# Impact of Frailty on Emergency Department Encounters for Cardiovascular Disease: A Retrospective Cohort Study



Balamrit Singh Sokhal<sup>a,b</sup>, Andrija Matetić, MD, PhD<sup>b,c</sup>, Abhishek Abhishek, MD, PhD<sup>d</sup>, Amitava Banerjee, MBChB, DPhil<sup>e</sup>, Richard Partington, MBBS, PhD<sup>a</sup>, Edward Roddy, MBBS, PhD<sup>a,f</sup>, Muhammad Rashid, MBBS, PhD<sup>b</sup>, Christian David Mallen, BMBS, PhD<sup>a</sup>, and Mamas Andreas Mamas, MBChB, DPhil<sup>b,\*</sup>

> Data are limited on whether the causes of emergency department (ED) encounters for cardiovascular diseases (CVDs) and associated clinical outcomes vary by frailty status. Using the United States Nationwide ED Sample, selected CVD encounters (acute myocardial infarction [AMI], ischemic stroke, atrial fibrillation [AF], heart failure [HF], pulmonary embolism, cardiac arrest, and hemorrhagic stroke) were stratified by hospital frailty risk score (HFRS). Logistic regression was used to determine the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) of ED mortality among the different frailty groups. A total of 8,577,028 selected CVD ED encounters were included. A total of 5,120,843 (59.7%) had a low HFRS (<5), 3,041,699 (35.5%) had an intermediate HFRS (5 to 15), and 414,485 (4.8%) had a high HFRS (>15). Ischemic stroke was the most common reason for the encounter in the high HFRS group (66.9%), followed by hemorrhagic stroke (11.7%) and AMI (7.2%). For the low HFRS group, AF was the most common reason for the encounter (30.2%), followed by AMI (23.6%) and HF (16.8%). Compared with the low-risk group, highrisk patients had a decreased ED mortality and an increased overall mortality across most CVD encounters (p <0.001). The strongest association with overall mortality was observed among patients with a high HFRS admitted for AF (aOR 27.14, 95% CI 25.03 to 29.43) and HF (aOR 13.71, 95% CI 12.95 to 14.51) compared with their low-risk counterparts. In conclusion, patients presenting to the ED with acute CVD have a significant frailty burden, with different patterns of CVD according to frailty status. Frailty is associated with an increased all-cause mortality in patients for most CVD encounters. © 2023 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) (Am J Cardiol 2023;206:210-218)

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Frailty is a clinical syndrome of multiple organ system impairment, leading to an increased vulnerability to stress, and is associated with an increased likelihood of adverse outcomes.<sup>1</sup> The proportion of subjects living with frailty is increasing.<sup>2</sup> Frail patients have a greater burden of cardiovascular disease (CVD)<sup>3,4</sup>; CVD is associated with a threefold increase in frailty, whereas frailty is independently associated with increased mortality from CVD.<sup>5</sup> Several studies have described the association between CVD and frailty in the hospital inpatient setting.<sup>6–8</sup> However, there remain little data on whether the type of CVD encounter varies by frailty status in the emergency department (ED) setting. The outcomes of a patient presentation to the ED vary: some presentations are resolved within the ED, including on-site treatment and discharge, others are admitted for specialist inpatient hospital care, whereas others may result in death during the encounter. Therefore, using data derived from inpatient hospital episodes alone may not provide a full picture on the patterns of CVD encounters in secondary care among patients with different frailty burdens and their associated outcomes. It is important to gain insight into the patterns of acute CVD presentations among frail patients in the ED to allow services to meet the needs of the growing frail population. Therefore, this study aimed to describe the relation between frailty status on the prevalence, clinical characteristics, causes, and outcomes of patients attending the ED with CVD using a national data set.

<sup>&</sup>lt;sup>a</sup>School of Medicine; <sup>b</sup>Keele Cardiovascular Research Group, Centre for Prognosis Research, Keele University, Keele, United Kingdom; <sup>c</sup>Department of Cardiology, University Hospital of Split, Split, Croatia; <sup>d</sup>Academic Rheumatology, University of Nottingham, Nottingham, United Kingdom; <sup>e</sup>Institute of Health Informatics, University College London, London, United Kingdom; and <sup>f</sup>Haywood Academic Rheumatology Centre, Midland Partnership Foundation Trust, Stoke-on-Trent, United Kingdom. Manuscript received July 30, 2023; revised manuscript received and accepted August 20, 2023.

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See page 217 for Declaration of Competing Interest.

<sup>\*</sup>Corresponding author: Tel: +44 1782 671654; fax: +44 1782 734719. *E-mail address:* mamasmamas1@yahoo.co.uk (M.A. Mamas).

## Methods

The National ED Sample (NEDS) was developed by the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality.<sup>9</sup> The NEDS provides accurate estimates of all hospital-owned ED encounters in the United States. This includes 989 hospitals located in 40 states amounting to approximately 145 million ED encounters. Patient demographics, outcomes, and comorbidities are all captured using the International Classification of Diseases, Tenth Revision (ICD-10) codes.<sup>9</sup>

The hospital frailty risk score (HFRS) was developed by Gilbert et al<sup>10</sup> to assess the risk of adverse outcomes in older persons using routinely collected health care data. A cohort of elderly patients admitted for diagnoses associated with frailty was identified using ICD-10 codes.<sup>10</sup> The HFRS was created using ICD-10 codes to group patients into low risk (HFRS <5), intermediate risk (HFRS 5 to 15), and high risk (HFRS >15).<sup>10</sup> The HFRS was validated using a local and national cohort in the United Kingdom.<sup>10</sup> Each component of the HFRS and the associated weighting is outlined in Supplementary Appendix 1.

The ICD-10 codes were used to identify all adult discharge records with a principal diagnosis of an acute CVD encounters between 2016 and 2018 (Supplementary Table 1). This sample was filtered using ICD-10 codes into 7 selected CVD groups: acute myocardial infarction (AMI), atrial fibrillation (AF), ischemic stroke, heart failure (HF), pulmonary embolism (PE), cardiac arrest, and hemorrhagic stroke. The sample was then stratified according to their frailty status measured by the HFRS into 3 groups: low risk (HFRS <5), intermediate risk (HFRS 5 to 15), and high risk (HFRS >15), as defined by Gilbert et al.<sup>10</sup>

The outcomes of this study were the following: (1) to calculate the proportion of encounters stratified by HFRS category (low, intermediate, and high); (2) to examine the discharge disposition (admission, discharge, and mortality), stratified by CVD diagnosis and HFRS category; and (3) to determine the association between frailty, CVD, and all-cause mortality in the ED.

Cases were excluded because of missing data for the following variables: age, gender, elective admission, ED mortality, primary expected payer, total ED and in-hospital charges, and length of stay (n = 40,341 [0.19%]). Because this is an observational study, it was appraised according to the Strengthening The Reporting of OBservational Studies in Epidemiology (STROBE) recommendations (Supplementary Appendix 2).<sup>11</sup>

Continuous variables, including age, length of stay, and total charges, were summarized using median and interquartile ranges and compared using the Kruskal–Wallis test. Categorical variables were compared using the chisquare test and summarized as percentages (%).

Multivariable logistic regression was performed to determine the adjusted odds ratios (aORs) with 95% confidence intervals (CIs) using the binomial multivariable logistic regression models ("enter" algorithm). Different sensitivity analyses were conducted by separately evaluating the subgroups of patients with 7 different cardiovascular causes of emergency encounters, namely, "acute myocardial infarction," "ischemic stroke," "atrial fibrillation/flutter,"

"heart failure," "pulmonary embolism," "cardiac arrest," and "haemorrhagic stroke." For each of the 7 different cardiovascular causes of emergency encounters, we evaluated 3 different binary outcomes (dependent variables), namely, "emergency department all-cause mortality," "overall allcause mortality" (ED + in-hospital all-cause mortality), and "hospitalization." The following independent variables were used in each multivariable logistic regression model: categorical frailty groups (low-frailty group as a reference group), age, gender, weekend admission, primary expected payer, median household income, hospital region and teaching status, previous AMI, thrombocytopenia, dyslipidemia, smoking, anemias, coagulopathy, diabetes mellitus, liver disease, malignancy, peripheral vascular disorders, chronic pulmonary disease, and chronic renal failure. Finally, to further explore the utility of the HFRS, we conducted additional analyses using the same previously mentioned settings but having the HFRS as a continuous variable (presented in the Supplements). All statistical analyses were weighted and performed using SPSS version 27 (IBM Corp, Armonk, New York).<sup>12</sup> The statistical significance was set at the level of p < 0.05.

This study did not require ethical approval. The NEDS is a publicly available national data set and does not contain any patient identifiable information.

## Results

A total of 8,577,028 selected ED encounters for CVD, including AMI, acute ischemic stroke, AF, HF, PE, cardiac arrest, and acute hemorrhagic stroke (Supplementary Figure 1), were recorded between 2016 and 2018. Overall, 5,120,843 (59.7%) had a low HFRS of <5, 3,041,699 (35.5%) had an intermediate HFRS of 5 to 15, and 414,485 (4.8%) had a high HFRS of >15 (Table 1).

Patients with a high HFRS had a higher prevalence of co-morbidities, such as dyslipidemia (55.7%), thrombocy-topenia (6.1%), anemia (25.0%), peripheral artery disease (3.5%), and chronic renal failure (34.7%), than patients with a low and intermediate HFRS (p <0.001 for all) (Table 1).

The most common cause of encounter was AF (24.0%), followed by AMI (20.9%), ischemic stroke (19.4%), HF (17.3%), PE (7.3%), cardiac arrest (5.8%), and hemorrhagic stroke (5.3%). The cohort admitted with ischemic stroke had the highest proportion of patients with a high HFRS (16.7%), followed by hemorrhagic stroke, AMI, and HF (10.6%, 1.7%, and 1.7%, respectively). The cohort admitted with ischemic stroke had the highest proportion of patients with an intermediate HFRS (57.5%), followed by hemorrhagic stroke (42.6%) and HF (40.5%). The cohort admitted with cardiac arrest had the highest proportion of patients with a low HFRS (89.1%), followed by AF (75.2%) and AMI (67.4%) (Figure 1, Table 2).

Acute ischemic stroke (66.9%) was the most common CVD encounter for the high HFRS group, followed by hemorrhagic stroke (11.7%) and AMI (7.2%). Ischemic stroke was also the most common CVD encounter for the intermediate HFRS group (31.4%), followed by HF (19.8%) and AMI (18.3%). The most common cause of CVD encounter

#### Table 1

Patient characteristics for selected emergency department cardiovascular admissions according to the hospital frailty risk score

Characteristics	Hospital Frailty Risk Score			
	Low <5 (59.7%)	Intermediate 5-15 (35.5%)	High >15 (4.8%)	
Number of weighted discharges	5,120,843	3,041,699	414,485	
Age (years), median (IQR)	66 (56, 77)	73 (62, 82)	77 (66, 86)	< 0.001
Female sex	43.5%	49.7%	55.0%	< 0.001
Weekend admission	25.5%	25.6%	26.4%	< 0.001
Primary expected payer				< 0.001
Medicare	55.1%	71.5%	76.8%	
Medicaid	10.0%	8.4%	8.0%	
Private Insurance	26.0%	14.9%	11.1%	
Self-pay	5.8%	3.1%	2.4%	
No charge	0.3%	0.2%	0.2%	
Other	2.6%	1.9%	1.5%	
Median Household Income (percentile)				< 0.001
0-25 <sup>th</sup>	30.5%	31.3%	30.7%	
26 <sup>th</sup> -50 <sup>th</sup>	27.9%	26.5%	25.1%	
51 <sup>st</sup> -75 <sup>th</sup>	22.5%	22.6%	23.0%	
76 <sup>th</sup> -100 <sup>th</sup>	19.2%	19.6%	21.3%	
Homelessness	0.4%	0.5%	0.4%	< 0.001
Comorbidities				
Dyslipidaemia	35.4%	54.4%	55.7%	< 0.001
Thrombocytopenia	1.6%	5.2%	6.1%	< 0.001
Smoking	13.0%	12.3%	10.3%	< 0.001
Previous AMI	7.7%	11.6%	8.5%	< 0.001
Previous PCI	7.5%	10.8%	7.1%	< 0.001
Previous CABG	5.8%	9.7%	7.0%	< 0.001
Anemias	6.9%	23.2%	25.0%	< 0.001
Valvular disease	6.9%	14.7%	12.2%	< 0.001
Peripheral artery disease	0.8%	2.9%	3.5%	< 0.001
Coagulopathy	1.2%	3.4%	2.8%	< 0.001
Diabetes Mellitus	25.2%	40.0%	39.2%	< 0.001
Liver disease	1.2%	3.4%	2.8%	< 0.001
Chronic renal failure	8.4%	32.4%	34.7%	< 0.001
Chronic pulmonary disease	13.0%	24.0%	18.4%	< 0.001
Hospital Region				< 0.001
Northeast	17.3%	17.5%	17.8%	
Midwest	23.6%	22.9%	24.7%	
South	39.4%	40.7%	39.8%	
West	19.7%	18.9%	17.6%	
Location/teaching status of hospital				< 0.001
Rural	27.4%	25.6%	20.2%	
Urban non-teaching	52.9%	63.0%	73.0%	
Urban teaching	19.7%	11.4%	6.9%	
Length of stay (days), median (IQR)	2 (2,4)	4 (2,6)	6 (4,11)	< 0.001
Total ED and in-hospital charges (USD), median (IQR)	33,663 (18,231, 65,201)	41,378 (23,395, 78,149)	62,859 (34,272, 124,400)	< 0.001
Hospitalization	47.2%	87.9%	98.3%	< 0.001
ED all-cause mortality	7.9%	0.8%	0.1%	< 0.001
Overall all-cause mortality	8.7%	6.3%	9.4%	< 0.001

AMI = acute myocardial infarction; CABG = coronary artery bypass graft; ED = emergency department; HFRS = hospital Frailty Risk Score; IQR = interquartile range; PCI = percutaneous coronary intervention; USD = United States dollar.

in the low HFRS group was AF (30.2%), followed by AMI (23.6%) and HF (16.8%) (Figure 2).

ischemic stroke, HF, AF, PE, cardiac arrest, and hemorrhagic stroke cohorts (Supplementary Tables 2 to 9).

Patients admitted for AMI with a high HFRS were more likely to be older and female than those with an intermediate or low HFRS. These patients were had more co-morbid conditions, such as anemia, thrombocytopenia, and peripheral vascular disorders, than patients with a low HFRS (p <0.001). Similar findings were observed among the Patients with a high HFRS were more likely to be admitted as an inpatient (98.3% vs 87.9% for intermediate HFRS and 47.2% for low HFRS) and less likely to be transferred to a short-term hospital (0.5% vs 3.6% for intermediate HFRS and 13.0% for low HFRS), discharged to home health care (0.2% vs 0.6% for intermediate HFRS and 0.4%



Figure 1. Distribution of each HFRS category within each of the selected ED cardiovascular admission causes.

for low HFRS), and discharged home (0.5% vs 5.7% for intermediate HFRS and 28.4% for low HFRS) (Supplementary Table 9).

Patients with a high HFRS generally had lower unadjusted rates of ED all-cause mortality than their lower frailty counterparts (0.1% vs 0.8% for intermediate HFRS group and 7.9% for low HFRS group; p < 0.001). However, a high HFRS was associated with increased rates of overall mortality (ED and in-hospital combined mortality) (9.4% vs 6.3% for the intermediate HFRS group and 8.7% for the

Table 2

Prevalence of the selected emergency department cardiovascular admission diagnoses and associated emergency department mortality based on the hospital frailty risk score

Admission diagnosis		Hospital Frailty Risk Score			P-value
		Low <5 (59.7%)	Intermediate 5-15 (35.5%)	High >15 (4.8%)	
Acute myocardial infarction	Prevalence	67.4%	30.9%	1.7%	< 0.001
(N =1,796,127)	ED mortality	0.8%	0.3%	0.1%	< 0.001
	<b>Overall mortality</b>	1.9%	8.9%	14.5%	< 0.001
Ischemic stroke	Prevalence	25.8%	57.5%	16.7%	< 0.001
(N =1,662,442)	ED mortality	0.2%	<0.1%	<0.1%	< 0.001
	<b>Overall mortality</b>	0.6%	2.6%	7.4%	< 0.001
Atrial fibrillation/flutter	Prevalence	75.2%	23.7%	1.1%	< 0.001
(N =2,056,294)	ED mortality	<0.1%	0.1%	<0.1%	< 0.001
	<b>Overall mortality</b>	0.1%	1.5%	5.9%	< 0.001
Heart failure	Prevalence	57.8%	40.5%	1.7%	< 0.001
(N =1,483,837)	ED mortality	0.2%	0.1%	<0.1%	< 0.001
	<b>Overall mortality</b>	0.5%	3.3%	9.1%	< 0.001
Pulmonary Embolism	Prevalence	67.2%	31.2%	1.6%	< 0.001
(N=627,547)	ED mortality	0.3%	0.1%	<0.1%	< 0.001
	<b>Overall mortality</b>	0.8%	5.4%	10.7%	< 0.001
Cardiac arrest	Prevalence	89.1%	10.3%	0.5%	< 0.001
(N=495,406)	ED mortality	88.2%	39.4%	5.7%	< 0.001
	<b>Overall mortality</b>	89.2%	78.0%	63.2%	< 0.001
Haemorrhagic stroke	Prevalence	46.9%	42.6%	10.6%	< 0.001
(N =458,987)	ED mortality	2.0%	0.6%	0.1%	< 0.001
	<b>Overall mortality</b>	7.0%	20.1%	16.0%	< 0.001

ED = emergency department; HFRS = hospital frailty risk score.

low HFRS group; p <0.001). This trend was observed across all CVD admissions, with lower crude rates of ED all-cause mortality and increased rates of overall mortality with increasing HFRS category (Table 2).

On adjustment for baseline covariates, the high HFRS group had decreased odds of ED mortality across all admission groups compared with their low frailty risk counterparts (p < 0.001). However, the high HFRS group had increased odds of overall (ED and in-hospital) all-cause mortality across all admission groups compared with their low frailty risk counterparts (p < 0.001). Looking at the effect size, patients with a high HFRS admitted for AF had the highest odds of overall mortality (aOR 27.14 95% CI 25.03 to 29.43) compared with their low frailty risk counterparts (Figure 3, Table 3).

With HFRS modeled as a continuous variable, increased HFRS was associated with significantly increased odds of hospitalization and ED mortality across all selected CVD admissions per 1-unit increase of the HFRS (all p <0.001) (Supplementary Table 10).

# Discussion

To the best of our knowledge, this is the first national analysis to examine the prevalence, clinical characteristics, cardiovascular phenotypes, and clinical outcomes of patients admitted to ED with a broad range of CVD conditions based on their frailty status. We report several important findings. Frailty is present in a significant proportion of patients with CVD admitted to the ED, with distinct cardiovascular phenotypes according to frailty status. Of the selected CVD diagnoses, ischemic stroke was the most common encounter in the high HFRS group, followed by hemorrhagic stroke and AMI. Cardiac arrest was the most common encounter for the low HFRS group, followed by AF and AMI. Finally, a higher frailty risk is associated with a lower ED mortality and increased admission to hospital and overall mortality across most CVD phenotypes.<sup>13–15</sup>

Previous studies using frailty measures in general populations have estimated the prevalence of frailty to range from 1% to 91%, whereas studies in CVD cohorts have estimated it to range from 15% and 41%.<sup>5,16</sup> This wide range in prevalence may relate to the heterogeneity between frailty measures and heterogenous populations.<sup>17</sup> There are few studies that utilize the HFRS and even fewer that use the HFRS in CVD cohorts, with most focusing on HF, acute coronary syndrome, and postprocedural outcomes from percutaneous coronary intervention or catheter ablation.<sup>7,18-20</sup> A single study used the HFRS in the ED cohort of 12,237 patients.<sup>21</sup> Interestingly, 17.5% of these patients had a high HFRS, 47.9% had an intermediate HFRS, and 34.5% had a low HFRS. However, the study did not investigate CVDspecific encounters but rather evaluated all encounters and only included patients aged over 75 years.<sup>21</sup> Elderly patients tend to be frailer; therefore, the different distribution of HFRS observed in our study may reflect that the nonage-restricted ED population admitted for CVD is less frail.

We report variations in frailty status across the different CVD phenotypes. AF was a rare cause of admission in the high HFRS group but, interestingly, was associated with the worst overall prognosis when accounting for the effect size. AF is associated with increasing age and co-morbidity burden and increases stroke risk.<sup>22–24</sup> Frailty is also linked



Figure 2. Distribution of selected ED cardiovascular admission causes within each HFRS category.

to the development of AF and its sequelae because of an aging myocardium predisposing to alterations of the electrophysiology of the heart and changes in left atrial volume.<sup>23,25</sup> Frailty can be described as a relative contraindication to anticoagulation, depending on the extent of the patient's frailty.<sup>26</sup> Therefore, highly frail patients are less likely to be anticoagulated, leading to the occurrence of thromboembolic complications.<sup>26</sup> Ischemic stroke was the most common cause of encounter in the high and intermediate HFRS groups. Similar to AF, stroke is considered a condition of older age, with 70% of strokes occurring after the age of 65 years.<sup>27</sup> There are no studies describing the prevalence of PE, cardiac arrest, and hemorrhagic stroke stratified by the presence of frailty in the ED setting.

Interestingly, cardiac arrest and had a high proportion of patients at a low or intermediate risk of frailty. This could also be because of potential selection bias, with only the most robust patients that are frail surviving to hospital admission. Cardiac arrest was associated with decreased odds of ED and overall mortality, which could be because of the inherent poor prognosis of the condition, independent of frailty status.  $^{\rm 28-30}$ 

Intermediate and high frailty risks were also highly prevalent among HF encounters. Previous studies have investigated the prevalence of frailty using the HFRS and other risk scores.<sup>6–8,31,32</sup> No studies have used the HFRS to study HF in the ED setting. Regarding in-hospital studies, the reported prevalence of intermediate and high HFRS in HF are variable.<sup>6,7</sup> An HF study of a US cohort estimated the prevalence of intermediate and high HFRS to be 19.9% and 0.1%, respectively, which agreed with an Australian study that reported a similar distribution and contrasts with another hospital study of Medicare beneficiaries who reported a prevalence of 47.4% and 25.0% for intermediate and high HFRS, respectively.<sup>6,7,33</sup> However, these variations may be explained because of the varying inclusion criteria for the studies (e.g., patients over the age of 65 years or insurers for specific at-risk patient groups).

There are several important clinical implications of this study. First, this study reaffirms that frailty represents a significant proportion of patients seen in ED, with over 40% of

Table 3

Adjusted odds of hospitalization, emergency department mortality and overall mortality in different hospital frailty risk score categories and selected emergency department cardiovascular admission diagnoses

Admission Diagnosis		Hospital Frailty Risk Score				
		Intermediate 5-15 (35.5%)		High >15 (4.8%)		
		aOR	P-value	aOR	P-value	
Acute myocardial infarction	Hospitalization	4.47 [4.41-4.54]	< 0.001	28.40 [25.09-32.14]	< 0.001	
(N = 1,796,127)	ED mortality	0.41 [0.39-0.44]	< 0.001	0.06 [0.04-0.11]	< 0.001	
	<b>Overall mortality</b>	4.10 [4.02-4.18]	< 0.001	5.69 [5.48-5.91]	< 0.001	
Ischemic stroke	Hospitalization	5.71 [5.65-5.77]	< 0.001	40.35 [39.11-41.63]	< 0.001	
(N =1,662,442)	ED mortality	0.36 [0.31-0.41]	< 0.001	0.12 [0.09-0.16]	< 0.001	
	Overall mortality	3.83 [3.67-4.00]	< 0.001	9.83 [9.42-10.26]	< 0.001	
Atrial fibrillation/flutter	Hospitalization	4.41 [4.37-4.45]	< 0.001	23.22 [21.66-24.89]	< 0.001	
(N =2,056,294)	ED mortality	1.79 [1.51-2.13]	< 0.001	0.11 [0.02-0.79]	< 0.001	
	Overall mortality	8.38 [7.91-8.89]	< 0.001	27.14 [25.03-29.43]	< 0.001	
Heart failure	Hospitalization	7.06 [6.98-7.13]	< 0.001	48.68 [44.12-53.70]	< 0.001	
(N =1,483,837)	ED mortality	0.74 [0.66-0.84]	< 0.001	0.24 [0.11-0.50]	< 0.001	
	<b>Overall mortality</b>	5.65 [5.45-5.86]	< 0.001	13.71 [12.95-14.51]	< 0.001	
Pulmonary Embolism	Hospitalization	4.61 [4.51-4.71]	< 0.001	28.44 [22.94-35.26]	< 0.001	
(N=627,547)	ED mortality	0.40 [0.34-0.47]	< 0.001	0.17 [0.06-0.46]	< 0.001	
	<b>Overall mortality</b>	5.61 [5.38-5.86]	< 0.001	10.98 [10.16-11.87]	< 0.001	
Cardiac arrest	Hospitalization	40.64 [39.22-42.12]	< 0.001	42.01 [35.19-49.21]	< 0.001	
(N=495,406)	ED mortality	0.12 [0.11-0.12]	< 0.001	0.02 [0.01-0.03]	< 0.001	
	Overall mortality	0.43 [0.42-0.45]	< 0.001	0.20 [0.18-0.22]	< 0.001	
Haemorrhagic stroke	Hospitalization	8.35 [8.20-8.50]	< 0.001	59.14 [57.32-61.03]	< 0.001	
(N =458,987)	ED mortality	0.30 [0.28-0.32]	< 0.001	0.04 [0.03-0.05]	< 0.001	
	<b>Overall mortality</b>	2.79 [2.73-2.86]	< 0.001	2.01 [1.95-2.08]	< 0.001	

Reference group is low HFRS score <5 for each CVD admission diagnosis.

Multivariable logistic regression model adjusted for: age, sex, weekend admission, primary expected payer, median household income, region and teaching status of the hospital, dyslipidemia, smoking, thrombocytopenia, previous AMI, anemia, coagulopathies, liver disease, diabetes, hypertension, malignancy, peripheral vascular disease, chronic pulmonary disease, chronic renal disease and valvular heart diseases.

aOR = adjusted odds ratio; CI = confidence interval; ED = emergency department; HFRS = hospital Frailty Risk Score.

patients at either intermediate or high risk of frailty. This outlines the importance of a frailty assessment in the ED, where the HFRS can assist in highlighting at-risk patients.<sup>34-36</sup> Frailty and CVD are closely related; the increasing age of the population and an improved survivorship of patients with acute and chronic CVD leads to the coexistence of CVD and frailty.<sup>37,38</sup> CVD and frailty share a bidirectional relation, with frailty associated with increased odds of CVD and vice versa.<sup>5</sup> It is important to identify patients at risk of frailty for appropriate management to prevent adverse complications and improve quality of life.<sup>39</sup> Moreover, frailty can be reversed, exemplifying the need for early identification and optimization of risk factors.<sup>40</sup> Second, the coexistence of frailty and co-morbidity among patients with CVD represents a challenge for health care services through increased length of stay, total costs, readmissions, and mortality. Knowledge of the trends and outcomes of CVD in frail patients is important to deliver improved care for this at-risk group. Finally, this study prompts the early recognition and management of CVD and frailty in the community, which could have an impact on acute and unplanned encounters.<sup>41</sup> The HFRS could be used as an automated tool to flag patients at a higher risk of frailty directly from their electronic health records. Flagged patients can be prioritized for further clinical assessment and optimization of risk factors.

This study includes several limitations inherent to the NEDS database. First, coded databases are susceptible to selection bias because of missing data, miscoding, and misdiagnosis. Second, given that this is an observational study, confounding bias could not be eliminated, despite the broad range of conditions covered by the NEDS. Third, useful clinical information that could provide a more granular analysis, such as race and pharmacologic management of patients, are not available in the NEDS. Most notably, previous studies have demonstrated that race and ethnicity are factors associated with inequality in access to care and increase risk of frailty.<sup>42,43</sup> Fourth, this analysis was based on US data, which cannot be generalized to other countries and health settings. Finally, a detailed analysis of longitudinal outcomes could not be assessed because the NEDS captures ED and in-hospital outcomes only.

In conclusion, ED encounters for CVD vary by frailty status, with ischemic stroke being the most common cause in high-risk patients, followed by hemorrhagic stroke and AMI, and cardiac arrest is the most common encounter in low-risk patients, followed by AF and AMI. Patient encounters for CVD in the ED have a high frailty burden, which is associated with a worse prognosis, including the highest overall mortality in patients with high HFRS, across most CVD phenotypes. Future studies are warranted to define the



Figure 3. Adjusted ED mortality rates for different frailty risk category and selected ED cardiovascular admission causes\*. (*A*) ED mortality, (*B*) Overall mortality. \*Reference group is low HFRS score <5 for each CVD admission diagnosis. Multivariable logistic regression model adjusted for: age, gender, weekend admission, primary expected payer, median household income, region and teaching status of the hospital, dyslipidemia, smoking, thrombocytopenia, previous AMI, anemia, coagulopathies, liver disease, diabetes, malignancy, peripheral vascular disease, chronic pulmonary disease, chronic renal disease and valvular heart diseases.

longitudinal association between frailty and mortality in this setting.

# **Declaration of Competing Interest**

The authors have no competing interests to declare.

### Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j. amjcard.2023.08.138.

- Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med* 2011;27:1–15.
- Ramsay SE, Arianayagam DS, Whincup PH, Lennon LT, Cryer J, Papacosta AO, Iliffe S, Wannamethee SG. Cardiovascular risk profile and frailty in a population-based study of older British men. *Heart* 2015;101:616–622.
- Stewart R. Cardiovascular disease and frailty: what are the mechanistic links? *Clin Chem* 2019;65:80–86.
- Wilkes JG, Evans JL, Prato BS, Hess SA, MacGillivray DC, Fitzgerald TL. Frailty cost: economic impact of frailty in the elective surgical patient. J Am Coll Surg 2019;228:861–870.
- Veronese N, Cereda E, Stubbs B, Solmi M, Luchini C, Manzato E, Sergi G, Manu P, Harris T, Fontana L, Strandberg T, Amieva H,

Dumurgier J, Elbaz A, Tzourio C, Eicholzer M, Rohrmann S, Moretti C, D'Ascenzo F, Quadri G, Polidoro A, Lourenço RA, Moreira VG, Sanchis J, Scotti V, Maggi S, Correll CU. Risk of cardiovascular disease morbidity and mortality in frail and pre-frail older adults: results from a meta-analysis and exploratory meta-regression analysis. *Ageing Res Rev* 2017;35:63–73.

- Kundi H, Wadhera RK, Strom JB, Valsdottir LR, Shen C, Kazi DS, Yeh RW. Association of frailty with 30-day outcomes for acute myocardial infarction, heart failure, and pneumonia among elderly adults. *JAMA Cardiol* 2019;4:1084–1091.
- Kwok CS, Zieroth S, Van Spall HGC, Helliwell T, Clarson L, Mohamed M, Mallen C, Duckett S, Mamas MA. The Hospital Frailty Risk Score and its association with in-hospital mortality, cost, length of stay and discharge location in patients with heart failure short running title: frailty and outcomes in heart failure. *Int J Cardiol* 2020;300:184–190.
- Sokhal BS, Matetić A, Rashid M, Protheroe J, Partington R, Mallen C, Mamas MA. Association of frailty status on the causes and outcomes of patients admitted with cardiovascular disease. *Am J Cardiol* 2023;192:7–15.
- Nationwide Emergency Department Sample (NEDS) under the Healthcare Cost and Utilization Project (HCUP), 2011, Agency for Healthcare Research and Quality; Rockville, MD. Available at: https://hcup-us.ahrq. gov/nedsoverview.jsp. Accessed on July 24, 2023.
- 10. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, Arora S, Street A, Parker S, Roberts HC, Bardsley M, Conroy S. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet* 2018;391:1775–1782.

- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Epidemiology* 2007;18:800– 804.
- NHS. NHS core surgical training portfolio requirements 2022. Available at: https://medical.hee.nhs.uk/medical-training-recruitment/medical-specialty-training/surgery/core-surgery/core-surgical-training-self-assessmentscoring-guidance-for-candidates. Accessed on July 24, 2023.
- Anand T, Khurrum M, Chehab M, Bible L, Asmar S, Douglas M, Ditillo M, Gries L, Joseph B. Racial and ethnic disparities in frail geriatric trauma patients. *World J Surg* 2021;45:1330–1339.
- Keeble E, Roberts HC, Williams CD, Van Oppen J, Conroy SP. Outcomes of hospital admissions among frail older people: a 2-year cohort study. *Br J Gen Pract* 2019;69:e555–e560.
- Limpawattana P, Phungoen P, Mitsungnern T, Laosuangkoon W, Tansangworn N. Atypical presentations of older adults at the emergency department and associated factors. *Arch Gerontol Geriatr* 2016;62:97–102.
- O'Caoimh R, Sezgin D, O'Donovan MR, Molloy DW, Clegg A, Rockwood K, Liew A. Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies. *Age Ageing* 2021;50:96–104.
- Faller JW, Pereira DDN, de Souza S, Nampo FK, Orlandi FS, Matumoto S. Instruments for the detection of frailty syndrome in older adults: A systematic review. *PLoS One* 2019;14:e0216166.
- McAlister FA, Savu A, Ezekowitz JA, Armstrong PW, Kaul P. The hospital frailty risk score in patients with heart failure is strongly associated with outcomes but less so with pharmacotherapy. *J Intern Med* 2020;287:322–332.
- Kwok CS, Lundberg G, Al-Faleh H, Sirker A, Van Spall HGC, Michos ED, Rashid M, Mohamed M, Bagur R, Mamas MA. Relation of frailty to outcomes in patients with acute coronary syndromes. *Am J Cardiol* 2019;124:1002–1011.
- 20. Kilkenny MF, Phan HT, Lindley RI, Kim J, Lopez D, Dalli LL, Grimley R, Sundararajan V, Thrift AG, Andrew NE, Donnan GA, Cadilhac DA, Stroke123 Investigators and the AuSCR Consortium. Utility of the hospital frailty risk score derived from administrative data and the association with stroke outcomes. *Stroke* 2021;52:2874–2881.
- Alshibani A, Coats T, Maynou L, Lecky F, Banerjee J, Conroy S. A comparison between the clinical frailty scale and the hospital frailty risk score to risk stratify older people with emergency care needs. *BMC Emerg Med* 2022;22:171.
- Staerk L, Sherer JA, Ko D, Benjamin EJ, Helm RH. Atrial fibrillation: epidemiology, pathophysiology, and clinical outcomes. *Circ Res* 2017;120:1501–1517.
- Guo Q, Du X, Ma CS. Atrial fibrillation and frailty. J Geriatr Cardiol 2020;17:105–109.
- Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;98:946–952.
- Triposkiadis F, Xanthopoulos A, Butler J. Cardiovascular aging and heart failure: JACC review topic of the week. J Am Coll Cardiol 2019;74:804–813.
- 26. Presta R, Brunetti E, Polidori MC, Bo M. Impact of frailty models on the prescription of oral anticoagulants and on the incidence of stroke, bleeding, and mortality in older patients with atrial fibrillation: a systematic review. *Ageing Res Rev* 2022;82:101761.
- Kelly-Hayes M. Influence of age and health behaviors on stroke risk: lessons from longitudinal studies. J Am Geriatr Soc 2010;58(suppl 2): S325–S328.
- Andersen LW, Holmberg MJ, Berg KM, Donnino MW, Granfeldt A. In-hospital cardiac arrest: a review. JAMA 2019;321:1200–1210.
- Myat A, Song KJ, Rea T. Out-of-hospital cardiac arrest: current concepts. *Lancet* 2018;391:970–979.
- van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral

haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol* 2010;9:167–176.

- 31. Martín-Sánchez FJ, Rodríguez-Adrada E, Mueller C, Vidán MT, Christ M, Frank Peacock W, Rizzi MA, Alquezar A, Piñera P, Aragues PL, Llorens P, Herrero P, Jacob J, Fernández C, Miró Ò. The Effect of frailty on 30-day mortality risk in older patients with acute heart failure attended in the emergency department. *Acad Emerg Med* 2017;24:298–307.
- 32. Vidán MT, Blaya-Novakova V, Sánchez E, Ortiz J, Serra-Rexach JA, Bueno H. Prevalence and prognostic impact of frailty and its components in non-dependent elderly patients with heart failure. *Eur J Heart Fail* 2016;18:869–875.
- 33. Sharma Y, Horwood C, Hakendorf P, Shahi R, Thompson C. External validation of the hospital frailty-risk score in predicting clinical outcomes in older heart-failure patients in Australia. J Clin Med 2022;11:2193.
- Jørgensen R, Brabrand M. Screening of the frail patient in the emergency department: A systematic review. *Eur J Intern Med* 2017;45:71–73.
- Elliott A, Hull L, Conroy SP. Frailty identification in the emergency department-a systematic review focusing on feasibility. *Age Ageing* 2017;46:509–513.
- **36.** Alakare J, Kemp K, Strandberg T, Castrén M, Jakovljević D, Tolonen J, Harjola VP. Systematic geriatric assessment for older patients with frailty in the emergency department: a randomised controlled trial. *BMC Geriatr* 2021;21:408.
- 37. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, Bonny A, Brauer M, Brodmann M, Cahill TJ, Carapetis J, Catapano AL, Chugh SS, Cooper LT, Coresh J, Criqui M, DeCleene N, Eagle KA, Emmons-Bell S, Feigin VL, Fernández-Solà J, Fowkes G, Gakidou E, Grundy SM, He FJ, Howard G, Hu F, Inker L, Karthikeyan G, Kassebaum N, Koroshetz W, Lavie C, Lloyd-Jones D, Lu HS, Mirijello A, Temesgen AM, Mokdad A, Moran AE, Muntner P, Narula J, Neal B, Ntsekhe M, Moraes de Oliveira G, Otto C, Owolabi M, Pratt M, Rajagopalan S, Reitsma M, Ribeiro ALP, Rigotti N, Rodgers A, Sable C, Shakil S, Sliwa-Hahnle K, Stark B, Sundström J, Timpel P, Tleyjeh IM, Valgimigli M, Vos T, Whelton PK, Yacoub M, Zuhlke L, Murray C, Fuster V, GBD-NHLBI-JACC Global Burden of Cardiovascular Diseases Writing Group. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 study. J Am Coll Cardiol 2020;76:2982-3021.
- 38. Ofori-Asenso R, Chin KL, Mazidi M, Zomer E, Ilomaki J, Zullo AR, Gasevic D, Ademi Z, Korhonen MJ, LoGiudice D, Bell JS, Liew D. Global incidence of frailty and prefrailty among community-dwelling older adults: a systematic review and meta-analysis. *JAMA Netw Open* 2019;2:e198398.
- 39. Rowe R, Iqbal J, Murali-Krishnan R, Sultan A, Orme R, Briffa N, Denvir M, Gunn J. Role of frailty assessment in patients undergoing cardiac interventions. *Open Heart* 2014;1:e000033.
- 40. Ijaz N, Buta B, Xue QL, Mohess DT, Bushan A, Tran H, Batchelor W, deFilippi CR, Walston JD, Bandeen-Roche K, Forman DE, Resar JR, O'Connor CM, Gerstenblith G, Damluji AA. Interventions for frailty among older adults with cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol 2022;79:482–503.
- Downing J, Rose TC, Saini P, Matata B, McIntosh Z, Comerford T, Wilson K, Pemberton A, Harper LM, Shaw M, Daras K, Barr B. Impact of a community-based cardiovascular disease service intervention in a highly deprived area. *Heart* 2020;106:374–379.
- 42. Javed Z, Haisum Maqsood M, Yahya T, Amin Z, Acquah I, Valero-Elizondo J, Andrieni J, Dubey P, Jackson RK, Daffin MA, Cainzos-Achirica M, Hyder AA, Nasir K. Race, racism, and cardiovascular health: applying a social determinants of health framework to racial/ ethnic disparities in cardiovascular disease. *Circ Cardiovasc Qual Outcomes* 2022;15:e007917.
- 43. Hirsch C, Anderson ML, Newman A, Kop W, Jackson S, Gottdiener J, Tracy R, Fried LP, Cardiovascular Health Study Research Group. The association of race with frailty: the cardiovascular health study. *Ann Epidemiol* 2006;16:545–553.