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ORIGINAL RESEARCH

Frailty in Older Patients with Acute Coronary Syndrome in Vietnam

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Background: There has been limited evidence about frailty in older patients with acute coronary syndrome (ACS) in Vietnam.

Aim: (1) To investigate the prevalence of frailty in older patients hospitalised with ACS and its associated factors; (2) To investigate the impact of frailty on percutaneous coronary intervention (PCI) and adverse outcomes in this population.

Methods: Patients aged ≥60 with ACS admitted to two teaching hospitals in Vietnam were recruited from 9/2017 to 4/2018. Frailty was defined by the Reported Edmonton Frail Scale. Multivariate logistic regression was applied to investigate the associated factors of frailty and the impact of frailty on PCI and adverse outcomes.

Results: There were 324 participants, mean age 73.5±8.3, 39.2% female. The prevalence of frailty was 48.1%. Advanced age, female gender, history of hypertension, heart failure, stroke and chronic kidney disease were significantly associated with a frailty status. Overall, 50.3% of the participants received PCI (58.3% in the non-frail vs 41.7% in the frail, p=0.003). However, frailty did not have an independent impact on PCI (adjusted OR 0.66, 95% CI 0.41–1.08). Frailty was significantly associated with increased risk of having arrhythmia during hospitalisation (adjusted OR 2.24, 95% CI 1.32–3.80), hospital-acquired pneumonia (adjusted OR 2.27, 95% CI 1.24–4.17), in-hospital mortality (adjusted OR 3.02, 95% CI 1.35–6.75), 30-day mortality (adjusted OR 3.28, 95% CI 1.59–6.76), and 30-day readmission (adjusted OR 2.53, 95% CI 1.38–4.63).

Conclusion: In this study, frailty was present in nearly half of older patients with ACS and was associated with increased adverse outcomes. These findings suggest that frailty screening should be performed in older patients with ACS in Vietnam.

Keywords: frailty, acute coronary syndrome, elderly, older patients, adverse outcomes, Vietnam

Introduction

Coronary heart disease is the world's leading cause of mortality.[1,2] Increasing age was associated with an increased incidence of acute coronary syndromes (ACS) and higher rates of adverse events after ACS.[3] In older patients with ACS, the presence of frailty, a state of increased vulnerability and reduced physiological reserve, can create a burden for these patients.[4,5] The development of frailty involves multiple physiological factors, including the cardiovascular systems.[6,7] Previous studies showed that frailty was common in older people with cardiovascular disease, and was associated with increased adverse outcomes.[8–19] In older people presenting to hospital with ACS, nearly one-third were frail, and they were less likely to receive an invasive coronary strategy and pharmacological therapies according to the current guidelines.[20]

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Over the past decades, the global burden of coronary heart disease has shifted towards low- and middle-income countries.[21] Vietnam is a lower-middle-income country in the Southeast Asia region with rapid urbanisation. In Vietnam, the proportion of older people (aged 60 or over) is increasing, with an estimate of 26.1% of the population in 2049.[22] Cardiovascular disease is the leading cause of death in Vietnam.[23–26] However, the evidence of frailty in older Vietnamese people is limited. In one study conducted in 2015, the prevalence of frailty in older hospitalised patients was 31.9%.[27] There has been no study of frailty in older patients with ACS. Therefore, this study aims to investigate the prevalence of frailty in older patients hospitalised with ACS and its associated factors, and to investigate the impact of frailty on percutaneous coronary intervention (PCI) and adverse outcomes in this population.

Methods

Participants

A prospective cohort study was conducted in patients with ACS admitted to Thong Nhat Hospital in Ho Chi Minh City (Interventional Cardiology Department) and Cho Ray Hospital (Interventional Cardiology Department, Cardiology Department) from 9/2017 to 4/2018.

Inclusion criteria: age ≥60 and was diagnosed with ACS at this admission. Exclusion criteria include: (1) severe illness (dying or receiving intensive care), (2) blind or deaf, (3) severe dementia or delirium, (4) unable to speak or understand Vietnamese language.

The study was approved by the ethics committees of the University of Medicine and Pharmacy in Ho Chi Minh City, Cho Ray Hospital and Thong Nhat Hospital. Written informed consent was obtained from all participants.

Sample Size Calculation

Sample size was calculated for the first aim of this study. The sample size was determined using a single population proportion formula: $n=Z^2_{1-\alpha/2} * [p*(1-p)/d^2]$, with n = the required sample size, $Z_{1-\alpha/2} = 1.96$ (with $\alpha = 0.05$ and 95% confidence interval), p = prevalence of frailty in older patients with ACS, and d = precision (assumed as 0.05). Previous studies showed that the prevalence of frailty in older patients with ACS ranged from 30.1% to 43.2%.[28–30] Therefore, the sample size for this study is calculated to be at least 324 participants.

Data Collection

Data were collected from patient interviews and from medical records. Information obtained from medical records included: demographic characteristics, height, weight, medical history, comorbidities, admission diagnosis, Killip class, PCI during hospitalisation, and events during hospitalisation (arrhythmia, acquired pneumonia, cardiogenic shock, stroke, major bleeding, recurrent myocardial infarction, death, and length of stays).

All participants were followed up for 30 days after discharged. Phone calls were conducted to the phone numbers provided by participants to obtain information about readmission and mortality.

Frailty Definition

In this study, frailty was defined by the Reported Edmonton Frail Scale (REFS). The REFS was chosen because it is a validated tool and more feasible for research in older hospitalized patients. This scale was also recommended by several guidelines to identify frailty, particularly in older patients after ACS.[31,32] The REFS has been applied in many studies.[27,33–38] In a recent study in the North of Vietnam, the REFS was shown to be as effective as Fried's frailty phenotype in detecting frailty and predicting mortality in older inpatients in Vietnam.[39] The REFS includes nine frailty domains: cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence and functional performance. The REFS has a maximum score of 18, and the cut point used to identify frailty was ≥8, as applied in previous studies using this scale.[27,33–38] The REFS is based on a questionnaire on how the patient functioned prior to the illness that brought them into the hospital, is not heavily influenced by the acute illness, easy to apply for older inpatients and less time-consuming (Supplementary Table S1).

Outcome Variables

The primary outcomes of this study are the proportion of receiving PCI, and the adverse event rates during hospitalisation and during 30 days after discharge. Adverse events during hospitalisation included arrhythmia (defined as any of the following arrhythmias: sinus tachycardia, sinus bradycardia, atrial fibrillation, atrial flutter, atrioventricular block, ventricular tachycardia, ventricular flutter), acquired pneumonia, cardiogenic shock, stroke, recurrent myocardial infarction, major bleeding (bleeding that required

blood transfusions), and all-cause mortality. Adverse events during 30 days after discharged included all-cause readmission and all-cause mortality.

Statistical Analysis

Analysis of the data was performed using SPSS for Windows 24.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as means ± standard deviation, and categorical variables as frequencies and percentages. Comparisons between frail and non-frail participants were conducted using the Chi-square test or Fisher's exact test for categorical variables and Student's *t*-test or Mann–Whitney test for continuous variables.

To identify the factors independently associated with frailty in older patients hospitalised with ACS, multivariable logistic regression analysis was applied. First, univariate logistic regression was performed on all the potential associated factors for frailty on the study data (such as age, sex, comorbidities). Variables that had a p-value <0.20 on univariate analysis were selected for multivariate analysis. A backward elimination method was applied so that the final model retained only those variables significant at p <0.05.

To investigate the impact of frailty on PCI and on adverse events, first, we conducted univariate logistic regression of frailty on the outcome variables. Only outcomes with the number of cases of at least 30 were selected for logistic regression analysis. We also performed univariate logistic regression of other factors that can be associated with PCI and adverse events based on the literature such as age, sex, ACS types, Killip class.[40–42] The relationship between frailty with PCI and adverse outcomes was then examined by multivariate logistic regression, adjusted to those variables that had a p-value <0.05 on univariate analyses.

All variables were examined for interaction and multicollinearity. Results were presented as odds ratios and 95% confidence intervals.

Results

There were 324 participants, mean age 73.5 ± 8.3 years, 39.2% female. The prevalence of frailty was 48.1% (40.6% in men, 59.8% in women, p<0.001).

In these studied participants, the most common comorbidity was hypertension, followed by diabetes. Compared to the non-frail, frail patients with ACS were older and had a significantly higher prevalence of hypertension, diabetes, heart failure, stroke, and chronic kidney disease. Frail patients were more likely to present with ST-segment elevation myocardial infarction (STEMI) or non-ST segment elevation myocardial infarction (NSTEMI) rather than unstable angina. Overall, 50.3% of the participants received PCI and this rate was significantly higher in the non-frail compared to the frail (58.3% vs 41.7%, p=0.003, respectively). (Table 1)

The components of the REFS in male and female participants are presented in Table 2. Multivariate logic regression showed that age (adjusted OR 1.12, 95% CI 1.08–1.16), female gender (adjusted OR 1.88, 95% CI 1.11–3.17), history of hypertension (adjusted OR 1.88, 95% CI 1.01–3.50), heart failure (adjusted OR 4.08, 95% CI 1.82–9.15), stroke (adjusted OR 4.03, 95% CI 1.80–9.01) and chronic kidney disease (adjusted OR 17.50, 95% CI 2.06–148.52) were significantly associated with a frailty status (Table 3).

Table 4 describes the event rates during hospitalisation and at 30 days after discharge. Overall, the most common adverse event during admission was arrhythmia (37.7%), followed by acquired pneumonia (24.4%). Compared to non-frail participants, frail participants had significantly higher rates of arrhythmia, acquired pneumonia, cardiogenic shock, major bleeding, recurrent myocardial infarction, in-hospital mortality, 30-day mortality and 30-day readmission.

On multivariable logistic regression analysis, frailty was independently associated with increased risk of arrhythmia, acquired pneumonia, in-hospital mortality, 30-day mortality, and 30-day readmission (Table 5). These multivariate logistic models were adjusted with the variables that showed a significant relationship with the outcome variables on univariate analyses (Table 6). Frailty was significantly associated with a reduced likelihood of receiving PCI on univariate logistic regression (unadjusted OR 0.51, 95% CI 0.33–0.79). However, the relationship became insignificant after allowing for age and sex (adjusted OR 0.66, 95% CI 0.41–1.08).

Discussion

In this study in older patients with ACS admitted to two teaching hospitals in Vietnam, frailty was present in nearly half of the participants. Advanced age, female gender, history of hypertension, heart failure, stroke and chronic kidney disease were significantly associated with a frailty status. Although frailty did not have an independent impact on whether the participants received PCI or not, it significantly increased the risk of adverse events during hospitalisation and during 30 days after discharge.

Table 1 Participant General Characteristics

Characteristics	All (N=324)	Non-Frail (N=168)	Frail (N=156)	P
Age, years	73.48 ± 8.32	70.42 ± 7.55	76.77 ± 7.87	<0.001
Female	127 (39.2)	51 (30.4)	76 (48.7)	0.001
Smoking	168 (51.9)	96 (57.1)	72 (46.2)	0.048
BMI				
Underweight (<18.5)	47 (14.5)	20 (11.9)	27 (17.3)	0.185
Normal (18.5–22.9)	161 (49.7)	91 (54.2)	70 (44.9)	
Overweight (≥23.0)	116 (35.8)	57 (33.9)	59 (37.8)	
Comorbidities:				
Hypertension	247 (76.2)	119 (70.8)	128 (82.1)	0.018
Diabetes	98 (30.2)	39 (23.2)	59 (37.8)	0.004
Dyslipidaemia	54 (16.7)	27 (16.1)	27 (17.3)	0.765
Heart failure	44 (13.6)	12 (7.1)	32 (20.5)	<0.001
Previous stroke	43 (13.3)	11 (6.5)	32 (20.5)	<0.001
Previous PCI	41 (12.7)	22 (13.1)	19 (12.2)	0.804
Previous myocardial infarction	24 (7.4)	8 (4.8)	16 (10.3)	0.059
Chronic kidney disease	13 (4.0)	1 (0.6)	12 (7.7)	0.001
Peripheral vascular disease	8 (2.5)	2 (1.2)	6 (3.8)	0.161
Previous CABG	2 (0.6)	0 (0)	2 (1.3)	0.231
ACS type:				
NSTEMI	133 (41.0)	57 (33.9)	76 (48.7)	0.002
STEMI	120 (37.0)	62 (36.9)	58 (37.2)	
Unstable angina	71 (21.9)	49 (29.2)	22 (14.1)	
PCI	163 (50.3)	98 (58.3)	65 (41.7)	0.003
Length of stay (days)	8.7 ± 5.6	8.05 ± 4.85	9.40 ± 6.30	0.031

Notes: Continuous data are presented as mean ± standard deviation. Categorical data are shown as n (%).
Abbreviations: BMI, body mass index; PCI, percutaneous coronary intervention; CABG, Coronary artery bypass grafting; ACS, Acute coronary syndromes; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

The prevalence of frailty in this study is similar to previous studies. Many studies around the world have reported a high prevalence of frailty in older patients with ACS, from around 30% to 49%.[10,28,30,43–46] However, when compared with studies using similar frailty definition, the prevalence of frailty in our study was higher. In the study conducted by Graham et al in 183 patients with ACS aged ≥65 in Canada, the prevalence of frailty was 30.5% using the Edmonton Frailty Scale.[29] In another study in 236 patients with ACS aged ≥80 in France, the prevalence of frailty defined by the Edmonton Frailty Scale was 20.8%.[47] Our study found that the prevalence of frailty in women was higher than in men, which is consistent with the literature on sex difference in frailty.[48,49]

Overall, only half of the participants received PCI and we found that frailty did not have an independent impact on whether the patients received PCI or not. In a recent published review of frailty in older patients with ACS, older people with frailty were significantly less likely to receive guideline-indicated ACS care, including percutaneous coronary intervention (from 6.7% to 43.7% in the frail compared to 30.4% - 69.5% in the non-frail).[20] However, these studies just reported the proportions and no logistic regression analysis was performed to examine the independent impact of frailty on PCI.

In this study, frail participants consistently had higher event rates across all of the study outcomes. The impact of frailty on adverse outcomes in our study is compatible with other studies. Previous studies showed that frailty was associated with longer length of stay, in-hospital complications and short-term mortality.[20,50] Notably, acquired pneumonia was the second most common adverse event during hospitalisation in the studied participants (24.4% overall, 13.7% in the non-frail and 35.9% in the frail). Frailty is a complex process that involves multiple system impairments, including the immune system.[4] The previous

Table 2 Components of the Reported Edmonton Frail Scale in the Studied Participants

Components	All (N=324)	Male (N=197)	Female (N=127)	P
Cognition: clock drawing test				
No errors	63 (19.4)	46 (23.4)	17 (13.4)	0.011
Minor spacing errors	147 (45.4)	93 (47.2)	54 (42.5)	
Other errors	114 (35.2)	58 (29.4)	56 (44.1)	
Health status:				
Admissions to hospital in the past year				
No admission	182 (56.2)	109 (55.3)	73 (57.5)	0.643
1–2 admissions	118 (36.4)	75 (38.1)	43 (33.9)	
>2 admissions	24 (7.4)	13 (6.6)	11 (8.7)	
Description of health				
Excellent/very good/good	24 (7.4)	17 (8.6)	7 (5.5)	0.148
Fair	281 (86.7)	172 (87.3)	109 (85.8)	
Poor	19 (5.9)	8 (4.1)	11 (8.7)	
Functional independence: activities requiring help				
0–1 activities	58 (17.9)	46 (23.4)	12 (9.4)	0.001
2–4 activities	169 (52.2)	104 (52.8)	65 (51.2)	
5–8 activities	97 (29.9)	47 (23.9)	50 (39.4)	
Social support: someone able to help				
Always	219 (67.6)	125 (63.5)	94 (74.0)	0.047
Sometimes	105 (32.4)	72 (36.5)	33 (26.0)	
Never	0	0	0	
Medication:				
Using ≥5 medications	149 (46.0)	80 (40.6)	69 (54.3)	0.016
Forget to take medication sometimes	70 (21.6)	50 (25.4)	20 (15.7)	0.040
Nutrition: weight loss	18 (5.6)	10 (5.1)	8 (6.3)	0.639
Mood: sadness or depression	98 (30.2)	55 (27.9)	43 (33.9)	0.256
Incontinence	79 (24.4)	50 (25.4)	29 (22.8)	0.602
Self-reported performance				
Can do heavy work around the house without help	70 (21.6)	52 (26.4)	18 (14.2)	0.009
Can go up and down stairs without help	209 (64.5)	145 (73.6)	64 (50.4)	<0.001
Can walk 1 km without help	68 (21.0)	47 (23.9)	21 (16.5)	0.114

Note: Data are shown as n (%).

study showed that frailty was associated with loss of physiological reserve in the respiratory.[51] There has been evidence of reduced responses to influenza and pneumococcal vaccines in frail people.[52–54]

In this study, the prevalence of frailty in older patients with ACS was high. As advanced age, female gender, history of hypertension, heart failure, stroke and chronic kidney disease were significantly associated with frailty status, older patients with ACS with these factors may require more attention in terms of frailty assessment. Future studies may target these high-risk patients for intervention to prevent frailty. This study is compatible with a previous study in Vietnam in older hospitalised patients, in which frailty was significantly associated with CVD.[27] These findings support the development of a frailty-screening program for older hospitalised patients in Vietnam, particularly for patients with coronary heart disease. Frailty assessment could provide an opportunity to prevent adverse outcomes related to frailty in this population. According to a recent systematic review and meta-analysis of 21 randomised controlled trials in 5262 participants, physical activity intervention, when compared to placebo and standard care, was associated with reductions in frailty.[55] Physical intervention for older people with coronary heart disease may not only help prevent frailty but also help reduce cardiovascular risk.

To our best knowledge, this is the first study investigating the prevalence and impact of frailty on PCI and adverse

Table 3 Factors Associated with Frailty in the Study Participants

Outcomes	Univariate Analysis		Multivariate Analysis	
	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Age (per year)	1.11 (1.08–1.15)	<0.001	1.12 (1.08–1.16)	<0.001
Sex				
Male (reference)	1	0.001	1	0.019
Female	2.18 (1.38–3.43)		1.88 (1.11–3.17)	
Underweight (BMI<18.5)	1.43 (0.76–2.70)	0.265	–	
Overweight (BMI≥23.0)	1.18 (0.75–1.87)	0.465	–	
History of chronic diseases:				
Hypertension	1.88 (1.11–3.19)	0.019	1.88 (1.01–3.50)	0.047
Diabetes	2.01 (1.24–3.26)	0.005	–	
Dyslipidaemia	1.09 (0.61–1.96)	0.765	–	
Heart failure	3.36 (1.66–6.78)	0.001	4.08 (1.82–9.15)	0.001
Previous stroke	3.68 (1.79–7.60)	<0.001	4.03 (1.80–9.01)	0.001
Previous PCI/CABG	0.92 (0.48–1.78)	0.804	–	
Previous myocardial infarction	2.29 (0.95–5.50)	0.065	–	
Chronic kidney disease	13.92 (1.79–108.33)	0.012	17.50 (2.06–148.52)	0.009
Peripheral vascular disease	3.32 (0.66–16.70)	0.145	–	

Notes: All variables with p value <0.20 on univariate analyses were selected for multivariable logistic regression. Backward elimination method was applied and the final model contained only variables with p<0.05.

Abbreviations: BMI, body mass index; PCI, percutaneous coronary intervention; CABG, Coronary artery bypass grafting.

outcomes in older patients with ACS in Vietnam. This study was conducted at two large hospitals in Ho Chi Minh City, Vietnam and contained high-quality detailed clinical information. This study has several limitations. First, socioeconomics information of the participants was not collected. In Vietnam, socioeconomic circumstances may have a significant impact on whether patients with ACS may receive PCI or not. Secondly, the follow-up time was short, and the sample size was calculated for the first aim of the study to investigate the prevalence of frailty. Therefore, the sample size may not be large enough to detect a significant association between frailty and PCI, and other adverse outcomes such as major bleeding, stroke, recurrent ischemia.

Conclusion

In this study, frailty was present in nearly half of older patients with ACS and was associated with increased adverse outcomes. These findings suggest that routine frailty screening should be performed in older patients with ACS in Vietnam.

Table 4 Adverse Events During Hospitalisation and at 30 Days After Discharged

Characteristics	All (N= 324)	Non-Frail (N=168)	Frail (N=156)	P
In-hospital outcomes:				
Arrhythmia	122 (37.7)	44 (26.2)	78 (50.0)	<0.001
Acquired pneumonia	79 (24.4)	23 (13.7)	56 (35.9)	<0.001
Death	48 (14.8)	10 (6.0)	38 (24.4)	<0.001
Cardiogenic shock	32 (9.9)	13 (7.7)	19 (12.2)	0.181
Major bleeding	15 (4.6)	4 (2.4)	11 (7.1)	0.046
Stroke	6 (1.9)	1 (0.6)	5 (3.2)	0.110
Recurrent myocardial infarction	5 (1.5)	0 (0)	5 (3.2)	0.025
30-day outcomes:				
30-day mortality	68 (21.0)	15 (8.9)	53 (34.0)	<0.001
30-day readmission	74 (27.9)	23 (17.2)	51 (38.9)	<0.001

Notes: Continuous data are presented as mean ± standard deviation. Categorical data are shown as n (%).

Table 5 The Impact of Frailty on PCI Treatment and Adverse Outcomes

Outcomes	Univariate Analysis		Multivariate Analysis	
	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Receiving PCI	0.51 (0.33–0.79)	0.003	0.66 (0.41–1.08)[a]	0.095
Cardiogenic shock during hospitalisation	1.65 (0.79–3.47)	0.184	1.13 (0.47–2.74)[b]	0.788
Arrhythmia during hospitalisation	2.82 (1.77–4.49)	<0.001	2.24 (1.32–3.80)[c]	0.003
Pneumonia during hospitalisation	3.53 (2.04–6.11)	<0.001	2.27 (1.24–4.17)[d]	0.008
Death during hospitalisation	5.09 (2.44–10.63)	<0.001	3.02 (1.35–6.75)[d]	0.007
30-day mortality	5.25 (2.81–9.81)	<0.001	3.28 (1.59–6.76)[c]	0.001
30-day readmission	3.08 (1.74–5.44)	<0.001	2.53 (1.38–4.63)[e]	0.003

Notes: [a]Adjusted to age, sex. [b]Adjusted to Killip class. [c]Adjusted to age, ACS type, Killip class, PCI. [d]Adjusted to ACS type, Killip class, PCI. [e]Adjusted to age.
Abbreviations: PCI, percutaneous coronary intervention; ACS, acute coronary syndrome.

Table 6 Univariate Regression of Potential Factors Associated with PCI and Adverse Outcomes

	Unadjusted OR (95% CI) for PCI	Unadjusted OR (95% CI) for Cardiogenic Shock	Unadjusted OR (95% CI) for Arrhythmia	Unadjusted OR (95% CI) for Pneumonia	Unadjusted OR (95% CI) for in-Hospital Mortality	Unadjusted OR (95% CI) for 30-Day Mortality	Unadjusted OR (95% CI) for 30-Day Readmission
Age (years)	0.96 (0.93–0.99), p=0.003	0.97 (0.92–1.01), p=0.152	1.03 (1.00–1.06), p=0.036	1.03 (1.00–1.06), p=0.057	1.02 (0.99–1.06), p=0.244	1.05 (1.01–1.08), p=0.007	1.05 (1.02–1.09), p=0.002
Sex:							
Female	Reference	1	1	1	1	1	1
Male	1.86 (1.19–2.93), p=0.007	1.47 (0.67–3.22), p=0.334	1.17 (0.74–1.86), p=0.508	0.71 (0.42–1.18), p=0.183	0.73 (0.39–1.35), p=0.309	0.72 (0.42–1.23), p=0.226	1.20 (0.69–2.09), p=0.516
ACS type:							
Unstable angina	Reference	N/A (event rates were too small for this analysis)	1	1	1	1	1
NSTEMI	1.06 (0.60–1.90), p=0.833		3.73 (1.80–7.74), p<0.001	35.80 (4.81–266.17), p<0.001	17.01 (2.26–128.21), p=0.006	25.98 (3.48–194.02), p=0.001	1.50 (0.70–3.22), p=0.292
STEMI	1.65 (0.91–2.98), p=0.097		4.94 (2.36–10.30), p<0.001	26.55 (3.54–199.00), p=0.001	14.85 (1.95–112.98), p=0.009	24.38 (3.25–183.03), p=0.002	1.59 (0.74–3.44), p=0.234
Killip class	0.80 (0.62–1.02), p=0.076	4.01 (2.75–5.85), p<0.001	1.78 (1.37–2.30), p<0.001	2.14 (1.64–2.80), p<0.001	2.08 (1.56–2.77), p<0.001	1.87 (1.44–2.45), p<0.001	0.80 (0.57–1.11), p=0.798
PCI	N/A	0.48 (0.23–1.04), p=0.062	0.61 (0.39–0.96), p=0.032	0.33 (0.19–0.57), p<0.001	0.13 (0.06–0.30), p<0.001	0.21 (0.11–0.39), p<0.001	0.93 (0.54–1.59), p=0.779

Notes: Killip class was treated as a continuous variable (values from 1 to 4).
Abbreviations: ACS, acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction.

Ethical Approval

The study protocol was approved by the ethics committees of the University of Medicine and Pharmacy in Ho Chi Minh City, Cho Ray Hospital and Thong Nhat Hospital, Ho Chi Minh City, Vietnam. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all participants for being included in the study. Participants could withdraw anytime without it affecting their current treatment. Their information was kept confidential and used only for research purposes.

Author Contributions

Conceptualization: T.V.N. and T.N.N. Methodology: T.V.N., D.L., K.D.T., K.X.B. and T.N.N. Software: T.V.N., D.L., K.D.T., K.X.B. and T.N.N. Validation: T.V.N. and T.N.N. Formal analysis, T.V.N., D.L. and T.N.N. Investigation: T.V.N., D.L. Resources: T.V.N. Data curation: T.V.N., D.L. Original draft preparation: T.V.N. and T.N.N. Supervision, T.V.N. Project administration, T.V.N., D.L. All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

All authors report no conflicts of interests in this work.

References

1. Clark H. NCDs: a challenge to sustainable human development. *Lancet (London, England)*. 2013;381(9866):510–511. doi:10.1016/S0140-6736(13)60058-6
2. World Health Organisation. The top 10 causes of death. Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death. Accessed September 10, 2019.
3. Avezum A, Makdisse M, Spencer F, et al. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J*. 2005;149(1):67–73. doi:10.1016/j.ahj.2004.06.003
4. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. 2013;381(9868):752–762. doi:10.1016/S0140-6736(12)62167-9
5. Raphael D, Cava M, Brown I, et al. Frailty: a public health perspective. *Can J Public Health*. 1995;86(4):224–227.
6. Chaves PHM, Semba RD, Leng SX, et al. Impact of anemia and cardiovascular disease on frailty status of community-dwelling older women: the women's health and aging studies I and II. *J Gerontol a Biol Sci Med Sci*. 2005;60(6):729–735. doi:10.1093/gerona/60.6.729
7. Kanapuru B, Ershler WB. Inflammation, coagulation, and the pathway to frailty. *Am J Med*. 2009;122(7):605–613. doi:10.1016/j.amjmed.2009.01.030
8. Von Haehling S, Anker SD, Doehner W, Morley JE, Vellas B. Frailty and heart disease. *Int J Cardiol*. 2013;168(3):1745–1747. doi:10.1016/j.ijcard.2013.07.068
9. Polidoro A, Stefanelli F, Ciacciarelli M, Pacelli A, Di Sanzo D, Alessandri C. Frailty in patients affected by atrial fibrillation. *Arch Gerontol Geriatr*. 2013;57(3):325–327. doi:10.1016/j.archger.2013.04.014
10. Ekerstad N, Swahn E, Janzon M, et al. Frailty is independently associated with short-term outcomes for elderly patients with non-ST-segment elevation myocardial infarction. *Circulation*. 2011;124(22):2397–2404. doi:10.1161/CIRCULATIONAHA.111.025452
11. Bo M, Puma FL, Martini MB, et al. Health status, geriatric syndromes and prescription of oral anticoagulant therapy in elderly medical in-patients with atrial fibrillation: a prospective observational study. *Int J Cardiol*. 2015;187(1):123–125. doi:10.1016/j.ijcard.2015.03.334
12. Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation*. 2010;121(8):973–978. doi:10.1161/CIRCULATIONAHA.108.841437
13. 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(5):496–502. doi:10.1161/CIRCOUTCOMES.111.961375
14. Ambler GK, Brooks DE, Al Zuhir N, et al. Effect of frailty on short- and mid-term outcomes in vascular surgical patients. *Br J Surg*. 2015;102(6):638–645. doi:10.1002/bjs.2015.102.issue-6
15. Singh I, Gallacher J, Davis K, Johansen A, Eeles E, Hubbard RE. Predictors of adverse outcomes on an acute geriatric rehabilitation ward. *Age Ageing*. 2012;41(2):242–246. doi:10.1093/ageing/afr179
16. Cacciatore F, Della-morte D, Basile C, et al. Long-term mortality in frail elderly subjects with osteoarthritis. *Rheumatology (UK)*. 2014;53(2):293–299. doi:10.1093/rheumatology/ket348
17. Le Maguet P, Roquilly A, Lasocki S, et al. Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study. *Intensive Care Med*. 2014;40(5):674–682. doi:10.1007/s00134-014-3253-4
18. Conroy S, Dowsing T. The ability of frailty to predict outcomes in older people attending an acute medical unit. *Acute Med*. 2013;12(2):74–76.
19. Cacciatore F, Abete P, Mazzella F, et al. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *Eur J Clin Invest*. 2005;35(12):723–730. doi:10.1111/eci.2005.35.issue-12
20. Bebb O, Smith FG, Clegg A, Hall M, Gale CP. Frailty and acute coronary syndrome: a structured literature review. *Eur Heart J Acute Cardiovasc Care*. 2018;7(2):166–175. doi:10.1177/2048872617700873
21. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. *Int J Cardiol*. 2013;168(2):934–945. doi:10.1016/j.ijcard.2012.10.046
22. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol*. 2009;8(4):355–369. doi:10.1016/S1474-4422(09)70025-0
23. Nhung NT, Long TK, Linh BN, Vos T, Huong NT, Anh ND. Estimation of Vietnam national burden of disease 2008. *Asia Pac J Public Health*. 2014;26(5):527–535. doi:10.1177/1010539513510556
24. Hoang VM, Dao LH, Wall S, Nguyen TK, Byass P. Cardiovascular disease mortality and its association with socioeconomic status: findings from a population-based cohort study in rural Vietnam, 1999–2003. *Prev Chronic Dis*. 2006;3(3):A89.
25. Islam SM, Purnat TD, Phuong NT, Mwingira U, Schacht K, Froschl G. Non-communicable diseases (NCDs) in developing countries: a symposium report. *Global Health*. 2014;10:81. doi:10.1186/s12992-014-0081-9

26. Ngo AD, Rao C, Hoa NP, Adair T, Chuc NT. Mortality patterns in Vietnam, 2006: findings from a national verbal autopsy survey. *BMC Res Notes*. 2010;3:78. doi:10.1186/1756-0500-3-78
27. Vu HTT, Nguyen TX, Nguyen TN, et al. Prevalence of frailty and its associated factors in older hospitalised patients in Vietnam. *BMC Geriatr*. 2017;17(1):216. doi:10.1186/s12877-017-0609-y
28. Kang L, Zhang SY, Zhu WL, et al. Is frailty associated with short-term outcomes for elderly patients with acute coronary syndrome? *J Geriatr Cardiol*. 2015;12(6):662–667. doi:10.11909/j.issn.1671-5411.2015.06.010
29. Graham MM, Galbraith PD, O'Neill D, Rolfson DB, Dando C, Norris CM. Frailty and outcome in elderly patients with acute coronary syndrome. *Can J Cardiol*. 2013;29(12):1610–1615. doi:10.1016/j.cjca.2013.08.016
30. Alonso Salinas GL, Sanmartin Fernandez M, Pascual Izco M, et al. Frailty is a short-term prognostic marker in acute coronary syndrome of elderly patients. *Eur Heart J Acute Cardiovasc Care*. 2016;5(5):434–440. doi:10.1177/2048872616644909
31. Diez-Villanueva P, Ariza-Sole A, Vidan MT, et al. Recommendations of the geriatric cardiology section of the spanish society of cardiology for the assessment of frailty in elderly patients with heart disease. *Rev Esp Cardiol (Engl Ed)*. 2019;72(1):63–71. doi:10.1016/j.rec.2018.06.035
32. Dent E, Lien C, Lim WS, et al. The Asia-Pacific clinical practice guidelines for the management of frailty. *J Am Med Dir Assoc*. 2017;18(7):564–575. doi:10.1016/j.jamda.2017.04.018
33. Hilmer SN, Perera V, Mitchell S, et al. The assessment of frailty in older people in acute care. *Australas J Ageing*. 2009;28(4):182–188. doi:10.1111/aja.2009.28.issue-4
34. Perera V, Bajorek BV, Matthews S, Hilmer SN. The impact of frailty on the utilisation of antithrombotic therapy in older patients with atrial fibrillation. *Age Ageing*. 2009;38(2):156–162. doi:10.1093/ageing/afn293
35. Rose M, Pan H, Levinson MR, Staples M. Can frailty predict complicated care needs and length of stay? *Intern Med J*. 2014;44(8):800–805. doi:10.1111/imj.2014.44.issue-8
36. Osborne C, Charles A, Hare A, Shipway D. Frailty predicts length of hospital stay in urology patients. *Eur Urol*. 2015;14(2):e658. doi:10.1016/S1569-9056(15)60651-0
37. Mitchell SJ, Hilmer SN, Murnion BP, Matthews S. Hepatotoxicity of therapeutic short-course paracetamol in hospital inpatients: impact of ageing and frailty. *J Clin Pharm Ther*. 2011;36(3):327–335. doi:10.1111/j.1365-2710.2010.01193.x
38. Bennett A, Gnjidic D, Gillett M, et al. Prevalence and impact of fall-risk-increasing drugs, polypharmacy, and drug-drug interactions in robust versus frail hospitalised falls patients: a prospective cohort study. *Drugs Aging*. 2014;31(3):225–232. doi:10.1007/s40266-013-0151-3
39. Nguyen AT, Nguyen TX, Nguyen TN, et al. The impact of frailty on prolonged hospitalization and mortality in elderly inpatients in Vietnam: a comparison between the frailty phenotype and the reported edmonton frail scale. *Clin Interv Aging*. 2019;14:381–388. doi:10.2147/CIA.S189122
40. Goldberg RJ, McCormick D, Gurwitz JH, Yarzebski J, Lessard D, Gore JM. Age-related trends in short- and long-term survival after acute myocardial infarction: a 20-year population-based perspective (1975–1995). *Am J Cardiol*. 1998;82(11):1311–1317. doi:10.1016/S0002-9149(98)00633-X
41. Vaccarino V, Parsons L, Peterson ED, Rogers WJ, Kiefe CI, Canto J. Sex differences in mortality after acute myocardial infarction: changes from 1994 to 2006. *Arch Intern Med*. 2009;169(19):1767–1774. doi:10.1001/archinternmed.2009.332
42. Khot UN, Jia G, Moliterno DJ, et al. Prognostic importance of physical examination for heart failure in non-ST-elevation acute coronary syndromes: the enduring value of Killip classification. *JAMA*. 2003;290(16):2174–2181. doi:10.1001/jama.290.16.2174
43. Sanchis J, Bonanad C, Ruiz V, et al. Frailty and other geriatric conditions for risk stratification of older patients with acute coronary syndrome. *Am Heart J*. 2014;168(5):784–791. doi:10.1016/j.ahj.2014.07.022
44. Alonso Salinas GL, Sanmartin M, Pascual Izco M, et al. The role of frailty in acute coronary syndromes in the elderly. *Gerontology*. 2018;64(5):422–429. doi:10.1159/000488390
45. Alonso Salinas GL, Sanmartin M, Pascual Izco M, et al. Frailty is an independent prognostic marker in elderly patients with myocardial infarction. *Clin Cardiol*. 2017;40(10):925–931. doi:10.1002/clc.2017.40.issue-10
46. Llao I, Ariza-Sole A, Sanchis J, et al. Invasive strategy and frailty in very elderly patients with acute coronary syndromes. *EuroIntervention*. 2018;14(3):e336–e42. doi:10.4244/EIJ-D-18-00099
47. Blanco S, Ferrieres J, Bongard V, et al. Prognosis impact of frailty assessed by the edmonton frail scale in the setting of acute coronary syndrome in the elderly. *Can J Cardiol*. 2017;33(7):933–939. doi:10.1016/j.cjca.2017.03.026
48. Gordon EH, Peel NM, Samanta M, Theou O, Howlett SE, Hubbard RE. Sex differences in frailty: a systematic review and meta-analysis. *Exp Gerontol*. 2017;89:30–40. doi:10.1016/j.exger.2016.12.021
49. Hubbard RE. Sex Differences in Frailty. *Interdiscip Top Gerontol Geriatr*. 2015;41:41–53.
50. Dou Q, Wang W, Wang H, et al. Prognostic value of frailty in elderly patients with acute coronary syndrome: a systematic review and meta-analysis. *BMC Geriatr*. 2019;19(1):222. doi:10.1186/s12877-019-1242-8
51. Vaz Fragoso CA, Enright PL, McAvay G, Van Ness PH, Gill TM. Frailty and respiratory impairment in older persons. *Am J Med*. 2012;125(1):79–86. doi:10.1016/j.amjmed.2011.06.024
52. Yao X, Hamilton RG, Weng NP, et al. Frailty is associated with impairment of vaccine-induced antibody response and increase in post-vaccination influenza infection in community-dwelling older adults. *Vaccine*. 2011;29(31):5015–5021. doi:10.1016/j.vaccine.2011.04.077
53. Ridda I, Macintyre CR, Lindley R, et al. Immunological responses to pneumococcal vaccine in frail older people. *Vaccine*. 2009;27(10):1628–1636. doi:10.1016/j.vaccine.2008.11.098
54. Jefferson T, Rivetti D, Rivetti A, Rudin M, Di Pietrantonj C, Demicheli V. Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet (London, England)*. 2005;366(9492):1165–1174. doi:10.1016/S0140-6736(05)67339-4
55. Negm AM, Kennedy CC, Thabane L, et al. Management of frailty: a systematic review and network meta-analysis of randomized controlled trials. *J Am Med Dir Assoc*. 2019;20(10):1190–1198. doi:10.1016/j.jamda.2019.08.009