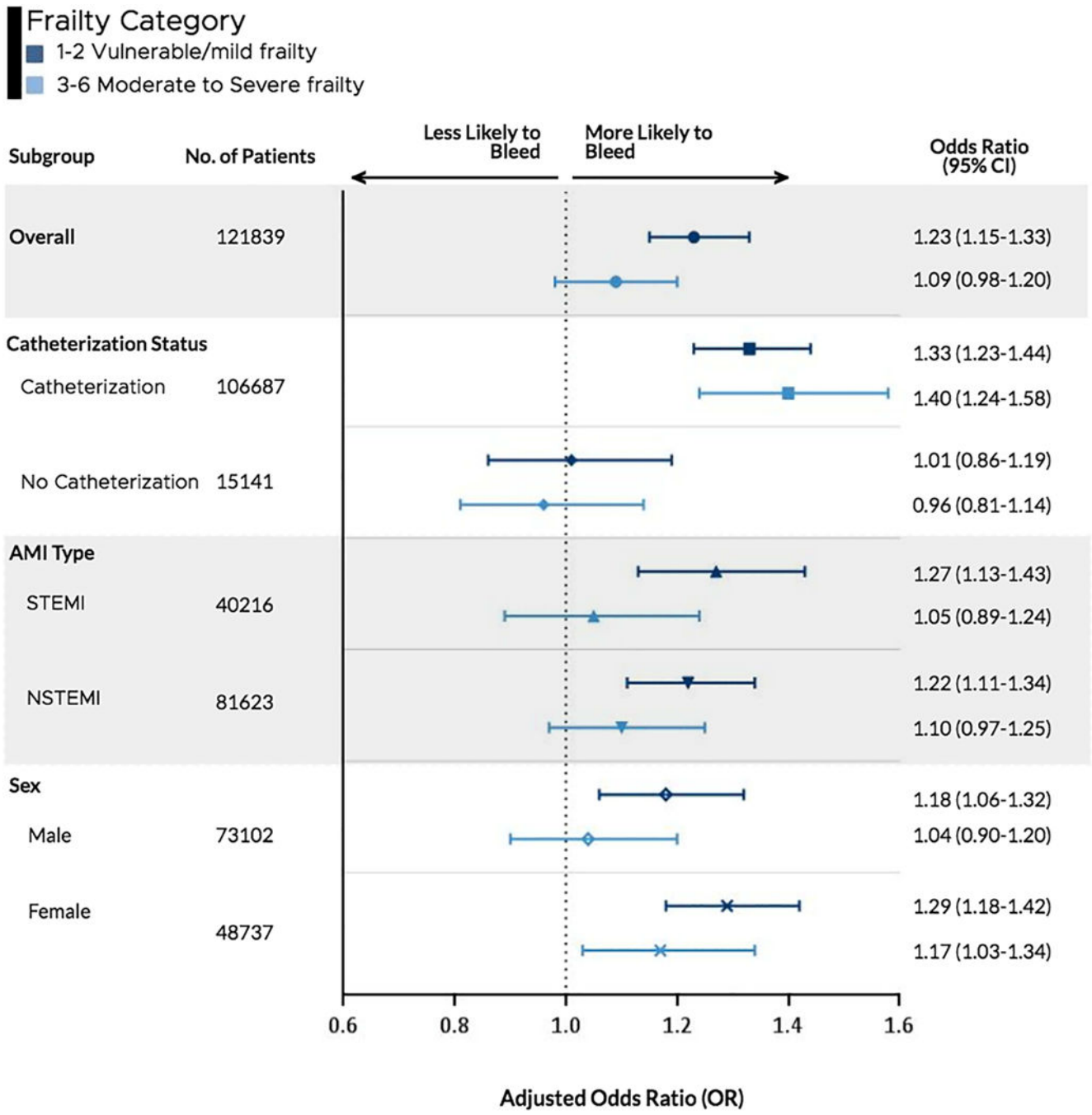

Figure 2. Adjusted odds ratios (95% confidence intervals) for bleeding by frailty categories.

Shown are adjusted odds ratios for bleeding by frailty category (reference group: no frailty) after adjusting for the ACTION Registry bleeding model. Among subgroups, higher adjusted bleeding rates were observed among patients who underwent catheterization but not those managed conservatively (interaction between frailty and catheterization status P<0.001). There were no interactions observed by subgroups of AMI type or sex.

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Table 1.

Frailty point scoring system

	Impairment level (Points):		
Walking:	Unassisted walking (0 points)	Assisted walking (1 point)	Wheelchair/non-ambulatory (2 points)
Cognition:	Normal cognition (0 points)	Mildly impaired (1 point)	Moderately/severely impaired (2 points)
Activities of daily living (ADLs):*	Independent in ADLs (0 points)	Partial assistance ≥1 ADL (1 point)	Full assistance ≥1 ADL (2 points)

Summary score (ranges from 0 to 6 points):

0 = no frailty (fit/well)

1–2 = vulnerable/mild frailty

3–6 = moderate to severe frailty

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Table 2.

Patient characteristics* by frailty categories

	Frailty categories				
	Overall (n=129,330)	**No frailty (n=108,059; 83.6%)**	**Vulnerable/ mild frailty (n=14,376; 11.1%)**	**Moderate to Severe frailty (n=6,895; 5.3%)**	**P value**
Baseline Factors					
Age (years)	75.3 ± 7.7	74.3 ± 7.2	79.6 ± 8.3	82.2 ± 8.6	<0.001
Weight (kg)	82.5 ± 19.9	83.4 ± 19.6	79.2 ± 21.3	74.7 ± 20.7	<0.001
Female sex	39.8	36.9	52.5	57.5	<0.001
Nonwhite race	15.5	15.1	16.8	20.1	<0.001
Hypertension	81.5	80.2	88.6	87.3	<0.001
Dyslipidemia	67.1	66.7	71.4	64.2	<0.001
Diabetes mellitus	37.3	35.8	45.7	43.8	<0.001
Atrial fibrillation/flutter	14.3	12.6	22.2	24.5	<0.001
Prior heart failure	15.0	12.0	28.1	33.6	<0.001
Prior stroke	9.1	7.0	17.0	25.6	<0.001
Prior PCI	26.1	25.9	29.1	22.4	<0.001
Prior coronary bypass	16.4	16.0	19.6	17.1	<0.001
Currently on dialysis	2.4	1.9	4.9	5.1	<0.001
Presentation characteristics					
Cardiogenic shock	3.4	3.3	3.2	5.6	<0.001
Signs of heart failure	15.2	12.9	25.4	30.0	<0.001
Heart rate (beats/min)	83.9 ± 24.2	83.1 ± 24.1	87.7 ± 23.9	88.7 ± 25.1	<0.001
Systolic blood pressure (mmHg)	148.1 ± 35.0	149.2 ± 35.0	145.4 ± 34.3	137.1 ± 35.0	<0.001
Initial serum creatinine (mg/dl), excluding dialysis	1.2 ± 0.7	1.2 ± 0.7	1.3 ± 0.8	1.4 ± 0.9	<0.001
Initial hemoglobin (g/dL)	13.4 ± 2.1	13.6 ± 2.1	12.4 ± 2.2	12.0 ± 2.1	<0.001
NSTEMI	67.4	65.4	77.6	76.2	<0.001
Treatments received					
Diagnostic cath	86.6	91.1	72.1	46.6	<0.001
Any anticoagulant use (cath)	96.0	96.1	94.8	94.1	<0.001
No Diagnostic cath	13.4	8.9	27.9	53.4	<0.001
Any anticoagulant use (no cath)	79.5	80.8	78.6	76.9	<0.001
PCI overall	61.0	64.8	46.5	30.9	<0.001
PCI among NSTEMI	47.8	51.7	36.1	19.8	<0.001
Primary PCI among STEMI	90.9	91.6	88.8	78.2	<0.001

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		Frailty categories			
	Overall (n=129,330)	**No frailty (n=108,059; 83.6%)**	**Vulnerable/ mild frailty (n=14,376; 11.1%)**	**Moderate to Severe frailty (n=6,895; 5.3%)**	**P value**
Radial access among PCI	30.5	31.0	28.4	19.1	<0.001
Bivalirudin use	26.7	28.4	20.0	13.6	
Excess initial UFH or LMWH†	52.3	52.6	51.6	49.5	<0.001
Among cath	53.4	53.2	53.8	56.2	0.009
Among no cath	44.1	44.5	44.8	42.3	0.128
Excess GP IIb/IIIa†	12.1	10.9	22.3	26.7	<0.001
Among cath	12.0	10.9	21.7	26.4	<0.001
Among no cath	18.5	13.1	40.0	35.0	<0.001

*Data are presented either mean ± SD or %

†Rates for anticoagulant dosing calculated among patients receiving anticoagulants. For UFH or LMWH is among 104,930 (81%) of total study population patients; for GP IIb/IIIa is among 20,552 (16.0%) of total study population.

cath = catheterization; GP IIb/IIIa = glycoprotein IIb/IIIa inhibitor; LMWH = low molecular weight heparin; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; UFH = unfractionated heparin

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Table 3.

Observed in-hospital major bleeding * by frailty categories for overall and among subgroups

	Overall	No frailty	Vulnerable/ mild frailty	Moderate to Severe frailty	P value
Overall major bleeding (n=121,839)	7.0	6.5	9.4	9.9	<0.001
Major bleeding by subgroup					
Catheterization (n=106,687)	7.0	6.4	10.3	13.6	<0.001
No catheterization (n=15,141)	7.1	7.4	7.0	6.7	0.38
STEMI (n=40,216)	9.5	8.9	13.6	14.4	<0.001
NSTEMI (n=81,623)	5.7	5.1	8.1	8.5	<0.001
Male (n=73,102)	6.0	5.7	8.4	9.0	<0.001
Female (n=48,737)	8.4	7.8	10.3	10.5	<0.001
Excess UFH or LMWH (n=51,871)	8.1	7.6	10.7	12.9	<0.001
No excess UFH or LMWH (n=46,946)	6.2	5.7	8.2	9.1	<0.001
Excess GP IIb/IIIa (n=2,382)	18.5	17.6	22.2	25.0	0.029
No excess GP IIb/IIIa (n=17,464)	10.0	9.6	13.9	19.3	<0.001

* Data are presented as %

All other abbreviations can be found in Table 1.