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ORIGINAL RESEARCH

The Impact of Frailty on Patients With AF and HFrEF Undergoing Catheter Ablation

A Nationwide Population Study

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ABSTRACT

BACKGROUND Frailty is a common geriatric syndrome often coexisting with cardiovascular diseases such as atrial fibrillation (AF) and heart failure (HF) with reduced ejection fraction (HFrEF). While catheter ablation (CA) has demonstrated efficacy in reducing major adverse cardiovascular events and improving mortality and quality of life, the influence of frailty among this population remains unknown.

OBJECTIVES The authors aimed to identify the prevalence of frailty among patients with HFrEF and AF undergoing CA and its influence on cardiovascular mortality and discharge disposition.

METHODS From January 2016 to December 2019, we used the Nationwide Inpatient Sample to identify patients with AF and HFrEF. Frailty was identified by the presence of ≥1 diagnostic cluster utilizing the Johns Hopkins Adjusted Clinical Groups with malnutrition, dementia, impaired vision, decubitus ulcer, urinary incontinence, loss of weight, poverty, barriers to access to care, difficulty walking, and falls as indicators. We compared clinical outcomes among frail vs nonfrail patients, including all-cause in-hospital mortality, major adverse cardiovascular events, other major complications, discharge disposition, and hospital length of stay using multivariable regression analysis.

RESULTS Of 113,115 weighted admissions, 11,725 (10.4%) were classified as frail. Frail patients were older (median age: 76 [IQR: 15] years vs 70 [IQR: 15] years, $P < 0.001$) than nonfrail patients. Frailty was associated with increased odds of all-cause hospital mortality (adjusted odds ratio [aOR]: 2.64; 95% CI: 1.87-3.72; $P < 0.001$), major adverse cardiovascular events (aOR: 2.00; 95% CI: 1.62-2.47; $P < 0.001$), and nonhome discharge (aOR: 3.31; 95% CI: 2.78-3.94; $P < 0.001$). Frail patients also experienced longer hospital length of stay (median 9 [IQR: 10] days vs 5 [IQR: 5] days, $P < 0.001$) after adjustment by Poisson regression (coefficient: 0.53; 95% CI: 0.46-0.59; $P < 0.001$).

CONCLUSIONS Frailty is associated with worse outcomes in patients with HFrEF undergoing CA for AF. The integration of frailty models in clinical practice may facilitate prognostication and risk stratification to optimize patient selection for CA. (JACC Adv. 2024;3:101358) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

ACG = Adjusted Clinical Groups

ACCP = American College of Chest Physicians

AF = atrial fibrillation

AHA = American Heart Association

CA = catheter ablation

HF = heart failure

HFrEF = heart failure with reduced ejection fraction

HRS = Heart Rhythm Society

ICD-10 = International Classification of Disease-10th Edition

MACE = major adverse cardiovascular events

NIS = Nationwide Inpatient Sample

Life expectancy of the U.S. population is increasing, but this paradoxically coincides with rising incidence and prevalence of age-related cardiovascular disease (CVD).[1] Atrial fibrillation (AF) and heart failure (HF) with reduced ejection fraction (HFrEF) often co-exist in the older adult population,[2] where frailty is also highly prevalent.[3] Frailty is a geriatric syndrome that renders individuals highly susceptible to increased vulnerability to stressors due to diminishing biological reserves that ultimately impairs the ability to cope with physiological demands, which exacerbates rapid physical decline, reduces the success from CVD interventions, and increases overall mortality.[3-8]

In recent years, there has been growing recognition of frailty status as it relates to the management of CVD[9,10] because previous studies have identified poor clinical outcomes in frail patients living with either AF[11] or HFrEF.[12] Additionally, it has been shown that frail patients undergoing catheter ablation (CA) for AF have a risk for greater perioperative and postoperative complications, including longer length of stay, higher rates of mortality, and more readmissions.[13,14]

However, less is known about how frailty impacts outcomes when older adults with both conditions are treated using a rhythm control strategy with CA. CA has recently garnered a Class I indication from the 2023 American College of Cardiology (ACC)/American Heart Association (AHA)/American College of Chest Physicians (ACCP)/Heart Rhythm Society (HRS) guidelines for the management of AF with underlying HF,[15] established from high-quality evidence that exhibited several important benefits, including reduction in HF readmissions, composite major adverse cardiovascular events (MACE), mortality, and improvement in quality of life, thereby underscoring critical importance of patient stratification and selection.[16-18] In this study, we aimed to examine the influence of frailty on cardiovascular mortality and outcomes among patients with AF and HFrEF undergoing CA utilizing the Johns Hopkins Adjusted Clinical Groups (ACG) frailty indicator clusters.[19]

METHODS

DATABASE. The Nationwide Inpatient Sample (NIS) is a publicly available, all-payer database belonging to the Healthcare Cost and Utilization Project as part of the Agency for Healthcare Research and Quality.[20] The database includes approximately 98% of the U.S. population, from which a representative sample of 20% of all hospital discharges from 48 states are included.[21] Discharge weights are applied to a representative sample of 7 million hospitalizations to obtain a population of 35 million inpatient hospitalizations reflecting national estimates. This database utilizes hospitalizations as the primary unit instead of individual patients, which is noteworthy because an individual patient may be reflected in several entries in the database.[22] NIS utilizes a single primary diagnosis and a maximum of 39 secondary diagnoses identified as pre-existing or newly diagnosed. Well-validated International Classification of Diseases-10th edition (ICD-10) codes[23] are used to select patient demographics, diagnoses, and procedures for the study of relevant variables. This information was made available to the investigator team (J.D.M.) through Healthcare Cost and Utilization Project. Although institutionalized review board approval was sought, an exemption was granted since the NIS is a limited, de-identified database according to the regulations set forth by the Health Insurance Portability and Accountability Act.

STUDY DESIGN. We utilized the NIS from January 1, 2016, to December 31, 2019, to select a cohort of adult admissions ≥18 years old with either primary or secondary diagnoses of both heart failure with reduced ejection fraction (HFrEF) and AF, utilizing ICD-10 codes I48.0 to 9 and I50, I50.20, I50.21, I50.22, and I50.23, respectively. We excluded patients with a history of atrial flutter, supraventricular tachycardia, ventricular tachycardia/fibrillation, other conduction diseases, or prior permanent pacemaker identified with the appropriate ICD-10 codes (Supplemental Table 1). We then selected admissions that received catheter ablation, identified by procedural codes 02583ZZ and 02584ZZ. These patients were subsequently stratified by frailty, defined as a binary variable frail or nonfrail (**Figure 1**). This was delineated by the presence of ≥1 diagnostic cluster using the

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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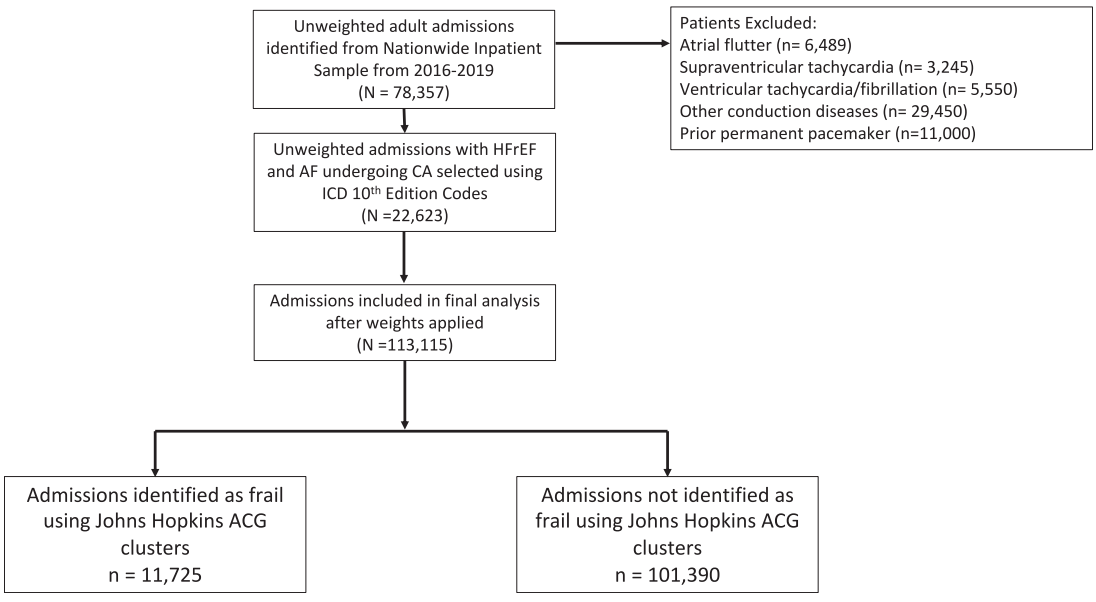
FIGURE 1 Flow Diagram for Study Inclusion Criteria



ACG = adjusted clinical groups; AF = atrial fibrillation; CA = catheter ablation; HFrEF = heart failure with reduced ejection fraction; ICD = International Classification of Disease.

ICD-10th edition codes corresponding to diagnoses included in the Johns Hopkins ACG score: malnutrition, dementia, impaired vision, decubitus ulcer, urinary incontinence, loss of weight, poverty, barriers to access to care, difficulty walking, and falls.[24] The Johns Hopkins ACG cluster has been previously validated to measure patients' frailty status.[21,25,26]

CLINICAL VARIABLES OF INTEREST. Using ICD-10th edition codes when appropriate (Supplemental Table 1), we obtained pertinent hospital and patient characteristics including patient frailty status, gender, age, median household income, hospital teaching status, hospital bed size and region, primary payer insurance, and several clinical variables, including prior cardiovascular and other medical comorbidities. We also separately calculated the Elixhauser Comorbidity Index, which incorporates 31 comorbid conditions that are used to calculate odds of in-hospital mortality.[12]

OUTCOMES. The primary outcome of interest was all-cause in-hospital mortality during index admission for CA stratifying by frailty status. Secondary and exploratory outcomes included in-hospital MACE (all strokes, myocardial infarctions, sudden cardiac death), the association of frailty with other in-hospital major complications, length of stay, and discharge disposition. We defined major complications as any peri- or post-procedural complications including pericardial complications (tamponade or perforation), vascular complications, significant bleeding events, ischemic or hemorrhagic strokes, thromboembolic events, the need for coronary revascularization, or sudden cardiac arrest. Discharge disposition was defined either by home or nonhome discharge (skilled nursing facility, long-term acute care, or hospice).

STATISTICAL ANALYSIS. Using the discharge-level weight variable (DISCWT), national estimates were obtained from these variables using the NIS.[21,22] Chi-squared test was used to compare categorical variables, and results were reflected as frequency and percentages. Student *t*-test or Mann-Whitney U test was used to compare continuous variables denoted as mean ± SD or median (IQR), respectively, depending on the skewness of the variables. Multivariable logistic and Poisson regression models were conducted to identify the association of covariates with our primary and secondary outcomes as appropriate. These results were reflected as OR or coefficients with respective 95% CIs. Variables in the regression model included patient age, gender, race, hospital bed size, hospital teaching status and location, median household income, insurance status, socioeconomic status as reflected by primary payer status, diabetes

with and without complications, hypertension with and without complications, chronic kidney disease, coronary artery disease, primary myocardial infarction, peripheral vascular disease, body mass index, chronic obstructive pulmonary disease, liver disease, electrolyte/acid base imbalances, prior coronary artery bypass graft, prior percutaneous coronary intervention, gastrointestinal bleeding, and coagulopathies. These variables were selected in the final regression model if statistical significance was met at $P < 0.20$ during univariable screening. We also forced demographic variables well-associated with increased mortality, longer length of stay, and overall worse clinical prognosis aligning with the primary and secondary outcomes into our final regression model, including socioeconomic predictors such as race, median household income, and primary insurance status.[27,28] To better understand the impact of age on these clinical variables of interest, we first performed interaction analysis between age and frailty. We then performed subgroup analysis stratifying patients based on age, indicated as either less than or equal to 65 years old (younger adults) or above 65 years old (older adults). Statistical significance was met for variables with P values <0.05 in the final regression model as well as the other statistical tests. We utilized the NIS checklist provided by Agency for Healthcare Research and Quality to ensure appropriate and consistent data analysis.[29] Statistical analyses were performed using STATA-17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, Texas: StataCorp LLC.).

RESULTS

BASELINE CHARACTERISTICS. Of 113,115 weighted admissions meeting inclusion criteria, 11,725 (10.4%) were identified as frail (**Figure 1**). Median age of frail patients was 76 (±15) years compared to 70 ± 15 years in nonfrail patients ($P < 0.001$). The distribution of frailty across age groupings is found in Supplemental Figure 1. A majority of frail patients receiving CA were White (78.2%) and more likely to be female than nonfrail patients (45.5% vs 36.9%, $P < 0.001$). Comorbidities more prevalent among frail patients included complicated hypertension (69.6% vs 66.8%, $P = 0.043$), diabetes mellitus with chronic complications (26.7% vs 21.6%, $P < 0.001$), chronic kidney disease (46.5% vs 35.5%, $P < 0.001$), peripheral vascular disease (13.0% vs 10.0%, $P < 0.001$), coagulopathy (15.0% vs 8.0%, $P < 0.001$), prior ischemic stroke or transient ischemic attack (3.9% vs 2.4%, $P < 0.001$), and hemorrhagic stroke (0.3% vs 0.1%, $P = 0.016$). Frail patients had a higher median Elixhauser Scale Mortality Score of 23 (IQR: 12) vs 14 (IQR: 18) for nonfrail patients, while median CHA_2DS_2-VASc scores were similar in frail (4) and nonfrail patients (3) (IQR: 2 for both). The remaining baseline characteristics are found in **Table 1**.

All-cause in-hospital mortality rate was significantly higher in frail patients than for nonfrail patients (5.4% vs 1.3%, $P < 0.001$), and univariable and multivariable logistic regression analyses corroborated this association (OR: 4.21; 95% CI: 3.17-5.58; $P < 0.001$) and (adjusted odds ratio [aOR]: 2.64; 95% CI: 1.87-3.72; $P < 0.001$), respectively. Although there was a notable trend, we did not detect statistically significant interaction effects of age and frail status on mortality after multivariable adjustment (P interaction = 0.068). Subgroup analysis of these patients stratified by age revealed similar results on adjusted multivariable regression, as both groups were more likely to experience higher rates of mortality. Still, compared to patients identified as 65 years old or younger (aOR: 2.19; 95% CI: 1.69-2.84; $P < 0.001$), patients greater than 65 years old were at increased odds of all-cause mortality (aOR: 4.06; 95% CI: 2.48-6.66; $P < 0.001$). Full results are found in Supplemental Table 3A and 3B. Other clinical predictors of mortality are found in **Figure 2**.

Frailty was also associated with a higher association of MACE in CA recipients (aOR: 2.00; 95% CI: 1.62-2.47; $P < 0.001$). The overall rate of major complications for all patients was 14.4%, higher in frail (19.7%) vs nonfrail patients (13.9%), $P < 0.001$. This corresponded to a statistically significant association after adjusting for potential confounders (aOR: 1.49; 95% CI: 1.27-1.76; $P < 0.001$). Frail patients had a higher likelihood of ST-elevation myocardial infarction (0.7% vs 0.3%, $P < 0.001$), bleeding events (5.8% vs 2.8%, $P < 0.001$), ischemic stroke (16.0% vs 10.2%, $P < 0.001$), other thromboembolic events (3.7% vs 2.6%, $P = 0.002$), postprocedural hemorrhage or hematoma (1.3% vs 0.7%, $P = 0.004$), need for pacemaker implantation (11.5% vs 7.0%, $P < 0.001$), and sudden cardiac arrest during index hospitalization (2.6% vs 1.2%, $P < 0.001$) (**Central Illustration**). In subgroup analyses, we also identified a strong association between frailty and increased odds of electrolyte or acid-base disturbances (OR: 2.14; 95% CI: 1.92-2.39; $P < 0.001$), gastrointestinal bleeding (OR: 2.32; 95% CI: 1.71-3.15;

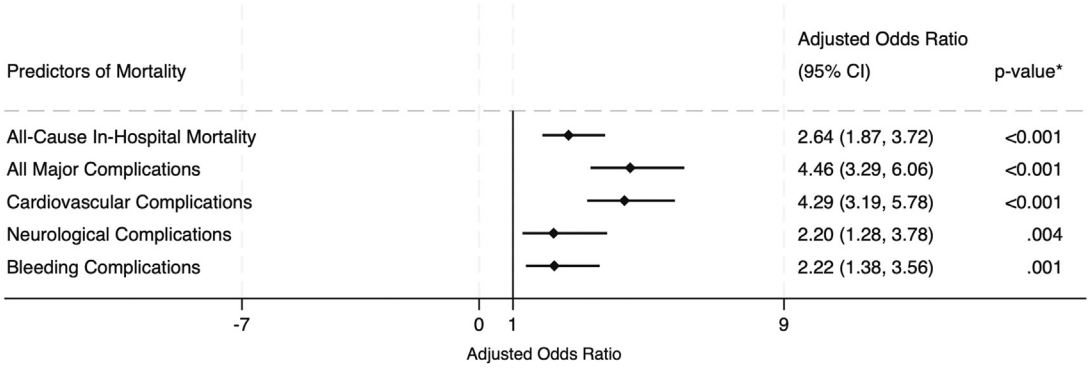
TABLE 1 Baseline Characteristics of HFrEF Patients Undergoing CA for AF Identified as Frail vs Nonfrail

	Frail (n = 11,725)	Nonfrail (n = 101,390)	Total Admissions (n = 113,115)	*P* Value
Age, y median (IQR)	76 (15)	70 (15)	71 (16)	<0.001
Sex[a]				<0.001
Female	5,335 (45.5)	37,360 (36.9)	42,695 (37.8)	
Male	6,390 (54.5)	64,015 (63.1)	70,405 (62.2)	
Race[b]				0.483
Black	1,350 (11.9)	13,385 (13.6)	14,735 (13.0)	
Hispanic	695 (6.0)	5,935 (5.9)	6,630 (5.9)	
Other	435 (3.7)	3,680 (3.6)	4,115 (3.6)	
White	8,895 (75.9)	75,745 (74.7)	84,640 (74.8)	
Bed size category of hospital				0.040
Small	1,400 (11.9)	11,420 (11.3)	12,820 (11.3)	
Medium	2,555 (21.8)	25,275 (24.9)	27,830 (24.6)	
Large	7,770 (66.3)	64,695 (63.8)	72,465 (64.1)	
Median household income[c]				0.536
0-25th percentile	3,165 (27.0)	27,640 (27.3)	30,805 (27.2)	
26th-50th percentile	2,790 (23.8)	25,480 (25.1)	28,270 (25.0)	
51st-75th percentile	3,090 (26.4)	25,210 (24.9)	28,300 (25.0)	
>75th percentile	2,475 (21.1)	21,325 (21.0)	23,800 (21.0)	
Teaching status of hospital				0.670
Nonteaching	255 (2.2)	2,400 (2.4)	2,655 (2.3)	
Rural teaching	1,390 (11.9)	12,715 (12.5)	14,105 (12.5)	
Urban teaching	10,080 (85.9)	86,275 (85.1)	96,355 (85.2)	
CHA_2DS_2-VASc score				<0.001
0	160 (1.4)	1,730 (1.7)	1,890 (1.7)	
1	610 (5.2)	8,450 (8.3)	9,060 (8.0)	
2	1,330 (11.3)	17,240 (17.0)	18,570 (16.4)	
3+	9,615 (82.0)	73,955 (72.9)	83,570 (73.9)	
Comorbidities				
Elixhauser Scaled Score for Mortality, median (IQR)	23 (12)	14 (18)	-	-
Coronary artery disease	6,175 (52.7)	53,775 (53.0)	59,950 (53.0)	0.794
Prior MI	1,680 (14.3)	15,965 (15.7)	17,645 (15.6)	0.166
Prior PCI	1,545 (13.2)	15,060 (14.9)	16,605 (14.7)	0.091
Prior CABG	2,730 (23.3)	27,815 (27.4)	30,545 (27.0)	<0.001
Valvular disease	3,845 (32.8)	30,975 (30.6)	34,820 (30.8)	0.075
Hypertension (uncomplicated)	1,050 (9.0)	13,290 (13.1)	14,340 (12.7)	<0.001
Hypertension (complicated)	8,155 (69.6)	67,770 (66.8)	75,925 (67.1)	0.043
Diabetes (uncomplicated)	4,315 (36.8)	38,440 (37.9)	42,755 (37.8)	0.402
Diabetes (complicated)	3,130 (26.7)	21,900 (21.6)	25,030 (22.1)	<0.001
Chronic kidney disease	5,460 (46.6)	36,025 (35.5)	41,485 (36.7)	<0.001
Peripheral vascular diseases	1,530 (13.0)	10,175 (10.0)	11,705 (10.3)	<0.001
Hyperlipidemia	365 (3.1)	3,860 (3.9)	4,225 (3.7)	0.172
Prior stroke	1,600 (13.6)	11,255 (11.1)	12,855 (11.4)	0.003
Obstructive sleep apnea	1,640 (14.0)	23,155 (22.8)	24,795 (21.9)	0.577
Chronic obstructive pulmonary disease	3,790 (32.3)	29,760 (29.4)	33,550 (29.7)	0.018
Pulmonary hypertension	2,310 (19.7)	15,725 (15.5)	18,035 (15.9)	<0.001
Metastatic cancer	130 (1.1)	615 (0.6)	745 (0.7)	0.024
Acid-base and electrolyte disorders	5,680 (48.4)	30,885 (30.5)	36,565 (32.3)	<0.001
Deficiency anemias	2,115 (18.0)	9,855 (9.7)	11,970 (10.6)	<0.001
Hypothyroidism	2,555 (21.8)	18,535 (18.3)	21,090 (18.6)	<0.001

Values are n (%) unless otherwise indicated. [a]15 patients missing from analysis for sex. [b]2,995 patients missing from analysis for race. [c]1,940 patients missing from analysis for median household income.

AF = atrial fibrillation; CA = catheter ablation; CABG = coronary artery bypass graft; HFrEF = heart failure with reduced ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

FIGURE 2 Forest Plot With Odds Ratios and Their Respective 95% CI Depicting Clinical Variables Association With Mortality



*Statistically significant at $P < 0.05$.

$P < 0.001$), and coagulopathy (OR: 2.03; 95% CI: 1.73-2.36; $P < 0.001$).

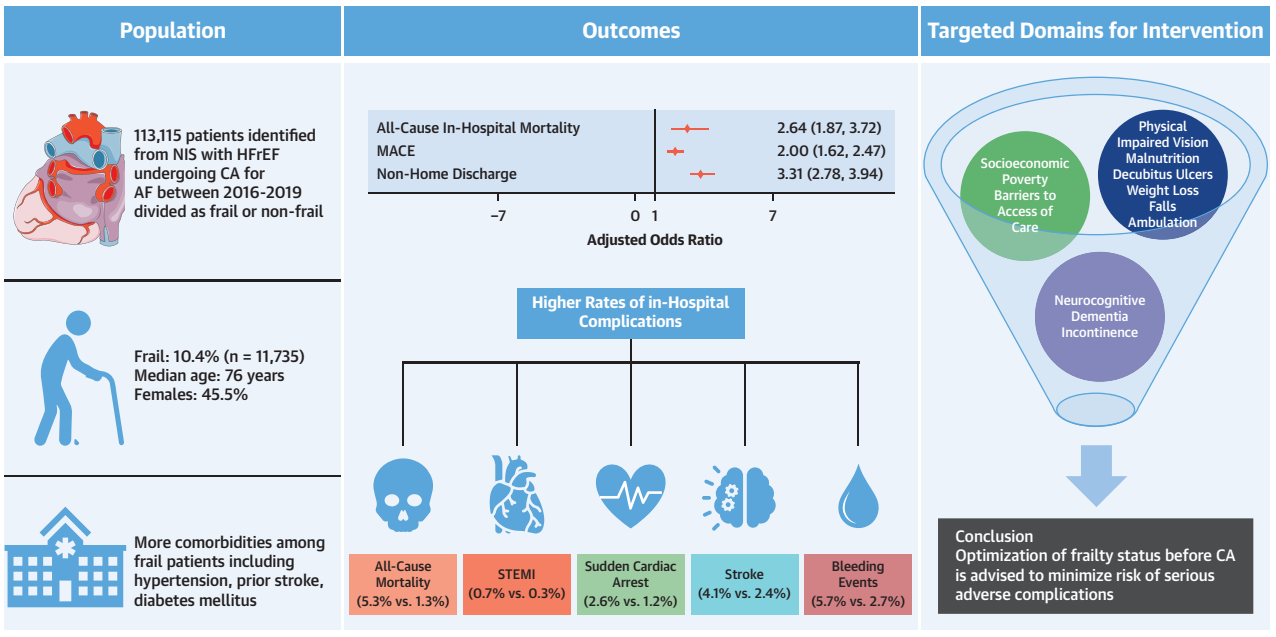
Frail patients experienced higher median total hospital charges ($157,105 vs $134,137, $P < 0.001$) and were more likely to be discharged to a skilled nursing facility, long-term acute care, or hospice compared to discharge home (aOR: 3.31; 95% CI: 2.78-3.94; $P < 0.001$). Frail patients also experienced longer median length of stay compared to nonfrail patients (9 [IQR: 10] vs 5 [IQR: 5], $P < 0.001$), which was also consistent in multivariable Poisson regression (coefficient: 0.53; 95% CI: 0.46-0.59; $P < 0.001$).

DISCUSSION

In this large retrospective cohort study, we investigated the impact of frailty on short-term outcomes in patients with HFrEF undergoing CA for AF (**Central Illustration**). Using the Johns Hopkins ACG criteria, we identified 10.4% of included patients as frail. We sought to extend the clinical utility of this system to stratify patients with AF and HFrEF who may initially not be the ideal candidate for CA. In doing so, we demonstrated a statistically significant association of higher risk of mortality in frail patients compared to nonfrail patients receiving CA, regardless of age. Patients were also at a higher predisposition for MACE and major periprocedural and postprocedural complications, including myocardial infarction, major bleeding events, stroke, and sudden cardiac arrest, which was associated with longer length of hospitalization, higher total charges, and nonhome discharge.

The reported prevalence of frailty in adults varies depending on the instrument used, ranging from 4.0% to 59.1% among community-dwelling older adults.[30] Prior authors have importantly noted the increased association of frailty in HFrEF patients, with higher predisposition to recurrent hospitalizations, worsening of HF, and all-cause death,[31] an effect that is further multiplied when underlying AF is present[12] as corroborated by our findings. As we detected frailty in approximately 10% of patients with both AF and HFrEF, and as prior estimates have varied between 15% and 74% for HF,[32] and 6% and 75% in AF,[11,33-35] we suspect this heterogeneity is due to differences in the populations studied and the various frailty measurements used. Given this administrative dataset, there are some concerns regarding coding reliability and variability as well as capturing some frailty measures, and instability may also arise in response to changes in local payment structures, which are tied to diagnostic codes.[36,37] Nonetheless, the Johns Hopkins ACG criteria have been successfully implemented to robustly ascertain frailty using 10 clusters of conditions that reflect functional and nutritional status, poverty, weight loss, falls, and barriers to care.[38-41] Although the Rockwood Clinical Frailty Scoring System and Fried phenotype are commonly used in HF patients, other tools utilizing ICD-10 codes have been shown to reliably assess frailty status and predict clinical outcomes, regardless of ejection fraction.[42] Sun et al identified similar reliability when comparing the ACG criteria to other indicators of frailty in recipients of

CENTRAL ILLUSTRATION **Impact of Frailty in Patients Undergoing Catheter Ablation for Atrial Fibrillation With Underlying Heart Failure With Reduced Ejection Fraction**



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cardiac surgeries.[26] Akin to previous studies that utilized the Hospital Frailty Risk Score for frail AF patients receiving interventions,[13,14,43] we extended this finding by demonstrating an associated four-fold increase in all-cause in-hospital mortality for frail AF patients with HFrEF, which remains an especially vulnerable population to intervene on with procedures. While we used one reliable scoring system to identify patients falling under the frailty syndrome, it still may be useful to further validate our findings with additional models.

Major adverse cardiac, vascular, and bleeding complications were significantly higher in frail patients included in our cohort. As noted in prior studies, frail patients with other cardiac and surgical comorbidities are also at a higher risk of suffering MACE.[44-46] On a biomolecular level, frail patients are more vulnerable due to age-related inflammation, accumulated oxidative stress, and damage to critical cellular components.[47] This renders difficulty for the maintenance of homeostasis, which thereby appears to potentiate coagulopathies and thromboses.[47] Of note, frail patients had a higher likelihood of experiencing major bleeding events periprocedurally or postprocedurally, which also warrants careful consideration of whether these patients may tolerate initiation of anticoagulation following CA. These findings lend support to the use of multidisciplinary patient assessments for a patient-centered, holistic approach and, in the frail population, attention should be given to interventions targeting improvement in frailty and functional status before electing for CA and the need for prolonged anticoagulation.

As concomitant presence of AF and HFrEF worsens outcomes for patients through several electrophysiological and structural mechanisms, our results strongly suggest short-term outcomes are likely exceedingly worse in frail patients. Longstanding AF is known to induce tachycardia-related HF through decreased cardiac output resulting from diminished diastolic filling times and altered calcium cycling.[48] Pro-arrhythmogenic atrial dilation worsens over time alongside AF-induced loss of atrial systole and preload, ultimately portending left ventricular remodeling and worsening contractility.[49,50] Higher morbidity and mortality are noted through repeated

exacerbations of HF presentations,[51] readmissions for AF sequelae,[52] and longer lengths of stay, thus implicating careful clinical decision-making when considering rhythm or rate control strategies in frail patients due to decreasing physiological reserves that renders them more vulnerable to these age-related effects.[5,7]

Recently, ACC/AHA/ACCP/HRS guidelines upgraded CA to a Class 1 indication for select patients following positive results from several studies.[15] CASTLE-AF randomized symptomatic AF patients with HFrEF comparing CA to pharmacological rhythm control, showing favorable outcomes in reduction of hospitalizations for HF or all-cause mortality in CA recipients.[17] Similarly, CASTLE-HTx demonstrated a reduction in composite death from any cause in AF patients with end-stage HFrEF receiving both CA and pharmacological guideline-directed medical therapy (GDMT) compared to GDMT alone.[18] Although EAST-AFNET 4 showed favorability when electing for early rhythm control in newly diagnosed AF,[53] these studies did not consider the impact of frailty, as we and a multitude of other studies show is a crucial clinical predictor of morbidity and mortality in CVD.[9,44,54-58] It is well known that frail patients are less likely to receive GDMT,[12] and underutilization of appropriate and indicated treatments potentially precludes these at-risk patients from receiving the benefits of optimal medical therapy. The risks of these therapies may be real or perceived, and there may be a bias for frail patients with HFrEF and AF, which would limit the application of these useful therapies to those who may benefit from them. Thus, rather than completely avoiding CA in frail patients, we strongly advocate for improved risk stratification using frailty models to identify patients who are at highest risk for complications, rather than excluding them from the potential benefits of CA, in order to intervene upon modifiable factors to mitigate poor outcomes.

Our findings are meaningful given the current paucity of literature that has not yet fully ascertained how co-existing frailty in HF affects CA, while coinciding with significant real-world barriers that exist in applying a widespread rhythm control approach with CA. Candidates for CA are selected based on absence of serious comorbidities that result in poor life expectancy, decreased duration and persistence of AF, favorable cardiovascular anatomy, and whether CA is the best strategy vs pharmacologic therapy.[59] Older patients are more likely to have longstanding AF and HFrEF and may not benefit from ablation, potentially due to increased left atrial size and burden of fibrosis, which makes CA less effective.[60] However, frailty status alone should not preclude these patients from consideration of this guideline-directed therapy, further warranting pragmatic stratification and optimization of frailty status before receiving CA to potentially lessen the burden of these three reciprocating conditions as patients reach advanced age.[57] Improvement of frailty burden in these patients may be obtained through a variety of well-validated methods, including nutritional supplementation,[61] multidomain physical therapy,[62] exercise training,[63] and cognitive therapies.[64]

STUDY LIMITATIONS. We acknowledge there are several important limitations to our study given the nature of the NIS database. First, accuracy of diagnoses and therapies are inherently dependent on clinician exactness of coding during hospitalizations.[22] Second, we could not establish causal relationships due to the observational nature of this retrospective study with a lack of control groups for various rhythm control strategies. Third, we were unable to stratify patients based on their functional class of heart failure or ejection fraction due to an inability to utilize ICD-10 codes for this purpose. Fourth, we could not identify medications, electrocardiographic, or echocardiographic features, thereby limiting a true assessment of our patient population. Fifth, the Johns Hopkins ACG criteria is not necessarily a HF-specific frailty method, thus warranting subsequent studies using other frailty scoring systems to further confirm and validate our findings. Sixth, we did not identify any patients with sarcopenia using the ICD-10 code M62.84, which may limit full generalizability as sarcopenia and frailty are distinct entities. Finally, we were not able to determine long-term outcomes for patients receiving CA.

CONCLUSIONS

By applying the Johns Hopkins ACG criteria to patients with HFrEF and AF undergoing CA, we identified a statistically significant association between frailty and increased all-cause in-hospital mortality. We also showed that frail patients are at a higher risk for major in-hospital cardiac, vascular, hematological, and neurological complications, resulting in longer length of stay and higher hospital charges. Our study lends support for the utilization of frailty status to prognosticate, guide clinical decision-making, and

optimize patients when electing for guideline-directed rhythm control with CA, while furthering the need for prospective studies.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The prevalence of frailty in older adults with concomitant age-related CVDs is rising. In patients with HFrEF and AF undergoing CA, frailty is associated with worsening cardiovascular outcomes and higher mortality.

COMPETENCY IN PATIENT CARE: Older adults with HFrEF and AF are more likely to be frail, which is associated with worse morbidity and mortality. With growing recognition and consideration of frailty status before undergoing cardiovascular interventions, the use of frailty models should better inform clinical decision-making for patient selection, preprocedural stratification, and optimization for CA in this highly vulnerable population.

TRANSLATIONAL OUTLOOK: Biological models of frailty integrating genetic, proteomic, and physiological data are needed to accurately identify frail patients who may benefit from a tailored treatment plan before catheter ablation. External validation studies are needed to validate these models and facilitate their translation from the laboratory to the bedside and integrate this approach into standard practice.

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KEY WORDS atrial fibrillation, catheter ablation, frailty, older adults, outcomes research, systolic heart failure

APPENDIX For supplemental tables and figures, please see the online version of this paper.