

The Frail Scale – A Risk Stratification in Older Patients with Acute Coronary Syndrome

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Purpose: The aim of this study was to explore the impact of frailty on in-hospital adverse outcomes and net adverse clinical events (NACE) in older patients with acute coronary syndrome.

Patients and Methods: This observational study included elderly patients (≥ 60 years old), diagnosed with acute coronary syndrome (ACS) at admission from February 2021 to August 2021. The primary outcome was net adverse clinical events (NACE) defined as a composite of all-cause mortality, stroke, and major bleeding. Secondary outcome was in-hospital adverse outcomes including arrhythmia, acquired pneumonia, stroke, major bleeding, and all-cause mortality. Frailty was assessed using the Frail scale (FS). Data about socio-demographics, comorbidities, body mass index, ACS type, coronary angiography, left ventricular ejection fraction, and length of hospital stay were also collected. Univariate and multivariate logistic regressions were employed to identify the potential association between frailty and outcomes.

Results: Of the 116 ACS patients, 38 patients were frail (32.76%). Frail subjects were more often female (50%) and older ($p < 0.01$) and had higher rates of in-hospital adverse outcomes (OR = 2.37, $p = 0.05$) and NACE (OR = 7.12; $p < 0.01$). In univariate analysis, the increased frail score was significantly associated with increased odds of NACE (unadjusted OR = 1.98, 95% CI 1.17–3.35 for each score increase in Frail Score). In multivariable logistic regression, models controlling for age, gender, PCI, LVEF, and coronary angiography (adjusted OR 2.19, 95% CI 1.12–4.29 for each score increase in Frail Score).

Conclusion: This study revealed the reference data of frailty assessment in older patients with ACS in Vietnam. Our result indicated that over 30% of ACS older patients presented with frailty which was associated with an increased risk of in-hospital adverse outcomes and NACE. This study also provided promising information about the simple FRAIL scale's potential role in the risk stratification of older patients with ACS.

Keywords: Frail scale, elderly, acute coronary syndrome

Introduction

Cardiovascular disease (CVD) is a major healthcare and economic burden worldwide.¹ It remains the leading cause of morbidity and mortality in older populations in developing countries.^{2,3} Acute coronary syndrome (ACS) is a medical emergency with significant ACS morbidity and mortality, the percentage of total mortality by developing region ranges from 5% to 30%.⁴ The incidence of ACS and adverse events due to ACS increases with advanced age. About 60% of hospital admissions for ACS are for patients older than 65 years of age, and approximately 85% of ACS-related deaths occur in this age group.⁴

Along with population aging, geriatric syndromes especially frailty increase the risk of adverse events and increase the burden of management in the elderly.^{2,3} Frailty is a biological condition with reduced storage and resistance to stressors, resulting in a loss of homeostasis and vulnerability to adverse outcomes.^{5–7} It has been found that frailty is

common in older patients with ACS with a prevalence of frailty ranging from 30.1% to 43.2%.^{3,8,9} In Vietnam, the prevalence of frailty in older hospitalised patients and older patients with ACS were reported to be 35.9% and 48.1%, respectively.^{10,11} More evidence is needed to elucidate whether frailty can be considered as an indicator that can be used to stratify the risk in older patients with ACS, which in turn may influence treatment decisions.

Despite the higher risk, older patients with ACS are often not screened for frailty at the time of admission. Most frailty diagnostic tools focused on basic phenotypic categories of frailty as assessed by physical performance tests, utilizing specific difficult-to-measure items (walking speed, handgrip strength).^{12–15} During the acute phase of ACS, the clinical condition limits the use of physical tests, so cumulative functional deficit testing is recommended. In this practical situation, the Frail scale (FS) is a simple questionnaire providing a simple approach (brief, interview-based and simple to administer, score and interpret) with good predictive value.^{16–18} The contribution of frailty according to FS to overall prognosis assessment after ACS has been published in the world^{19,20} but has not been previously investigated in Vietnam. Therefore, we conducted this study to explore the impact of frailty on in-hospital adverse outcomes, and net adverse clinical events (NACE) in this population.

Material and Methods

Study Design and Participants

This prospective, observational study design was conducted in older patients with ACS admitted to Vietnam National Heart Institute, Bach Mai Hospital, Hanoi, Vietnam from February 2021 to August 2021.

Participants were included if they: (1) were ≥ 60 years old according to the WHO definition of an older Vietnamese adult;²¹ (2) were diagnosed with ACS at admission according to 2021 American Heart Association (AHA) and American College of Cardiology (ACC) guideline.^{22,23} Participants were excluded if they: (1) were unable to understand and/or answer the questions, (2) suffered from other acute or severe illness or received intensive care, (3) had cognitive impairment or dementia or delirium, or (4) did not agree to participate in the study. Sixteen patients were excluded on account of study exclusion criteria.

Sample Size Calculation

The sample size was calculated using a formula: $n = Z_{1-\alpha/2}^2 \times (p \times (1-p)/d^2)$, with n = the required sample size, $Z_{1-\alpha/2} = 1.96$ with $\alpha = 0.05$ and 95% confidence interval, $p = 0.481$ (the prevalence of frail in ACS patients in Vietnam¹¹) and d = precision (assumed to be 0.1). Therefore, our study's sample size was calculated to be at least 96 participants.

Data Collection

Data were collected using a structured questionnaire on general characteristics (age, gender, comorbidities, body mass index) and from medical records (admission diagnosis, ACS type, angiography results, treatment therapy, left ventricular EF, and length of hospital stay). The face-to-face interviews were conducted on the day of admission by cardiologists working at the Vietnam National Heart Institute, Bach Mai Hospital. The flow chart of the study population is shown in Figure 1.

Measurements

Frailty Definition

Frailty was assessed using the Frail scale (FS). The Frail scale (FS) was developed by the International Association of Nutrition and Aging to provide a simple approach with good predictive value.¹⁶ The score evaluates 5 specific domains including fatigue, resistance, ambulation, illnesses, and loss of weight.

The score ranges from very fit (FS = 0) to frail (FS = 5). Frailty is defined as $FS \geq 2$ (cut-off with AUC = 0.86).^{24–26}

Outcome Variables

In-hospital adverse outcomes included arrhythmia (defined as any of the following arrhythmias: atrial fibrillation, atrioventricular block, ventricular tachycardia, ventricular flutter), acquired pneumonia, stroke, major bleeding (bleeding

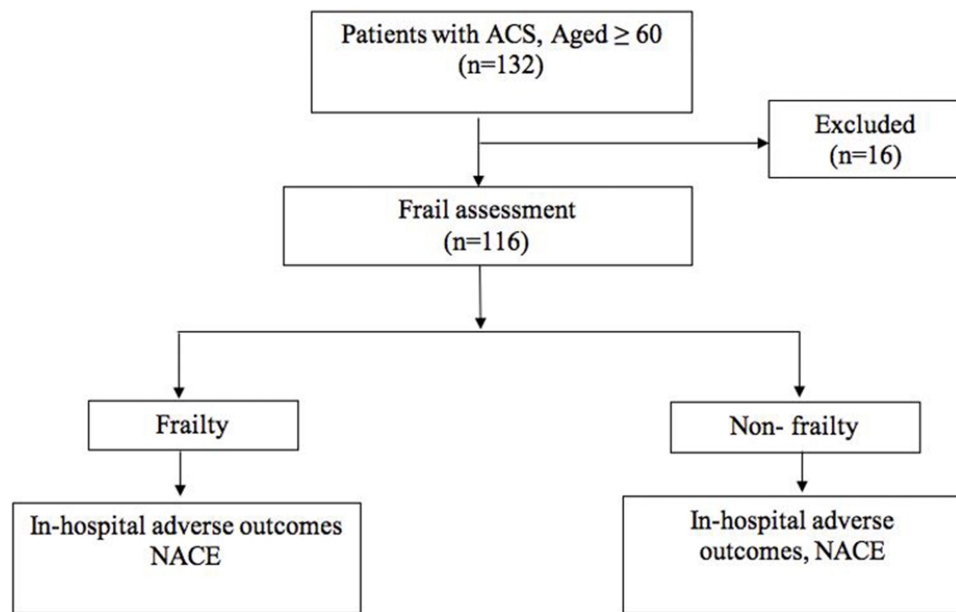


Figure 1 Flow chart of the study population.

that provoked a decrease of over 5g/dl hemoglobin or 15% hematocrit or required blood transfusions) and all-cause mortality. Net adverse clinical events (NACE) were defined as a composite of all-cause mortality, stroke, and major bleeding).

Other Measures

Socio-demographic variables comprised sex (male and female), and age (years). Comorbidities included hypertension, diabetes, dyslipidemia, previous stroke, chronic obstructive pulmonary disease (COPD), and heart failure. Comorbidities were obtained from medical records based on doctors' diagnoses.

Weight and height were measured and used to calculate the body mass index (BMI) using the formula $\text{weight}/\text{height}^2$ (kg/m^2). BMI was categorized into three groups: underweight (<18.5), normal ($18.5\text{--}22.9$), overweight and obesity (≥ 23).

Information obtained from medical records included: ACS type (including ST-elevation myocardial infarction; non-ST elevation myocardial infarction and unstable angina), coronary angiography assessed by Quantitative Coronary Angiography (one-vessel coronary artery disease (CAD) was defined as over 70% stenosis in one major coronary vessel, two-vessel CAD was defined as over 70% stenosis in two major coronary vessels or in left main, three-vessel CAD was defined as over 70% stenosis in three major coronary vessels or in left main and right coronary artery), treatment therapy (percutaneous coronary intervention – PCI during hospitalization or medication treatment). Left ventricular ejection fraction (LVEF) in echocardiography at the time of admission was divided into two groups: heart failure with reduced ejection fraction LVEF $<53\%$ and normal ejection fraction with LVEF $\geq 53\%$ (according to the American Society of Echocardiography²⁷ and the European Association of Cardiovascular Imaging). Length of hospital stay (days) was also collected from medical records.

Statistical Analysis

All data analysis used the Stata/SE 16.0. Characteristic variables were expressed in numbers, percentages, and mean (and standard deviations, SD). The qualitative variables are presented with their distribution of frequency. *T*-test and Chi-squared test were used to measure relationships between frail and non-frail groups and other characteristics. This study evaluated if the variable was parametric or non-parametric via a histogram. Non-parametric data such as length of hospital stay were analyzed using the Wilcoxon-Mann-Whitney test. A *p*-value <0.05 was considered a statistical significance. Univariate logistic regression was performed to analyze the association between potential factors with in-

hospital adverse outcomes and NACE based on the literature such as age, gender, treatment therapy, LVEF, and coronary angiography characteristics. Multivariate logistic regression was employed to identify the potential association between NACE and frailty status. Variables that had a p-value <0.20 on univariate analysis or variables that have potential association with NACE²⁸ were selected for multivariate analysis.

Ethical Consideration

The investigation conforms with the principles outlined in the Declaration of Helsinki. The study protocol was approved by the institutional review board of Hanoi Medical University (Reference number: 3916/QD-DHYHN). All participants or their representative/guardian were asked to give their written informed consent, and they could withdraw anytime. Their information was kept confidential and used only for research purposes.

Results

Study Population Characteristics

Of the 116 patients, the mean age was 72.91, (SD = 6.22) years old, and 76 (65.52%) were male. A total of 38 patients were frail (32.76%). Patients who were frail were more often female (50%) versus 26% in the group non-frail ($p < 0.01$). The prevalence of comorbidities such as hypertension was significantly higher in patients with frailty criteria. In addition, patients in the frailty group had significantly reduced left ventricular systolic function and longer hospitalization (Table 1).

Table 2 describes the in-hospital adverse outcomes and NACE in 27 patients (23.27%) and 8 (6.89%) patients, respectively. The cause of death was related to pneumonia and intracranial bleeding. The major bleeding rate was 4.3%, of which the majority was upper gastrointestinal bleeding. Compared to non-frail participants, frail participants had significantly higher rates of in-hospital adverse outcomes (OR = 2.37, $p = 0.05$) and NACE (OR = 7.12; $p < 0.01$) on univariate analysis.

Table 1 Patient Demographic and Clinical Characteristics (FS)

	N = 116	FS		
		Non Frail (78)	Frail (38)	P
Age	72.91 ± 6.22(60–88)	71.88±5.94	75.02±6.33	P=0.01
Female	40(34.48%)	21(26.92%)	19(50%)	0.01
Comorbidity				
Hypertension	94(81.03%)	58(74.36%)	36(94.74%)	<0.01
Diabetes	38(32.76%)	22(28.21%)	16(42.11%)	0.13
Dyslipidaemia	16(13.79%)	10(12.82%)	6(15.79%)	0.66
Previous stroke	12(10.34%)	7(8.97%)	5(13.16%)	0.48
COPD	7(6.03%)	3(3.85%)	4(10.53%)	0.21
Heart failure	18(15.52%)	7(8.97%)	5(13.16%)	0.48
BMI	21.69± 2.29	21.85±2.20	21.35±2.45	0.26
Underweight	7(6.03%)	3(3.85%)	4(10.53%)	0.29
Normal	101(87.07%)	70(89.74%)	31(81.58%)	
Overweight	8(6.90%)	5(6.41%)	3(7.89%)	
ACS type				
STEMI	38(32.76%)	27(34.62%)	11(28.95%)	0.49
NSTEMI	18(15.52%)	10(12.82%)	8(21.05%)	
Unstable Angina	60(51.72%)	41(62.56%)	19(50.0%)	

(Continued)

Table 1 (Continued).

	N = 116	FS		
		Non Frail (78)	Frail (38)	P
Angiography				
One-vessel CAD	48(41.38%)	34(43.59%)	14(36.84%)	0.71
Two-vessel CAD	42(36.21%)	28(35.90%)	14(36.84%)	
Three-vessel CAD	26(22.41%)	16(20.51%)	10(26.32%)	
Treatment				
PCI	88(75.86%)	62(79.49%)	26(68.42%)	0.19
Medical treatment	28(24.14%)	16(20.51%)	12(31.58%)	
Left ventricular EF	53.87±13.45	54.56±13.58	49.42±12.64	0.05
Length of hospital stay (Days)	6.27 ± 3.83(2–23)	5.66±3.16	7.52±4.74	0.01
In-hospital adverse Outcomes				
Arrhythmia	8(6.89%)	6(7.69%)	2(5.26%)	
Pneumonia	11(9.4%)	6(7.69%)	5(13.6%)	
Stroke	1(0.86%)	0(0%)	1(2.63%)	
Major bleeding	5(4.30%)	2(2.56%)	3(7.89%)	
In-hospital death	2(1.70%)	1(1.28%)	1(2.63%)	
Net adverse clinical outcome (NACE)				
Stroke	1(0.86%)	0(0%)	1(2.63%)	
In-hospital death	2(1.70%)	1(1.28%)	1(2.63%)	
Major bleeding	5(4.30%)	2(2.56%)	3(7.89%)	

Abbreviations: COPD, Chronic Obstructive Pulmonary Disease; BMI, Body Mass Index; ACS, Acute Coronary Syndrome; STEMI, ST Elevation Myocardial Infarction; NSTEMI, Non-ST Elevation Myocardial Infarction; CAD, Coronary Artery Disease; PCI, Percutaneous Coronary Intervention; LVEF, Left Ventricular Ejection Fraction.

Table 2 Relation Between In-Hospital Adverse Outcomes, Net Adverse Clinical Outcome (NACE) and Frailty

FS	Frail (38)	Non Frail (78)	OR (95% CI)	P
In-hospital adverse outcomes, n (%)	13 (34.21)	14 (17.95)	2.37 (0.96–5.86)	0.05
NACE, n (%)	6 (15.79)	2 (2.56)	7.12 (1.28–39.47)	<0.01

Patients with frailty in the subgroup of males, under 70 years old, with one vessel CAD had significantly higher rates of in-hospital adverse outcomes ($p < 0.05$). Similarly, patients with frailty in the subgroup of males, over 70 years old, with LV function over 53% and one-vessel CAD significantly increased the ratio of NACE ($p < 0.05$). (Table 3)

In univariate analysis, the increased frail score was significantly associated with increased odds of NACE (unadjusted OR = 1.98, 95% CI 1.17–3.35 for each score increase in FS) (Table 4). This association remained significant in multivariable logistic regression models controlling for age, gender, PCI, LVEF, and coronary angiography (adjusted OR 2.19, 95% CI 1.12–4.29 for each score increase in FS).

Discussion

The primary finding of this study was that ACS patients with frailty had more than doubled the risk of in-hospital adverse outcomes and NACE. This finding is in line with some prior studies showing that frail older patients were more likely to have poor results, a shorter recovery rate, more iatrogenic complications, and a higher mortality rate.^{2,29,30} Frailty was also linked to an increased risk of death, hospitalization, and falls.^{31–33} Furthermore, older patients with ACS are likely to

Table 3 Analysis of In-Hospital Adverse Outcomes, NACE and Potential Factors Associated with Frailty

		OR (95% CI) for In-Hospital Adverse Outcomes	OR (95% CI) for NACE
Frail			
Frail adjusted for Gender	Female	1.23(0.72–2.10) <i>p</i> =0.43	1.99(0.67–5.16) <i>p</i> =0.15
	Male	1.55(1.01–2.40) <i>p</i> =0.04	2.04(1.07–3.87) <i>p</i> =0.02
Frail adjusted for Age	<70 years	2.76(1.07–7.03) <i>p</i> =0.03	1.85(0.59–5.76) <i>p</i> =0.28
	≥70 years	1.22(0.84–1.77) <i>p</i> =0.28	1.85(1.05–3.61) <i>p</i> =0.03
Frail adjusted for PCI		1.13(0.78–1.66) <i>p</i> =0.49	1.26(0.63–2.54) <i>p</i> =0.504
Frail adjusted for LVEF	LVEF≥53%	1.64(0.88–3.04) <i>p</i> =0.11	6.58(1.07–43.74) <i>p</i> =0.04
	LVEF<53%	1.38(0.92–2.06) <i>p</i> =0.11	1.49(0.80–2.76) <i>p</i> =0.20
Frail adjusted for Angiography	One-vessel CAD	1.87(1.09–2.90) <i>p</i> =0.02	2.66(0.98–7.23) <i>p</i> =0.05
	Two-vessel CAD	1.16(0.60–2.22) <i>p</i> =0.65	1.82(0.71–4.66) <i>p</i> =0.20
	Three-vessel CAD	1.31(0.65–2.65) <i>p</i> =0.44	1.85(0.63–5.44) <i>p</i> =0.25

Abbreviations: PCI, Percutaneous Coronary Intervention; LVEF, Left Ventricular Ejection Fraction; CAD, Coronary Artery Disease.

Table 4 Results from Logistic Regression Models Examining Association Between NACE and Frailty Status

	OR for NACE	95% CI
Un adjusted Model		
Model 1	1.98	1.17–3.35
Adjusted Model		
Model 2	2.08	1.20–3.61
Model 3	2.19	1.12–4.29

Notes: Model 1: unadjusted; Model 2: adjusted for age, gender; Model 3: adjusted for age, gender, PCI, LVEF, Coronary Angiography.

get poorer outcomes^{3,12–15,34–36} in the previous studies using classical scales such as Fried and Edmonton which are inherently inappropriate for ACS patients, during the early days due to physical activity such as walk speed or handgrip strength.^{3,12,13} Some other previous reports that frailty is strongly associated with in-hospital mortality and adverse

events.^{34,37,38} However, most of these studies used classical frailty tools such as Frailty Index or Canadian Frailty Scale in very old patients. In this context, the Frail scale only uses brief, interview-based and simple questions, which seems to be a suitable tool.

The FRAIL scale has been proven in initial investigations to predict adverse effects.^{39,40} Furthermore, prior research has demonstrated that the FRAIL scale performs as well as or better than other known frailty instruments, such as Fried's frailty^{3,12,13,41} in terms of predicting outcomes.⁴² Despite the fact that a FRAIL scale is an excellent tool for screening frailty in the general population, there is little data on its stratification value in patients with ACS. In a previous study, the FRAIL scale independently predicted outcomes in very elderly ACS patients over 80 years old.¹⁹ Recently, there is a study comparing 4 scales including FS,²⁰ but there is little difference in outcomes with the primary endpoint being all-cause mortality and the secondary endpoint being unscheduled rehospitalization. However, to our knowledge, there is little evidence assessing the role of the FRAIL scale in risk stratification in older ACS patients over 60 years old with NACE.

The FRAIL scale allows a reliable assessment of frailty at baseline so that the proportion of patients fulfilling frailty criteria in our series is similar to other research.^{3,11,12} In line with prior studies, frail patients in our study had more comorbidities and a greater risk profile such as advanced age and reduced left ventricular systolic function.¹⁹ Importantly, a significant correlation between frailty and in-hospital adverse outcomes and Net adverse clinical events (NACE) was observed. Interestingly, after adjustment for age, gender, PCI, LVEF, and coronary angiography, the risk of NACE associated with frailty persisted. A previous study showed that frailty was strongly and independently associated with in-hospital mortality and the primary composite outcome.³⁴ However, very elderly patients in this study with higher frailty rate according to the CFS scale (48.5%) probably lead to discrepancies with our study. Besides, our findings suggest that the FRAIL scale is associated with the outcomes of older patients with ACS, in addition to currently recommended risk scores. Besides, a previous meta-analysis discovered that older individuals had worse long-term results following PCI, and conventional cardiac risk factors play a less role than in younger patients.^{43,44} This data indirectly support the Frail scale as a new risk stratification in older ACS persons. As far as we know, our study justified the first use of the FRAIL scale for improved risk classification in ACS patients over 60 years old. This is appropriate with recent guidelines where the recommendation of careful consideration of the risks and benefits of using a Heart Team while accounting for frailty is vital in decisions about the suitable revascularization plan for older patients.²³ Previous study showed that frail scales and physical performance could provide improvements in risk stratification in older ACS patients.⁴⁵ Refining the risk assessment of elderly patients with ACS could help to improve clinical outcomes, potentially leading to significant clinical benefits. Older patients should be screened for frailty routinely at hospital admission for ACS patients.

Our study has some limitations, such as a single-center study, a small sample size, and its observational nature. As a result, we cannot rule out the possibility of selection bias and unmeasured confounding. Despite these limitations, this study reveals intriguing information about the simple FRAIL scale's potential role in the risk stratification of older patients with ACS in coronary care settings although the evidence for the Frail scale is also not representative of populations in different subgroups. In addition, this study did not explore the association between adverse events and classic risk scores (such as GRACE score and/or TIMI risk score). Therefore, further and longer-term research is needed on this issue.

Conclusion

This study revealed the reference data of frailty assessment in older patients with ACS in Vietnam. Our result indicated that over 30% of ACS older patients presented with frailty which was associated with an increased risk of adverse outcomes. This study also provided promising information about the simple FRAIL scale's potential role in the risk stratification of older patients with ACS.

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Disclosure

The authors declare that there is no conflict of interest regarding the publication of this paper.

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