

Original Article

Association of Frailty With In-hospital and Long-term Outcomes Among STEMI Patients Receiving Primary Percutaneous Coronary Intervention

Farshad Hosseini, MD,^a Ian Pitcher, MD,^a Mehima Kang, MD,^b Martha Mackay, PhD, RN,^{c,d} Joel Singer, PhD,^c Terry Lee, PhD,^a Kenneth Madden, MD, MSc,^{e,f} John A. Cairns, MD,^{a,g} Graham C. Wong, MD, MPH,^{a,g} and Christopher B. Fordyce, MD, MHS, MSc^{a,g}

^aDivision of Cardiology, Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

^bDivision of Internal Medicine, University of British Columbia, Vancouver, British Columbia, Canada

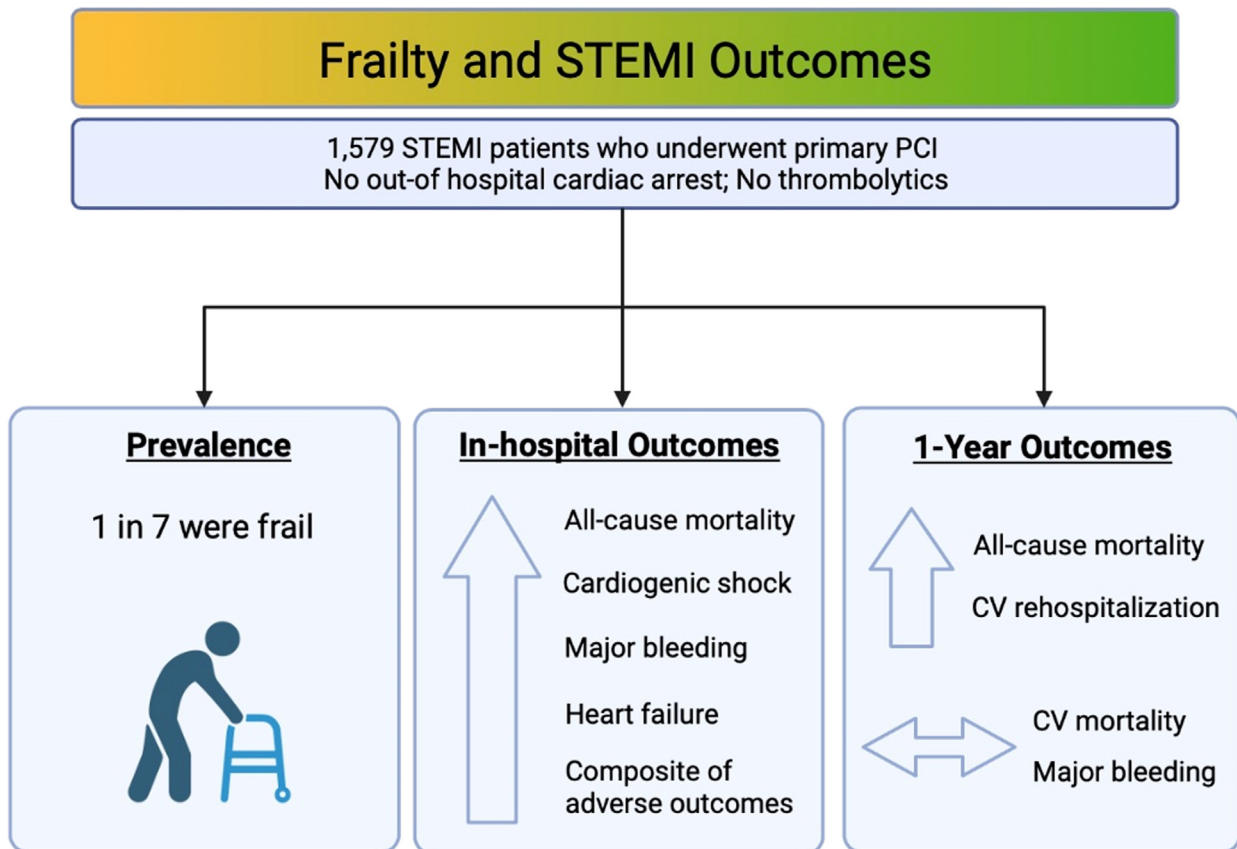
^cCentre for Health Evaluation and Outcome Sciences, University of British Columbia, Vancouver, British Columbia, Canada

^dSchool of Nursing, University of British Columbia, Vancouver, British Columbia, Canada

^eDivision of Geriatric Medicine, Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada

^fCentre for Hip Health and Mobility, University of British Columbia, Vancouver, British Columbia, Canada

^gCentre for Cardiovascular Innovation, University of British Columbia, Vancouver, British Columbia, Canada



ABSTRACT

Background: Frailty is generally a marker of worse prognosis. The impact of frailty on both in-hospital and long-term outcomes in ST-segment-elevation myocardial infarction (STEMI) patients has not been well described. Given this context, we aimed to determine the prevalence and impact of frailty on in-hospital and 1-year outcomes in STEMI patients undergoing primary percutaneous coronary intervention (pPCI).

Methods: This retrospective study reviewed STEMI patients aged ≥ 65 years who underwent pPCI at 1 of the 2 pPCI-capable hospitals at Vancouver Coastal Health. A frailty index (FI) was determined using a deficit-accumulation model, with those with an FI > 0.25 being defined as frail. The primary outcome was 1-year all-cause mortality. The secondary outcomes included in-hospital all-cause mortality, a composite of adverse in-hospital outcomes (all-cause mortality, cardiogenic shock, heart failure, reinfarction, major bleeding, or stroke), and the individual components of the composite.

Results: A total of 1579 patients were reviewed, of which 228 (14.4%) were determined to be frail. After multivariable adjustment, greater frailty (ie, increasing FI) was associated with increased in-hospital all-cause mortality (odds ratio [OR], 1.88; 95% confidence interval [CI], 1.50-2.35, $P < 0.001$), the composite adverse in-hospital outcome (OR, 1.46; 95% CI, 1.27-1.68, $P < 0.001$), and 1-year all-cause mortality (OR, 1.48; 95% CI, 1.10-2.00, $P = 0.011$).

Conclusions: In a contemporary STEMI cohort of older patients receiving pPCI, 1 in 7 patients were frail, with greater frailty being independently associated with increased in-hospital and long-term adverse outcomes. These findings highlight the need for the early recognition of frailty and implementation of an interdisciplinary approach toward the management of frail STEMI patients.

Frailty is a state of increased vulnerability in which the body has a decreased reserve to respond to stressors.¹ This state, in turn, leads to a higher chance of adverse events and mortality. Although interest in frailty in the cardiac population has been increasing, developing a unified approach that enables accurate and reproducible identification of frailty has presented difficulty.² Several scores have been validated to identify frailty,³⁻⁷ but many are difficult to implement into clinical practice, especially in the setting of acute ST-segment-elevation myocardial infarction (STEMI). Prior studies have

RÉSUMÉ

Contexte : La fragilité est généralement un marqueur de mauvais pronostic. Les conséquences de la fragilité sur l'état de santé des patients hospitalisés et sur l'évolution de l'état de santé à long terme après un infarctus du myocarde avec élévation du segment ST (STEMI) ne sont pas bien établies. Nous avons donc cherché à déterminer la prévalence et les conséquences de la fragilité durant une hospitalisation et après un an chez des patients ayant eu un STEMI et devant subir une première intervention coronarienne percutanée (ICP).

Méthodologie : Cette étude rétrospective visait à évaluer les patients de ≥ 65 ans ayant présenté un STEMI et ayant subi une première ICP dans l'un des deux hôpitaux de Vancouver Coastal Health capables d'effectuer une telle intervention. Un indice de fragilité a été établi à l'aide d'un modèle d'accumulation de déficit, les patients ayant un indice $> 0,25$ étant définis comme fragiles. Le critère d'évaluation principal était la mortalité toutes causes confondues après un an. Les critères d'évaluation secondaires comprenaient la mortalité toutes causes confondues à l'hôpital, un critère composé regroupant les résultats défavorables obtenus à l'hôpital (mortalité toutes causes confondues, choc cardiogénique, insuffisance cardiaque, nouvel infarctus, hémorragie majeure ou accident vasculaire cérébral) et les composants individuels du critère composé.

Résultats : Au total, 1579 patients ont été évalués, dont 228 (14,4 %) ont été jugés fragiles. Après un ajustement à variables multiples, une plus grande fragilité (c.-à-d. une augmentation de l'indice de fragilité) était associée à une augmentation de la mortalité toutes causes confondues à l'hôpital (rapport de cote [RC] : 1,88; intervalle de confiance [IC] à 95 % : 1,50 à 2,35; $p < 0,001$), à des résultats défavorables obtenus à l'hôpital selon le critère composé (RC : 1,46; IC à 95 % : 1,27 à 1,68; $p < 0,001$) et à la mortalité toutes causes confondues après un an (RC : 1,48; IC à 95 % : 1,10 à 2,00; $p = 0,011$).

Conclusions : Dans une cohorte contemporaine de patients âgés ayant présenté un STEMI et ayant subi une première ICP, un patient sur sept était fragile, une plus grande fragilité étant associée de manière indépendante à une augmentation des résultats défavorables à l'hôpital et à long terme. Ces résultats soulignent la nécessité de reconnaître rapidement la fragilité et de mettre en œuvre une approche interdisciplinaire pour prendre en charge les patients fragiles présentant un STEMI.

found frailty to be an independent predictor of adverse outcomes in patients with acute coronary syndrome (ACS).⁸⁻¹⁴ Data, however, on the in-hospital impact of frailty in a STEMI-specific population who have undergone primary percutaneous coronary intervention (pPCI) are limited,^{15,16} and only one published study, with a small sample size, previously has assessed the long-term impact of frailty in this specific population.⁹

Given the gaps in the literature, the specific objectives of this analysis were as follows: (i) to determine the prevalence of frailty in a modern STEMI population undergoing pPCI; (ii) to describe the association of baseline frailty with major adverse in-hospital events post-pPCI in STEMI patients; (iii) to investigate the association of baseline frailty with 1-year adverse outcomes post-STEMI discharge. We hypothesized that frailty would be common and would be independently associated with increased rates of in-hospital and 1-year adverse outcomes.

Received for publication March 30, 2024. Accepted April 21, 2024.

Corresponding author: Dr Christopher Fordyce, 2775 Laurel St, 9th Floor, Vancouver, British Columbia V5Z 1M9, Canada. Tel.: +1-604-875-5230; fax: +1-604-675-3007.

E-mail: cfordyce@mail.ubc.ca

See page 1011 for disclosure information.

Methods

Study population

We performed a retrospective analysis of the Vancouver Coastal Health (VCHA) STEMI database, which provides prospective, population-based, granular pre- and in-hospital information on all STEMI patients treated at the 2 PCI-capable quaternary hospitals within the VCHA region.^{17,18} Hospital records also were reviewed for all included patients, to provide additional information on frailty, functional status (geriatric and paralleled health assessments), residential location, and postdischarge long-term outcomes. We included all patients aged ≥ 65 years who were admitted with STEMI and underwent pPCI between June 1, 2007 and September 1, 2020. We excluded patients who had presented with out-of-hospital cardiac arrest and those who had received fibrinolytic therapy. The study was conducted according to the Declaration of Helsinki and received institutional research ethics board approval.

Definitions and outcomes

Frailty was measured using a frailty index (FI) that employs a deficit-accumulation model that includes 31 variables identified from the baseline data.^{7,19} A health deficit can be defined as any health variable that increases with age and is associated with death.⁷ These variables represented documented measures of cognition, functional status, psychological state, and burden of comorbidities. A full table of the variables is included in [Supplemental Table S1](#). Variables were coded dichotomously (0 for absent, 1 for present), with each patient receiving a score between 0 and 31, and the FI was calculated as the frailty score divided by 31. Frail patients were defined as those with an FI > 0.25 (ie, frailty score ≥ 8). Measures of cognitive function and psychological state were obtained on all patients from prior history or by reviewing assessment by an allied health provider.

Patient place of residence (long-term care facility [LTCF] or not) was documented from the admitting note of the occupational therapist or geriatrician or from review of the home address. An LTCF was defined as a facility being documented as such under the British Columbia Health Care (Consent) and Care Facility (Admission) Act.²⁰

In-hospital heart failure was defined as the presence of symptoms, physical findings, or imaging evidence of pulmonary edema at the time of admission. In-hospital mortality was defined as death from any cause. Cardiovascular (CV) mortality was defined as a death resulting from an acute myocardial infarction, sudden cardiac death, heart failure, stroke, CV procedures, CV hemorrhage, or other CV causes.²¹ Cardiogenic shock was characterized as systolic blood pressure < 90 mm Hg persisting for > 30 minutes. Major bleeding was identified as a bleeding event that was associated with significant blood loss (hemoglobin drop of ≥ 30 g/L) requiring transfusion of ≥ 1 unit of packed red blood cells or use of a procedural intervention to manage the bleeding. First medical contact (FMC) was defined as the time at which the patient was first evaluated by either emergency health services or the earliest recorded time of assessment in the emergency department, whichever was first.²² A prolonged reperfusion time was defined as an FMC-to-device time of > 90 minutes

and > 120 minutes in PCI-capable and PCI-noncapable hospitals, respectively, per the most-recent Canadian Cardiovascular Society guidelines.²²

The primary outcome was 1-year all-cause mortality. The secondary outcomes included the following: in-hospital all-cause mortality; a composite of adverse in-hospital outcomes (all-cause mortality, cardiogenic shock, heart failure, reinfarction, major bleeding, or stroke); and the individual components of the composite.

Statistical analysis

Patients were grouped according to the presence of frailty on admission. Continuous variables were reported as means with standard deviation (SD), or medians with interquartile range (IQR), and categorical values were reported as proportions using percentages (%). Between-group comparisons were performed using the Kruskal–Wallis test or analysis of variance for continuous variables, and the χ^2 or Fisher's exact test for categorical variables, as appropriate. Unadjusted and adjusted odds ratios (ORs) were calculated using a logistic regression model. The impact of frailty was assessed in a multivariable model performed for frailty as both a binary variable (ie, frail vs nonfrail), as well as a continuous variable (ie, greater frailty) with ORs expressed as per 0.1 unit increase in FI. Adjustment variables included the following prognostically important clinical characteristics: age, sex, heart failure on presentation, infarct territory, prolonged reperfusion time, initial heart rate, and systolic blood pressure.²³ A sensitivity analysis was performed in which the multivariable model was also adjusted for residency in an LTCF. Statistical significance was defined as a *P*-value of < 0.05 . All data were analyzed with Statistical Analysis System (SAS) software, version 9.4 (SAS Institute, Cary, NC).

Results

FI distribution

A total of 1579 patients were reviewed, of whom 228 (14.4%) were frail ([Fig. 1](#)). The median baseline FI of the study population was 0.097 (IQR, 0.065–0.194), with a median FI of 0.290 (IQR, 0.258–0.323) in the frail cohort, and of 0.097 (IQR, 0.032–0.161) in the nonfrail cohort ([Fig. 2](#)).

Baseline clinical characteristics

[Table 1](#) displays the baseline demographics, comorbidities, and presentation characteristics of the patients. Patients who were frail more often presented with heart failure and/or cardiogenic shock on arrival, experienced a greater incidence of in-hospital cardiac arrest, and had longer FMC-to-device time. No significant difference was present in the infarct territory between the 2 groups. A total of 100 patients (6.3%) were admitted from an LTCF, of whom 32 (32.0%) were frail.

Medical management

Aspirin administration on presentation was similar between frail and nonfrail patients ([Supplemental Table S2](#)).

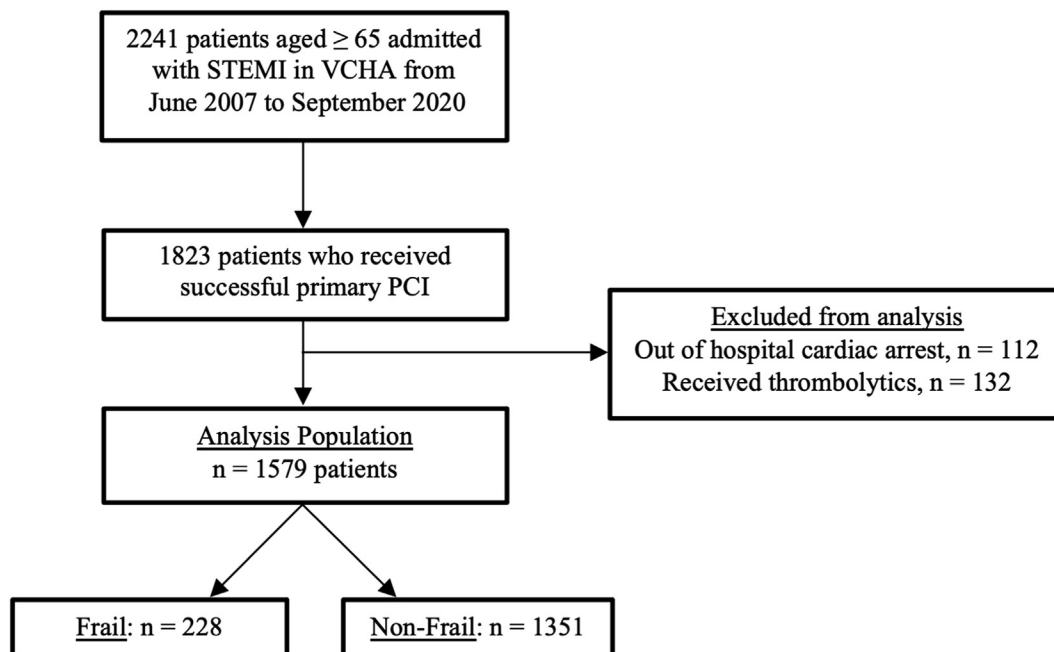


Figure 1. Study cohort derivation. PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation myocardial infarction; VCHA, Vancouver Coastal Health Authority.

The 2 groups did not differ in terms of use of anticoagulant therapy upon presentation. Frail patients, however, were less likely to be started on a beta-blocker, an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker, and statin upon hospitalization. At discharge from the hospital, frail patients were less likely to be referred to cardiac rehabilitation and prescribed aspirin, but they were more likely to be prescribed an anticoagulant.

Outcome analysis

The unadjusted outcomes by frailty status are presented in [Table 2](#). Frailty was associated with increased rates of in-hospital all-cause mortality (OR, 7.84; 95% confidence interval [CI], 5.19-11.84; $P < 0.001$), the composite adverse outcome (OR, 3.04; 95% CI, 2.28-4.06; $P < 0.001$), and 1-year all-cause mortality (OR, 3.58; 95% CI, 1.97-6.49; $P < 0.001$).

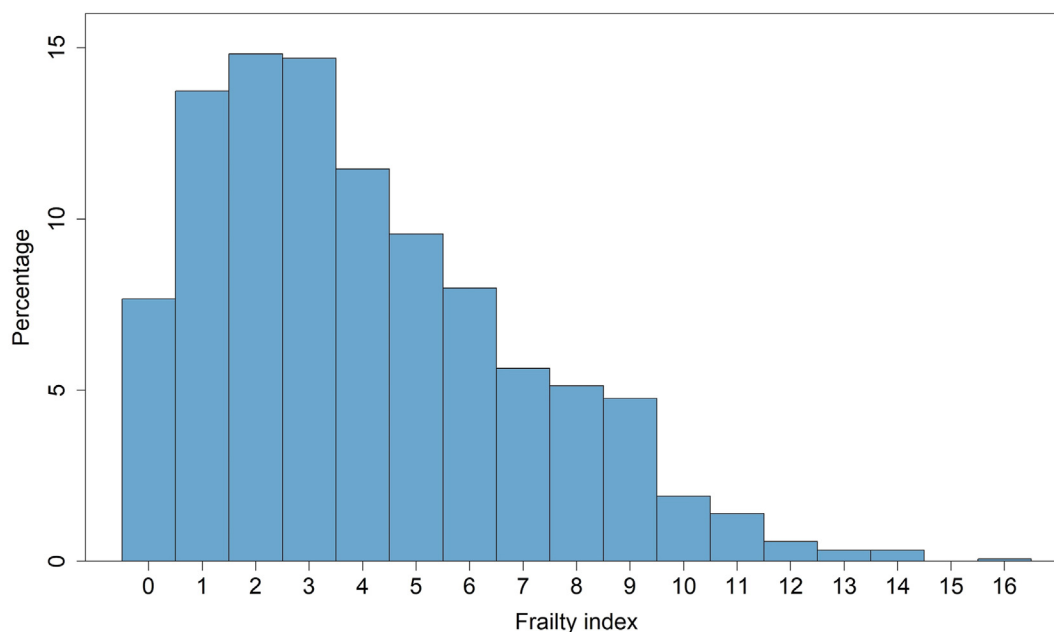


Figure 2. Frailty index distribution among the study population. The frailty index was calculated as the frailty score divided by 31.

Table 1. Baseline characteristics of the study population

Characteristic	All (n = 1579)	Frailty status		P
		Frail (n = 228)	Nonfrail (n = 1351)	
Baseline demographics				
Age, y				
65–74	824 (52.2)	62 (27.2)	762 (56.4)	< 0.001
75–84	486 (30.8)	90 (39.5)	396 (29.3)	
≥ 85	269 (17.0)	76 (33.3)	193 (14.3)	
Female sex	505 (32.0)	102 (44.7)	403 (29.8)	< 0.001
Weight < 60, kg	278 (17.6)	63 (27.6)	215 (15.9)	< 0.001
BMI > 30, kg/m ²	201 (12.7)	35 (15.5)	166 (12.3)	0.199
Impaired mobility	310 (19.6)	130 (57.0)	180 (13.3)	< 0.001
Functional dependence	386 (24.4)	134 (58.8)	252 (18.7)	< 0.001
In an LTCF	100 (6.3)	32 (14.0)	68 (5.0)	< 0.001
Baseline comorbidities				
Cognitive impairment	135 (8.5)	72 (31.6)	63 (4.7)	< 0.001
Anxiety/depression	181 (11.5)	82 (36.0)	99 (7.3)	< 0.001
Polypharmacy	232 (14.7)	141 (61.8)	91 (6.7)	< 0.001
Lung disease	229 (14.5)	92 (40.4)	137 (10.1)	< 0.001
Liver disease	35 (2.2)	20 (8.8)	15 (1.1)	< 0.001
CKD	280 (17.7)	127 (55.7)	153 (11.3)	< 0.001
Dialysis dependence	17 (1.1)	15 (6.6)	2 (0.1)	< 0.001
Prior MSK fractures	184 (11.7)	84 (36.8)	100 (7.4)	< 0.001
Prior major bleeds	52 (3.3)	23 (10.1)	29 (2.1)	< 0.001
Prior VTE	27 (1.7)	13 (5.7)	14 (1.0)	< 0.001
Hemoglobin, < 100 g/L	57 (3.6)	23 (10.1)	34 (2.5)	< 0.001
Life-limiting cancer	130 (8.2)	49 (21.5)	81 (6.0)	< 0.001
Hypertension	1059 (67.1)	215 (94.3)	844 (62.5)	< 0.001
Dyslipidemia	783 (49.6)	181 (79.4)	602 (44.6)	< 0.001
Diabetes	392 (24.8)	112 (49.1)	280 (20.7)	< 0.001
Current/recent smoker	249 (15.8)	57 (25.0)	192 (14.2)	< 0.001
Prior stroke	177 (11.2)	68 (29.8)	109 (8.1)	< 0.001
Prior heart failure	77 (4.9)	49 (21.5)	28 (2.1)	< 0.001
Prior MI	306 (19.4)	106 (46.5)	200 (14.8)	< 0.001
Prior PCI	229 (14.5)	83 (36.4)	146 (10.8)	< 0.001
Prior CABG	61 (3.9)	29 (12.7)	32 (2.4)	< 0.001
Prior PAD	82 (5.2)	44 (19.3)	38 (2.8)	< 0.001
Prior AF	197 (12.5)	71 (31.1)	126 (9.3)	< 0.001
Mechanical valves	5 (0.3)	3 (1.3)	2 (0.1)	0.024
PPM	9 (0.6)	1 (0.4)	8 (0.6)	0.776
ICD	3 (0.2)	2 (0.9)	1 (0.1)	0.056
Presentation characteristics				
Initial heart rate, bpm, mean (SD)	76 (23)	80 (25)	75 (22)	0.007
Initial systolic BP, mm Hg, mean (SD)	139 (34)	132 (35)	141 (33)	< 0.001
Initial hemoglobin, g/L, mean (SD)	137 (18)	128 (22)	138 (17)	< 0.001
Initial creatinine, mmol/L, median (IQR)	96 (79–114)	107 (85–139)	94 (79–111)	< 0.001
Heart failure on presentation	114 (7.2)	40 (17.6)	74 (5.5)	< 0.001
Cardiogenic shock on arrival	96 (7.2)	31 (15.8)	65 (5.7)	< 0.001
Anterior infarct	738 (46.7)	115 (50.4)	623 (46.1)	0.226
In-hospital arrest				
Pre-angiogram	65 (4.1)	20 (8.8)	45 (3.3)	< 0.001
Post-angiogram	60 (3.8)	28 (12.4)	32 (2.4)	
FMC-to-device time, min, median (IQR)	107 (87–140)	119 (93–156)	105 (86–134)	< 0.001
Unknown	58 (3.7)	2 (0.9)	56 (4.1)	< 0.001
≤ 90/120	608 (38.5)	62 (27.2)	546 (40.4)	
> 90/120	913 (57.8)	164 (71.9)	749 (55.4)	

Values are n (%), unless otherwise indicated.

AF, atrial fibrillation; BMI, body mass index; BP, blood pressure; bpm, beats per minute; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; FMC, first medical contact; ICD, implantable cardioverter defibrillator; IQR, interquartile range; LTCF, long-term care facility; MI, myocardial infarction; MSK, musculoskeletal; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; PPM, permanent pacemaker; SD, standard deviation; VTE, venous thromboembolism.

After multivariable adjustment, greater frailty severity upon index STEMI hospitalization was significantly associated with in-hospital all-cause mortality (OR, 1.88; 95% CI, 1.50–2.35; $P < 0.001$), the composite adverse outcome (OR, 1.46; 95% CI, 1.27–1.68; $P < 0.001$), and 1-year all-cause mortality

(OR, 1.48; 95% CI, 1.10–2.00; $P = 0.011$; Fig. 3). An independent association was found between greater frailty and the individual components of the composite, including in-hospital major bleeding (OR, 1.31; 95% CI, 1.11–1.55; $P = 0.001$). In a sensitivity analysis in which the multivariable

Table 2. Unadjusted odds ratios (ORs) of in-hospital and 1-year outcomes by frailty status as a binary variable

Outcome	Frailty status		OR (95% CI)	P
	Frail (n = 228)	Nonfrail (n = 1351)		
In-hospital				
All-cause mortality	54 (23.9)	52 (3.9)	7.84 (5.19, 11.84)	< 0.001
Composite adverse outcome	117 (51.3)	347 (25.7)	3.04 (2.28, 4.06)	< 0.001
Major bleeding	46 (20.2)	157 (11.6)	1.92 (1.34, 2.77)	< 0.001
FMC-to-device time > 90/120 min	164 (72.6)	749 (57.8)	1.93 (1.41, 2.63)	< 0.001
Cardiogenic shock	62 (27.4)	95 (7.1)	4.97 (3.47, 7.12)	< 0.001
Heart failure	86 (38.2)	217 (16.1)	3.22 (2.37, 4.37)	< 0.001
LVEF ≤ 40%	99 (45.2)	394 (29.5)	1.97 (1.47, 2.63)	< 0.001
Reinfarction	5 (2.2)	10 (0.7)	3.03 (1.03, 8.95)	0.05
Stroke	10 (4.4)	20 (1.5)	3.08 (1.42, 6.67)	0.004
Cardiac rehabilitation referral	112 (65.5)	995 (76.8)	0.58 (0.42, 0.82)	0.002
1-years^b				
All-cause mortality	17 (9.8)	38 (2.9)	3.58 (1.97, 6.49)	< 0.001
CV mortality	7 (4.0)	22 (1.7)	2.42 (1.02, 5.76)	0.045
Major bleeding	15 (8.6)	65 (5.0)	1.78 (0.99, 3.20)	0.053
CV rehospitalization	50 (28.7)	324 (25.0)	1.21 (0.85, 1.72)	0.294

Values are n (%), unless otherwise indicated.

CV, cardiovascular; FMC, first medical contact; LVEF, left ventricular ejection fraction; pPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

model was also adjusted for residency in an LTCF, the estimated effect of greater frailty severity on adverse outcomes was unchanged (Supplemental Fig. S1). When frailty was assessed as a binary variable (ie, frail vs nonfrail) in the multivariable model, frailty status remained significantly associated with increased adverse in-hospital and 1-year outcomes (Supplemental Table S3). To account for the impact of the evolution of invasive strategies and antithrombotic therapies during the study period, a time-stratified analysis of the major outcomes of interest was performed according to the phases of VCHA STEMI program implementation, as outlined previously and presented in Supplemental Table S4.²⁴

Discussion

Prior work has demonstrated frailty to be an independent risk factor for adverse outcomes in ACS patients, with these studies using a variety of definitions for frailty.⁸⁻¹⁴ In this study, we showed that frailty was common in our population of STEMI patients receiving pPCI. Greater frailty was demonstrated to be an independent predictor of adverse in-hospital and 1-year outcomes. This study adds to the limited body of evidence assessing the in-hospital impact of frailty on STEMI outcomes in patients receiving pPCI, and it is the largest study to evaluate the long-term implications of frailty in a STEMI-specific population.

The high prevalence of frailty (14%) reported in our study adds to the range of frailty prevalence (3% to 28%) reported in prior literature assessing frailty in STEMI patients.^{9,15,16} In these studies, frailty was expressed as a binary variable (frail or not frail), using different cutoffs, tools, inclusion criteria, and variable sample sizes. Specifically, the referenced studies used a wide agecutoff in the overall included STEMI study population, with patients as young as age 18 years included in one analysis.¹⁵ However, we selected a large cohort of adults, with a realistic age cutoff of ≥ 65 years, with specific inclusion and exclusion criteria, to evaluate frailty as both a binary and a continuous variable using a model that has been validated

previously over a long follow-up period in post-myocardial infarction patients.^{9,10,15,16} Furthermore, we focused on frailty as a continuous variable, rather than as being binary, for our multivariable analysis, as frailty is considered to lie on a spectrum, and specific cutoffs to define this entity in one group of patients may not apply to another group. With the multi-system involvement of frailty,^{19,25} a frailty cumulative index allows for its easier recognition, in addition to providing increased flexibility in the index composition in different clinical settings based on available resources and health records. Future large-scale studies, similar to the **Frailty-Aortic Valve Replacement (FRAILTY-AVR)** study in the aortic stenosis population, are required to compare different frailty tools, to determine which is best at predicting adverse outcomes in the ACS population.²⁶

This analysis has important implications for STEMI patients undergoing pPCI. First, the increased rates of adverse in-hospital outcomes with greater frailty call for its early recognition as an independent risk factor among patients with coronary artery disease. Although establishing a uniform definition for frailty in clinical practice is challenging, with up to 20 different tools having been used to measure frailty,²⁷ our study used the frailty deficit-accumulation model to evaluate for frailty, as this tool recognizes that frailty lies on a continuous spectrum, rather than being an all-or-none phenomenon. Furthermore, phenotypic assessment of frailty using other models, such as the Clinical Frailty Score, in patients with acute illness is difficult, unreliable, and tends to predict mortality less well than do deficit models.²⁸ With that limitation in mind, the implementation of electronic medical records allows for frailty accumulation-deficit models potentially to be built into electronic medical records, to allow for early and easy identification of these individuals. This modality has been utilized previously as a successful strategy for identifying frailty in primary care.²⁹ Early recognition of patients with frailty could lead to an increase in comprehensive, interdisciplinary care for these patients, which may decrease the incidence of

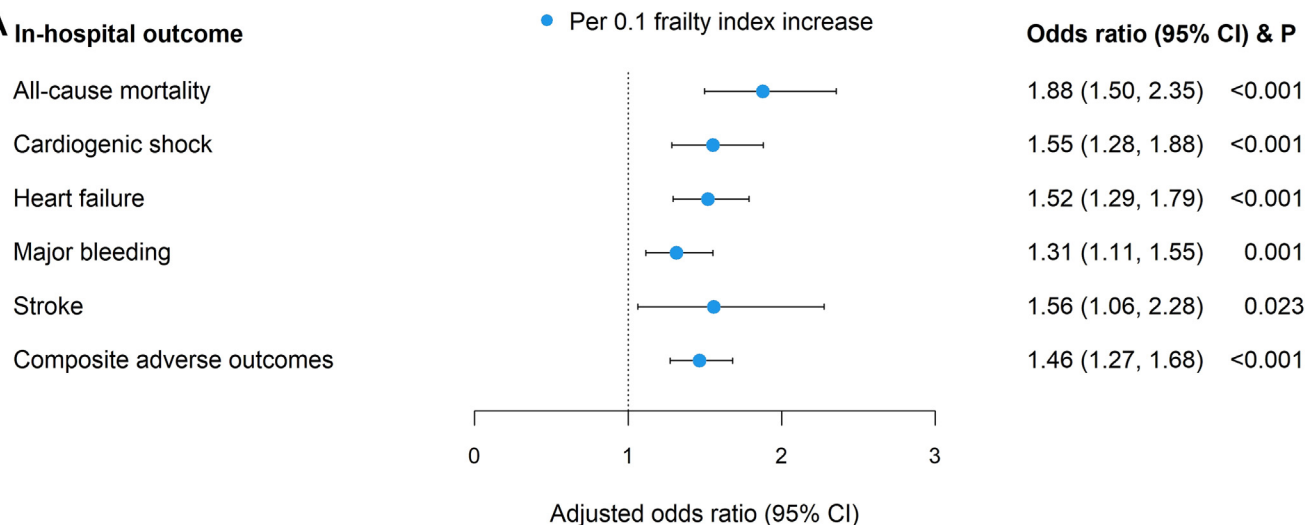
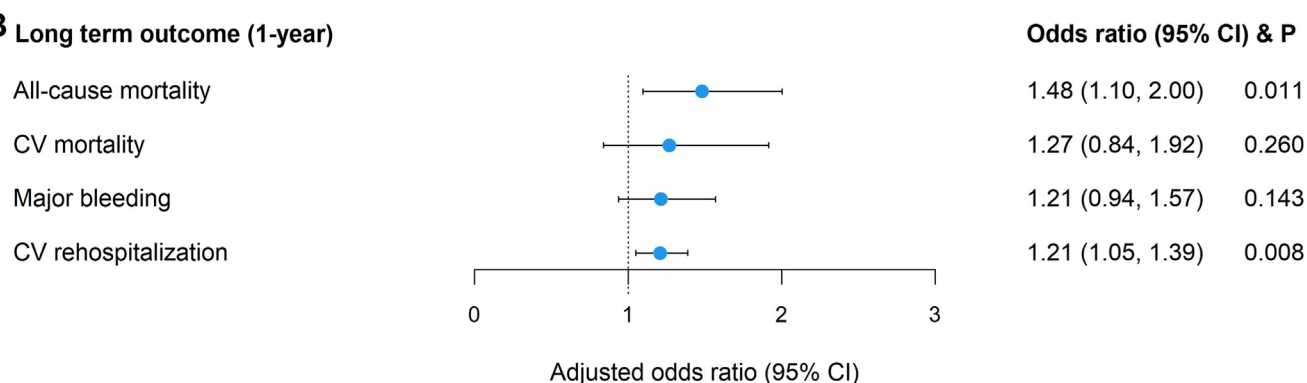
A In-hospital outcome**B Long term outcome (1-year)**

Figure 3. Adjusted odds ratios of in-hospital and 1-year outcomes by degree of frailty. Composite outcomes include all-cause mortality, cardiogenic shock, heart failure, reinfarction, major bleeding, and stroke. The odds ratios were adjusted for age, sex, heart failure on presentation, infarct territory, first-medical-contact-to-device time > 90 (or 120) minutes, initial heart rate, and systolic blood pressure. CI, confidence interval; CV, cardiovascular.

subsequent acute coronary events, although more evidence is required to show modification of outcomes.

Second, we showed that in addition to greater frailty severity putting STEMI patients at an elevated risk for adverse short-term outcomes, this risk also seems to persist post-discharge, largely due to the competing risk imposed by non-CV comorbidities in these individuals. In a recent analysis of over 3 million outpatient US veterans aged ≥ 65 years, both the presence and severity of frailty was tightly correlated with CV death over time, independent of underlying CV disease.³⁰ We extend these findings to STEMI patients by showing the association of greater frailty with increased all-cause mortality at 1 year, with a similar trend being seen for CV mortality, although it did not reach statistical significance, given the low number of cardiac deaths. Our results are in keeping with those reported by Yoshioka et al., who found that greater frailty severity, as determined by the Canadian Frailty Scale, was associated with higher 1-year all-cause mortality in a small cohort of STEMI patients.⁹ These findings are not surprising, as frailty is a multidimensional condition affecting different organ systems in addition to cognitive and functional domains, all of which can lead to noncardiac mortality. This

possibility underlines the need for routine assessment and global optimization of frail patients in longitudinal, interdisciplinary clinics, involving experts in geriatrics, nutrition, physiotherapy, and social supports, all of which are considered areas of potential vulnerability for these individuals.

Third, our data shed light on the importance of incorporating frailty-status assessment in the evaluation of adults being considered for pPCI. Such assessment is important, as recognizing frailty and the associated risk of adverse outcomes in these individuals may help guide an informed, shared decision-making process about revascularization among patients and care providers. Lastly, greater frailty was associated with increased incidence of major in-hospital bleeding, in keeping with the findings reported by Borovac et al.,¹⁶ which suggest the need for potential risk-reducing strategies in the care of patients with frailty, including careful attention to renal dosing of antithrombotics, use of a proton-pump inhibitor, and use of radial access whenever possible.^{31,32}

We are aware that our study has some limitations. First, given that this study is retrospective, causation cannot be inferred. Second, we are aware that our sample is from a single-region study population, although rigorous chart review

was performed, allowing for the collection of data that may not be obtainable through administrative data collection. Third, our study included those patients with frailty who underwent pPCI, which may introduce an element of recruitment bias, as some frail STEMI patients may not be deemed suitable to undergo pPCI. Fourth, our FI did not include phenotypic parameters, such as gait speed, as variables, which would have added to the accuracy of our model. Despite this, assessment of patient phenotype in the context of a STEMI event is not reliable, and it may be affected falsely relative to the patient's true baseline. Lastly, frailty was assessed only at a single point at the time of the index STEMI event, and therefore, changes in frailty status over time are not known. Even given these limitations, our study presents novel findings that can be beneficial to the scientific community and in the care of STEMI patients. We welcome confirmation of these findings by other investigations around the world that have different healthcare and social systems.

Conclusion

In a contemporary model of STEMI patients receiving pPCI, frailty is prevalent and it is independently associated with increased adverse in-hospital and long-term outcomes. These results highlight the significant need to identify frailty, as doing so provides potential opportunities for clinicians to improve the care and outcomes of this vulnerable population. Ongoing research is needed to study interventions, both medical and by means of multidisciplinary care, to improve outcomes in patients with frailty.

Ethics Statement

The study adhered to local ethical guidelines and received institutional research ethics board approval.

Patient Consent

The authors confirm that patient consent is not applicable to this article.

Funding Sources

The authors have no funding sources to declare.

Disclosures

C.B.F. reports serving on advisory boards for Bayer, Novo Nordisk, Boehringer Ingelheim, Sanofi, Pfizer, Amgen, Novartis, and Pendopharm. C.B.F. reports receiving research grant support from Bayer, Canadian Cardiovascular Society, and BMS-Pfizer. J.A.C. reports receiving research grants from Astra Zeneca, Edwards Life Sciences, and Boston Scientific, and personal fees from Abbott Vascular. The other authors have no conflicts of interest to disclose. All authors have read and agreed to the manuscript as written.

References

1. Clegg A, Young J, Iliffe S, Rikkert M, Rockwood K. Frailty in elderly people. *Lancet* 2013;381:752-62.
2. Damluji AA, Forman DE, van Diepen S, et al. Older adults in the cardiac intensive care unit: factoring geriatric syndromes in the management, prognosis, and process of care: a scientific statement from the American Heart Association. *Circulation* 2020;141:e6-32.
3. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-56.
4. Clegg A, Rogers L, Young J. Diagnostic test accuracy of simple instruments for identifying frailty in community-dwelling older people: a systematic review. *Age Ageing* 2015;44:148-52.
5. Parker SG, McCue P, Phelps K, et al. What is comprehensive geriatric assessment (CGA)? An umbrella review. *Age Ageing* 2018;47:149-55.
6. Pilotto A, Cella A, Pilotto A, et al. Three decades of comprehensive geriatric assessment: evidence coming from different healthcare settings and specific clinical conditions. *J Am Med Dir Assoc* 2017;18:192.e1-11.
7. Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. *J Gerontol A Biol Sci Med Sci* 2007;62:722-7.
8. Patel A, Goodman S, Yan A, et al. Frailty and outcomes after myocardial infarction: insights from the CONCORDANCE Registry. *J Am Heart Assoc* 2018;7:e009859.
9. Yoshioka N, Takagi K, Morita Y, et al. Impact of the clinical frailty scale on mid-term mortality in patients with ST-elevation myocardial infarction. *Int J Cardiol Heart Vasc* 2019;22:192-8.
10. Myers V, Drory Y, Gerber Y. Clinical relevance of frailty trajectory post myocardial infarction. *Eur J Prev Cardiol* 2014;21:758-66.
11. Damluji AA, Huang J, Bandeen-Roche K, et al. Frailty among older adults with acute myocardial infarction and outcomes from percutaneous coronary interventions. *J Am Heart Assoc* 2019;8:e013686.
12. 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;124:2397-404.
13. Alegre O, Formiga F, López-Palop R, et al. An easy assessment of frailty at baseline independently predicts prognosis in very elderly patients with acute coronary syndromes. *J Am Med Dir Assoc* 2018;19:296-303.
14. White HD, Westerhout CM, Alexander KP, et al. Frailty is associated with worse outcomes in non-ST-segment elevation acute coronary syndromes: insights from the Targeted platelet Inhibition to Clarify the Optimal strategy to medically manage Acute Coronary Syndromes (TRILOGY ACS) trial. *Eur Heart J Acute Cardiovasc Care* 2016;5:231-42.
15. Rubens M, Ramamoorthy V, Saxena A, et al. Management and outcomes of ST-segment elevation myocardial infarction in hospitalized frail patients in the United States. *Am J Cardiol* 2022;175:1-7.
16. Borovac JA, Mohamed MO, Kontopantelis E, et al. Frailty among patients with acute ST-elevation myocardial infarction in the United States: the impact of the primary percutaneous coronary intervention on in-hospital outcomes. *J Invasive Cardiol* 2022;34:E55-64.
17. Fordyce CB, Cairns JA, Singer J, et al. Evolution and impact of a regional reperfusion system for ST-elevation myocardial infarction. *Can J Cardiol* 2016;32:1222-30.
18. Moghaddam N, Wong GC, Cairns JA, et al. Association of anemia with outcomes among ST-segment-elevation myocardial infarction patients receiving primary percutaneous coronary intervention. *Circ Cardiovasc Interv* 2018;11:e007175.
19. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr* 2008;8:24.

20. Government of British Columbia. Health care (consent) and care facility (admission) act. Available at: https://www.bclaws.gov.bc.ca/civix/document/id/complete/statreg/96181_01. Accessed February 18, 2022.
21. Hicks KA, Mahaffey KW, Mehran R, et al. 2017 cardiovascular and stroke endpoint definitions for clinical trials. *Circulation* 2018;137:961-72.
22. Wong GC, Welsford M, Ainsworth C, et al. 2019 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology guidelines on the acute management of ST-elevation myocardial infarction: focused update on regionalization and reperfusion. *Can J Cardiol* 2019;35:107-32.
23. Morrow D, Antman E, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation* 2000;102:2031-7.
24. Williams C, Fordyce CB, Cairns JA, et al. Temporal trends in reperfusion delivery and clinical outcomes following implementation of a regional STEMI protocol: a 12-year perspective. *CJC Open* 2023;5:181-90.
25. Rockwood K. Frailty and its definition: a worthy challenge. *J Am Geriatr Soc* 2005;53:1069-70.
26. Afilalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: the FRAILTY-AVR study. *J Am Coll Cardiol* 2017;70:689-700.
27. de Vries NM, Staal JB, van Ravensberg CD, et al. Outcome instruments to measure frailty: a systematic review. *Ageing Res Rev* 2011;10:104-14.
28. Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61:1537-51.
29. Lansbury LN, Roberts HC, Clift E, et al. Use of the electronic Frailty Index to identify vulnerable patients: a pilot study in primary care. *Br J Gen Pract* 2017;67:e751-6.
30. Shrauner W, Lord EM, Nguyen XMT, et al. Frailty and cardiovascular mortality in more than 3 million US veterans. *Eur Heart J* 2022;43:818-26.
31. Steg PG, Huber K, Andreotti F, et al. Bleeding in acute coronary syndromes and percutaneous coronary interventions: position paper by the Working Group on Thrombosis of the European Society of Cardiology. *Eur Heart J* 2011;32:1854-64.
32. Bhatt DL, Cryer BL, Contant CF, et al. Clopidogrel with or without omeprazole in coronary artery disease. *N Engl J Med* 2010;363:1909-17.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at <https://www.cjopen.ca/> and at <https://doi.org/10.1016/j.cjco.2024.04.005>.