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Frailty as an independent predictor for midterm adverse outcomes in the elderly undergoing primary percutaneous coronary intervention: A longitudinal cohort study

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Abstract

Background: Frailty is associated with poor health outcomes in elderly population. However, its effect on midterm outcomes in elderly patients undergoing primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) remains unknown.

Aims: This study aimed to evaluate the association between frailty, as classified by the Clinical Frailty Scale (CFS), and midterm adverse outcomes in elderly STEMI patients after primary PCI.

Methods: In this prospective, observational, multicenter cohort study, frailty status of 426 STEMI patients aged ≥60 years undergoing primary PCI was determined using the nine-point CFS 2 weeks before the occurrence of STEMI. Patients scoring at least four points on the CFS were considered frail. The primary outcome was a composite of cardiovascular death or readmission. Secondary outcomes included cardiovascular death, cardiovascular readmission, heart failure-related death or readmission, and myocardial reinfarction. Follow-up data were collected through medical record reviews and/or telephone interviews.

Results: Of 426 elderly patients, 116 were frail. The median follow-up period was 15 months (interquartile range 5–19 months). Primary outcome events occurred in 87 (75.0%) frail and 75 (24.2%) nonfrail patients. The adjusted hazard ratio was 3.278 after model selection using the Bayesian Model Averaging approach (95% confidence interval 2.372–4.531). Multivariate Cox proportional hazard survival analysis showed that frailty was significantly associated with a higher prevalence of all secondary outcome events after adjusting for TIMI, PAMI, and CADILLAC risk scores.

Conclusions: Frailty, as defined by the CFS, was independently associated with midterm adverse outcomes in elderly patients undergoing primary PCI for STEMI.

KEYWORDS
adverse outcomes, elderly, frailty, primary PCI, STEMI

1 | INTRODUCTION

Primary percutaneous coronary intervention (PCI) is widely used as the core management for ST-elevation myocardial infarction (STEMI). However, adverse outcomes after primary PCI remain high and have not significantly changed over the decades, especially in elderly patients. In 2023, a registry in Germany evaluating mortality trends over 20 years after performing primary PCI in 25,792 patients with STEMI showed that the overall in-hospital mortality rate decreased significantly from 12.8% in 2000 to 9.2% in 2019. However, in-hospital mortality remained highest and unchanged in female patients aged ≥75 years (25.1% in 2000 vs. 23.6% in 2019).[1] In addition, the in-hospital mortality rate of patients aged <75 years decreased significantly during the study period and remained significantly lower than that of elderly patients. Reports from Asia have also recorded remarkably higher mortality rates following primary PCI in the elderly than in young individuals. In 2015, a registry in Singapore on 1268 patients diagnosed with STEMI and undergoing primary PCI recorded a significantly higher in-hospital mortality rate in elderly patients (≥70 years) compared with younger patients (11.9% vs. 3.6%, respectively).[2] Moreover, in 2015, a cohort study in China included 116 patients ≥60 years and 68 patients <60 years to compare in-hospital mortality rates. Results showed that in-hospital mortality was significantly higher in the elderly (8.62%) than in the younger group (1.47%).[3] Data on mortality and adverse outcomes after primary PCI in Vietnam are scarce.

Recommendations for the management of cardiovascular diseases have emphasized that biological age (i.e., life expectancy based on biological status but not chronological age) is the determining factor in treatment decisions.[4,5] Frailty is a multidimensional syndrome characterized by increased vulnerability and decreased physiological reserve and can be used as a marker of biological age.[6,7] Frailty has been verified as an independent predictor of adverse outcomes in the elderly, including hospitalization, disability, and death.[8,9]

Frailty measurement tools have been advocated for risk stratification of adverse outcomes in elderly patients with myocardial infarction (MI) and non-ST elevation MI (NSTEMI).[10–12] However, data on the prognostic value of frailty and its ability to predict adverse outcomes in elderly patients with STEMI after primary PCI are scarce, particularly in developing countries, such as Vietnam. Therefore, further research is needed in this area.

This study aimed to evaluate the association between frailty, classified using the Clinical Frailty Scale (CFS), and midterm adverse outcomes in elderly patients with STEMI after primary PCI. We hypothesized that frailty, defined as CFS ≥ 4, is independently associated with midterm adverse outcomes.

2 | METHODS

2.1 | Study design and population

This study was a longitudinal cohort study. We prospectively collected data from the cardiovascular centers of two national hospitals in southern Vietnam, including patients hospitalized for suspected STEMI, between February 2017 and April 2018. Basic information included demographics, medical history, management during the hospital stay, treatment at discharge, and final diagnosis. Information on adverse outcomes was obtained from the medical records of the two cardiovascular centers and through direct telephone interviews with the patients or their relatives. Each patient was followed up every 3 months until the outcomes occurred or the study ended.

STEMI was defined according to the 2023 European Society of Cardiology (ESC) guideline for the management of acute coronary syndromes as follows[5]: (a) clinical presentation of myocardial ischemia (including chest pain, epigastric pain, and shortness of breath); (b) electrocardiogram showing new ST elevation at the J-point in two contiguous leads, with a cutoff point of ≥2 mm in men and ≥1.5 mm in women in leads V2–V3 or ≥1 mm in the other leads; and (c) at least one high-sensitivity cardiac troponin level above the 99th percentile of the normal reference during the first 24 h after admission. Patients were excluded if they met the following criteria: (a) age < 60 years; (b) suspected STEMI but did not undergo coronary angiography; or (c) culprit lesions but did not undergo primary PCI.

All primary PCI procedures and medications were administered using standard techniques and in accordance with the current practice guidelines.

This study was approved by the local ethics committee of the University of Medicine and Pharmacy at Ho Chi Minh City.

2.2 | Clinical outcome measures

The primary outcome was a composite event of cardiovascular death (MI, heart failure, stroke, ventricular tachycardia/fibrillation, or sudden death) or cardiovascular readmission (myocardial reinfarction, heart failure, stroke, arrhythmia, or target lesion revascularization). Secondary outcomes included components of the primary outcome, such as cardiovascular death, cardiovascular readmission, death or readmission due to heart failure, and myocardial reinfarction.

2.3 | Risk factors

2.3.1 | Frailty assessment

The CFS version 2.0 is a nine-level scale based on the cumulative deficit model of frailty. It serves as a simple clinical measure of biological age, taking into account factors including illness severity, comorbidities, disability, and cognitive impairment.[13] The CFS has been suggested as the most valuable tool for assessing frailty in patients with acute coronary syndrome scenarios.[14] It demonstrated strong predictive capabilities and was straightforward to implement in clinical settings.[10,15]

The CFS was accessed through direct patient interview or communication with patients' relatives. The goal was to assess frailty levels 2 weeks before admission to mitigate any deterioration resulting from hospitalization. Unlike other frailty scales, which require specialized testing tools in certain domains, the CFS is a fully questionnaire-based scale, acquired through direct patients' or their relatives' recalls of their basic and instrumental activities of daily living.[13] Therefore, a retrospective interview of the patient's CFS 2 weeks before the onset of STEMI was reasonably feasible, as their health status was considered stable at that time. Trained collaborators, who were geriatrics resident physicians, conducted the CFS assessments and documented the data in medical records. This information was collected independently and blinded to the principal investigators, who were responsible for collecting clinical outcomes' data.

The CFS questionnaire, when collected directly from patients, was deemed the most reliable. In cases where the patient was unable to communicate at the time of the interview (e.g., patients in cardiogenic shock or those who were intubated), their relatives were interviewed instead. If the patient regained the ability to communicate during their hospital stay, all information previously obtained from their relatives was replaced by new information provided directly by the patient.

According to the latest update of the CFS version 2.0, patients were classified as frailty when they had a CFS score of at least FOUR points.[13]

2.3.2 | Conventional risk models and their parameters

Baseline patient characteristics, including age, sex, systolic blood pressure, and heart rate, were recorded at the time of admission. In this study, three well-known mortality risk models were used to coordinate with frailty, including TIMI, PAMI, and CADILLAC risk scores along with their parameters.[16–18] Hypertension was characterized by either current or prior treatment with antihypertensive medications. Diabetes mellitus was defined as current or previous use of antidiabetic medication or a hemoglobin A1c level ≥6.5%. Dyslipidemia was identified by current or past use of antidyslipidemic medications. Patient history, including smoking, previous MI, heart failure, stroke, peripheral artery disease, PCI, and coronary bypass grafting, was documented through interviews with patients and/or their relatives upon admission. The Killip classification was determined based on physical examination findings. The time from symptom onset of STEMI to admission and wiring through the culprit lesions was recorded. Electrocardiography (ECG) is used to diagnose anterior STEMI and left bundle branch block (LBBB). Laboratory findings, including baseline hemoglobin and creatinine levels, were recorded on admission. Renal insufficiency was defined as a baseline estimated glomerular filtration rate <60 mL/min/1.73 m.[2,18] Anemia was defined as a hemoglobin level <130 g/L in men and <120 g/dL in women.[18] Information on the coronary angiography and PCI procedures, including vascular access sites, coronary lesion characteristics, and TIMI blood flow of the culprit lesions before and after PCI, was recorded based on the attending physician's discretion.

2.4 | Statistics

Continuous variables were summarized as means (with standard deviations) or as medians with interquartile ranges (interquartile range: 25%–75%). Categorical variables were presented as counts (percentages). Chi-square test or Fisher's exact test was used for comparing categorical data, while Student's t-test or the Mann–Whitney U test was employed for continuous data, depending on the normality of the variable. Event-free survival comparisons (Kaplan-Meier curves) were conducted using the log-rank test. Additionally, Cox proportional hazard survival analysis was performed with selected covariates to identify independent predictors of primary and secondary outcomes. Outcomes are presented as hazard ratios (HRs) and 95% confidence intervals (CIs). Frailty was the only explanatory variable in the first model. In the second, third, and fourth models, three widely used risk factors for STEMI prognosis were added: TIMI, PAMI, and CADILLAC risk scores, respectively. The parameters of the TIMI risk score include age 65–74/ ≥ 75, systolic blood pressure < 100 mmHg, heart rate > 100 bpm, Killip class ≥ II, anterior STEMI or LBBB, history of diabetes, hypertension or angina, weight <67 kg, and symptom onset to wiring >4 h.[16] Parameters of the PAMI risk score include 65–75/ > 75, heart rate > 100 bpm, Killip class ≥ II, anterior STEMI or LBBB, and a history of diabetes.[17] Parameters of CADILLAC risk score consist of age >65, LVEF ≤ 40%, Killip class ≥ II, renal insufficiency, post-PCI TIMI blood flow < 3, anemia, and three-vessel disease.[18] Subgroup analyses were performed for age, sex, history of diabetes, LVEF, Killip class, and three-vessel disease. All p-values were two-tailed, and results with $p < 0.05$ were considered statistically significant for all analyses. Statistical analyses were performed using R software.

Bayesian Model Averaging (BMA) was employed to identify the most concise models among the variables, including frailty, and all parameters from the three conventional risk models.[19] This approach has demonstrated superior performance compared to stepwise regression.[20] In the BMA approach, regression analysis was conducted for 2^M competing models (where M represents the number of potential risk factors). The BMA-averaged point estimates of the regression coefficients across all possible models yielded a posterior probability for each model.

Some variables had a 1%–2% rate of missing, including LVEF in eight cases (1.9%), creatinine in six cases (1.4%), and history of smoking in five cases (1.2%), while other variables had less than 1% missing data. Missing values were assumed to be completely and randomly missing. A multiple imputation method was performed using the 'mice' package in R

software.[21] Multiple imputation comprises two primary stages: 1) Generating surrogate values for missing data: During this stage, surrogate values are generated to replace missing data. This process is repeated multiple times, resulting in several datasets, each containing different imputed values. 2) Once the imputed datasets are obtained, any analysis can be performed within each data set as if there were no missing data. The results from these analyses are then combined to provide a more robust and complete understanding of the data.

3 | RESULTS

The study population comprised of 426 consecutive elderly patients with STEMI who underwent primary PCI. Of these, 310 (72.8%) were classified as nonfrailty (CFS < 4) and 116 (27.2%) were classified as frailty (CFS ≥ 4). The median follow-up period was 15 months (interquartile range, 5–19). The total time at risk was 5595 person-months, of which 4601 person-months were in the nonfrail group and 994 were in the frail group. No patient was lost to follow-up (Figure 1).

The baseline clinical, laboratory, medical treatment, and procedural characteristics of the CFS are shown in Table 1. Frailty patients were more often female and older than nonfrail patients, with a mean age of 74.6 in frailty patients and 69.4 in nonfrailty patients ($p < 0.001$). Frail patients have more comorbidities, including higher rates of diabetes, hypertension, and chronic kidney disease. Frail patients presented more frequently with anterior STEMI or LBBB ($p = 0.013$) and lower LVEF ($p < 0.001$). Baseline creatinine and hemoglobin levels were higher and lower, respectively, in frail patients ($p = 0.035$ and $p = 0.031$, respectively). Regarding angiographic features, frail patients appeared to have more severe coronary lesions than nonfrail patients ($p = 0.039$). There were no differences in the time from symptom onset to wiring, vascular access sites, post-PCI TIMI blood flow, or medications at discharge between the two groups of patients.

The primary and secondary outcomes are presented in Table 2. During the follow-up period, 162 (38.0%) patients experienced the primary composite outcome at a rate of 2.9 cases/100 person-months, of which 87 (75.0%) were in the frailty arm at a rate of 8.8 cases/100 person-months, and 75 (24.2%) were in the non-frailty arm at a rate of 1.6 cases/100 person-months. Frailty was associated with higher rates of the primary composite outcome, cardiovascular readmission, cardiovascular death, heart failure death or readmission, and myocardial reinfarction (all $p < 0.001$). Figures 2 and 3 show the Kaplan–Meier analyses of primary and secondary outcomes, stratified by frailty status, with all log-rank tests showing $p < 0.001$.

The five most likely models selected by the BMA included frailty, heart failure, and three-vessel disease as their key parameters, in which model 1 had the highest posterior probability (Supporting Information S1: Table S1). In model 1, frailty significantly increased the risk of the primary outcome, independent of heart failure and three-vessel disease (Table 3). In the remaining models, frailty maintained its prognostic value with the hazard ratio ranging from 3.2 to 3.3 (all p-Value < 0.001).

4 | DISCUSSION

Scientific statements from the ESC have emphasized the importance of frailty and comorbidity assessments in elderly patients with acute coronary syndromes.[4,5] Frailty assessment has no gold standard, and up to 20

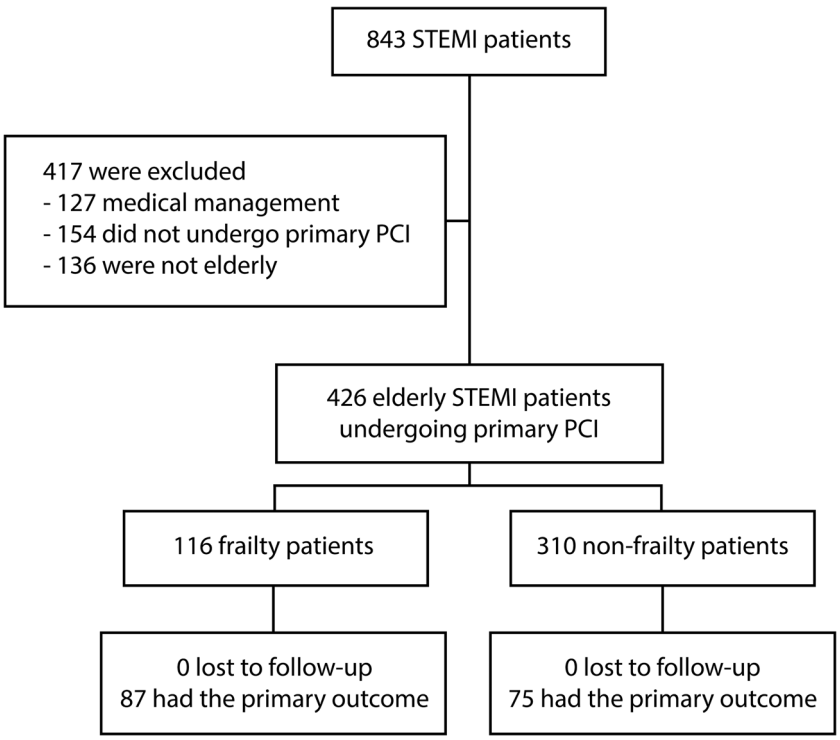

FIGURE 1 Enrollment and follow-up. PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

TABLE 1 Baseline patient characteristics.

		All *N* = 426	Nonfrailty *N* = 310	Frailty *N* = 116	*p*-Value
Age		70.8 (8.1)	69.4 (7.60)	74.6 (8.09)	<0.001
Age ≥75		134 (31.5%)	74 (23.9%)	60 (51.7%)	<0.001
Gender	Male	274 (64.3%)	220 (71.0%)	54 (46.6%)	<0.001
	Female	152 (35.7%)	90 (29.0%)	62 (53.4%)	
Medical history					
Smoking		158 (37.1%)	129 (41.6%)	29 (25.0%)	0.002
Hypertension		312 (73.2%)	219 (70.6%)	93 (80.2%)	0.064
Diabetes		88 (20.7%)	53 (17.1%)	35 (30.2%)	0.005
Dyslipidemia		42 (9.9%)	30 (9.68%)	12 (10.3%)	0.982
Chronic kidney disease		16 (3.8%)	6 (1.94%)	10 (8.62%)	0.003
Stroke		23 (5.4%)	15 (4.84%)	8 (6.90%)	0.551
Peripheral artery disease		1 (0.2%)	1 (0.32%)	0 (0.00%)	1
Myocardial infarction		21 (4.9%)	14 (4.52%)	7 (6.03%)	0.694
Heart failure		5 (1.2%)	4 (1.29%)	1 (0.86%)	1
Coronary angioplasty		16 (3.8%)	13 (4.19%)	3 (2.59%)	0.574
Coronary bypass grafting		1 (0.2%)	1 (0.32%)	0 (0.00%)	1
Presentations at admission					
Heart rate (bpm)		81.5 (21.9)	81.4 (20.8)	84.9 (23.0)	0.389
Heart rate > 100 bpm		48 (11.3%)	31 (10.0%)	17 (14.7%)	0.238
Systolic BP (mmHg)		115.0 (30.4)	115.6 (30.0)	113.3 (31.6)	0.348
Systolic BP < 100 mmHg		94 (22.1%)	65 (21.0%)	29 (25.0%)	0.446
Killip class	I	332 (77.9%)	249 (80.3%)	83 (71.6%)	0.132
	II	42 (9.9%)	29 (9.35%)	13 (11.2%)	
	III	20 (4.7%)	14 (4.52%)	6 (5.17%)	
	IV	32 (7.5%)	18 (5.81%)	14 (12.1%)	
Killip class > I		94 (22.1%)	61 (19.7%)	33 (28.4%)	0.07
Symptom onset to admission (hours)		8.0 (5.0-11.0)	8.0 (5.0-11.0)	9.0 (6.0-15.5)	0.307
Clinical Frailty Scale (points)		2.0 (2.0-5.0)	2.0 (2.0-3.0)	5.0 (5.0-6.0)	<0.001
Anterior STEMI/LBBB		206 (48.4%)	138 (44.5%)	68 (58.6%)	0.013
LVEF (%)		44.9 (11.8)	46.4 (12.0)	40.9 (10.4)	<0.001
LVEF ≤ 40%		222 (52.1%)	138 (44.5%)	84 (72.4%)	<0.001
Creatinine (mg/dL)		1.2 (0.4)	1.13 (0.28)	1.24 (0.52)	0.035
Renal insufficiency		283 (66.4%)	208 (67.1%)	75 (64.7%)	0.719
Hemoglobin (g/L)		131.9 (19.9)	133.6 (19.0)	127.3 (21.6)	0.031
Anemia		134 (31.5%)	93 (30.0%)	41 (35.3%)	0.347
Angiographic features					
Symptom onset to wiring (hours)		12.5 (8.5–19.0)	12.2 (8.5–18.0)	13.5 (9.0–24.3)	0.427
Symptom onset to wiring > 4 h		413 (96.9%)	301 (97.1%)	112 (96.6%)	0.757
Access sites	Radial artery	342 (80.3%)	249 (80.3%)	93 (80.2%)	1
	Femoral artery	84 (19.7%)	61 (19.7%)	23 (19.8%)	

(Continues)

TABLE 1 (Continued)

		All *N* = 426	Nonfrailty *N* = 310	Frailty *N* = 116	*p*-Value
TIMI flow, pre-PCI	0	222 (52.1%)	164 (52.9%)	58 (50.0%)	0.386
	1	51 (12.0%)	33 (10.6%)	18 (15.5%)	
	2	153 (35.9%)	113 (36.5%)	40 (34.5%)	
TIMI flow, post-PCI	2	23 (5.4%)	13 (4.19%)	10 (8.62%)	0.119
	3	403 (94.6%)	297 (95.8%)	106 (91.4%)	
TIMI flow, post-PCI < 3		23 (5.4%)	13 (4.19%)	10 (8.62%)	0.119
Three vessel disease		121 (28.4%)	79 (25.5%)	42 (36.2%)	0.039
Medications at discharge					
Aspirin		419 (98.4%)	306 (98.7%)	113 (97.4%)	0.396
Clopidogrel		327 (76.8%)	233 (75.2%)	94 (81.0%)	0.251
Ticagrelor		95 (22.3%)	73 (23.5%)	22 (19.0%)	0.378
Statin		410 (96.2%)	299 (96.5%)	111 (95.7%)	0.775
Beta blockers		134 (31.5%)	103 (33.2%)	31 (26.7%)	0.242
ACE inhibitors		298 (70.0%)	223 (71.9%)	75 (64.7%)	0.180
ARBs		66 (15.5%)	43 (13.9%)	23 (19.8%)	0.173
Aldosterone antagonists		124 (29.1%)	80 (25.8%)	44 (37.9%)	0.020

Abbreviations: LBBB, left bundle branch block; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

TABLE 2 Primary and secondary outcomes.

	All *N* = 426	Nonfrailty *N* = 310	Frailty *N* = 116	*p*-Value
Primary outcome	162 (38.0%)	75 (24.2%)	87 (75.0%)	<0.001
Secondary outcomes				
Cardiovascular readmission	94 (22.1%)	41 (13.2%)	53 (45.7%)	<0.001
Cardiovascular death	69 (16.2%)	35 (11.3%)	34 (29.3%)	<0.001
Heart failure death or readmission	76 (17.8%)	28 (9.03%)	48 (41.4%)	<0.001
Myocardial reinfarction	27 (6.3%)	15 (4.84%)	12 (10.3%)	<0.001

tools have been developed.[22] Phenotypic assessment of frailty can be difficult in patients with acute illness, leading to less accurate predictions of adverse outcomes. The CFS serves as a simple and effective semi-quantitative tool for objectively assessing frailty status in routine clinical practice. It offers a global evaluation of prior home daily function and is not compromised by measurement inaccuracies resulting from hospitalization. To date, the CFS stands as the most rigorously validated instrument for the accumulated deficit model of frailty, specifically tailored for risk prediction.[23]

In developed countries, frailty was identified in approximately 15%–20% of elderly patients with STEMI.[10,12,24] Meanwhile, our study recorded a higher prevalence of frailty (27.2%), reflecting a distinctive characteristic of elderly healthcare status in developing countries. A key factor contributing to the higher frailty rate observed in our study, compared to prior studies, was our selection of CFS ≥ 4 for diagnosing frailty, rather than the threshold of CFS ≥ 5 in previous studies.[10,12,24] This choice was partly supported by the CFS level distribution chart (Supporting Information S1: Figure S1), which demonstrated that, at CFS = 2 and CFS = 3, the number of patients experiencing the primary outcome was lower than those who were outcome-free. In contrast, at CFS ≥ 4, the opposite trend was observed, supporting our decision to define frailty at CFS ≥ 4. Additionally, the Kaplan–Meier curves at each CFS point (Supporting Information S1: Figure S2) revealed that CFS ≥ 4 significantly exhibited an earlier discrimination in the primary outcome than CFS ≥ 3, and had a narrower 95% confidence interval than CFS ≥ 5, indicating greater prognostic stability at CFS ≥ 4. Lastly, the most crucial reason was that, in the latest

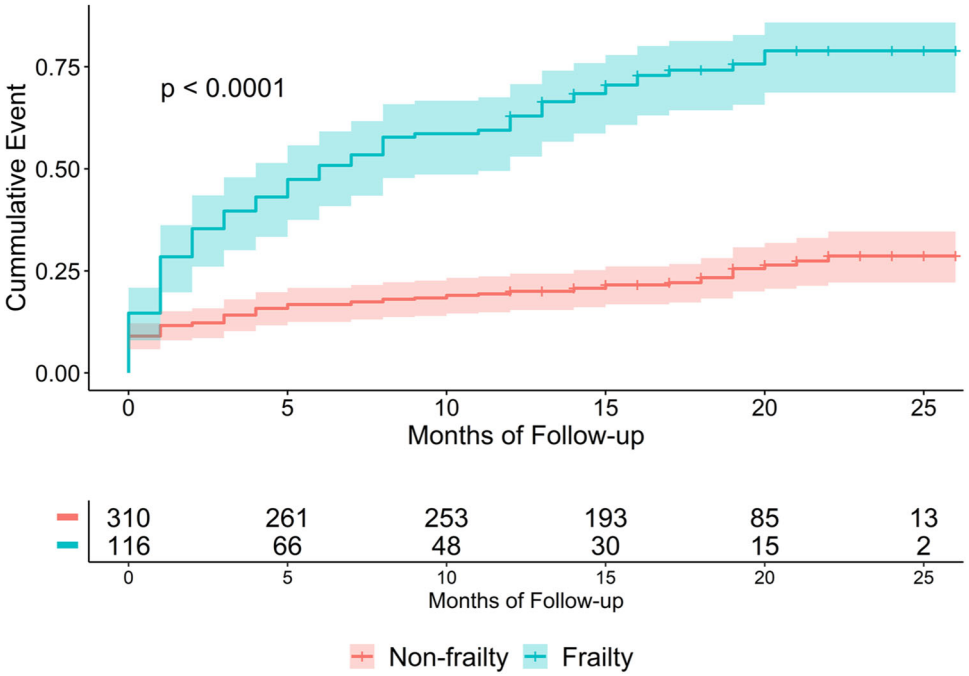

FIGURE 2 Kaplan–Meier. Association between frailty (CFS ≥ 4) and primary outcome. CFS, Clinical Frailty Scale. [Color figure can be viewed at wileyonlinelibrary.com]

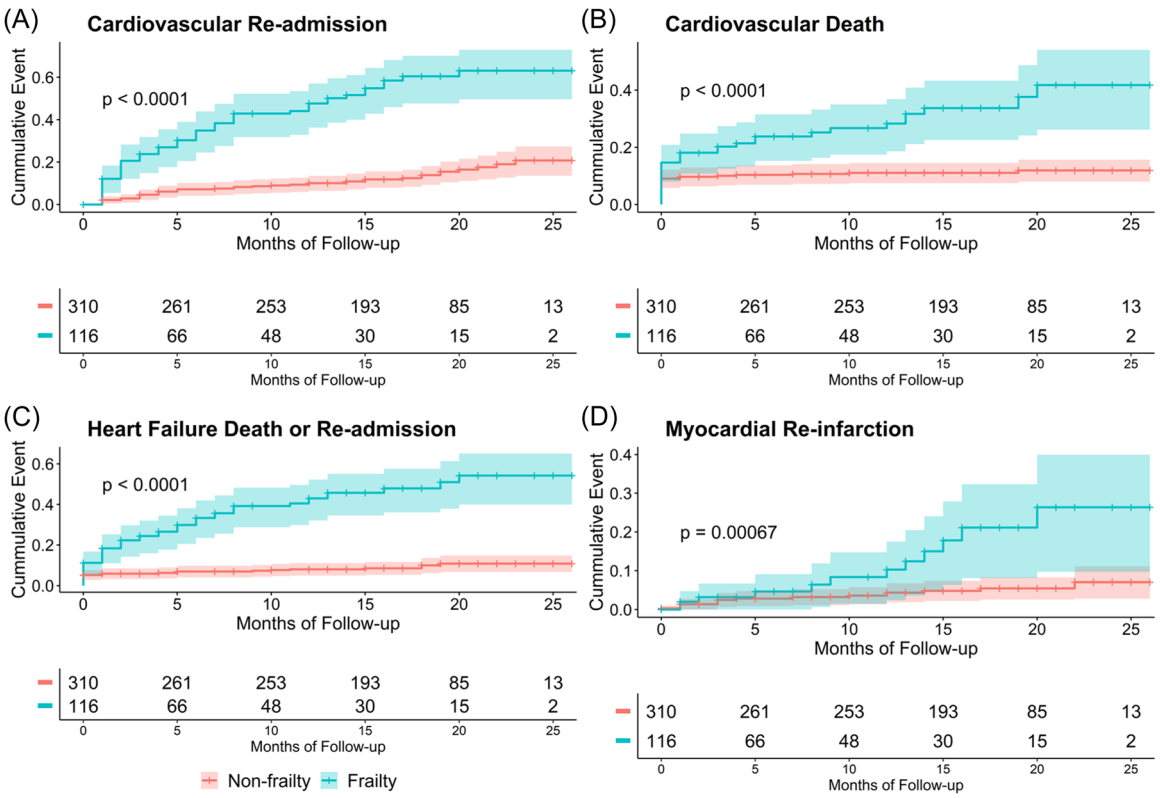

FIGURE 3 Kaplan–Meier. Association between frailty (CFS ≥ 4) and secondary outcomes. (A) Cardiovascular readmission. (B) Cardiovascular death. (C) Heart failure death or readmission. (D) Myocardial reinfarction. CFS, Clinical Frailty Scale. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Multivariate Cox regression analyses between five models from the BMA approach and primary outcome.

Model	Parameters	HR	95% CI	*p*-Value
Model 1	LVEF ≤ 40%	2.337	1.639–3.333	<0.001
	Three vessel disease	2.034	1.487–2.782	<0.001
	Frailty	3.278	2.372–4.531	<0.001
Model 2	TIMI flow, post-PCI < 3	2.117	1.226–3.657	0.007
	LVEF ≤ 40%	2.175	1.515–3.123	<0.001
	Three vessel disease	2.088	1.526–2.857	<0.001
	Frailty	3.295	2.386–4.551	<0.001
Model 3	Killip class > I	1.294	0.920–1.818	0.138
	LVEF ≤ 40%	2.259	1.579–3.229	<0.001
	Three vessel disease	1.969	1.434–2.703	<0.001
	Frailty	3.236	2.341–4.474	<0.001
Model 4	Anemia	1.266	0.913–1.755	0.158
	LVEF ≤ 40%	2.394	1.678–3.414	<0.001
	Three vessel disease	2.05	1.499–2.804	<0.001
	Frailty	3.311	2.399–4.571	0.001
Model 5	Renal insufficiency	1.256	0.895–1.763	0.188
	LVEF ≤ 40%	2.352	1.651–3.35	<0.001
	Three vessel disease	2.028	1.484–2.773	<0.001
	Frailty	3.37	2.436–4.662	<0.001

update of the CFS version 2.0, the authors have reclassified CFS = 4 from "Vulnerable" to "Very mild frailty."[13] Our patients with frailty were older, more commonly women, and presented with a greater burden of comorbidities.

Frailty is characterized by multisystemic dysregulation that leads to the loss of dynamic homeostasis, reduced physiological reserves, and increased vulnerability to subsequent morbidity and mortality.[25] This is often manifested as a maladaptive response to stressors, including acute events (i.e., MI), leading to a vicious cycle of functional decline and an increase in the serious adverse consequences of acute stressors. To the best of our knowledge, this is the first study to show that CFS is independently and strongly associated with adverse outcomes, including death and readmission rates, over 1-year of follow-up in elderly patients undergoing primary PCI for STEMI.

As shown in Table 3, frailty was present in all five of the most parsimonious models suggested by the BMA. When adjusted for other parameters in each model, a more than threefold risk of the primary composite outcome was observed in patients with frailty. These results remained consistent when multivariate Cox proportional hazards survival analyses were performed. The risk of the primary outcome and all 4 secondary outcomes remained significant after comprehensive adjustment for other well-validated STEMI prognostic risk scores, including TIMI, PAMI, and CADILLAC, which may add important predictive value to these risk scores (Supporting Information S1: Figures S3 and S4). These results are consistent with those of previous studies. found that slow gait speed, a marker of frailty, significantly correlated with an elevated risk of cardiovascular events in a prospective cohort study of 472 STEMI patients, irrespective of age, over an average follow-up period of 5.5 years.[26] In another retrospective cohort of 354 consecutive STEMI patients, Yoshioka et al. demonstrated that a higher CFS score was significantly associated with an increased risk of all-cause mortality, with a median follow-up of 474 days.[24] Recently, a study using data from the Swedish SWEDEHEART registry investigated the impact of frailty, as defined by the CFS, on 6-month mortality in MI patients, regardless of age.[10] Among a subgroup of 1486 STEMI patients, both frailty (CFS ≥ 5) and vulnerability (CFS = 4) were significantly linked to a higher risk of 6-month all-cause mortality.

Our findings remained consistent across both men and women aged 75 years or older, as well as those younger, and in certain conditions coexisting with STEMI (i.e., low or high LVEF, history of diabetes, and three-vessel disease), implying good generalizability of the study results (Supporting Information S1: Figure S5). In emphasizing the role of frailty as a surrogate for biological age in contrast to chronological age, our analysis revealed a notably elevated risk of the primary outcome among frail patients aged less than 75 years, compared to nonfrail patients aged 75 years or older (Supporting Information S1: Figure S6). Therefore, older patients without frailty may have a better prognosis than younger patients with frailty. These findings support the idea of developing a prognostic risk score model exclusively for elderly patients with STEMI, in which frailty may be included as a core parameter to improve the discriminatory ability of traditional risk scores.

In our study, frailty was prospectively assessed using the CFS, which is considered the reference standard for diagnosing frailty in cardiovascular diseases. To the best of our knowledge, this study represents the first attempt to assess the association between frailty and adverse outcomes in elderly STEMI patients undergoing primary PCI in Vietnam. Additionally, this study contributes to our understanding of the impact of frailty on adverse outcomes after primary PCI in a Southeast Asian country. Understanding the association between frailty and adverse outcomes among elderly patients with STEMI undergoing primary PCI will help geriatricians and cardiologists recognize the importance of frailty screening and predict and discuss possible periprocedural outcomes with patients and their families. In addition, this study will assist healthcare providers in developing appropriate care plans for frail patients after primary PCI.

5 | LIMITATIONS

First, the quality of life (QoL), length of hospital stay, burden, and differences in symptoms between frail and nonfrail patients were not assessed. QoL and length of hospital stay are important outcome measures in the elderly because these parameters also affect long-term adverse events. Second, the CFS was self-reported and evaluated 2 weeks before admission. Hence, a recall bias is inevitable. Third, although

we adjusted for well-established risk scores, unmeasured residual confounders could not be ruled out. Finally, because frail patients usually have more comorbidities, it is difficult to determine whether frailty itself has a direct impact on adverse outcomes.

6 | CONCLUSION

Frailty, assessed using the CFS, was independently and strongly associated with midterm adverse outcomes in elderly patients with STEMI undergoing primary PCI. This association persisted after adjustment for some well-known prognostic risk scores, holding promise for the addition of frailty status as a new parameter to conventional STEMI risk indicators.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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