



ARTICLE

The impact of frailty on in-hospital outcomes in patients with HFrEF

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Abstract

Frailty is a marker of poor prognosis and is often undertreated and predisposed to adverse outcomes. This study aimed to determine the association between frailty and outcomes in hospitalized patients with heart failure with reduced ejection fraction (HFrEF). A retrospective cross-sectional analysis of the National Inpatient Sample (2016-2020) was conducted to evaluate hospitalizations for HFrEF. Frailty was defined as a hospital frailty risk score of ≥ 5 . Patient demographics, comorbidities, and hospital characteristics were compared between frail and non-frail groups. Multivariable logistic regression, adjusted for confounders, was used to assess the association between frailty and in-hospital outcomes. Among 5,526,303 weighted HFrEF hospitalizations, 53% ($n=2,931,329$) were classified as frail. Frail patients had a median age of 74 years vs 67 years in non-frail patients. In-hospital mortality was 5.9% in frail vs 1.2% in non-frail patients (adjusted OR [aOR]: 3.8; 95% CI: 3.68-3.92). Adverse events were significantly higher in the frail group, including cardiogenic shock (5.3% vs 2.1%; aOR: 2.58), acute stroke (4.5% vs 0.8%; aOR: 6.63), acute kidney injury (47.8% vs 12.5%; aOR: 5.16), sepsis (13.4% vs 1.6%; aOR: 11.00), major bleeding (4.2% vs 2.0%; aOR: 1.90), acute pulmonary edema (0.47% vs 0.31%; aOR: 1.60), and mechanical ventilation (8.1% vs 1.7%; aOR: 5.33). Additionally, non-home discharge occurred more frequently (35.4% vs 15%; aOR: 2.77), with higher median hospital costs (\$46,706 vs \$34,793) and prolonged length of stay (5 vs 3 days). Frailty is independently associated with worse in-hospital outcomes in HFrEF patients, underscoring the need for targeted strategies to improve care in this high-risk population.

Key words: frailty; heart failure with reduced ejection fraction (HFrEF).

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Introduction

Heart failure (HF) remains a significant public health challenge in the United States (U.S.), affecting approximately 6.7 million Americans over the age of 20, with projections rising to 8.7 million by 2030. Among its subtypes, heart failure with reduced ejection fraction (HFrEF) accounts for 40% to 50% of all cases.¹

Frailty is a prevalent but often underrecognized contributor to adverse outcomes in HF. It reflects a diminished physiological reserve resulting from age-related decline, comorbidities, chronic inflammation, symptomatic burden, nutritional deficits, and cognitive impairment.² Despite their higher clin-

ical vulnerability, frail patients with HFrEF are often undertreated due to concerns about medication-related adverse effects. As a result, fewer than 40% of patients receive guideline-directed medical therapy (GDMT), and those who do are often prescribed suboptimal doses.^{3,4}

While frailty is widely acknowledged as a poor prognostic indicator, its incorporation into routine HF management remains inconsistent. Moreover, large-scale investigations assessing its impact on in-hospital outcomes remain limited. This study aims to evaluate the impact of frailty on outcomes in patients with HFrEF, utilizing nationally representative data to enhance clinical understanding and guide future management strategies for this vulnerable population.

Methods

Study design and data source

This study is a retrospective, cross-sectional analysis of inpatient admissions for HFREF using data from the NIS database, spanning from January 1, 2016, to December 31, 2020. The NIS, a part of the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ), is the largest publicly available database of inpatient healthcare records in the U.S.⁵ This database represents approximately 20% of all U.S. hospitalizations, recording over 7 million un-weighted cases annually. When weighted appropriately, the database provides estimates of approximately 35 million hospitalizations each year. The dataset includes both patient and hospital-level information from over 4,500 hospitals across 48 states. Each hospitalization includes up to 40 discharge diagnoses and 25 procedures, documented using International Classification of Diseases, 10th Revision (ICD-10) diagnostic codes, providing a comprehensive record of clinical events and interventions. As data are de-identified and publicly available, this study is exempted from approval by the institutional review board. This study conforms to the NIS data-use agreement with HCUP.



Figure 1. Reported numbers based on survey-weighted analysis.

Study population

HFREF hospitalizations were identified in the database using ICD-10 diagnostic codes: I50.20, I50.21, I50.22, and I50.23. The cohort was further categorized into patients with or without frailty. Individuals without complete data on main study variables and outcomes were excluded using listwise deletion. Patients under the age of 20 years were also excluded from this study (Figure 1). Baseline demographic characteristics, including age, sex and race, are available in the dataset. Comorbidities were identified from the database using ICD-10 diagnostic codes and Charlson comorbidities as reported in the HCUP dataset (Supplementary Table 1).

Definition of frailty

To define frailty, we adopted the hospital frailty risk score (HFRS), a previously developed algorithm by Gilbert et al. for identifying frailty traits in electronic databases.⁶ The HFRS, derived from both primary and secondary ICD-10 codes, is advantageous as it can be applied wherever ICD-10 coding systems are in use. This algorithm has been validated and is being increasingly utilized in multiple countries across various clinical settings.⁷⁻⁹ In the present study, patients with an HFRS ≥ 5 were classified as frail, while those with an HFRS < 5 were considered nonfrail. The codes used to assess HFRS are summarized in Supplementary Table 2.

Study outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included cardiogenic shock, acute stroke, acute kidney injury, sepsis, major bleeding, acute pulmonary edema, mechanical ventilation, discharge disposition, total hospital cost and prolonged length of stay, defined as $> 75^{\text{th}}$ length of stay.

Statistical analysis

Continuous variables were reported as mean \pm SD or median with interquartile range (IQR) and compared using linear regression for weighted estimates. Categorical variables were expressed as proportions and analyzed using Pearson's chi-square test.

A multivariable logistic regression model was constructed to assess the association of frailty with in-hospital outcomes, adjusting for i) patient-level factors: age, sex, race, income quartile, primary payer, and comorbidities including hypertension, diabetes, ischemic heart disease, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, hyperlipidemia, anemia, and obstructive sleep apnea, and Elixhauser Comorbidity Index score;¹⁰ and ii) hospital-level characteristics: bed size, location/teaching status, and geographic region. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Multicollinearity was assessed using variance inflation factors, all of which were found to be < 5 .

Survey-weighted analysis was performed to generate nationally representative estimates using discharge weights from the NIS database. Inflation-adjusted total hospital costs were calculated using cost-to-charge ratios from the HCUP database. A p -value of < 0.05 was considered statistically significant. All statistical analyses were conducted using Stata v17.0 (StataCorp, College Station, TX, USA).

Table 1. Baseline characteristics of HFREF patients identified as frail vs nonfrail.

Study variables	Total (n=5,526,303)	Frail (n=2,931,329)	Nonfrail (n=2,594,974)	p-value
Age, median (IQR)	71.0 (60.0-81.0)	74.0 (63.0-83.0)	67.0 (57.0-78.0)	<0.001
Age groups				<0.001
20–39	139,100 (2.5)	51,125 (1.7)	87,975 (3.4)	
40–59	910,250 (16.5)	363,295 (12.4)	546,955 (21.1)	
60–79	2,150,949 (39.0)	1,119,200 (38.2)	1,031,750 (39.8)	
80 +	2,326,004 (42.1)	1,397,709 (47.7)	928,295 (35.8)	
Sex				<0.001
Male	3,520,419 (63.7)	1,814,610 (62.0)	1,705,810 (65.7)	
Female	2,005,329 (36.3)	1,116,430 (38.1)	888,900 (34.3)	
Race				<0.001
White	3,596,784 (66.7)	1,952,874 (68.3)	1,643,909 (65.0)	
Black	1,042,630 (19.3)	519,450 (18.2)	523,180 (20.7)	
Hispanic	459,500 (8.5)	233,670 (8.1)	225,830 (8.9)	
Others	289,765 (5.3)	151,825 (5.3)	137,940 (5.4)	
Missing				
Median household income				<0.001
Quartile1 (\$1-\$51,999)	182,7714 (33.8)	947,660 (33.0)	880,055 (34.7)	
Quartile2 (\$52,000 - \$65,999)	1,453,775 (26.8)	770,570 (26.8)	683,205 (27.0)	
Quartile3 (\$66,000 - \$87,999)	1,210,225 (22.3)	650,850 (22.6)	559,375 (22.0)	
Quartile4 (\$88,000 or more)	923,575 (17.1)	507,825 (17.7)	415,750 (16.4)	
Missing				
Expected primary payer				<0.001
Medicare	3,797,654 (68.8)	2,199,644 (75.1)	1,598,009 (61.7)	
Medicaid	633,785 (11.5)	270,130 (9.2)	363,655 (14.0)	
Private	773,680 (14.0)	329,005 (11.2)	444,675 (17.2)	
Self-pay, none, other	314,670 (5.7)	129,480 (4.4)	185,190 (7.1)	
Elixhauser groups*				<0.001
<4	616,060 (11.1)	137,875 (4.7)	478,185 (18.4)	
4-6	3,066,904 (55.5)	1,445,485 (49.3)	1,621,419 (62.5)	
>6	1,843,339 (33.4)	1,347,970 (46.0)	495,370 (19.1)	
Comorbidities				
Hypertension	4,373,754 (79.1)	2,321,540 (79.2)	2,052,215 (79.1)	0.371
Diabetes mellitus	2,472,844 (44.7)	1,397,955 (47.7)	1,074,890 (41.1)	<0.001
Obesity	215,830 (20.0)	112,895 (18.7)	102,935 (21.8)	<0.001
Chronic IHD	3,402,779 (61.6)	1,818,260 (62.0)	1,584,520 (61.1)	<0.001
Atrial fibrillation / flutter	2,381,514 (43.1)	1,347,329 (46.0)	1,034,185 (40.0)	<0.001
CKD	2,387,654 (43.2)	1,655,435 (56.5)	732,220 (28.2)	<0.001
COPD	1,645,334 (29.8)	935,995 (32.0)	709,340 (27.3)	<0.001
Hyperlipidemia	2,968,174 (53.7)	1,578,695 (54.0)	1,389,480 (53.5)	0.021
Anemia	381,235 (7.0)	241,085 (8.2)	140,150 (5.4)	<0.001
Obstructive sleep apnea	661,660 (12.0)	345,025 (11.8)	316,635 (12.2)	<0.001
Hospital bed size				0.063
Small	1,047,943 (19.0)	555,694 (19.0)	492,249 (19.0)	
Medium	1,591,974 (28.8)	849,739 (29.0)	742,234 (28.6)	
Large	2,886,386 (52.2)	1,525,896 (52.1)	1,360,491 (52.4)	
Hospital location/teaching status				0.014
Rural	494,450 (9.0)	259,515 (8.8)	234,935 (9.0)	
Urban nonteaching	1,147,010 (20.8)	612,895 (21.0)	534,115 (20.6)	
Urban teaching	3,884,844 (70.3)	2,058,919 (70.2)	1,825,924 (70.4)	
Hospital region				<0.001
Northeast	1,036,875 (18.8)	531,765 (18.1)	505,110 (19.5)	
Midwest	1,104,900 (20.0)	610,145 (20.8)	494,755 (19.1)	
South	2,340,200 (42.3)	1,228,660 (42.0)	1,111,540 (42.8)	
West	1,044,329 (19.0)	560,759 (19.1)	483,569 (18.6)	

*Elixhauser comorbidity index is a method of categorizing comorbidities of patients based on ICD diagnosis codes found in administrative data; Group <4 represents patients with fewer than 4 comorbidities, Groups 4-6 includes patients with four to six comorbidities and >6 comprises patients with more than six comorbidities. Values are n (%) unless otherwise indicated. All values are survey-weighted national estimates. IHD, ischemic heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

Table 2. In-hospital outcomes of HFREF patients by frailty status.

Outcomes	Total (n=5,526,303)	Frail (n=2,931,329)	Nonfrail (n=2,594,974)	p-value
In-hospital mortality	205,010 (3.7)	172,035 (5.9)	32,975 (1.2)	<0.001
Cardiogenic shock	210,195 (3.8)	154,700 (5.3)	55,495 (2.1)	<0.001
Acute stroke (hemorrhagic or ischemic)	153,495 (2.9)	131,035 (4.5)	22,460 (0.8)	<0.001
Acute kidney injury	1,725,800 (31.2)	1,401,755 (47.8)	324,045 (12.5)	<0.001
Sepsis	434,615 (7.8)	393,715 (13.4)	40,900 (1.6)	<0.001
Major bleeding	176,155 (3.2)	123,650 (4.2)	52,505 (2.0)	<0.001
Acute pulmonary edema	21,890 (0.40)	13,825 (0.47)	8,065 (0.31)	<0.001
Mechanical ventilation	285,865 (5.1)	239,745 (8.1)	46,120 (1.7)	<0.001
Discharge disposition				<0.001
Home	3,954,289 (74.3)	1,781,285 (64.6)	2,173,004 (85.0)	
Short term care facility	185,350 (3.5)	96,980 (3.5)	88,370 (3.4)	
Long term care facility	1,083,710 (20.4)	839,825 (30.5)	243,885 (9.5)	
Left against medical advise	94,175 (1.7)	39,270 (1.4)	54,905 (2.1)	
Total charges (\$), median (IQR)	40,679 (21,840–82,033)	46,706 (25,117–93,850)	34,793 (18,973–69,155)	<0.001
Length of stay (days), median (IQR)	4 (2-7)	5 (3-9)	3 (2-5)	<0.001

Hospital costs were inflation-adjusted to 2020 USD using HCUP cost-to-charge ratios. All values are survey-weighted national estimates. IQR, interquartile range.

Results

Baseline characteristics

Between 2016 and 2020, a total of 5,526,303 weighted hospitalizations for HFREF were identified, of which 2,931,329 (53%) were classified as frail. Frail patients were older than nonfrail patients, with a median age of 74 (63 to 83) years, compared to 67 (57 to 78) years in nonfrail patients ($p<0.001$). Males comprised 62.0% of frail patients vs 65.7% of nonfrail patients ($p<0.001$). Frail patients were more likely to have Medicare as their primary payer (75.1% vs 61.7%, $p<0.001$). Clinically, frail patients had a higher prevalence of diabetes (47.7% vs. 41.1%, $p<0.001$), atrial fibrillation/flutter (46.0% vs 40.0%, $p<0.001$), chronic kidney disease (56.5% vs 28.2%, $p<0.001$), and a higher Elixhauser Comorbidity Index score ($p<0.001$). In terms of hospital distribution, significant differences existed for hospital location or teaching status ($p<0.001$) and hospital region ($p<0.001$). The remaining baseline characteristics are detailed in Table 1.

Outcomes

The overall in-hospital mortality rate among patients with HFREF was 3.7% (205,010 admissions), with frail patients experiencing significantly higher mortality rates compared to nonfrail individuals (5.9% vs 1.2%, $p<0.001$). Multivariable logistic regression confirmed frailty as an independent predictor of in-hospital mortality, with frail patients having 3.8 times higher odds of mortality (aOR: 3.8; 95% CI: 3.68-3.92; $p<0.001$).

Frailty was also associated with significantly increased risks across multiple adverse clinical outcomes in patients with HFREF. Cardiogenic shock was more frequent among frail indi-

viduals, occurring in 5.3% of cases compared to 2.1% in nonfrail patients ($p<0.001$) (aOR: 2.58; 95% CI: 2.51-2.65; $p<0.001$). Similarly, acute stroke was observed at a higher rate in frail patients (4.5% vs 0.8%, $p<0.001$), (aOR: 6.63; 95% CI: 6.38-6.90; $p<0.001$). Acute kidney injury followed the same pattern, occurring in 47.8% of frail individuals compared to 12.5% of nonfrail patients ($p<0.001$), (aOR: 5.16; 95% CI: 5.10-5.22; $p<0.001$).

The likelihood of sepsis was also markedly elevated in frail patients, occurring in 13.4% compared to 1.6% in nonfrail individuals ($p<0.001$), (aOR: 11.00; 95% CI: 10.64-11.24; $p<0.001$). Additionally, frail patients demonstrated a greater risk of major bleeding (4.2% vs 2.0%, $p<0.001$), (aOR: 1.90; 95% CI: 1.84-1.95; $p<0.001$) and acute pulmonary edema (0.47% vs 0.31%, $p<0.001$), (aOR: 1.60; 95% CI: 1.48-1.72; $p<0.001$).

The need for mechanical ventilation was substantially greater among frail patients with HFREF, occurring in 8.1% of cases compared to 1.7% in nonfrail individuals ($p<0.001$). After adjusting for confounders, frail patients exhibited significantly increased odds of requiring mechanical ventilation during hospitalization (aOR: 5.33; 95% CI: 5.18-5.48; $p<0.001$). Discharge to locations other than home was also significantly more common among frail patients with HFREF compared to nonfrail individuals (35.4% vs 15%, $p<0.001$), (aOR: 2.77; 95% CI: 2.75-2.80; $p<0.001$).

Hospitalization costs were notably higher among frail patients with HFREF, with a median total charge of \$46,706 ± \$34,733, compared to \$34,793 ± \$25,820 in nonfrail individuals ($p<0.001$). The length of stay was similarly prolonged, with frail patients spending a median of 5±6 days in the hospital, while nonfrail individuals had a shorter stay of 3±3 days ($p<0.001$). Detailed results are available in Table 2, with aORs available in Table 3.

Table 3. Association of frailty with in-hospital outcomes in hospitalized patients HF_rEF.

In-hospital outcomes	Adjusted odds ratio*	95% Confidence interval	p-value
In-hospital mortality	3.80	3.68-3.92	<0.001
Cardiogenic shock	2.58	2.51-2.65	<0.001
Acute stroke	6.63	6.38-6.90	<0.001
Acute kidney injury	5.16	5.10-5.22	<0.001
Sepsis	11.00	10.64-11.24	<0.001
Major bleeding	1.90	1.84-1.95	<0.001
Acute pulmonary edema	1.60	1.48-1.72	<0.001
Mechanical ventilation	5.33	5.18-5.48	<0.001
Non-home discharge	2.77	2.75-2.80	<0.001

*Based on multivariable logistic regression model adjusted for age, sex, race, income quartile, primary payer, hypertension, diabetes, ischemic heart disease, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease, hyperlipidemia, anemia, and obstructive sleep apnea, and Elixhauser comorbidity index score, hospital bed size, hospital location/teaching status, and hospital geographic region.

Discussion

This large-scale nationwide study evaluates the impact of frailty on hospital outcomes among patients hospitalized with HF_rEF (Figure 2). By analyzing 5.5 million weighted hospitalizations from 2016 to 2020, our study provides key insights into how frail patients compare to their nonfrail counterparts in terms of in-hospital mortality, total hospital costs, length of stay, and other major complications. Frail patients faced markedly higher odds of in-hospital mortality, cardiogenic shock, and acute stroke

while also being at a substantially greater risk for complications such as acute kidney injury, sepsis, major bleeding, and acute pulmonary edema. They were also more likely to require mechanical ventilation, indicating a higher severity of illness. This may explain why frail patients were observed to have longer hospital stays and higher healthcare costs. Furthermore, they were far less likely to be discharged home. These findings highlight the association of frailty with clinical outcomes in hospitalized HF_rEF patients and emphasize the need for targeted interventions to improve their prognosis.

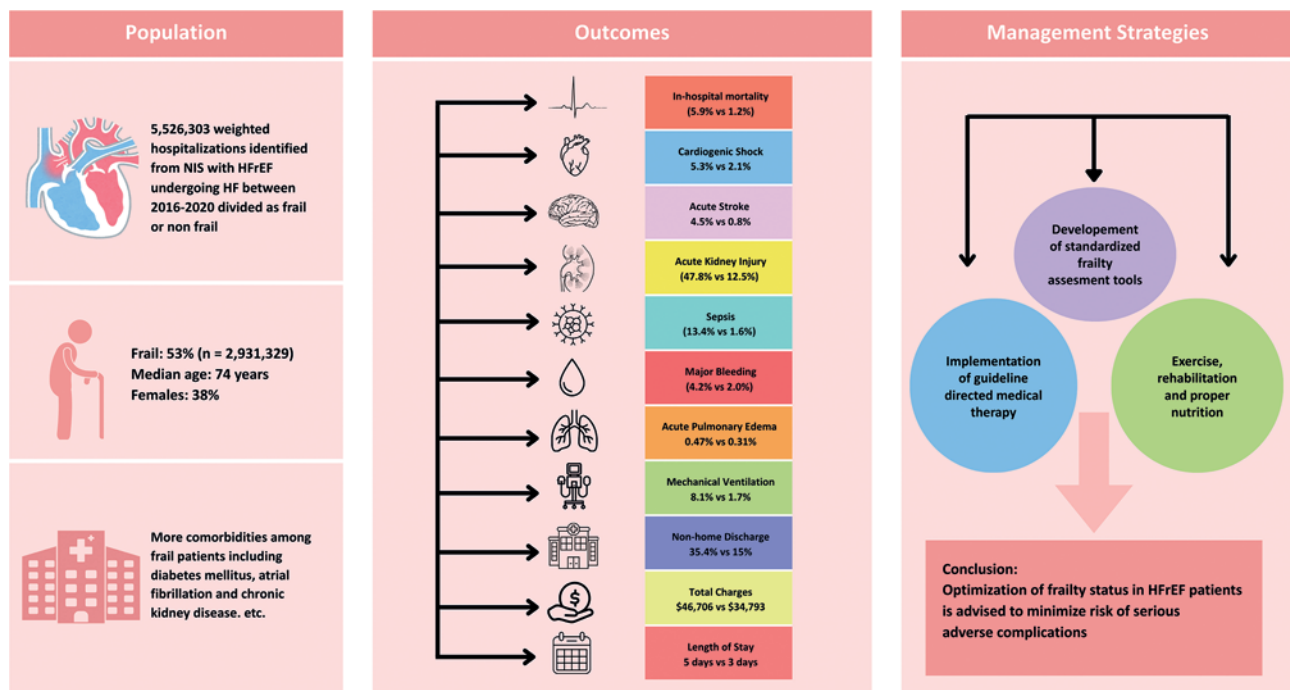


Figure 2. Impact of frailty on patients with underlying HF_rEF. Frailty is independently associated with worse in-hospital outcomes, including significantly higher odds of mortality (aOR: 3.8), acute kidney injury (aOR: 5.16), acute stroke (aOR: 6.63) and sepsis (aOR: 11.00). All reported outcomes, and the prevalence of frailty are survey-weighted national estimates.

Frailty has increasingly been recognized as a key determinant of adverse outcomes in heart failure, particularly in patients with HF_rEF. Consistent with prior studies, our findings show that frail patients tend to be older and carry a higher burden of comorbidities; however, frailty is not exclusive to geriatric populations and may present across a wider age range.^{11,12} In our study of HF_rEF hospitalizations, the HF_rES enabled efficient identification of frail patients using administrative data, supporting its utility in U.S. inpatient populations. HF_rES has demonstrated strong predictive value for adverse outcomes across international settings and serves as a scalable, cost-effective tool for early risk stratification.^{13,14} Our results reinforce existing evidence linking frailty with significantly worse in-hospital outcomes.^{2,15} A pooled analysis by Yang *et al.* reported a 50% increase in mortality among frail HF patients, further supporting our findings.³

Moreover, our study extends the literature by quantifying the impact of frailty on hospital length of stay and healthcare costs, emphasizing its substantial economic and clinical burden.¹⁶ Frail patients exhibited a nearly fourfold higher risk of in-hospital mortality. This elevated risk likely stems from a complex interplay of chronic inflammation, mitochondrial dysfunction, and sarcopenia.^{4,17,18} Frailty in HF_rEF may also mirror features of cachexia and cardiac wasting, where skeletal muscle dysfunction contributes to dyspnea and reduced functional capacity.^{19,20} Sarcopenia, a hallmark of frailty, is also independently linked to poor prognosis and a higher incidence of acute stroke in HF_rEF patients.^{23,24} Our analysis revealed a six-fold increase in acute stroke risk, likely associated with atrial fibrillation and a prothrombotic state.^{25,26} These findings highlight the urgent need for early frailty recognition and targeted intervention.

Beyond mortality, frailty in HF_rEF patients is linked to a higher risk of complications, such as acute kidney injury, sepsis, major bleeding, acute pulmonary edema, and increased need for mechanical ventilation. Endothelial dysfunction, reduced renal perfusion, and dehydration predispose frail individuals to acute kidney injury.^{27,28} Immune dysregulation and malnutrition (hallmarks of frailty) exacerbate sepsis risk, especially with prolonged hospital stays increasing exposure to nosocomial infections.^{29,30} Frailty also alters coagulation pathways and increases vascular fragility, raising bleeding risk, particularly in patients on anticoagulation.^{31,32} Impaired fluid regulation, diminished cardiac reserve, and respiratory muscle weakness contribute to pulmonary edema and respiratory failure, frequently necessitating mechanical ventilation.³³ These complications often lead to longer hospital stays, intensive care use, and discharge to long-term care facilities, reflecting greater functional decline and higher healthcare utilization.³⁴⁻³⁶

Our findings corroborate those from previous trials. A post hoc analysis of the FRAGILE-HF study identified sarcopenia as a predictor of poor prognosis in HF_rEF patients. Despite similar prevalence across heart failure phenotypes, outcomes were worse in sarcopenic patients. Likewise, a post hoc analysis from the GUIDE-IT trial demonstrated that increased frailty burden correlated with higher mortality and hospitalization

risk. Notably, frail patients were less likely to receive GDMT, possibly due to polypharmacy, clinical variability, and concern over adverse effects.³⁷ These barriers may partially explain the poor outcomes in this population and highlight the importance of addressing frailty in HF_rEF management.

Frailty and HF_rEF form a bidirectional cycle, each exacerbating the other. Despite known benefits of GDMT, frail patients are frequently undertreated due to perceived therapeutic futility, elevated risk profiles, and management complexity, particularly in the presence of comorbidities like chronic kidney disease, diabetes, and anemia.³⁷ This underscores the need for standardized frailty assessment tools tailored to HF_rEF - a task that remains challenging, particularly with regard to endpoint definition and patient selection.³⁸ Non-pharmacological strategies - such as exercise training, rehabilitation, and nutritional support - are also vital in improving functional status and mitigating frailty, especially during hospitalization.³⁹⁻⁴¹ However, there remains a lack of high-quality evidence supporting these interventions. Future research should focus on developing personalized treatment strategies, validating frailty assessment tools specific to HF_rEF, and evaluating the effectiveness of multidisciplinary care models aimed at improving outcomes in this vulnerable population.

Limitations

This study should be considered within the context of several limitations. First, we could not distinguish between age-related frailty and frailty that may arise from disease severity or the cumulative effects of HF_rEF management. Second, accuracy of diagnoses and therapies are inherently dependent on clinician exactness of coding during hospitalizations.⁴² Third, we could not establish causal relationships due to the observational nature of this retrospective study. Fourth, although the HF_rES is a validated tool, it may partially reflect acute illness severity rather than underlying frailty alone, which could influence the observed associations. Fifth, the NIS lacks granular clinical data such as NYHA class, echocardiographic parameters, and biomarkers like BNP, limiting assessment of HF_rEF severity and frailty. Sixth, the absence of data on nutritional interventions and pharmacologic therapies restricts evaluation of key confounders influencing outcomes. Finally, we were not able to compare long-term outcomes for frail and nonfrail patients with HF_rEF.

Conclusions

In conclusion, this large-scale nationwide study highlights frailty as a significant independent predictor associated with poor hospital outcomes in patients with HF_rEF. Frail patients experienced higher mortality and an increased risk of complications such as acute stroke, cardiogenic shock, acute kidney injury, sepsis, and major bleeding. They also had longer hos-

pital stays, higher healthcare costs, and a greater need for mechanical ventilation. Additionally, frail patients were less likely to be discharged to home and more frequently transferred to long-term care facilities. These findings highlight the crucial impact of frailty on clinical outcomes in hospitalized HFrEF patients, emphasizing the need for targeted interventions to improve prognosis in this high-risk population.

Contributions

All authors made a substantive intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest

Dr Anker has received grants from Vifor International and Abbott; has received consulting fees from CVRx, AstraZeneca, Bioventrix, Repairon, Novo Nordisk, Brahms, Novartis, Actimed Therapeutics, Faraday Pharmaceuticals, Cytokinetics, HeartKinetics, GSK, Vectorious, Scirent, Sensible Medical. Edwards, Relaxera, Repairon, Regeneron Pharmaceuticals, and Cordio; has served on steering or advisory committees work for Vifor International, Bayer AG, Boehringer Ingelheim, Medtronic, Abbott, Impulse Dynamics, Cardior, V-Wave, Pfizer, Cardiac Dimensions, and Occlutech; and was named inventor on patent applications regarding MR-proANP (DE 102007010834 & DE 102007022367), but he does not benefit personally from the related issued patents. All other authors declare that they have no competing interests, and all authors confirm accuracy.

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Online supplementary material:

Supplementary Table 1. ICD-10 CM of medical comorbidities.

Supplementary Table 2. ICD-10 codes used to assess Hospital Frailty Risk Score (HFRS).