Validation of Cognitive Impairment in Combination With Physical Frailty as a Predictor of Mortality in Patients With Advanced Heart Failure Referred for Heart Transplantation

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Background. The aim of this study was to validate our previous finding that frailty predicts early mortality in patients with advanced heart failure (AHF) and that including cognition in the frailty assessment enhances the prediction of mortality. **Methods.** Patients with AHF referred to our Transplant Unit between November 2015 and April 2020 underwent physical frailty assessment using the modified Fried physical frailty (PF) phenotype as well as cognitive assessment using the Montreal Cognitive Assessment to identify patients who were cognitively frail (CogF). We assessed the predictive value of the 2 frailty measures (PF ≥ 3 of 5 = frail; CogF ≥ 3 of 6 = frail) for pretransplant mortality. **Results.** Three hundred thirteen patients (233 male and 80 female; age 53 ± 13 y) were assessed. Of these, 224 patients (72%) were nonfrail and 89 (28%) were frail using the PF. The CogF assessment identified an additional 30 patients as frail: 119 (38%). Frail patients had significantly increased mortality as compared to nonfrail patients. Ventricular assist device and heart transplant-censored survival at 12 mo was 92 ± 2 % for nonfrail and 69 ± 5% for frail patients ($P < 0.0001$) using the CogF instrument. **Conclusions.** This study validates our previously published findings that frailty is prevalent in patients with AHF referred for heart transplantation. PF predicts early mortality. The addition of cognitive assessment to the physical assessment of frailty identifies an additional cohort of patients with a similarly poor prognosis.

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INTRODUCTION

Heart transplantation (HTx) is indicated for patients with advanced heart failure (AHF) who have failed medical and device therapies.[1,2] As the need for HTx has always exceeded the availability of suitable heart donors, only a small proportion of patients who might benefit are able to be transplanted. The 2016 ISHLT patient assessment guideline[1] recommended that potential recipients should undergo frailty assessment. However, due to the paucity of published studies on frailty in AHF, there was no recommendation

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regarding which frailty assessment tool should be applied, nor advice on the implications of a finding of frailty.

Frailty (defined as a reduction in a person's physiologic reserve resulting in a reduced ability to withstand minor stressors) has gained increased attention as an objective stratifier of those who are "biologically aged" as opposed to "chronologically aged." While the large majority of frailty studies have been conducted in elderly populations, frailty is also prevalent in younger patients with AHF.[3]

The most widely reported frailty assessment tool is the physical frailty (PF) phenotype developed by Fried et al.[4] It assesses 5 physical domains: exhaustion, weakness, slowness, physical inactivity, and shrinkage (sarcopenia).[4] We previously reported that frailty as determined by a modification of the PF phenotype was an independent predictor of mortality in patients with AHF who were referred to our institution for HTx assessment.[3] We subsequently reported that the inclusion of cognitive impairment in the definition of frailty further enhanced the utility of frailty in identifying those patients at highest risk of death.[5] In that study, we assessed cognitive impairment using the Montreal Cognitive Assessment tool[6] and developed a 6-point scoring system with a score of ≥3 indicative of frailty (cognitive frailty [CogF]): 42% of patients were identified as frail.[5] Medically treated frail patients had a very high mortality, approaching 50% at 1 y compared with approximately 20% in nonfrail patients.[5]

The aim of this study was to confirm the validity of our PF and CogF assessment tools in a subsequent cohort of patients with AHF who were referred to our program for HTx assessment. We also examined the predictive value of grip strength and walking speed as both have been proposed as simpler single-item measures of frailty.[7,8]

MATERIALS AND METHODS

This study was approved by the St Vincent's Hospital Research Ethics Committee, (Reference number 2019/ETH03097). All data were obtained with informed consent and entered prospectively into a dedicated database.

Study Population

The study population was derived from 343 consecutive patients who were referred for HTx assessment between November 2015 and April 2020. Thirty patients were excluded: 18 patients in cardiogenic shock, 8 patients who were assessed for heart retransplantation, and 4 who were referred for heart-lung transplant. PF and cognition were assessed in 313 patients together with measures of heart failure severity. These included New York Heart Association (NYHA) class, heart failure duration, left ventricular end-diastolic diameter, and left ventricular ejection fraction by echocardiography, central hemodynamic pressures, and cardiac index by right heart catheterization. Estimated glomerular filtration rate (eGFR), serum creatinine, bilirubin, albumin, blood hemoglobin levels, and body mass index were also recorded.

Measures of Frailty

Physical Frailty

A modification of the frailty phenotype[4] was used to classify patients as frail or nonfrail as described previously.[3] The main modification was to replace unexpected weight loss with loss of appetite due to concern that edema may mask weight loss in this patient group. Walking speed was assessed over a 5-m distance.[5] Grip strength was measured in both hands with a Jamar dynamometer set to the second position using a standardized protocol.[9] Grip strength was considered reduced if the average of 3 attempts in the stronger hand was >2 SDs below age- and gender-matched normative values.[10,11] Nonambulatory patients were scored 1 point on this domain. Patients were classified as frail if 3 or more (of 5) domains were present, and nonfrail if <3 were present.[3]

Cognitive Frailty

The Montreal Cognitive Assessment (version 7.1) was used to assess cognition.[5,6] If the score was <26 (out of 30), the patient was deemed cognitively impaired. The CogF score is a composite 6-domain score which combines the 5 physical domains with the addition of cognitive impairment. Patients were identified as cognitively frail if ≥3 domains were present from the 6-item scale, and nonfrail if <3. The Depression in Medical Illness (DMI-10) questionnaire[12] was also performed in all patients but not used in the frailty instrument. Patients with a score of 9 or greater (out of 30) were classified as depressed.

Statistical Analyses

Baseline characteristics are presented as mean ± SD for continuous variables and as the frequency (percent) for categorical variables. Baseline characteristics were compared between frail and nonfrail patients using unpaired *t*-tests for continuous variables and chi-square tests for categorical variables. For comparison of outcomes, survival time was defined as the time between the date of frailty assessment and the date of death or date of censoring (date of ventricular assist device [VAD] implantation, HTx, or most recent follow-up). Three patients who were considered not medically suitable for HTx were lost to follow-up between 3 and 13 mo after assessment. Kaplan-Meier cumulative survival curves were generated for each frailty category, and the log-rank test was used to compare survival rates between frail and nonfrail groups. Cox proportional-hazards model was used to assess the impact of CogF on survival after adjusting for selected covariates: age (younger than or older than 60 y), sex, NYHA class, heart failure category (heart failure with reduced ejection fraction or heart failure with preserved ejection fraction) depression, anemia, renal function (eGFR < 60 versus > 60 mL/min per m^2), serum albumin (<35 versus ≥35 mmol/L), and the presence or absence of right heart failure (central venous pressure > or ≤10 mm Hg). Competing outcomes analysis was performed using the date of the initial event for censoring (VAD, HTx, death, or at follow-up date). A $P < 0.05$ was considered statistically significant. Data analysis was conducted using Statview Version 5.0, SAS Institute.

RESULTS

Prevalence of Frailty

Frailty was assessed in 313 patients (233 men and 80 women; age 53 ± 13 y, range 16–75 y, left ventricular ejection fraction 27 ± 14%) as part of their transplant referral work up. The cause of heart failure was dilated cardiomyopathy (48%), ischemic heart disease (30%), hypertrophic or restrictive cardiomyopathy (12%), and other cardiac

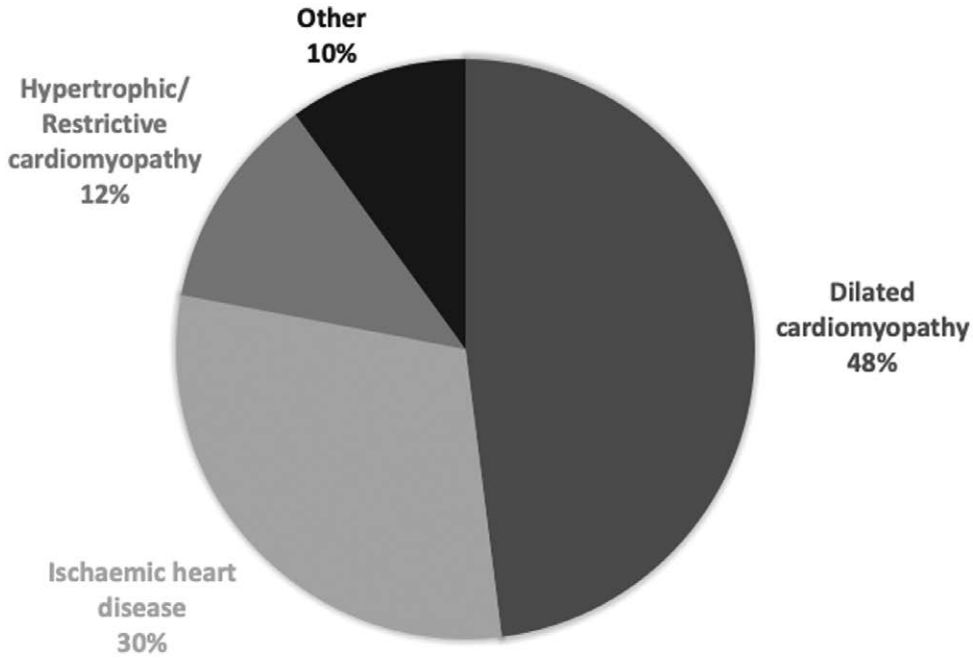

FIGURE 1. Pie graph depicting the underlying causes of heart failure in the study population (N = 313).

diseases (10%) (Figure 1). These proportions were similar in the frail and nonfrail cohorts (Table 1).

Using the PF phenotype, 89 (28%) patients were classified as frail. Using the CogF phenotype, 119 (38%) were classified as frail. Table 1 summarizes the baseline characteristics of the study population stratified by frailty status. For both frailty instruments, frail patients were significantly older and more likely to be female compared with nonfrail patients. They were also more likely to be NYHA Class IV with hemodynamic changes indicative of more severe right heart failure. Frail patients had significantly higher serum bilirubin, lower serum albumin, and lower hemoglobin levels. Renal function as assessed by eGFR was also lower in the frail group. Depression score was significantly higher in the frail cohort for both PF and CogF instruments. Body mass index was similar in frail and nonfrail patients (Table 1).

Figure 2 shows the distribution of frailty across different age and BMI categories. Although age was on average 4 y older in frail patients, frailty was observed in all age categories. Similarly, frailty was observed across all BMI categories. Only 6 patients (4 frail and 2 nonfrail) were underweight (BMI < 18.5) at the time of frailty assessment.

Outcome of Assessment

Of the 313 patients who underwent frailty assessment, 208 (66%) were accepted for transplant, 55 (18%) were considered not sufficiently impaired for active listing, and 50 (16%) were determined to be medically unsuitable (Table 2). Regardless of the frailty instrument used, a similar proportion of frail and nonfrail patients were accepted for transplant. Significantly more frail patients were deemed medically unsuitable whereas significantly more nonfrail patients were considered not sufficiently impaired for transplant listing (P < 0.0001 for PF and P < 0.0015 for CogF; Table 2).

The subsequent outcome of accepted patients stratified by CogF frailty status is summarized in Figure 3. Sixty-three patients underwent VAD implantation (39 nonfrail [35 LVAD and 4 BVAD] and 24 frail [22 LVAD and 2 BVAD]) with 41 patients (27 nonfrail and 14 frail) proceeding to HTx. The median time between frailty assessment and VAD implantation was 0 mo (interquartile range [IQR] 0–1 mo) in frail patients and 1 mo (IQR 0–4 mo) in nonfrail patients (P < 0.01 versus frail patients). Eight of 24 frail patients died during VAD support compared with 4 of 39 nonfrail patients (P < 0.05). One hundred fifty-two patients underwent HTx—100 nonfrail and 52 frail patients. The median time between frailty assessment and HTx was 5 mo (IQR 2–9 mo) in both frail and nonfrail groups. Survival to 3 mo posttransplant was 95 ± 2% in nonfrail patients and 90 ± 4% in frail patients (P = NS). Of the 34 patients who remained on medical treatment, 5 of 14 nonfrail patients and 15 of 20 frail patients died (P < 0.05).

Survival

VAD/HTx-censored survival stratified by frailty status and frailty instrument is shown in Figure 4A and B, and actuarial survival (including those that underwent VAD implantation and/or HTx) is shown in Figure 4C and D. Frailty predicted early mortality with similar survival curves for the 2 frailty instruments. VAD/HTx-censored survival at 12 mo was 92 ± 2% for nonfrail and 69 ± 5% for frail patients (P < 0.0001) using the CogF instrument (Figure 4B). The main difference between the 2 instruments was that an additional 30 patients were reclassified as frail using the CogF instrument. The survival curve for the 30 patients reclassified as frail based on the CogF instrument was superimposable on that of the 89 patients classified as frail based on the PF Instrument (Figure 5). Using Cox proportional-hazards model, CogF and right heart failure were the only independent predictors of mortality with hazard ratios of 3.97 (95% confidence interval, 1.85-8.54, P < 0.0005) and 3.05 (95% confidence interval, 1.05-8.84, P < 0.05), respectively.

TABLE 1.

Baseline patient demographics stratified by the different frailty measures (physical frailty and cognitive frailty)

	Physical frailty			Cognitive frailty		
Variable	**Nonfrail (n = 224) (72%)**	**Frail (n = 89) (28%)**	***P***	**Nonfrail (n = 194) (62%)**	**Frail (n = 119) (38%)**	***P***
Age (y)	51.7 ± 13.1	56.2 ± 11.1	0.001	51.4 ± 13.1	55.5 ± 11.7	0.002
Gender						
Male	174 (78%)	59 (66%)	<0.05	156 (80%)	77 (65%)	<0.001
Female	50 (22%)	30 (34%)		38 (20%)	42 (35%)	
BMI (Kg/m^2)	27.0 ± 5.2	25.9 ± 5.3	NS	26.9 ± 5.1	26.2 ± 5.5	NS
Cause of heart failure			NS			NS
Dilated CM	115 (51%)	32 (36%)		98 (51%)	49 (41%)	
Restrictive CM	18 (8%)	9 (10%)		15 (8%)	12 (10%)	
Hypertrophic CM	8 (4%)	2 (2%)		7 (4%)	3 (3%)	
IHD	61 (27%)	34 (38%)		57 (29%)	38 (32%)	
Other	22 (10%)	12 (13%)		17 (9%)	17 (14%)	
Heart failure duration (y)	5.1 ± 5.6	5.7 ± 5.6	NS	5.1 ± 5.8	5.5 ± 5.3	NS
LVEDD (mm)	66 ± 13	62 ± 12	0.01	67 ± 13	62 ± 12	0.002
LVEF (%)	26 ± 14	28 ± 15	NS	26 ± 13	29 ± 16	<0.05
NYHA class						
III	132 (59%)	14 (16%)	<0.0001	120 (62%)	26 (22%)	<0.0001
IV	92 (41%)	75 (84%)		74 (38%)	93 (78%)	
RAP (mm Hg)	14 ± 7	17 ± 7	0.0005	14 ± 6	17 ± 7	<0.0001
PAWP (mm Hg)	24 ± 9	25 ± 7	NS	24 ± 9	25 ± 7	NS
CI (L/min/m^2)	2 ± 0.6	2 ± 0.6	NS	2 ± 0.6	2 ± 0.6	NS
Serum creatinine (μmol/L)	124 ± 75	148 ± 136	NS	126 ± 78	140 ± 121	NS
eGFR (L/min/1.73m$^{2)}$	64 ± 21	57 ± 25	<0.05	64 ± 21	59 ± 24	<0.05
Serum bilirubin (μmol/L)	20 ± 14	29 ± 22	<0.001	19 ± 13	27 ± 20	<0.0005
Serum albumin (g/L)	40 ± 6	37 ± 6	<0.0001	40 ± 6	38 ± 6	<0.0005
Hypoalbuminemia	19 (8%)	30 (34%)	<0.0001	15 (8%)	32 (36)	<0.0001
Hemoglobin (g/L)	136 ± 18	126 ± 22	<0.0001	137 ± 18	127 ± 21	<0.0001
Anemia	32 (14%)	36 (40%)	<0.0001	27 (14%)	32 (27%)	<0.005
MOCA score	26 ± 3	24 ± 4	<0.005	27 ± 2	24 ± 4	<0.0001
Abnormal MOCA	37 (17%)	48 (53%)	<0.0001	29 (15%)	59 (50%)	<0.0001
DMI-10 score	6 ± 6	9 ± 7	0.005	6 ± 6	8 ± 7	<0.005
Abnormal DMI-10	21 (10%)	35 (39%)	<0.0001	19 (12%)	32 (26%)	<0.0001
Comorbidities						
Diabetes	47 (21%)	29(33%)	<0.05	39 (20%)	37 (31%)	<0.05
Chronic lung disease	24 (11%)	14 (16%)	NS	21 (11%)	17 (14%)	NS
Implanted device			NS			NS
ICD	119 (53%)	51 (58%)		96 (49%)	74 (62%)	
CRT ICD	50 (22%)	15 (18%)		47 (24%)	18 (15%)	
PPM	7 (3%)	1 (1%)		6 (3%)	2 (2%)	
Chronic/recurrent AF	86 (38%)	49 (56%)	<0.01	74 (38%)	61 (51%)	<0.05

BMI, body mass index; CI, cardiac index; CM, cardiomyopathy; DMI, Depression in Medical Illness; eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; IHD, ischemic heart disease; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MOCA, Montreal Cognitive Assessment; NYHA, New York Heart Association; PAWP, pulmonary artery wedge pressure; RAP, right atrial pressure.

Thirteen patients died within 1 m of undergoing frailty assessment. Ten were classified as physically frail and 12 were classified as cognitively frail. Both frailty measures were highly predictive of death during this time period ($P < 0.0005$, frail versus nonfrail for both PF and CogF). Conditional survival analyses after exclusion of deaths within the first month of frailty assessment are shown in Figure S1 (**SDC,** http://links.lww.com/TP/C125). As shown in the figure, both frailty measures remained highly predictive of mortality beyond the first month.

We also performed a competing risks survival analysis stratified by CogF status. The results of this analysis are shown in Figure S2 (**SDC,** http://links.lww.com/TP/C125). The cumulative mortality curves highlight the high early mortality of frail heart failure patients in the absence of VAD implantation or HTx.

Single-item Measures of Frailty

As grip strength and walking speed have been proposed as single-item measures of frailty,[7,8,13-15] we also assessed

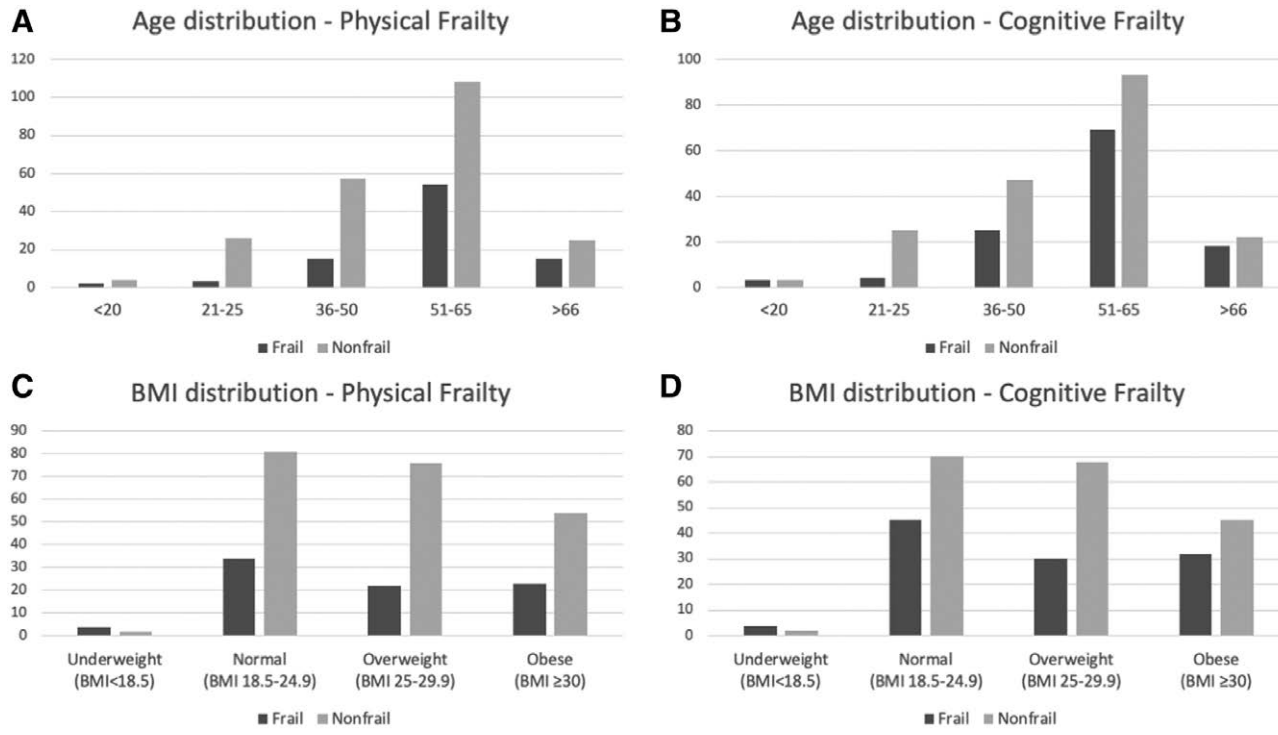

FIGURE 2. Distribution of physical frailty and cognitive frailty across different age categories and body mass index (BMI) categories.

the prognostic significance of reduced grip strength and slowed walking speed in our cohort.

Grip Strength

One hundred thirty-nine patients had reduced grip strength. As shown in Figure 6 (left panel), their VAD/HTx-censored survival was significantly less than the group with normal grip strength (88 ± 3% versus 76 ± 5%, $P = 0.007$), however, the level of significance was less than that observed for the more comprehensive frailty measures.

Walking Speed

Eighty-five patients had reduced walking speed. This number included 32 patients who were nonambulatory at the time of frailty assessment. VAD/HTx-censored survival stratified by walking speed is shown in Figure 6 (right panel). Survival of the 53 patients who were able to complete the test with a reduced walking speed was significantly worse than the survival of those with normal walking speed. The VAD/HTx-censored survival of these 53 patients was similar to that of patients classified as physically or cognitively frail. The VAD/HTx-censored survival of the 32 patients who were unable to perform the test was even worse. All 32 patients were inpatients at the time of assessment with most having been transferred from another hospital for transplant assessment. Twenty-six patients were on intravenous inotropic therapy and 13 progressed to VAD implant during the same admission. Twenty of the 32 nonambulatory patients had reduced grip strength, 25 were classified as physically frail and 29 were classified as cognitively frail. Eleven of these patients died before VAD or Htx with 9 deaths occurring within 1 m of the frailty assessment. All 11 deceased patients were classified as cognitively frail, 10 were classified as physically frail and 9 had reduced grip strength.

Cognition and Depression

We also examined the predictive value of cognitive impairment and depression as single-item measures. VAD/HTx-censored survival stratified by cognitive assessment and depression are shown in Figure 7. Cognitive impairment was associated with significantly reduced survival; however depression was not.

TABLE 2.

Assessment outcome stratified by frailty status

	Nonfrail		Frail		Total
	No. of patients (%)		No. of patients (%)		No. of patients (%)
	PF	CogF	PF	CogF	Both
Accepted for transplant	146 (65)	126 (65)	62 (70)	82 (69)	208 (66)
Not sufficiently impaired	49 (22)	48 (25)	6 (7)	7 (6)	55 (18)
Not medically suitable	29 (13)	20 (10)	21 (24)	30 (25)	50 (16)
Total	224	194	89	119	313 (100)

CogF, cognitive frailty; PF, physical frailty.

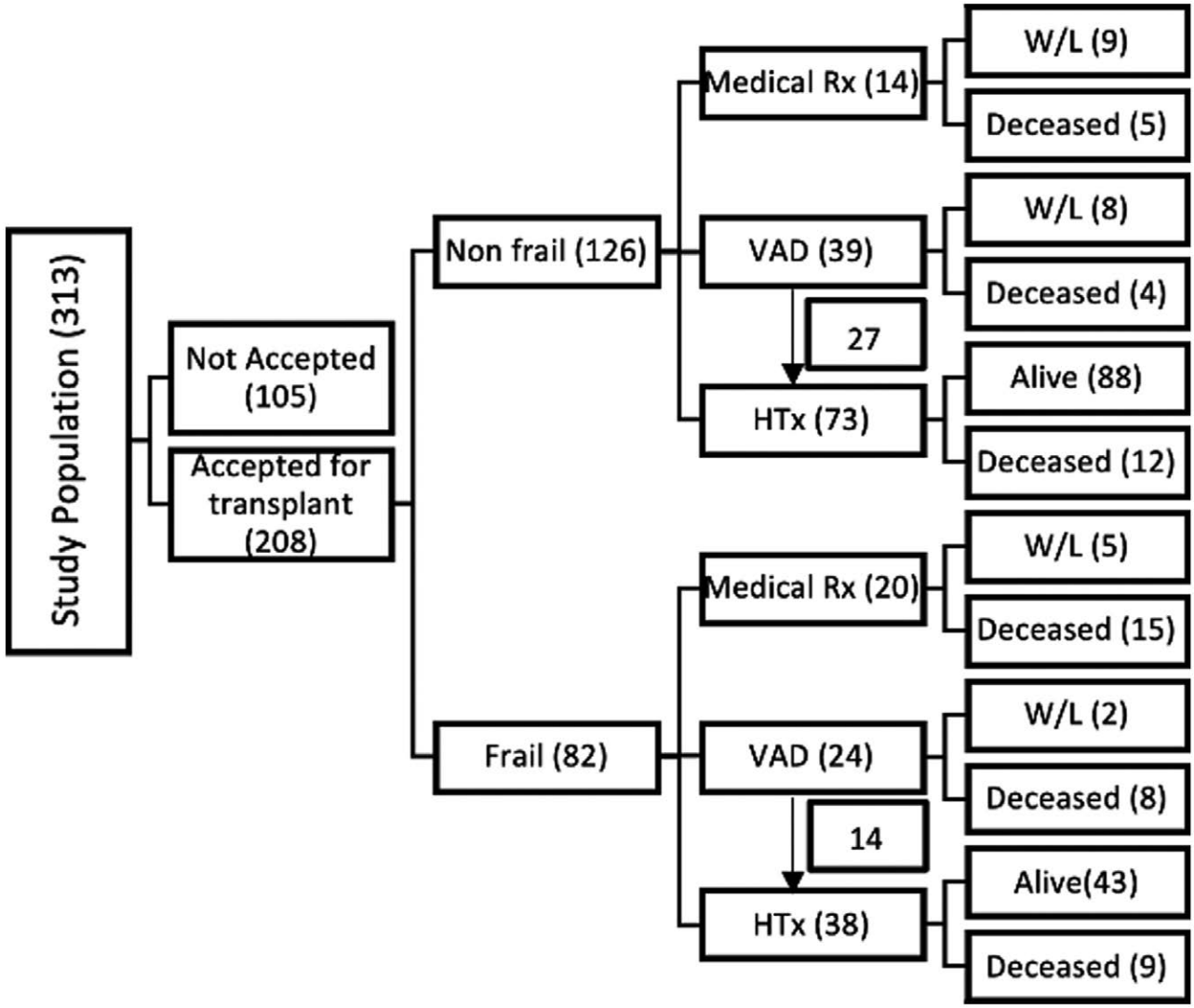

FIGURE 3. Outcome of all patients referred for HTx stratified by cognitive frailty. Thirty-nine nonfrail patients underwent VAD implantation and 27 of these proceeded to HTx. Twenty-four frail patients underwent VAD implantation and 14 of these proceeded to HTx. HTx, heart transplantation; Rx, treatment; VAD, ventricular assist device; W/L, waiting list.

DISCUSSION

The major findings of this study are first, that frailty defined either as PF or CogF is prevalent in patients with AHF. In our previous studies, the prevalence of PF in AHF was 33% increasing to 42% for CogF.[3,5] In the present study, 28% of AHF patients were classified as physically frail and 38% as cognitively frail. Second, frailty as assessed by either PF or CogF was associated with more severe symptoms, more advanced right heart failure, lower albumin, and lower hemoglobin levels, all findings that were observed in our previous studies.[3,5] In this study, we also observed higher rates of diabetes and chronic/recurrent atrial fibrillation in the frail cohort. Third, frailty was associated with markedly reduced survival in medically treated patients, validating of our previously published findings.[3,5] The adverse impact of frailty on survival was apparent within the first month after assessment and remained significant throughout the observation period.

Two findings in the present study which differed from our previous findings were the relationship between frailty and age and between frailty and BMI. In our previous studies, the mean age of the study population was 53 y with no difference between the frail and nonfrail groups.[3,5] In the current study, the mean age for the study population was also 53 y; however, the frail group was on average 4 y older than the nonfrail group (Table 1). This finding is more in keeping with what we expected to find in our previous studies,[16] that is, increasing frailty with increasing age, nonetheless, the current study findings together with our previously published findings[3,5] and a recent systematic review[17] highlight the fact that frailty can occur at any age in an AHF population. It remains to be determined whether the underlying pathophysiology of frailty associated with advanced disease is different from that associated with aging.[18] In our previous studies, we found that average BMI was lower in the frail cohort.[3,5] This was not found in the present study, however, as observed in our previous studies we found that frailty (PF or CogF) was seen in all BMI categories including the obese.[3,5] It is noteworthy that only a small proportion of the study population (2%) were underweight, while a substantial proportion of frail patients were obese. These observations may help explain why formal frailty measures are much better at identifying vulnerable patients than "end of the bed" assessments.[19-21]

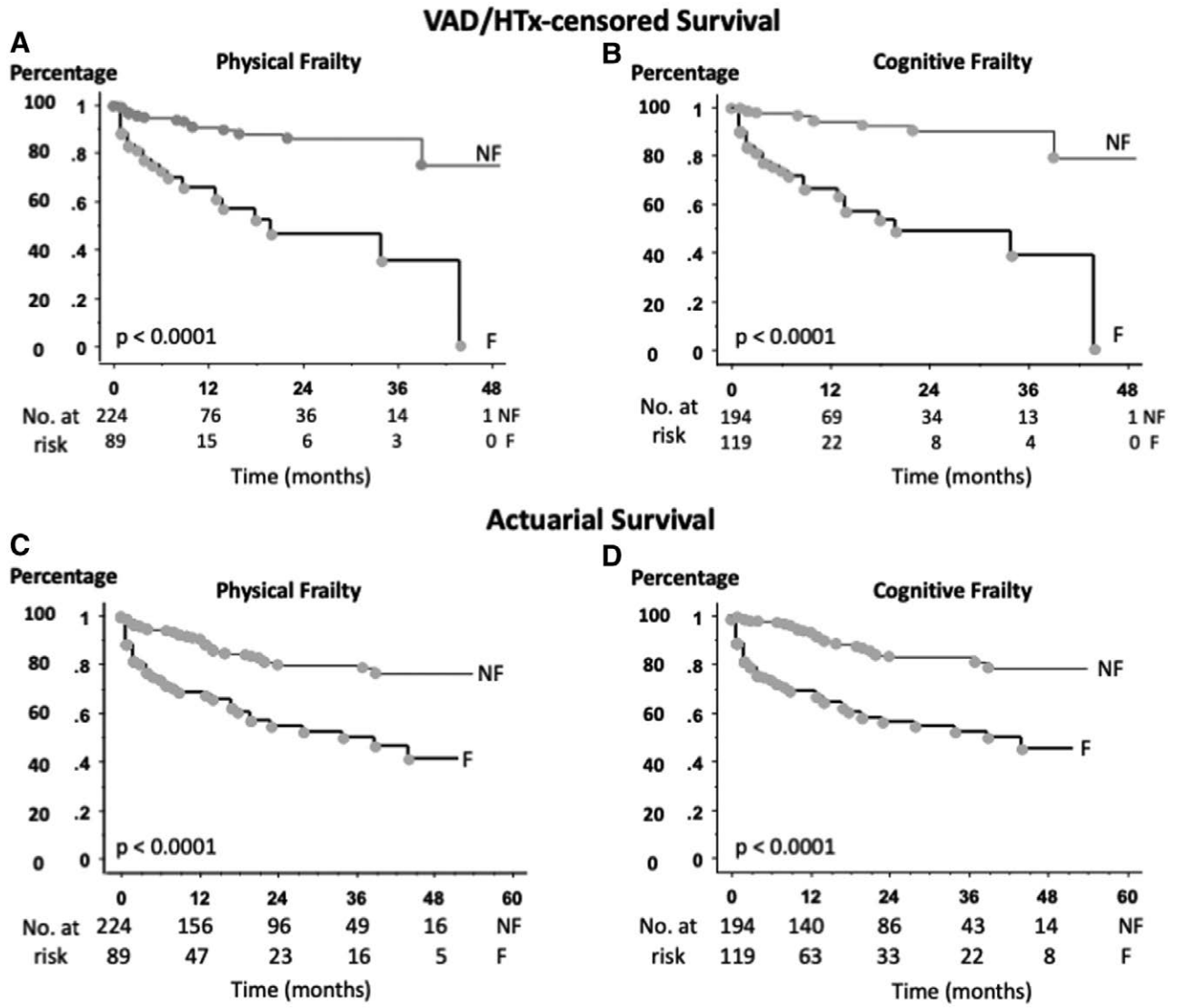

FIGURE 4. Patient survival stratified by frailty status. Panels (A) and (B) show ventricular assist device (VAD) and heart transplant (HTx) censored survival stratified by frailty status (nonfrail [NF] and frail [F]) using the physical frailty and cognitive frailty scores. Patients undergoing VAD or HTx were censored as alive at the time of surgery. Panels (C) and (D) show actuarial survival stratified by frailty status. Survival curves include deaths after VAD or HTx.

Grip strength and walking speed have been proposed as simpler single measures of frailty.[7,22,23] Assessment of grip strength has the added advantage of being able to be performed in nonambulatory patients. In the present study, reduced grip strength was present in 20 of 32 nonambulatory patients and was associated with a trend to increased mortality (9 of 20 patients with reduced grip strength compared with 2 of 12 patients with normal group strength). Chung and coworkers reported that reduced grip strength was associated with increased early mortality after VAD implantation for bridge-to-transplant or destination therapy in patients with AHF.[8] A recent meta-analysis of patients with cardiac diseases reported that reduced grip strength predicted increased mortality and heart failure hospitalizations.[24] Here, we found that reduced grip strength was common in our patient cohort, affecting 44% of patients with AHF. In univariate analysis, it was associated with significantly increased mortality but was less predictive of this outcome compared to PF or CogF. Slowed walking speed was less prevalent in the AHF patients, affecting 27% of the study population but was strongly associated with increased mortality and was similarly predictive of this outcome as the more comprehensive PF measurement. The advantage of the CogF measurement is that it identified an additional cohort of AHF patients with a similarly poor prognosis.

In a recent consensus statement issued by the American Society of Transplantation and the American Society of Transplant Surgeons,[25] the heart working group concluded that the modified PF was the most appropriate instrument to measure frailty in ambulant heart failure patients and that grip strength alone could be considered in more critically ill or bedbound patients. The findings of the present study support those conclusions. The working group also concluded that cognition and depression were important, but that the additive predictive value of these domains required further validation. Our study directly addressed these 2 domains and has provided further evidence that in patients with AHF, cognitive impairment but not depression adds significant predictive value to the assessment of mortality risk in this population.

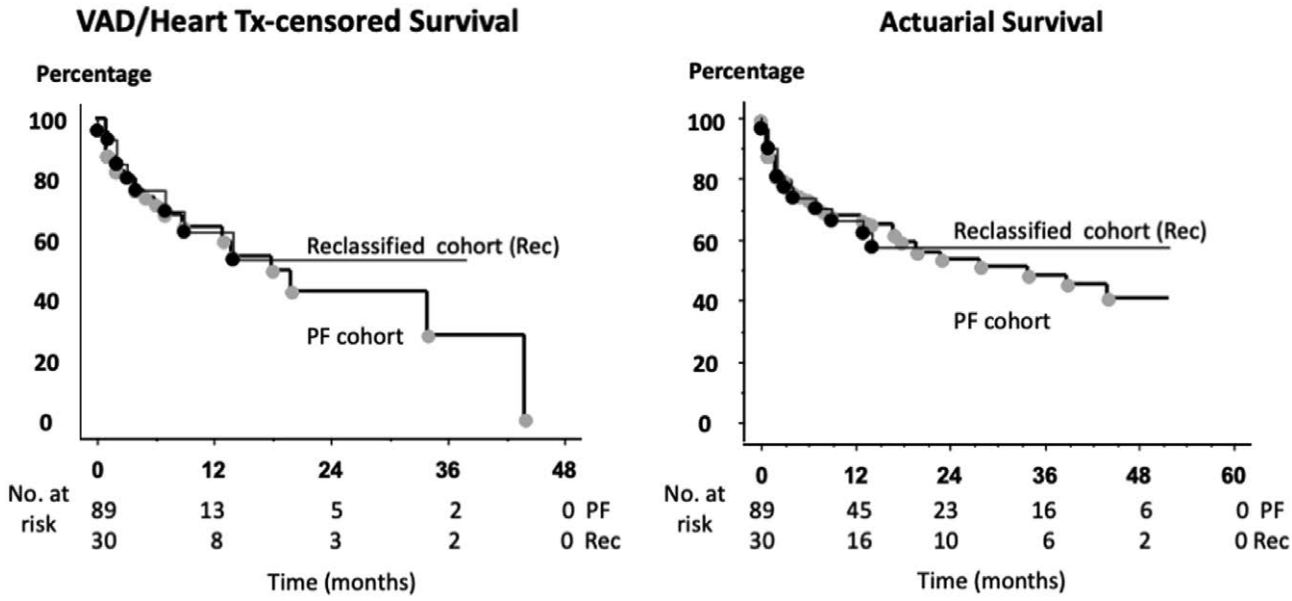

FIGURE 5. VAD- and heart transplant-censored survival as well as actuarial survival of patients defined as frail using the 2 frailty scales. Gray circles represent patients identified as frail using the physical frailty (PF) score, black circles shows the extra 30 patients identified as frail using the cognitive frailty score, which were reclassified as frail (Rec). VAD, ventricular assist device.

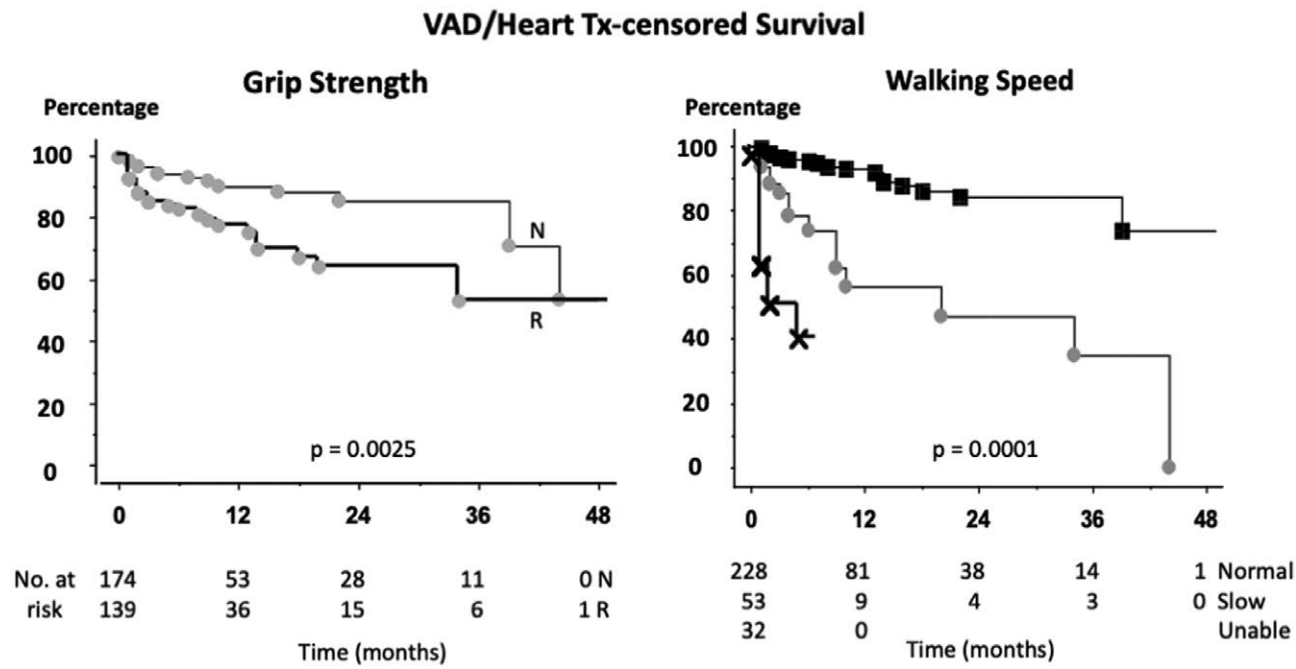

FIGURE 6. VAD/heart transplant (HTx)–censored survival of patients based on components of the frailty score. The left graph shows survival of patients with normal (N) or reduced (R) grip strength, and the graph on the right shows survival of patients with different walking speeds, normal (black squares), slow (gray circles), or (unable black crosses). VAD, ventricular assist device.

Although not the primary focus of this article, we also analyzed the impact of frailty on post-VAD and postheart transplant survival. All patients who underwent VAD implantation did so as a bridge-to-transplant. Frailty was associated with an approximate 3-fold increase in mortality after VAD implantation, consistent with the findings of previous studies in patients undergoing either bridge-to-transplant or destination VAD implantation.[8,26] This increased perioperative mortality risk needs to be balanced against our previous finding that PF is potentially reversible after VAD implantation.[27] It is less clear that cognitive impairment is reversible after VAD or HTx. While a previous review concluded that cognitive function was more likely to worsen than improve after cardiac surgery,[28] a more recent study of patients undergoing VAD implantation reported significant improvement in cognition 8 mo after the surgery.[29] The mean age of patients reported in that study was 58 y, similar to the age of patients included in our study. This is an area where further research is needed.

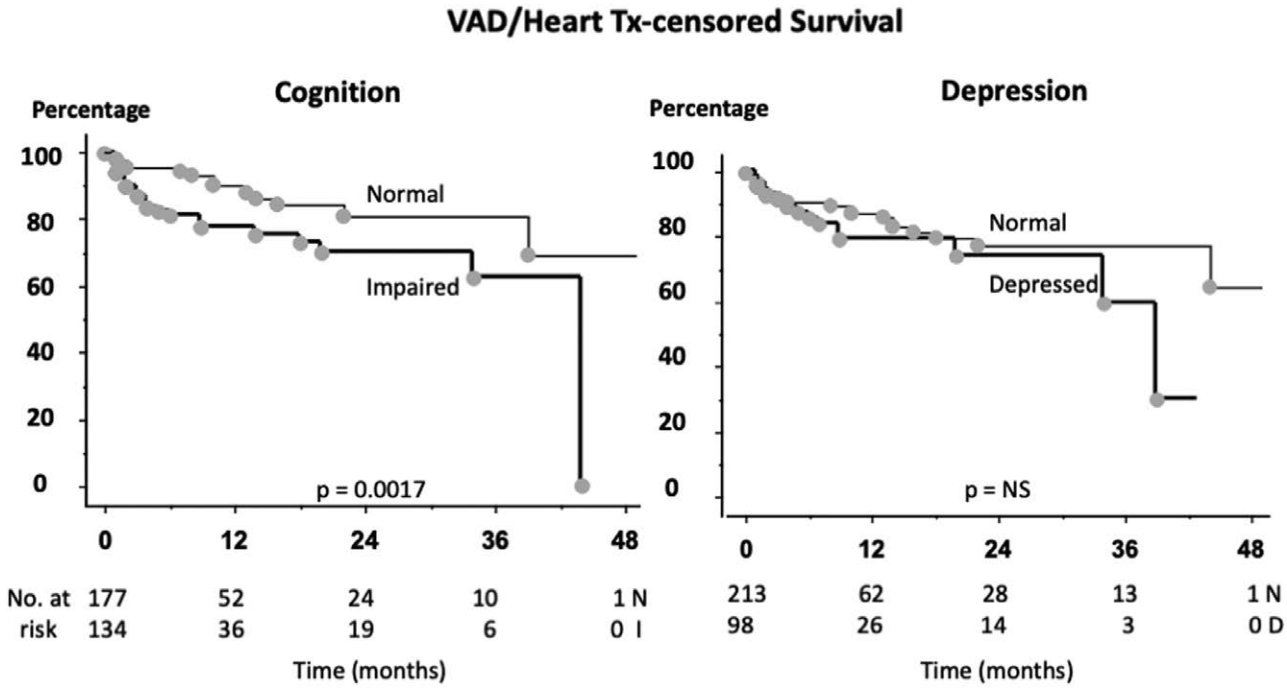

FIGURE 7. VAD/heart transplant (HTx)–censored survival of patients based on cognition or depression score using the MOCA and DMI, respectively. The left graph shows survival of patients with normal (N) or impaired (I) cognition, and the right graph shows survival of normal or depressed (D) patients. DMI, depression in medical illness; MOCA, Montreal Cognitive Assessment; VAD, ventricular assist device.

LIMITATIONS

The major limitation is that this is a single-center study with limited sample size. Nonetheless, our findings are consistent with and validate our previous published findings regarding the prevalence and prognostic implications of both frailty models in a study population double the size of our original cohort. We also included nonambulatory inpatients who accounted for 10% of our study population. Most were on intravenous inotropic support. It is well recognized that these patients face an extremely high mortality risk without further intervention[30,31] and our own experience highlights the poor outcome of this group of patients. Nonetheless, we thought it was important to assess the frailty status of these patients in part to provide a baseline for future comparison in those that proceeded to VAD or HTx. The large majority of nonambulatory patients were assessed as frail and all deaths within 1 m of assessment occurred in those who were frail based on CogF assessment. While pretransplant frailty appeared to have less of an adverse impact on survival after HTx, there was a long and variable delay between frailty assessment and transplantation. This is unavoidable due to the unpredictable timing of HTx and further study is needed to assess the impact of frailty on posttransplant outcomes. This limitation also raises the question of how often frailty should be reassessed in patients listed for transplant and the potential role of prehabilitation in mitigating the adverse health consequences.[32-34] The answers to these questions are beyond the scope of this study but are important for future research.

CONCLUSIONS

In conclusion, the results of this study validate our previously published findings that frailty is prevalent in patients with AHF referred for HTx. PF as determined by a modified version of the PF phenotype predicts early mortality. The addition of cognitive assessment to the physical assessment of frailty identifies an additional cohort of patients with a similarly poor prognosis.

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