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Benefits of both physical assessment and electronic health record review to assess frailty prior to heart transplant

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Abstract

Introduction: Frailty status affects outcomes after heart transplantation, but the optimal way to assess frailty prior to transplant remains unknown.

Methods: This single-center, observational study assessed 44 heart transplant candidates for frailty using three methods. The Short Physical Performance Battery (SPPB) and Fried Frailty Phenotype (FFP) were used as two physical assessments of frailty. The Frailty Risk Score (FRS) was used as a chart-review based assessment measuring 20 different biopsychosocial and functional components, including biomarkers, depression, cognitive impairment, and sleep.

Results: We determined the correlation between FRS, SPPB, and FFP and how each correlated with clinical outcomes. Of 44 participants, mean age was 60 years. FRS correlated with SPPB and FFP ($P = .043$, $P < .001$, respectively). Higher frailty as measured by SPPB and FRS was significantly associated with lack of achieving waitlist status ($P = .022$; $P = .002$) and not being transplanted ($P = .026$; $P = .008$). Higher frailty by SPPB and FFP was also associated with mortality ($P = .010$; $P = .025$).

Conclusion: SPPB and chart-review FRS showed potential for predicting waitlist and transplant status of heart transplant candidates, while SPPB and FFP were associated with mortality. Additional studies may serve to validate these observations.

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1 | INTRODUCTION

Heart transplantation serves as the treatment of choice for patients with end stage heart failure (HF) not responsive to medical therapy. With an aging population, there has been an increased number of older adults with advanced heart failure.[1] In turn, the age of those evaluated for heart transplant is also increasing, with 10.8% of heart transplant candidates 65 years old in 2003[2] increasing to 18.7% in 2018.[3] The 2016 ISHLT guideline for heart transplant candidacy, addresses the concerns of an older population by recommending the consideration of frailty in heart transplant criteria,[4] as has also been recommended by the American Society of Transplantation.[5]

Frailty is a syndrome of multiorgan deterioration associated with decreased resiliency resulting in an increased risk for adverse outcomes after hospitalizations or surgical procedures. Older surgical patients who are frail have increased risk for postoperative morbidity, mortality, length-of-stay (LOS), complications, and discharge to a residential care facility.[6-10] In a study of 120 heart transplant candidates, one-third were frail, and frailty was associated with all-cause mortality and a trend toward longer ICU and hospital stays.[11]

Previously, physicians assessed the frailty of a transplant candidates through the "eyeball test."[12] Given the subjective nature of this assessment, more objective frailty assessments have developed. One of the most common frailty assessments is the Fried Frailty Phenotype (FFP)[13] test, which evaluates for weight loss, exhaustion, low physical activity, and weakness. Another frailty assessment, the Short Physical Performance Battery (SPPB), measures lower extremity strength and balance.[14] As compared to the FFP, the SPPB is composed only of objective measures of function without subjective questions. Both the SPPB and FFP involve additional tests that must be conducted during an in person assessment by the care team. An alternative approach is to perform a chart-based review for frailty assessment, which eliminates the need for additional in person assessments by utilizing biopsychosocial data previously captured in the electronic medical record. Using 16 biopsychosocial risk factors, the Frailty Risk Score (FRS), has been shown to correlate with risk of in-hospital mortality and rehospitalization, showing EMR to be an effective method of frailty assessment.[15] The FRS has since been shown to be associated with increased LOS and number of readmissions in kidney transplant recipients,[16] but has not yet been evaluated in the heart transplant population.

Although a few studies have shown that frailty status impacts outcomes after heart transplants standard approach to frailty assessment during transplant candidacy evaluation does not yet exist. Further, different frailty assessments may be best for predicting different aspects of surgical care,[10] but there is a lack of extensive comparison across different frailty assessments in heart transplant patients. Given the growing data on use of SPPB and FFP in transplant candidates coupled with our center's previous experience in application of FRS assessment in kidney transplant recipients, we selected these three approaches

for further study in candidates for heart transplantation. This study aims to address these gaps of understanding by determining the relationship between SPPB, FFP, and FRS frailty assessments, analyzing their individual predictive abilities of clinical outcomes, and elucidating the potential for use of a biopsychosocial EMR frailty assessment in clinical settings. In this study, we compared the SPPB, FFP, and FRS assessments against each other and how each assessment predicts clinical outcomes in heart transplant candidates.

2 | METHODS

2.1 | Sampling selection

In this single-center, observational study, 44 patients undergoing evaluation for heart transplant candidacy by the UCLA Heart Transplant Patient Selection Committee also underwent frailty assessment. Patients were admitted at the time of transplant evaluation and frailty assessment but could be discharged from the hospital prior to organ transplantation. Inclusion criteria for selection was patients 55 years or older. Younger patients were included if the clinical team requested a frailty evaluation.

2.2 | Frailty assessments

Patients were evaluated for frailty using three different assessments from June 2018 to May 2020 as described below as part of the standard pre-transplant workup for hospitalized patients. Patients were retrospectively evaluated for frailty using a modified Frailty Risk Score (FRS).[15] Based on Lekan et al., our modified FRS assessed 20 different biopsychosocial and functional components: social support, activities of daily living (ADL), depression, sleep, current smoking status, history of smoking, falls, fall risk, visual impairment, hearing impairment, dyspnea/shortness of breath (SOB), fatigue, weakness, chronic pain, incontinence, nutrition/weight-loss, cognitive impairment, low albumin (< 3.9 g/dL), low hemoglobin (female < 11.6 g/dL, male < 13.5 g/dL), and abnormal white blood cell count ($< 4.16 \times 10^3$/uL or $> 9.95 \times 10^3$/uL) (Table 1).

Prospective frailty assessments included the SPPB and the FFP. The SPPB tested balance, gait speed, and lower extremity strength using tandem stand, chair rise, and 5 m walk. Each activity was scored on a scale of 0–4 points for a total of 12 points, with higher scores indicating less frailty.[14] The FFP tested gait speed and grip strength and surveyed for weight loss, exhaustion, and physical activity.[13] Each activity was given a score of 0 or 1 for a total of 5 points, with higher scores indicating greater frailty. Patients were not included for SPPB or FFP testing if there was a logistical issue such as an incomplete or non-interpretable test. Those who were too weak to perform the tests were scored as frail for that category.

All frailty assessments (FFP, SPPB, and FRS) were performed within two weeks of transplant candidacy evaluation. The SPPB and FFP tests were performed by a team of nurses, transplant coordinators and geriatric cardiologists who had been trained in the assessments.

2.3 | Data collection

Demographic and clinical data were collected from the hospital admission during which transplant candidacy was evaluated. For the patients who were not admitted during evaluation, data were collected from the clinic visits dedicated to transplant candidacy evaluation. In addition to the data necessary for FRS calculation, demographic and clinical data included age, sex, race/ethnicity, etiology of heart failure, body mass index (BMI), inotrope dependence, presence of mechanical circulatory support (MCS), and length of initial hospitalization. The Charlson comorbidity index (CCI) and the sequential organ failure assessment (SOFA) score were also calculated for each patient to capture medical complexity and severity of illness, respectively. The CCI predicts 10-year mortality in patients with multiple comorbidities and is calculated based on presence of the following: myocardial infarction, peripheral vascular disease, congestive heart failure, stroke, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes, hemiplegia, moderate to severe chronic kidney disease, malignancy, leukemia, lymphoma, and acquired immunodeficiency syndrome.[17] The SOFA score predicts intensive care unit mortality and is calculated with the following information: partial pressure of oxygen, presence of mechanical ventilation, platelet count, Glasgow coma scale, bilirubin level, supplemental oxygen requirement, mean arterial pressure or dependence on pressor support, creatinine level.[18] The FRS was manually calculated based on lab results and chart notes from services including but not limited to physical therapy, psychiatry, social work, general medicine, and cardiovascular disease.

2.4 | Outcomes

Final chart review was done May 14, 2020. Waitlist and transplant status were noted based on the decision of the Selection Committee. Patient mortality was based on death after SPPB and FFP assessment date, not after transplant. Only one patient died after transplant. One patient was missing a waitlist status because the patient died. This patient was counted as not listed during analysis.

2.5 | Data analysis

Demographic data was analyzed using percentage or mean and median, as appropriate.

Statistical analyses were performed through JMP Pro 14.2 (SAS Software). t tests and Chi-squared tests were used to determine differences in baseline demographic and clinical variables in frail versus non-frail individuals, as appropriate. Patients with an SPPB score < 6 were considered frail, the standard cutoff for frailty with this measure. Bivariate linear fit was performed to assess the correlation between different assessments. t tests and one-way ANOVA based on frailty status were performed to determine differences in post-assessment outcomes.

2.6 | Ethics declaration

The UCLA IRB approved the retrospective review of data collected.

3 | RESULTS

44 patients were assessed for frailty as part of their pre-transplant evaluation (Figure 1). Mean age was 60 ± 12 years. The majority were male (80%), non-white (54%), and had a non-ischemic cardiomyopathy (61%) as the etiology of heart failure (Table 2). Frailty scores for SPPB, FFP, and FRS are presented in in Table 2. In all three assessment types, there were no significant difference between scores for sex or race (data not shown). To explore whether frail patients were different in demographics, medical complexity, or degree of illness as compared to non-frail patients, we compared individuals who met criteria for frailty based on an SBBP score 6 versus those who were not frail with SBBP > 6. There were no significant differences between frail and non-frail groups (Table 3). There was also no significant difference in demographic characteristics between patients determined to be frail by FFP or FRS (data not shown).

FRS scores correlated with both SPPB and FFP scores, although the correlation was much stronger with FFP ($R^2 = .101$, $P = .043$; $R^2 = .313$, P .001, respectively) (Figure 2). The two physical frailty assessments, SPPB and FFP, correlated well with each other ($R^2 = .408$, P .001). There was no significant association between any of the frailty scores and age.

Clinical outcomes for the entire cohort are reported in Table 2. Individuals on the transplant waitlist were significantly less frail as compared to those not waitlisted, as measured by both SPPB and FRS ($P = .022$; $P = .002$, respectively), but not FFP ($P = .111$) (Figure 3).

Two of the frailty assessments demonstrated that frail candidates were less likely to receive a heart transplant. Patients who received heart transplants were significantly less frail, as measured by SPPB and FRS ($P = .026$; $P = .008$, respectively) but not FFP ($P = .131$) (Figure 4). In a secondary analysis of the subpopulation including only waitlisted patients, none of the assessments showed significant differences in scores between those who did or did not receive a heart transplant (SPPB $P = .340$; FFP $P = .508$; FRS $P = .441$).

Pre-transplant frailty status is also associated with mortality. Higher frailty as measured by SPPB and FFP was significantly associated with mortality ($P = .010$; $P = .025$, respectively), while FRS ($P = .182$) was not (Figure 5). In a secondary analysis of heart transplant candidates 55 years old, higher frailty as measured by SPPB and FFP was seen in deceased versus alive older patients (n = 33; P .001; $P = .004$, respectively), whereas FRS ($P = .672$) showed no difference. However, none of the assessments showed significant differences for those < 55 (n = 11; SPPB $P = .799$; FFP $P = .751$; FRS $P = .148$).

4 | DISCUSSION

In this study, we performed SPPB, FFP, and FRS frailty assessments on heart transplant candidates. We found that FRS, a chart-review based frailty assessment, correlates with prospective SPPB and FFP frailty assessments, which include more objective measures of physical frailty such at gait speed, grip strength, and balance. The relatively weak correlation between FRS and SPPB suggests that these two assessments measure different aspects of frailty (Figure 2A). The stronger relationship between FRS and FFP is likely due to the fact that the FFP includes subjective questions as part of its evaluation,[13] which are similar

to those found in the FRS measure (Figure 2B). We also found that patients who were waitlisted and eventually transplanted were significantly less frail than their non-waitlisted and non-transplanted counterparts, as measured by the SPPB and FRS (Figures 3 and 4), indicating that these frailty assessments may have an important role in heart transplant candidacy evaluations. Finally, we found that higher frailty, as measured SPPB and FFP but not FRS, was related to patient mortality (Figure 5). This suggests that, as opposed to chart-based retrospective frailty assessments, the role of more objective prospective functional frailty evaluations may be an important element of risk stratification. This is an important observation both for the field of transplantation as well as for more general pre-surgical evaluation, as most applications of SPPB and FFP have been studied in the outpatient setting as opposed to in a cohort of critically ill inpatients with severe end organ disease.

In secondary analyses, the subpopulation of patients age 55 and older was significant for mortality, but this association was not seen in the younger subpopulation. This suggests the older subpopulation drives the results from Figure 5. This may be due to the presence of other factors in older heart transplant candidates that increase their mortality risk. Some of these factors may be immune senescence or inflammation associated with aging, suggesting that the relationship between immune function and frailty as may be another interesting area to study. Additional analyses in a larger patient cohort would be able to confirm whether the impact of frailty analysis is stronger in candidacy evaluation in older as opposed to younger patients.

Overall, in our study, different assessments provide insight on different aspects about the patient, suggesting a role for both prospective physical frailty evaluations in addition to relevant frailty data obtained by chart review. Given that although statistical significance was demonstrated, observed correlations were low for each individual frailty assessment. Since frailty assessments have different strengths, performing a variety of frailty assessments may be the best way to capture pre-transplant frailty status and inform risk stratification leading to a combined approach including aspects of different frailty metrics that are most strongly predictive of clinical outcomes of interest. We hope to confirm the strength of these findings through a larger cohort to determine whether a combination approach of physical frailty evaluation supplemented by chart review would be most effective for transplant candidate evaluation.

There are a number of study limitations. Although we found differences in frailty status based on a number of patient outcomes, a larger sample size is necessary to explore the predictive value of these variables and validate their use in risk stratification. The patients analyzed in this cohort included a large proportion of patients receiving inotrope support, however, few patients underwent MCS implantation, which may limit application of these findings to patients with higher clinical acuity or those receiving mechanical support, additionally given that a number of patients were not critically ill enough to require ongoing inpatient support while awaiting transplantation. If sufficient resources had been available, evaluation of all candidates for heart transplantation may have identified additional frail patients who were younger than age 55 and did not appear to be frail by the "eyeball test". Another limitation was that some of the frailty results were available for discussion during the selection committee process and may have influenced waitlist and

transplant status. However, this confounding aspect of the study would not have affected successful progression to transplantation once waitlisted or death after transplantation. Finally, patient frailty status may have changed over time between date of evaluation and date of transplantation; further studies should explore the durability of frailty assessment and whether longitudinal change as observed before or after transplantation.

Overall, pre-transplant frailty status offers potential to serve as a method of risk stratification for heart transplant candidates. Since frail candidates are less likely to progress to transplantation, frailty assessment can be used to identify those who may benefit from pre-habilitation and other targeted interventions. Pre-habilitation may improve the likelihood of receiving a transplant and improve the recovery process after transplant. Frailty assessment can also serve to indicate which patients are at greater risk of mortality, giving early notice to the healthcare team to closely monitor and these patients and possibly target interventions.

Further research in a larger cohort is ongoing. A larger dataset will confirm the reliability of using retrospective chart-review frailty assessments versus prospective physical frailty assessments, and determine which approach is most optimal for prediction of clinical outcomes. Future research will also compare how frailty associates with other clinical outcomes such as length-of-stay post-transplant, number of readmissions within 6 months and 1 year, total days in hospital within 6 months and 1 year, as well as whether frailty evaluations improve after transplantation. An additional future area of study will be to further explore potential differences in performance of frailty measures in cohorts of different ages, and with different etiologies of heart failure, which may be more strongly linked to frailty and its concurrent inflammation. These approaches may improve ability to evaluate transplant candidates and pre-habilitate when indicated, improving outcomes after transplantation for the growing numbers of older patients with end stage heart failure.

## ACKNOWLEDGMENTS

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to concern regarding compromising privacy and confidentiality of research participants.
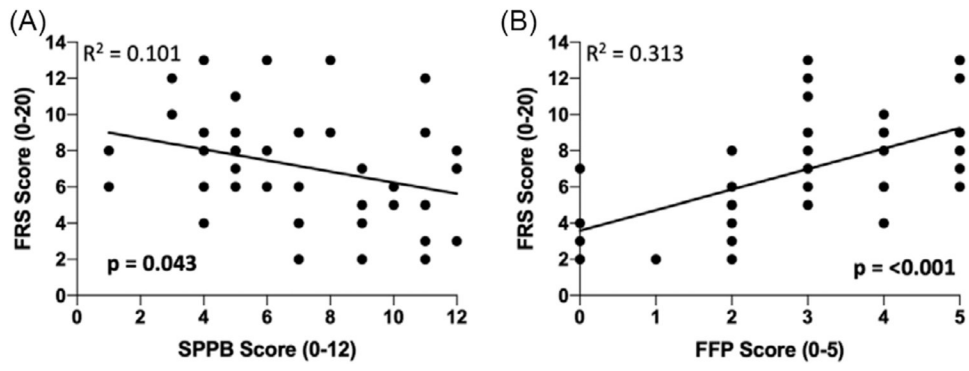
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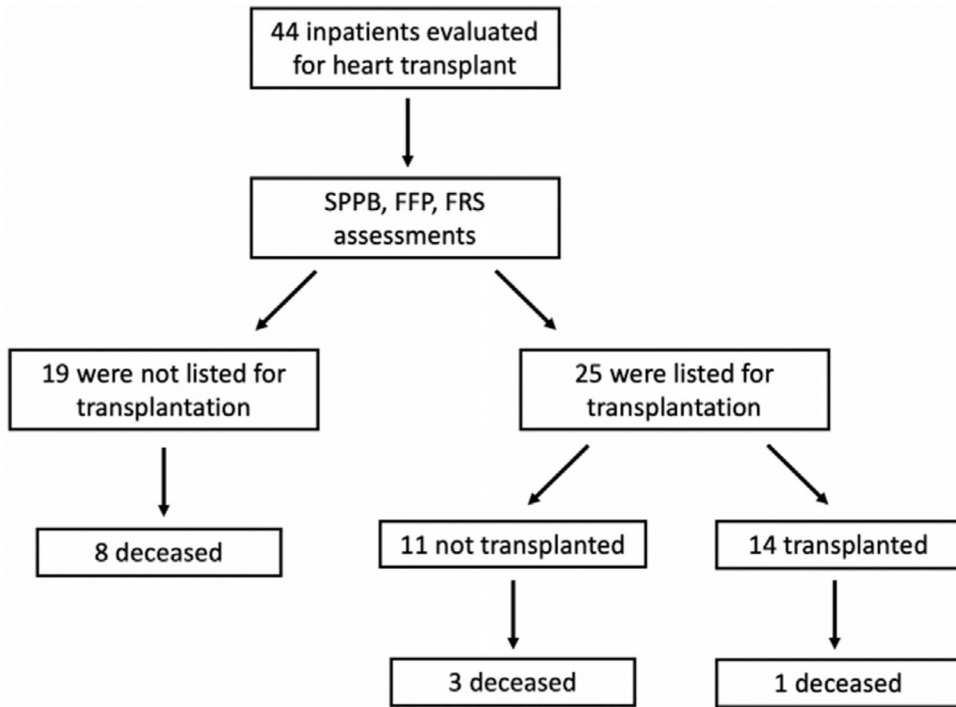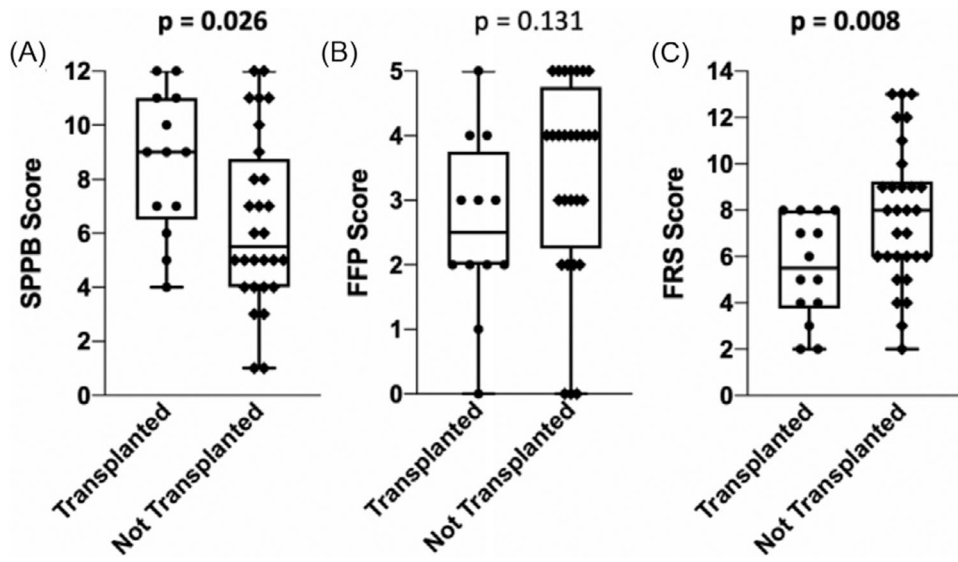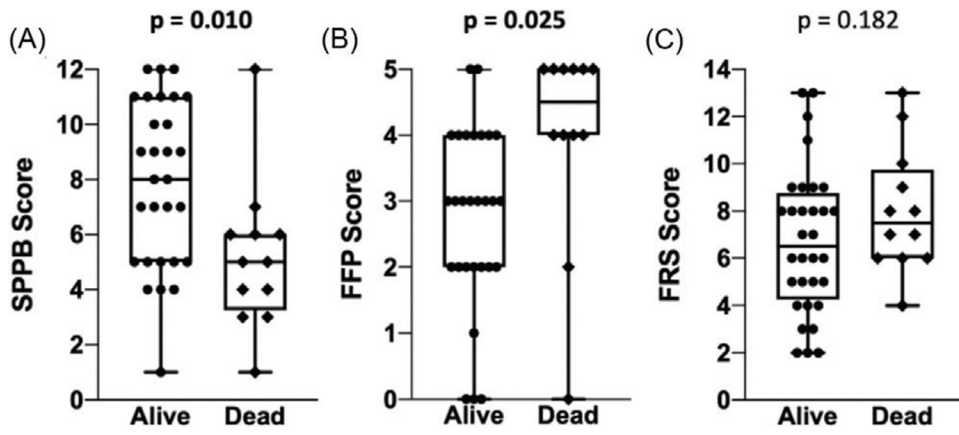
FIGURE 1.
Flow diagram showing methods

FIGURE 2.
Linear correlation between SPPB and FRS (B) and FFP and FRS (A) scores. Correlation depicted by line. *P*-values are indicated, *P* < .05 highlighted in bold
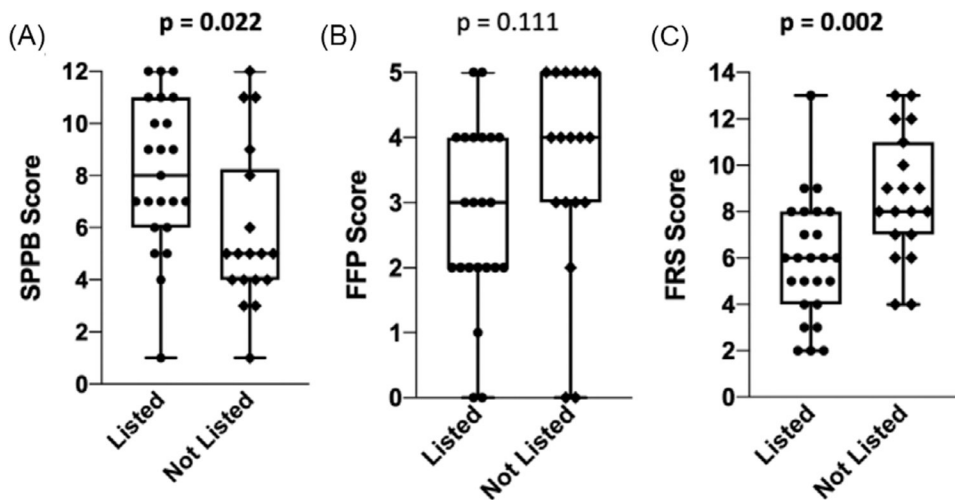
FIGURE 3.
Frailty differences by waitlist status (listed or not listed) as measured by SPPB (A), FFP (B), and FRS (C) scores. Box and whisker plot shown with median at central line and range at whiskers. Statistical analysis by unpaired t test, assuming unequal variances and Gaussian distribution. *P*-values are indicated, *P* < .05 highlighted in bold

FIGURE 4.
Frailty differences by transplant status (transplanted or not transplanted) as measured by SPPB (A), FFP (B), and FRS (C) scores. Box and whisker plot shown with median at central line and range at whiskers. Statistical analysis by *t* test. *P* values are indicated, *P* < .05 highlighted in bold

FIGURE 5.
Difference in frailty status by mortality (alive or dead) as measured by SPPB (A), FFP (B), and FRS (C) scores. Box and whisker plot shown with median at central line and range at whiskers. Statistical analysis by *t* test. *P* values are indicated, *P* < .05 in bold

TABLE 1

Summary of demographics of heart transplant candidates

Frailty Assessment	Type	Components	Scale	Scoring
Short Physical Performance Battery (SPPB)	Prospective	Balance, gaitspeed, and chair stand	0–12	Higher = less frail
Fried Frailty Phenotype (FFP)	Prospective	Exhaustion, gaitspeed, grip strength, weight loss, and physical activity	0–5	Higher = more frail
Frailty Risk Score (FRS)	Retrospective (Chart-review, EMR, Biopsychosocial)	Social support, depression, current smoking status, falls, visual impairment, dyspnea/shortness of breath (SOB), fatigue, weakness, chronic pain, incontinence, nutrition/weight-loss, cognitive impairment, low albumin, low hemoglobin, and abnormal white blood cell count, ADL, sleep, smoking history, fall risk, hearing impairment	0–20	Higher = more frail

TABLE 2

Demographic and clinical features of the total cohort

Clinical Feature	Total cohort n = 44[a]
Age (years), mean (SD)	60 (12)
Sex, Male, n (%)	35 (80)
Race/Ethnicity, n, (%)	
White (Non-Hispanic)	20 (46)
Black	8 (18)
Asian	5 (11)
Hispanic (White + Non-White)	10 (23)
Other	1 (2)
Etiology, n (%)	
Ischemic Cardiomyopathy	17 (39)
Non-Ischemic Cardiomyopathy	27 (61)
Body mass index, mean (SD)	25 (5.2)
Charlson comorbidity index (CCI), median (range)	4
Mechanical circulatory support pre-transplant, n (%)	2 (4)
On inotropes pre-transplant, n (%)	19 (43)
Sequential Organ Failure Assessment (SOFA) Score, median (range)	3 (0-10)
Days of initial hospitalization, mean (SD)	25.5 (17.8)
Short Physical Performance Battery (SPPB)[a]	7 (1-12)
Fried Frailty Phenotype (FFP)[a]	3 (0-5)
Frailty Risk Score (FRS)	7 (2-13)
Listed, n (%)	25 (57)
Transplanted, n (%)	14 (32)
Deceased, n (%)	12 (27)

[a]SPPB and FFP had n = 41 and n = 40, respectively.

TABLE 3

Demographic and clinical features in frail versus non-frail patients

Clinical Feature	Frail (SPPB ≤ 6) n = 18	Non-frail (SPPB > 6) n = 23	p
Age (years), mean (SD)	60 (13)	59 (13)	NS
Sex, Male, n (%)	15 (79)	19 (86)	NS
Race/Ethnicity, n, (%)			nsNS
White (Non-Hispanic)	11 (58)	9 (41)	
Black	3 (16)	3 (13)	
Asian	0	5 (23)	
Hispanic (White + Non-White)	5 (26)	4 (18)	
Other	0	1 (4)	
Etiology, n (%)			NS
Ischemic Cardiomyopathy	9 (53)	8 (64)	
Non-Ischemic Cardiomyopathy	10 (47)	14 (36)	
Body mass index, mean (SD)	25 (5)	25 (5)	NS
Charlson comorbidity index (CCI), median (range)	4 (1-7)	4 (1-8)	NS
Mechanical circulatory support pre-transplant, n (%)	0	1 (4)	NS
On inotropes pre-transplant, n (%)	7 (37)	10 (45)	NS
Sequential Organ Failure Assessment (SOFA) Score, median (range)	4 (0-6)	2 (0-10)	NS
Days of initial hospitalization, mean (SD)	22 (15)	27 (18)	NS

SPPB, Short physical performance battery.