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Reversibility of Frailty After Bridge-to-Transplant Ventricular Assist Device Implantation or Heart Transplantation

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Background. We recently reported that frailty is independently predictive of increased mortality in patients with advanced heart failure referred for heart transplantation (HTx). The aim of this study was to assess the impact of frailty on short-term outcomes after bridge-to-transplant ventricular assist device (BTT-VAD) implantation and/or HTx and to determine if frailty is reversible after these procedures. **Methods.** Between August 2013 and August 2016, 100 of 126 consecutive patients underwent frailty assessment using Fried's Frailty Phenotype before surgical intervention: 40 (21 nonfrail, 19 frail) BTT-VAD and 77 (60 nonfrail, 17 frail) HTx—including 17 of the 40 BTT-VAD supported patients. Postprocedural survival, intubation time, intensive care unit, and hospital length of stay were compared between frail and nonfrail groups. Twenty-six frail patients were reassessed at 2 months or longer postintervention. **Results.** Frail patients had lower survival (63 ± 10% vs 94 ± 3% at 1 year, $P = 0.012$) and experienced significantly longer intensive care unit (11 vs 5 days, $P = 0.002$) and hospital (49 vs 25 days, $P = 0.003$) length of stay after surgical intervention compared with nonfrail patients. Twelve of 13 frail patients improved their frailty score after VAD (4.0 ± 0.8 to 1.4 ± 1.1, $P < 0.001$) and 12 of 13 frail patients improved their frailty score after HTx (3.2 ± 0.4 to 0.9 ± 0.9, $P < 0.001$). Handgrip strength and depression improved postintervention. Only a slight improvement in cognitive function was seen postintervention. **Conclusions.** Frail patients with advanced heart failure experience increased mortality and morbidity after surgical intervention with BTT-VAD or HTx. Among those who survive frailty is partly or completely reversible underscoring the importance of considering this factor as a dynamic not fixed entity.

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Frailty has recently been identified as an important consideration in the assessment of patients referred for heart transplantation (HTx).[1] Although previously considered synonymous with advancing age, frailty is commonly identified among patients with advanced heart failure (AHF) across all ages. Several studies have identified that frailty provides a simple and effective means of risk stratification in patients undergoing cardiac surgical interventions,[2] including younger heart transplant patients.[3] In our previous studies of frailty in patients referred for HTx, frailty was reflective of increased vulnerability and was associated with an increased waitlist mortality and adverse postinterventional outcomes.[3,4]

In light of the growing body of evidence highlighting the risks associated with being frail, and the ageing demographic of patients being referred for and undergoing transplantation,[5] Indeed, the 2016 ISHLT listing criteria recommended that all patients undergoing transplant referral be assessed for frailty[1] in response to the growing body of evidence highlighting the risks associated with facility and the ageing demographic of patients being referred for and undergoing transplantation.[5]

Although frail patients may face increased morbidity and mortality risks from interventions, such as ventricular assist device (VAD) implantation and/or HTx, these interventions also have the potential to improve frailty severity. It has been hypothesized that the key to differentiating between patients who have positive and negative postinterventional outcomes in of a patient's frailty syndrome may lie in determining whether their frailty is predominantly cardiovascular or noncardiovascular in nature).[6]

Although there has yet to be any reports on the reversibility of physical frailty in patients undergoing bridge-to-transplant VAD (BTT-VAD) implantation or HTx, it is known that there is significant improvement in several factors associated with being frail (including cardiac cachexia and handgrip strength [HGS]) with these surgical interventions.[7,8] Given the high prevalence of frailty among those with AHF, the question of whether this syndrome is reversed after surgical intervention is of considerable clinical interest. The aims of this study were to assess the impact of frailty on short-term outcomes after BTT-VAD implantation and/or HTx and to determine if frailty, depression, and cognitive impairment are reversible after these procedures.

MATERIALS AND METHODS

Study Population

Patients for this study were recruited between August 1, 2013, and August 31, 2016. During that period, 126 consecutive patients underwent major surgical intervention for AHF at our institution—either BTT-VAD (n = 45) or HTx (n = 81). Seventeen of the 45 BTT-VAD patients proceeded to HTx during the same period, bringing the total number of HTx to 98. The study population of 100 patients who underwent frailty assessment before surgical intervention comprised 40 BTT-VAD (17 proceeded to HTx) and 60 HTx without prior VAD support. Of the 26 patients excluded from the study, 7 were already on VAD support before commencement of routine frailty testing in our institution and 19 were Intermacs class I and not able to be assessed. Twenty-six patients, who were frail preintervention, underwent repeat frailty assessment postintervention. This study was reviewed and approved by the hospital's research ethics committee (reference number LNR/13/SVH/21). Informed consent was obtained from all patients for their data to be entered prospectively into a dedicated database for subsequent analysis.

Frailty, Cognition, and Depression Assessment

Frailty was assessed using an adapted version of Fried's Frailty Phenotype. A detailed description of the assessment tool has been described previously[3] and are briefly outlined in Table 1. The 5 functional domains assessed were exhaustion, slowness, weakness, physical inactivity, and loss of appetite. Patients who were unable to mobilize out of bed or a chair at the time of assessment scored a point for slowness. A score of 3 or higher over 5 was classified as frailty. Cognitive impairment was assessed using the Montreal Cognitive Assessment (MoCA) questionnaire,[9] with scores less than 26 classified as cognitive impairment. The Depression in Medical Illnesses (DMI-10)[10] questionnaire was used to assess depression, with scores of 9 or higher classified as depression. Rationale for the use of the MoCA and DMI is given in our previous study. Briefly, the MoCA has a good sensitivity for the detection of mild levels of cardiac index (CI) in HF patients, and the DMI tool circumvents depressive elements (such as appetite and fatigue) which overlap with frailty elements.[4]

TABLE 1.

The 5 domains of physical frailty with a possible score of 0 or 1 for each domain

Modified version of Fried's Frailty Phenotype		
Domain		
Exhaustion	"In the last week, did you feel on at least 3 days, that everything you did was an effort?" and "In the last week, did you feel on at least 3 days, that you could not get going?" a response of "yes" to either question met the criteria for exhaustion	/5
Grip strength	Grip strength was considered weak if the average of 3 consecutive attempts on the left and right hand fell below 2 standard deviations of sex and age adjusted normative values	
Mobility	Walking speed was considered slow if the average of 3 attempts took 6 seconds or more to complete 5 meters	
Appetite	"Have you, in the last 3 months, been eating more/less than usual?" A response of "less" was classified as poor appetite	
Physical activity	"How often do you engage in activities that require a low or moderate level of energy, such as gardening, cleaning the car or going for a walk?" A response of "1 to 3 times a month or hardly ever" was classified as physical inactivity	

HGS

Reduced HGS—1 of the 5 items recorded during the full frailty assessment—has been proposed as a single-item surrogate measure of frailty.[8] HGS was assessed using a Jamar Hand Dynamometer. Grip strength was considered weak if the average of 3 consecutive attempts on the left and right hand was less than 2 standard deviations below the sex- and age-adjusted normative values. The higher of the right-hand and left-hand averages were recorded for baseline and follow-up HGS.

Assessment of Heart Failure Severity

As part of routine patient data collection, markers of heart failure severity were also obtained. These included New York Heart Association (NYHA) class, heart failure duration, left ventricular end-diastolic diameter (LVEDD) and left ventricular ejection fraction (LVEF) by echocardiography, central hemodynamic pressures including right atrial pressure (RAP), mean pulmonary artery pressure (MPAP) and pulmonary artery wedge pressure (PAWP) and CI by right heart catheterisation. Patients were also stratified by LVEF into those with heart failure and preserved ejection fraction (LVEF $\geq$ 40% heart failure with a reduced ejection fraction [HFPEF]) and those with heart failure and reduced ejection fraction (LVEF < 40%, HFREF). Estimated glomerular filtration rate (eGFR), calculated using the Modification of Diet in Renal Disease formula, serum creatinine, bilirubin and albumin, blood hemoglobin levels and body mass index (BMI) (calculated as weight/height^2 (kg/m^2), were also recorded.

Outcome Measures

Morbidity and Mortality

Postintervention intubation time, days in intensive care unit (ICU) and hospital length of stay (LOS) were recorded for all patients undergoing BTT-VAD or HTx. Postintervention survival was also recorded.

Assessment of Reversibility of Frailty

Follow-up assessments of frailty phenotype, HGS, cognitive impairment, and depression were conducted postintervention in patients who were classified as frail preintervention. All reassessments were performed at least 2 months postintervention.

Statistical Analysis

Descriptive statistics were calculated for all variables. The proportion of patients within each category (nonfrail and frail) was determined for the total study population. Association between the frailty category and age, sex, depression, cognitive impairment, markers of heart failure severity, hematological, and biochemical parameters were made using unpaired *t* tests or Mann-Whitney *U* test for continuous variables and χ^2 test for categorical variables. Baseline characteristics are presented as mean ± standard deviation or median with interquartile range for continuous variables and frequency (percent) for categorical variables. For comparison of outcomes, survival time was defined as the time between the date of intervention and the date of death or date of censoring (date of most recent follow-up). Kaplan-Meier cumulative survival curves were also generated for each frailty category and the log-rank test was used to compare survival rates between frail and nonfrail groups. A Cox proportional hazards model was used to assess the association between frailty and death adjusting for covariates. To assess changes in frailty, HGS, cognition, and depression at follow-up, related sample Wilcoxon signed ranked test was used for continuous data and McNemar for categorical data. A *P* value less than 0.05 was considered statistically significant. All the data analyses were conducted using the IBM SPSS Statistics software (version 24; IBM Corporation).

RESULTS

Frailty Prevalence

During the study period, 100 patients (65 men:35 women; age 51 ± 13 years; range, 16-71; LVEF, 27 ± 14%) underwent surgical intervention: 40 VAD implantations (17 of whom proceeded to HTx) and 60 heart transplants (Figure 1). The underlying causes of heart failure were dilated cardiomyopathy (58%), ischemic heart disease (22%), hypertrophic or restrictive cardiomyopathy (14%), and other cardiac diseases (6%). Thirty-two patients were identified as physically frail (32%). Selected baseline demographics by physical frailty are given in Table 2. Frailty was not associated with age, BMI, left ventricular end-diastolic dimension or ejection fraction, PAWP and MPAP, cardiac index, blood hemoglobin level or renal function (as assessed by serum creatinine or eGFR). Frailty was significantly associated with being female, NYHA class IV symptomatic status, higher RAP, higher serum bilirubin and lower serum albumin, as well as cognitive impairment and depression (both as continuous and categorical variables). The majority (70%) of frail patients within the intervention group were younger than 60 years.

Frailty and Postintervention Outcomes

(1) Overall Survival

Postintervention survival for all 100 patients is shown in Figure 2. For patients who underwent BTT-VAD followed by HTx, postintervention survival was assessed from the time of VAD implantation. Survival was significantly lower in patients who were frail before intervention. By 12 months postintervention, survival was 94 ± 3% in the nonfrail group compared with 63 ± 10% in the frail group (P = 0.012, Cox-Mantel test). Postoperative median ICU and total hospital LOS were significantly longer in frail patients (11 vs 5 days, P = 0.002 and 49 vs 25 days, P = 0.003, respectively).

We examined the impact of the following variables on postintervention survival: frailty category (nonfrail vs frail), age (younger than or older than 60 years), sex, LVEF (<27% vs $\geq$ 27%), depression, cognitive impairment, anemia, renal function (eGFR < 60 vs $\geq$ 60 mL/min per m^2), serum albumin (<35 vs or $\geq$ 35 mmol/L). Applying Cox proportional hazards model, only frailty and older than 60 years were independent predictors of postintervention mortality with the hazard ratios of 2.8 (95% confidence interval, 1.1-7.5) and 2.5 (95% confidence interval, 1.0-6.8), respectively.

(2) Post-VAD Outcomes

Forty patients underwent VAD implantation during this study, including 6 patients (3 frail and 3 nonfrail) who were placed on biventricular VAD support. There was a median of 22 (6-127) days between frailty assessment and VAD

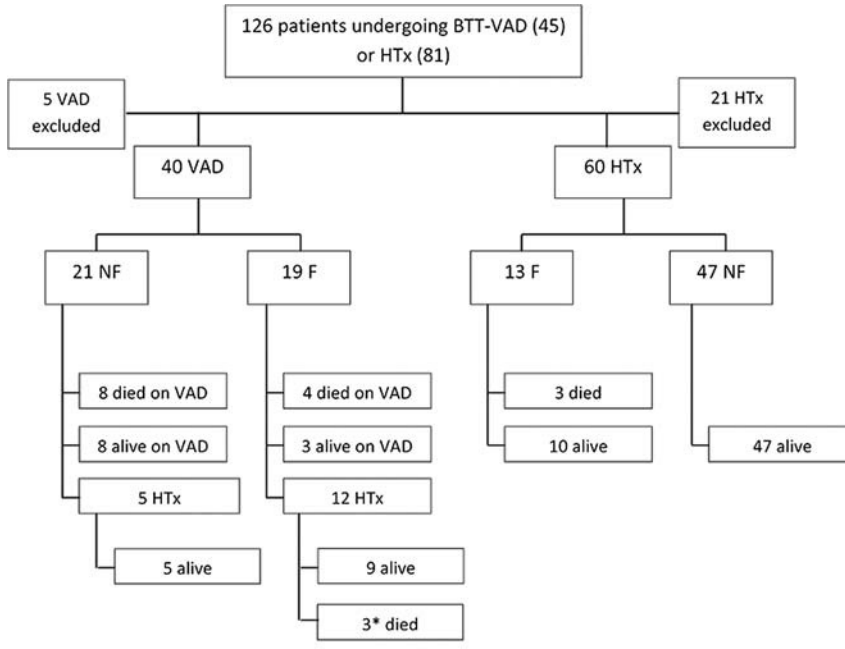


FIGURE 1. Consort diagram illustrating the derivation and outcome of the study population. F frail, NF nonfrail. *2 of 3 BTT-VAD patients were reclassified as nonfrail before HTx.

implantation. Post-VAD outcomes by frailty status are given in Table 3. Almost half of all VAD patients (19/40) were identified as frail; and indeed, there was a significant association with being frail and proceeding to VAD support ($P = 0.022$). Compared with their nonfrail counterparts, frail patients were intubated for an average of 3 hours longer, spent twice as long in ICU (median 6 vs 12 days, $P < 0.05$) and a month longer in hospital (median 31 vs 57 days, $P < 0.05$). Fifteen patients died post-VAD implant. Four of 19 frail patients died postimplant and another 3 died posttransplant. Eight of 21 nonfrail patients died postimplant. Post-VAD deaths tended to occur earlier in the frail patients: 6 month and 12-month survival post-VAD implant was lower in frail patients however the differences were not significant (Table 3). Seventeen patients proceeded from VAD to HTx: 12 were frail pre-VAD implantation. Nine of the 12 patients who were frail pre-VAD underwent frailty reassessment before HTx: all 9 improved their frailty score although 2 were still classified

TABLE 2.

Patient demographics by physical frailty

Physical frailty				
	Total (n = 100)	Nonfrail (n = 68)	Frail (n = 32)	*P*
Age, y	51 ± 13	52 ± 12	50 ± 15	ns
Sex (male/female)	65:35	50:18	15:17	0.018
BMI, kg/m^2	26.1 ± 4.8	26.5 ± 4.6	25.1 ± 5.4	ns
Heart failure duration, y	5.0 ± 5.3	5.1 ± 5.0	4.9 ± 6.2	ns
LVEDD, mm	67 ± 13	68 ± 13	66 ± 13	ns
LVEF, %	27 ± 14	27 ± 13	27 ± 16	ns
HF type: HFrEF:HFpEF	85:15	58:10	27:5	ns
NYHA class (III:IV)	27:73	24:44	3:29	0.012
RAP, mm Hg	14 ± 7	13 ± 6	17 ± 8	0.020
PAWP, mm Hg	25 ± 8	24 ± 7	27 ± 8	ns
MPAP, mm Hg	36 ± 10	35 ± 9	37 ± 10	ns
CI, L/min per m^2	1.9 ± 0.5	1.9 ± 0.6	1.8 ± 0.5	ns
Se creatinine, μmol/L	111 ± 36	111 ± 33	110 ± 40	ns
eGFR, L/min per 1.73 m^2	61 ± 19	62 ± 17	61 ± 22	ns
Se bilirubin, μmol/L	26 ± 18	23 ± 15	31 ± 21	0.047
Se albumin, g/L, hypoalbuminemia, n (%)	42 ± 5, 15 (1%)	42 ± 4, 5 (7%)	39 ± 6, 10 (31%)	0.006, 0.005
Hemoglobin, g/L anemia, n (%)	131 ± 18, 36 (36%)	133 ± 17, 23 (34%)	128 ± 17, 13 (41%)	ns, ns
Cognition MOCA score, abnormal MOCA, n (%)	26 ± 4, 36 (36%)	26 ± 3, 18 (26%)	24 ± 4, 18 (56%)	0.024, 0.007
Depression DMI score, abnormal DMI, n (%)	7 ± 6, 34 (34%)	6 ± 5, 18 (26%)	10 ± 8, 16 (50%)	0.002, 0.025

HFrEF, heart failure with a reduced ejection fraction; N, number; ns nonsignificant; Se, serum.

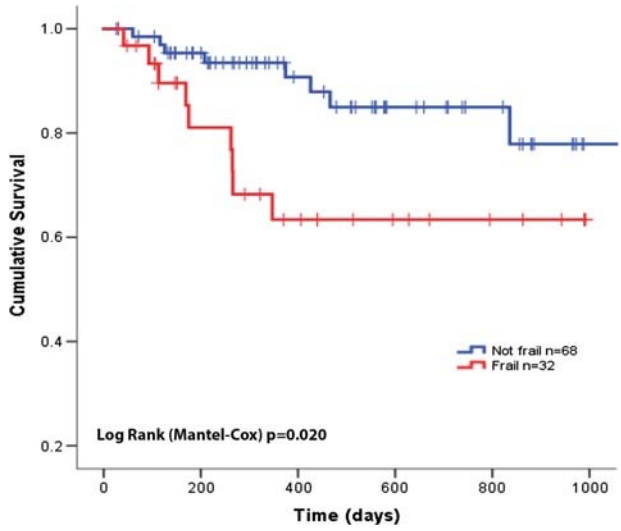


FIGURE 2. Postinterventional survival.

as frail. Three BTT-VAD patients died early posttransplant (at days 16, 44 and 56), 2 from primary graft failure and 1 from infection. All 3 patients had improved their frailty score post-VAD implant and before HTx although 1 patient whose score had improved from 5 to 3 was still classified as frail at the time of transplant. The results of serial frailty assessments in the 12 patients who were frail pre-VAD and who proceeded to HTx are illustrated in Figure 3.

(3) Postheart transplant outcomes

Seventy-seven patients underwent HTx during this study. There was a median of 183 (98-419) days between frailty assessment and transplantation. Eighteen (23%) patients were classified as frail before HTx: 5 BTT_VAD patients and 13 patients with AHF not requiring VAD support. Post-HTx outcomes by frailty status are shown in Table 4. Although nonsignificant, the median duration of intubation posttransplantation was 35 hours longer and ICU LOS 3 days longer for the frail group. Hospital LOS posttransplant was similar for frail and nonfrail groups. All 6 patients who died posttransplant had been found to be frail at their initial assessment, although as mentioned above 2 of 3 VAD-supported patients who died posttransplant had been reclassified as nonfrail before transplant. Posttransplant survival at 6 and 12 months was 96 ± 3% in nonfrail patients. Posttransplant survival for frail patients was 87 ± 8% at 6 months and 66 ± 16% at 12 months. In addition to the 3 VAD-supported patients who died posttransplant, 3 other patients died: a 57-year-old woman and 21-year-old woman died at days 104 and 265, respectively, from sepsis/multiorgan failure and a 29-year-old woman died at day 347 from uncontrollable acute cellular rejection.

Reversibility

Frail Preintervention

Of the 32 patients who were identified as frail preintervention, 6 died before reassessment (3 post-VAD and 3 post-HTx). A total of 26 frail patients underwent frailty reassessment postintervention: 13 post-VAD implantation and 13 posttransplantation. Follow-up assessments were performed 133 (96-185) days post-VAD and 184 (88-457) days post-HTx.

Among the frail pre-VAD patients, there was a significant improvement in frailty score postintervention (4.0 ± 0.8 to 1.4 ± 1.1, $P < 0.001$) with 10 of the 13 patients being recategorized to nonfrail at follow-up (Figure 4A). Of the 3 patients who remained frail postintervention, 2 had an improvement in frailty score, although the threshold for recategorization (<3/5) was not reached. No patients experienced worsening frailty postintervention, although 1 patient remained unchanged. Ten of the 13 frail pre-VAD patients had reduced HGS. At reassessment, there was a significant improvement in grip strength (from 24.5 ± 13.0 kg to 27.6 ± 10.3 kg, $P < 0.02$), with 3 weak patients being reclassified to normal grip strength postintervention (Figure 4B). There was also a nonsignificant improvement in DMI score (11.5 ± 8.3 vs 5.3 ± 4.3, $P = 0.10$), with 3 of 5 depressed patients being recategorized to being not depressed post-VAD. There was a no change in MOCA score (24.5 ± 4.7 vs 24.5 ± 3.5, P = ns).

Similar trends were seen among those identified as frail pre-HTx. There was a significant improvement in frailty score (3.3 ± 0.6 to 0.8 ± 1.0, $P < 0.001$) with all the frail patients being recategorized to nonfrail at follow-up (Figure 5A). Seven of the 13 frail pre-HTx patients had reduced HGS preintervention. At reassessment, there was a nonsignificant improvement in grip strength (from 22.9 ± 9.4 to 28.2 ± 10.0 kg, $P = 0.114$), with 3 of the weak patients being reclassified to normal grip strength postintervention (Figure 5B). There was a significant improvement in DMI score (from 8.9 ± 7.6 vs 3.2 ± 3.5, $P = 0.016$), with 3 of 5 depressed patients being reclassified as nondepressed postintervention. Although improved, the change in cognitive impairment at follow-up was nonsignificant (24.3 ± 3.4 vs 27.2 ± 2.4, $P = 0.100$), with 4 of 6 cognitively impaired patients being reclassified as normal cognition postintervention.

DISCUSSION

There were 2 major findings of this study. The first is that patients with documented frailty and AHF have an increased mortality after major surgical interventions (BTT-VAD or HTx). There was also increased morbidity, reflected by extended lengths of stay in the ICU and hospital after these

TABLE 3.

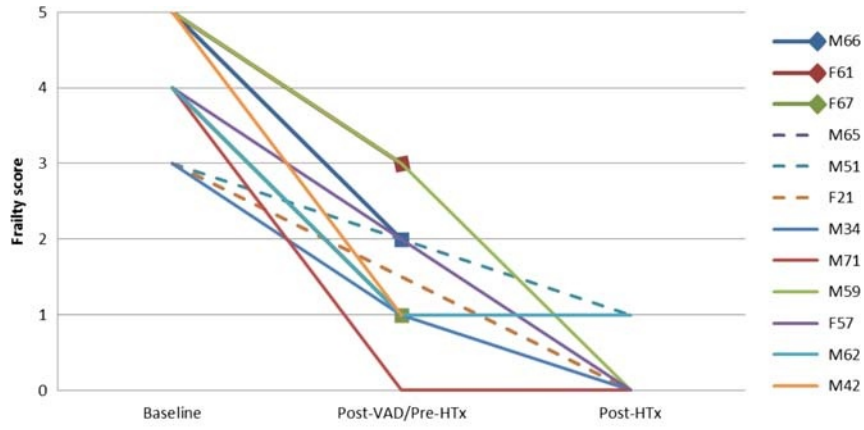
Post-VAD outcomes by physical frailty

Physical frailty			
	Total (n = 40)	Not-Frail (n = 21)	Frail (n = 19)
Age, y	55 ± 12	55 ± 11	55 ± 13
Sex (male/female)	31:9	19:2	12:7
LVAD/BiVAD	34:6	18:3	16:3
Intubation, h	24 (21-62)	24 (18-45)	27 (22-93)
ICU post-MCS, d	8 (5-17)	6 (4-10)	12 (7-21)*
LOS post-MCS, d	39 (23-58)	31 (22-45)	57 (28-71)*
Survival at 6 mo, %	80 ± 6	86 ± 8	74 ± 12
Survival at 12 mo, %	71 ± 7	80 ± 9	61 ± 12

Values are mean ± SD for normally distributed continuous data, median (interquartile range) for nonnormally distributed continuous data, and number for categorical data.

LVAD, left ventricular assist device; BiVAD, both a left and right VAD, MCS, mechanical circulatory support.

* $P < 0.05$ Frail versus nonfrail.



Abbreviations: F female, HTx heart transplant, M male, VAD ventricular assist device, BTT bridge to transplant.
Key: Solid line with diamond, patients died without post-HTx follow-up, only post-VAD follow-up (n=3).
Dotted line, patient received only a post-HTx follow-up, no post-VAD follow-up (n=3).
Solid line, patients received both post-VAD and post-HTx follow-up (n=6).

FIGURE 3. Follow-up frailty among the BTT-VAD/HTx subgroup. Key: solid line with diamond, patients died without post-HTx follow-up, only post-VAD follow-up (n = 3). Dotted line, patient received a post-HTx follow-up, no post-VAD follow-up (n = 3). Solid line, patients received both post-VAD and post-HTx follow-up (n = 6). F, female.

procedures. These findings are consistent with previous reports of patient groups undergoing major cardiac surgical interventions.[11,12] Other authors have reported increased mortality and duration of hospitalisation after VAD implantation however these studies were performed predominantly in older destination-VAD recipients.[8,13] To our knowledge, this is the first study to report these findings in a younger bridge-to-transplant VAD population and in patients undergoing HTx. Despite the increased postprocedural mortality risk for frail patients compared with their nonfrail counterparts, most frail patients survived the intervention: 15 of 19 frail patients undergoing VAD implantation and 13 of 17 frail patients undergoing HTx.

The second major finding was that the frailty phenotype was partly or completely reversible in the large majority of patients who could undergo reassessment post-VAD or posttransplant. Only 1 patient, a 67-year-old man, failed to improve on his frailty score when repeated 5 months after VAD implantation. We were concerned that older frail patients would demonstrate less reversibility than younger patients. Although the number of patients recruited for this study was too small to discount this possibility, it is noteworthy that the oldest patient, a 71-year-old man reversed his frailty score from 4 to 0 after VAD implant. He subsequently underwent HTx and remains well 6 months posttransplant.

Based on these findings, we believe that delisting all frail patients for BTT-VAD or HTx, due to increased procedural risks, is premature. Although our findings suggest that the frailty phenotype is wholly or partly reversible in most frail patients with AHF who undergo BTT-VAD or HTx transplantation, we speculate that reversal of frailty in BTT-VAD patients reduces the mortality and morbidity risks of subsequent HTx however this is also an area where further research is required. It would seem logical that there is a greater chance of reversal of frailty if related to cardiac factors rather than noncardiac ones. This raises the question of whether all items on frailty assessment are equal in their potential reversability.

The reversibility of frailty was initially suggested in the context of patient selection for destination left ventricular assist device therapy. Flint and colleagues[6] hypothesized that the relative proportion of cardiac- and non–cardiac-related factors that constitute a patient's frailty, was indicative of the extent to which frailty may be reversible postintervention. For instance, if a patient's frailty was largely the result of cardiac-related factors, the implant of VAD or HTx, would effectively ameliorate aspects of their heart failure-induced frailty.

To date, the small number of studies that have measured frailty pre and postintervention have suggested that this is the next step in frailty research. One such study by Chung and colleagues assessed a single item measure of frailty (reduced HGS, <25% body weight) monthly for 6 months after VAD implantation in 72 destination patients. This study found that HGS significantly improved at 3 months after VAD implantation and maintained significant improvement to 6 months. We observed a similar improvement in mean HGS in our frail cohort; however, this improvement was only significant for the BTT-VAD group. Comparatively, the improvements in total frailty score were significant among those undergoing either BTT-VAD or HTx. This may reflect the better relative sensitivity of a more comprehensive frailty tool

TABLE 4.

Post-HTx outcomes by physical frailty

Physical frailty			
	Total (n = 77)	Nonfrail (n = 59)	Frail (n = 18)
Age, y	50 ± 14	52 ± 13	46 ± 17
Sex (male/female)	47:30	42:18	5:12*
Ischemic time, min	205 ± 94	209 ± 93	188 ± 94
Intubation, h	35 (16-130)	31 (16-134)	66 (14-129)
ICU post-MCS, d	7 (3-10)	6 (3-10)	9 (3-16)
LOS post-MCS, d	25 (16-46)	25 (15-39)	25 (18-57)
Survival at 6 mo, %	94 ± 3	96 ± 3	87 ± 8
Survival at 12 mo, %	90 ± 4	96 ± 3	66 ± 16**

Values are mean ± SD for normally distributed continuous data, median (interquartile range) for non-normally distributed continuous data, and number for categorical data.

* $P < 0.05$, frail versus nonfrail.

** $P < 0.01$, frail versus nonfrail.

MCS mechanical circulatory support.

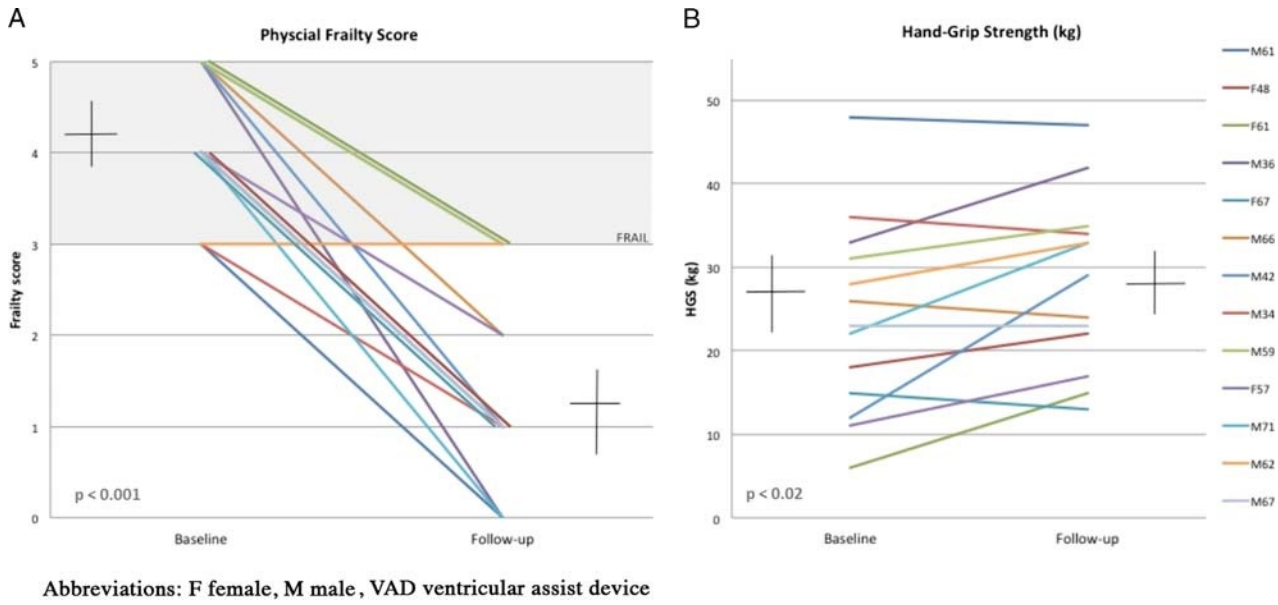


FIGURE 4. Changes in frailty score and HGS for patient's frail pre-VAD. F, female; M, male.

for detecting changing frailty status above that of a single-item measure, such as HGS. Other authors have reported that gait speed, another single frailty measure, predicts mortality and morbidity after heart surgery and may be more reliable than more complex frailty instruments[14,15]; however, this measure has limited application in a population with AHF because many are too sick to mobilize. In addition, to our knowledge there are no studies that have assessed gait speed before and after cardiac surgical interventions. Although there is currently limited evidence for reversibility of frailty within cardiac surgical populations, frailty has been shown to improve in patients of a similar age undergoing kidney transplantation. This study of 349 patients showed that although there was an initial worsening of frailty severity 1 month posttransplantation, by 3 months frailty had significantly improved. Furthermore, patients who were frail pretransplant were the ones most likely to improve their frailty score after transplantation.[16]

The question of cardiac and noncardiac causes is important here. If gait speed or hand grip are reduced because of heart failure-induced weakness, one would expect that they would improve postintervention, but if they were caused by some other problem, for example, a neurological condition, then they may not be reversible. Another important consideration is cognitive function. We have previously reported that the incorporation of cognitive impairment as an item in frailty assessment improves the prediction of mortality in patients with heart failure.[4] If the patient has cognitive slowing due to heart failure-induced apathy or even depression, this could be potentially reversed but if it is indicative of microvascular disease or hypoxic brain damage, it is unlikely to be reversible with improved cardiac function.

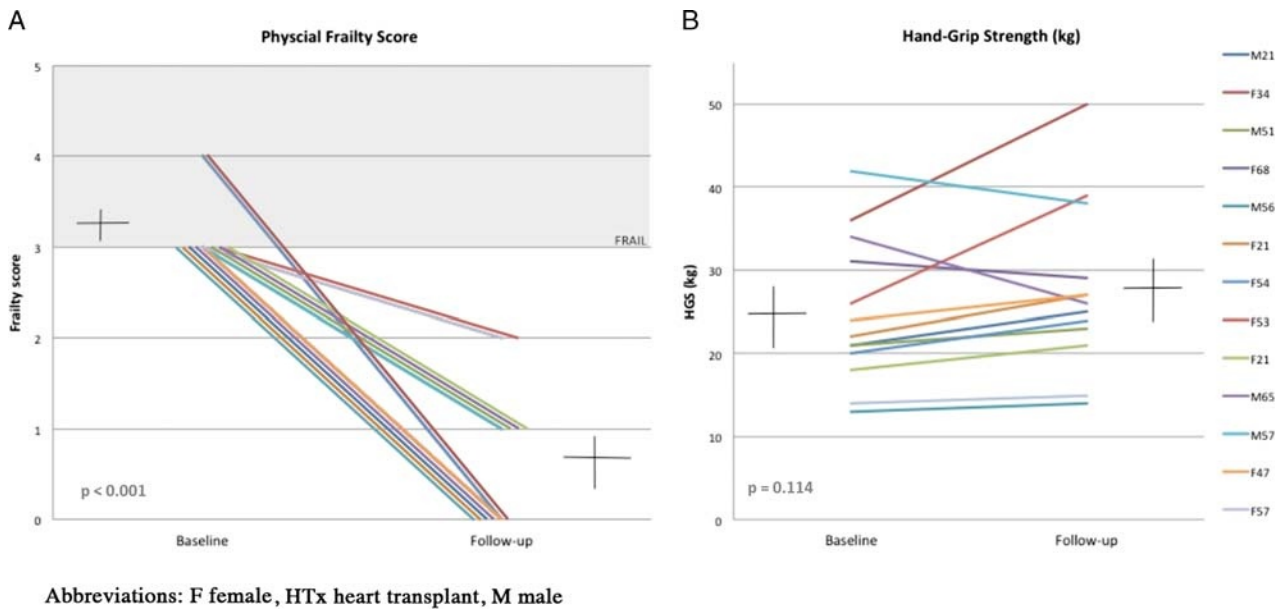


FIGURE 5. Changes in frailty score and HGS for patient's frail pre-HTx.

Limitations

To assess the impact of frailty on postoperative survival we examined the actuarial survival for all 100 patients from the date of their first intervention: VAD or HTx. It is possible that the impact of frailty on postoperative mortality may differ per the type of surgical intervention, however given the impact of frailty on outcomes after other major cardiac surgical procedures we believe that the adverse effect of frailty on operative mortality is likely to be similar for VAD and HTx. Another limitation of our study was the variable time between baseline frailty assessment and the surgical intervention. This was explained in part by the fact that patients underwent frailty assessment at the time of initial referral which did not necessarily coincide with the timing of BTT-VAD or HTx. There was also considerable variation in the timing of repeat frailty assessment postintervention. However, all patients were at least 2 months postintervention to allow adequate time for recovery from the surgical procedure. Regardless of the timing of postintervention frailty assessment, it does not affect the interpretation of our critical finding that the frailty phenotype is substantially reversible in most patients.

Decisions regarding the management of patients with AHF need to take into consideration the increased morbidity and mortality risks associated with frailty and the prospects of reversing frailty after the intervention. We initially hypothesized that frailty would be more prevalent and less reversible in older patients with AHF but so far have found this not to be the case.[3,4] We believe that future studies should focus on identification of measures to distinguish reversible from irreversible frailty and on the role of prehabilitation to see if frailty can be reversed at least in part before BTT-VAD or HTx.[17-19]

CONCLUSION

Frail patients with AHF experience increased mortality after surgical intervention with BTT-VAD or HTx. Frail patients also experience increased morbidity after these procedures as reflected by longer ICU and hospital stays; however, for those who survive, the perioperative period frailty is partly or completely reversible in the majority. Based on these data, measurement and monitoring frailty status is an important tool in planning clinical care.

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