Published in final edited form as:

J Heart Lung Transplant. 2014 April ; 33(4): 359–365. doi:10.1016/j.healun.2013.12.014.

Frailty and Outcomes Following Implantation of Left Ventricular Assist Device as Destination Therapy

Shannon M. Dunlay, MD MS*, Soon J. Park, MD, Lyle D. Joyce, MD, Richard C. Daly, MD, John M. Stulak, MD, Sheila M. McNallan, MPH†, Véronique L. Roger, MD, MPH*,†, and Sudhir S. Kushwaha, MD*

*Division of Cardiovascular Diseases in the Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota

†Department of Health Sciences Research, Mayo Clinic, Rochester, Minnesota

‡Division of Cardiothoracic Surgery in Department of Surgery, Mayo Clinic, Rochester, Minnesota

Abstract

Background—Frailty is recognized as an important prognostic indicator in heart failure. There has been interest in understanding whether pre-operative frailty is associated with worse outcomes after destination left ventricular assist device (LVAD).

Methods—Patients undergoing destination LVAD at the Mayo Clinic in Rochester, Minnesota from February 2007 to June 2012 were included. Frailty was assessed using the Deficit Index (31 impairments, disabilities, and comorbidities) and defined as the proportion of deficits present. We divided patients based on tertiles of the Deficit Index (>0.32 = frail, 0.23 – 0.32 = intermediate frail, <0.23 = not frail). Cox proportional hazard regression models were used to examine the association between frailty and death. Patients were censored at death or last follow-up through October 2013.

Results—Among 99 patients (mean age 65 years, 18% female, 55% ischemic HF), the Deficit Index ranged from 0.10 to 0.65 (mean 0.29). After a mean follow-up of 1.9 ± 1.6 years, 79% had been rehospitalized (range 0–17 hospitalizations, median 1 per person) and 45% had died. Compared to those who were not frail, patients who were intermediate frail (adjusted HR 1.70, 95% CI 0.71–4.31) and frail (HR 3.08, 95% CI 1.40–7.48) were at increased risk for death (p for trend=0.004). The mean (SD) days alive out of hospital the first year after LVAD was 293 (107), 266 (134), and 250 (132) in those who were not frail, intermediate frail, and frail, respectively.

Conclusions—Frailty pre-destination LVAD is associated with increased risk of death, and may represent an important patient selection consideration.

© 2013 International Society for Heart and Lung Transplantation. Published by Elsevier Inc. All rights reserved.

Address for correspondence: Shannon M. Dunlay MD MSc, Division of Cardiovascular Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 Telephone: (507) 284-8087; dunlay.shannon@mayo.edu.

Presented at the 2013 International Society for Heart and Lung Transplantation Annual Meeting, Featured Abstract at Plenary Session

DISCLOSURES: Dr. Park has consulted and received honoraria from Thoratec. Dr. Kushwaha has received a grant to study endothelial function from Thoratec. All other authors have no relationships to disclose.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Frailty is defined as a “state of increased vulnerability to adverse outcomes¹” and reflects biological rather than chronological age². While interrelated with comorbidity and disability¹, frailty has been strongly associated with increased morbidity and mortality in patients with cardiovascular disease^{3–6} and those undergoing cardiac surgery⁷. Frailty is more common in heart failure (HF) than in the general population^{4, 6}, and has been increasingly recognized as an important indicator of adverse prognosis. While frailty assessment has been applied to patients with a variety of medical conditions, it has never been used in patients undergoing left ventricular assist device implantation (LVAD) as destination therapy (DT).

There has been growing interest in understanding how frailty may impact prognosis after destination LVAD⁸. Patients undergoing LVAD as DT often have a variety of comorbidities including advanced age that render them ineligible for cardiac transplantation, but may put them at increased risk for frailty. The cachexia associated with advanced HF may have a large impact on a patient’s exercise capacity, ability to perform activities of daily living, and organ function. As the impact of left ventricular dysfunction on these limitations has the potential to be improved or reversed with LVAD therapy, it is unclear whether frailty preceding destination LVAD will still confer poor postoperative prognosis.

As no gold standard definition of frailty exists, there are many methods of assessing frailty, and most require prospective testing of grip strength or gait speed, which limits our ability to apply these definitions to populations. However, the Deficit Index is calculated based on information assessing a patient’s ability to perform their own activities of daily living (ADLs) and comorbidities^{2, 9}, and relies on data that is available in the medical record. It has been predictive of outcomes in the Cardiovascular Health Study¹⁰ and the Framingham Cohort¹¹ and has been associated with other measures of frailty in community patients with HF¹².

To evaluate the impact that preoperative frailty has on postoperative morbidity and mortality following destination LVAD, we assessed frailty using the Deficit Index in consecutive patients who underwent LVAD as DT and examined the association between frailty, rehospitalization and mortality.

METHODS

Identification of Patients

All patients undergoing LVAD as DT at the Mayo Clinic in Rochester, Minnesota from 2007 through July 2012 were eligible for inclusion. The study was approved by the Mayo Clinic Institutional Review Board.

Frailty Definition

The Deficit Index was based on 31 deficits obtained from the medical record and defined as the proportion of deficits present for each patient (Table 1). This index has been associated with other measures of frailty in a community population of patients with HF in Olmsted County, Minnesota (where the Mayo Clinic is located)¹². All deficits reflect their status pre-LVAD. The first fourteen items (ability to perform activities of daily living) were collected from a patient provided questionnaire (within 6 months pre-LVAD) that patients routinely complete while receiving care at the Mayo Clinic. The remaining items were collected by manual chart review. Clinicians’ diagnoses were used to define hypertension, hyperlipidemia, chronic obstructive pulmonary disease (COPD), depression, peripheral vascular disease, cerebrovascular disease, ulcer, hemiplegia, myocardial infarction (MI),

malignancy, dementia, and rheumatologic disease. Diabetes mellitus was defined by physician diagnosis or use of diabetes medications. Body mass index (BMI) (kg/m^2) was calculated using height and weight pre-LVAD. Underweight, overweight and obesity were defined by BMI <18.5 , 25 to <30 , and ≥ 30 kg/m^2 , respectively. Anemia and renal dysfunction were defined based on the hemoglobin and creatinine the day before LVAD surgery. Anemia was defined as a hemoglobin concentration <13.0 g/dL in men and <12.0 g/dL in women¹³. Moderate/severe renal dysfunction was defined as an estimated glomerular filtration rate <60 mL/min using the Modification of Diet in Renal Disease equation¹⁴. To examine the association between the Deficit Index and outcomes, we divided patients into tertiles of the Deficit Index (lowest tertile= not frail, middle tertile= intermediate frail, highest tertile= frail). In sensitivity analyses, we defined frailty as >0.25 , as suggested by Rockwood et al⁹.

Patients were eligible for inclusion if they completed the questionnaire administered routinely at Mayo Clinic to assess deficits in their ability to complete activities of daily living. In the case that only one item was missing in the questionnaire, the patient was retained in the analysis and the denominator of deficits adjusted accordingly.

Additional Data

Echocardiograms were performed and evaluated by the Mayo Clinic Echocardiographic Laboratory using M-mode, quantitative, and semiquantitative methods to measure left ventricular ejection fraction (EF) according to the American Society of Echocardiography guidelines¹⁵. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) patient profile has been used to describe the severity of illness prior to device implantation and ranges in score from 1 (critical cardiogenic shock) to 7 (advanced New York Heart Association class III symptoms)¹⁶. The Leitz Miller score (developed to predict in-hospital mortality, though never validated for use in patients with continuous flow LVADs) was calculated using pre-operative variables as: 7 points for platelets $<148,000/\mu\text{L}$, 5 points for albumin <3.3 g/dL, 4 points for INR >1.1 , 4 points for use of vasodilators, 3 points for mean pulmonary artery pressure >25 mm Hg, 2 points for AST >45 U/mL, 2 points for hematocrit $<34\%$, 2 points for blood urea nitrogen >51 U/dL, and 2 points for no intravenous intropes¹⁷.

Outcomes

Deaths were as noted in the medical record. Cause of death early after LVAD implantation was determined based on autopsy or review of the medical record. For patients who were still alive at last follow-up, they were censored at their date of last follow-up. Rehospitalizations were defined as all-cause hospitalizations at the Mayo Clinic in Rochester, MN that occurred during follow-up through October 31, 2013. The initial postoperative length of stay was defined as the number of days from the time of LVAD implantation to hospital discharge. Discharge destination (home vs. inpatient rehabilitation) was recorded. It is our practice to discharge patients who may benefit from additional physical therapy to our on-site inpatient rehabilitation facility prior to going home.

Statistical analysis

Trends in baseline characteristics across frailty tertiles were analyzed using generalized linear models for continuous variables and Mantel Haenszel χ^2 for categorical variables. The association between frailty tertiles, mortality, and rehospitalization was examined using Kaplan Meier curves and differences compared using the log-rank test. Cox proportional hazard regression models were used to assess the association between frailty tertiles and death adjusting for potential confounders. Andersen Gill models¹⁸ were used to examine the association between frailty tertiles and all-cause rehospitalization. Unlike traditional Cox

models, which only account for the first rehospitalization, Andersen Gill models account for the impact of multiple rehospitalizations in generating a hazard ratio. Patient characteristics to include in the multivariable models were chosen a priori based on prior work and included age, sex, and INTERMACS profile. Analyses were performed using STATA version 10.0. A p value of <0.05 was used as the level of significance.

RESULTS

Study Population

A total of 117 patients underwent destination LVAD from September 2007 to June 2012. Of these, 99 (84.6%) of patients completed patient-reported questionnaires allowing calculation of the Deficit Index and were included in analysis. Included patients had a similar age and sex distribution to those who did not complete questionnaires. The mean age of the study population was 65.1 years, 18 (18.2%) were women, and 55 (55.6%) had an ischemic etiology for their HF (Table 2). In total, 94 patients had a HeartMate II and 5 had a HeartWare LVAD.

Frailty Assessment

The mean (SD) Deficit Index in the study population was 0.29 (0.11) [range 0.10–0.65], indicating that, on average, LVAD patients had deficits in 29% of the areas assessed preoperatively. The age, sex, and EF distribution were similar across frailty tertiles (Table 2). When defining frailty by the Rockwood definition⁹ (Deficit Index >0.25), 61 (61.6%) patients were frail prior to LVAD.

Frailty and Outcomes

After a mean (SD) follow-up of 1.9 (1.6) years, 45 (45.5%) patients had died including 12 who died during the initial LVAD surgery hospitalization. The cause of death in those 12 patients was stroke (n=5), right ventricular failure (n=5), coagulopathy/bleeding (n=1) and encephalopathy (n=1). There was no difference in the risk of in-hospital death in patients with prior sternotomy (13.8%) vs. no prior sternotomy (9.8%, p=0.54). Among those who survived their initial hospitalization (n=87), there was no difference in time to hospital discharge in patients who were frail [median 19 days, 25th–75th percentile 12–23 days), intermediate frail (16, 12–25 days) and not frail (17 days, 11–29 days, p=0.81). A total of 59 (67.8%) patients were discharged to inpatient rehabilitation. There was a trend toward discharge to inpatient rehabilitation rather than home in those with higher Deficit Index (p=0.069).

There was a stepwise increase in one-year mortality with increasing Deficit Index (Figure 1). Patients who were not frail, intermediate frail, and frail had Kaplan-Meier estimated 1-year mortality rates of 16.2%, 21.2% and 39.9%, respectively (log rank p=0.007, Figure 2A). After adjustment for age, sex, and INTERMACS profile, the HR (95% CI) for death were 1.70 (0.71–4.31) in those who were intermediate frail and 3.08 (1.40–7.48) in those who were frail (Table 3). Alternatively, defining frailty as a Deficit Index >0.25⁹, frailty was associated with a hazard ratio (95% CI) for death of 2.31 (1.18–4.98, p=0.014). Findings were similar when the population was restricted to those with HeartMate II LVAD. By comparison, INTERMACS profile was not predictive of death (p=0.46).

In total, 235 rehospitalizations occurred during follow-up. Most (N=69, 79%) patients who survived to discharge after LVAD were rehospitalized at least once. The number of hospitalizations per person ranged from 0–17 (median 1). The 30-day rehospitalization rate was 37.9%. The most common reasons for rehospitalization were gastrointestinal bleeding, HF, and ventricular arrhythmias. Figure 2B shows the mean number of admissions over time

by frailty tertile, demonstrating that those who are frail and intermediate frail have more admissions over time than those who are not frail. The HR (95% CI) for rehospitalization were 1.70 (1.23–2.34) and 1.42 (0.98–2.06) in those who were intermediate frail and not frail, respectively (Table 3), indicating that rehospitalization risk may be highest in patients with intermediate frailty. To assess the impact that out of hospital death may have on rehospitalization risk, we performed a sensitivity analysis assuming that patients who died were rehospitalized on the date of death.

As those who were frail most often experienced out of hospital death, this increased the HR (95% CI) to 1.58 (1.14–2.18), though results were unchanged for intermediate frail patients (HR 1.74, 95% CI 1.28–2.35). The mean (SD) days alive out of hospital the first year after LVAD was 293 (107), 266 (134), and 250 (132) in those who were not frail, intermediate frail, and frail, respectively. Alternatively, defining frailty as a Deficit Index $>0.25^9$, frailty was associated with a HR (95% CI) for rehospitalization of 1.41 (1.07–1.85, $p=0.015$).

DISCUSSION

LVADs are increasingly implanted as DT for patients with advanced HF who are not candidates for cardiac transplantation, due to the presence of concomitant comorbidities or increased age. There has been recent interest in better understanding the role of preoperative frailty in this population, as it may have important implications for patient selection and assessment prior to implantation. Herein, we found that frailty, defined by the Deficit Index, was associated with an increased risk of postoperative mortality and rehospitalization.

Patient selection is the most important factor in attaining favorable outcomes following implantation of LVAD as DT¹⁹. Unlike heart transplantation, where established criteria exist for patient selection including the aid of tools such as oxygen consumption treadmill testing, guidelines for selecting appropriate candidates for LVAD are less well defined. In particular, DT candidates are often elderly with comorbidities making them ineligible for heart transplantation, but that may impact outcomes following LVAD independent of their cardiac disease. While a number of risk assessment tools have been developed for LVAD patients, such as the INTERMACS profile^{16, 20} and risk scores such as the Leitz-Miller score¹⁷, these were primarily studied in patients with first-generation pulsatile flow devices, and do little to account for the impact that comorbidity and functional limitation may have on patient outcome. While the cost-effectiveness of LVAD is improving²¹, morbidity and mortality remain substantial, with an estimated 26% of patients dying within one year of implantation²².

There has been increasing interest in understanding the role that pre-existing frailty may play in postoperative outcomes in patients undergoing LVAD as DT. Frailty increases with age, is more common in HF, and is associated with increased morbidity, mortality, and healthcare resource use^{1, 4, 6, 23}. As such, patients eligible for LVAD as DT are at high risk for frailty. However, in contrast to other HF populations, treatment with LVAD has the potential to greatly improve cardiac hemodynamics and HF symptoms, and may improve other organ function²⁴ via increased perfusion. As such, frailty prior to LVAD may have differential implications on postoperative outcomes compared with other disease states.

While no universal definition of frailty exists, a variety of approaches to identify frail individuals have been developed. The phenotypic definition of frailty is defined by specific signs of physical dysfunction (unintentional weight loss, poor grip strength, slow gait speed, low physical activity). An alternative approach, the Deficit Index, defines frailty by the quantity of health impairments in an individual⁹. It has been validated for use in a wide variety of populations, and has compared favorably with the phenotypic definition of frailty

in the Cardiovascular Health Study¹¹, Framingham Cohort¹⁰, and in an Olmsted County cohort with established HF¹². In our population of 99 patients treated with LVAD as DT, when defined by a Deficit Index $>0.25^9$, frailty was present in 62% of patients preoperatively. While the prevalence of frailty has varied in the literature, this is higher than community-dwelling patients with cardiovascular disease¹ and HF^{6, 23}, and underscores the vulnerability of this population.

When dividing the Deficit Index into tertiles, we found that mortality risk increased following DT LVAD as a function of increasing preoperative frailty. There was a more than 3-fold increased risk of death in patients in the highest frailty tertile compared with those who were not frail (lowest tertile). The association between frailty and rehospitalization risk was more complex. While frail and intermediate frail patients (highest two tertiles) were at higher risk for rehospitalization compared with those who were not frail, the HR for rehospitalization was greatest for those with intermediate frailty. By contrast, in community HF patients, rehospitalization risk progressively increases with increasing frailty²³. In our population, some of the difference in risk was mitigated by accounting for the impact of out of hospital death, which occurred most often in patients who were frail and would have resulted in hospitalization had the patient survived. Furthermore, the LVAD itself introduces a unique set of potential problems that can lead to rehospitalization, such as bleeding, driveline infection, and pump thrombosis, the risk of which may not be mediated by frailty or may occur in specific subgroups of patients. Notably, the number of days alive out of the hospital in the first year progressively decreased with increasing frailty. Patients who were not frail were alive and out of the hospital an average of 6 additional weeks their first year after LVAD than those who were frail.

There are important clinical implications to these data. First, frailty may represent a useful prognostic tool to aid in patient assessment prior to LVAD. While it is just one factor to consider, it may also represent an important high-risk marker to help identify patients who may necessitate closer follow-up or more aggressive rehabilitation postoperatively. While we used the Deficit Index to define frailty, an important next step in this line of work will be to compare the Deficit Index to other methods of assessing frailty (including grip strength and gait speed) to better understand whether one measure may best predict postoperative outcomes in DT LVAD patients. Second, while controversy exists as to whether frailty is modifiable, particularly in the setting of a life-threatening advanced illness such as HF, studies such as the Frailty Intervention Trial²⁵ are underway which may provide insight into potential methods to treat frail individuals. Our center is planning to investigate whether a rigorous rehabilitation protocol could be applied pre-LVAD as a method of improving frailty and post-LVAD outcomes. In addition, further work is needed to understand how frailty is modified following LVAD, and whether we are able to identify individuals who may have frailty reversed with LVAD therapy, as they may represent particularly good candidates for this therapy.

There are some limitations that should be acknowledged to aid in interpretation of these data. First, this is a single-center study and the experience of patients cared for at other centers may differ. The number of patients and outcomes in this study are relatively small and we were limited in the number of factors we could adjust for in the multivariable models. It will be important to investigate the association between frailty and outcomes in larger patient populations. Rehospitalizations at other institutions were not captured in this study. However, there is no reason to believe that the risk of rehospitalization at other institutions would differ by frailty status. However, there are several important strengths to consider. We were able to apply a rigorous definition of frailty to a group of patients prior to LVAD and follow them postoperatively for outcomes. Further, to the best of our knowledge,

we are the first to report on the association between frailty and outcomes following LVAD as DT, which has been highlighted as an area in need of analysis⁸.

As our use of mechanical circulatory support as DT in patients who are ineligible for cardiac transplantation continues to grow, it will be increasingly important to select patients who will have the best opportunity to benefit from these therapies. As frailty encompasses a vulnerability to stress and adverse outcomes, it may represent an important consideration in the selection of patients prior to LVAD implantation. We found frailty to be a strong predictor of adverse postoperative outcomes in patients undergoing LVAD as DT.

Acknowledgments

FUNDING SOURCES: Dr. Dunlay is funded by an NHLBI Career Development Award (K23HL 116643).

References

1. Afilalo J, Karunanathan S, Eisenberg MJ, Alexander KP, Bergman H. Role of frailty in patients with cardiovascular disease. *Am J Cardiol*. 2009; 103:1616–21. [PubMed: 19463525]
2. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr*. 2008; 8:24. [PubMed: 18826625]
3. Boxer R, Kleppinger A, Ahmad A, Annis K, Hager D, Kenny A. The 6-minute walk is associated with frailty and predicts mortality in older adults with heart failure. *Congest Heart Fail*. 2010; 16:208–13. [PubMed: 20887617]
4. Cacciatore F, Abete P, Mazzella F, et al. Frailty predicts long-term mortality in elderly subjects with chronic heart failure. *Eur J Clin Invest*. 2005; 35:723–30. [PubMed: 16313247]
5. Purser JL, Kuchibhatla MN, Fillenbaum GG, Harding T, Peterson ED, Alexander KP. Identifying frailty in hospitalized older adults with significant coronary artery disease. *J Am Geriatr Soc*. 2006; 54:1674–81. [PubMed: 17087693]
6. Lupon J, Gonzalez B, Santa-eugenia S, et al. Prognostic implication of frailty and depressive symptoms in an outpatient population with heart failure. *Rev Esp Cardiol*. 2008; 61:835–42. [PubMed: 18684366]
7. Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation*. 2010; 121:973–8. [PubMed: 20159833]
8. Flint KM, Matlock DD, Lindenfeld J, Allen LA. Frailty and the selection of patients for destination therapy left ventricular assist device. *Circ Heart Fail*. 2012; 5:286–93. [PubMed: 22438521]
9. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci*. 2007; 62:738–43. [PubMed: 17634321]
10. Kulminski AM, Ukraintseva SV, Kulminskaya A IV, et al. Cumulative deficits and physiological indices as predictors of mortality and long life. *J Gerontol A Biol Sci Med Sci*. 2008; 63:1053–9. [PubMed: 18948555]
11. Kulminski AM, Ukraintseva SV, Kulminskaya IV, Arbeev KG, Land K, Yashin AI. Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: Lessons from the cardiovascular health study. *J Am Geriatr Soc*. 2008; 56:898–903. [PubMed: 18363679]
12. McNallan SM, Chamberlain AM, Gerber Y, et al. Measuring frailty in heart failure: A community perspective. *Am Heart J*. 2013; 166:768–74. [PubMed: 24093859]
13. WHO. Nutritional anemias: Report of a who scientific group. WHO Technical Report Series. 1968; 405:1.
14. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of diet in renal disease study group. *Ann Intern Med*. 1999; 130:461–70. [PubMed: 10075613]
15. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: A report from the american society of echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the european association of

- echocardiography, a branch of the european society of cardiology. *J Am Soc Echocardiogr*. 2005; 18:1440–63. [PubMed: 16376782]
16. Stevenson LW, Pagani FD, Young JB, et al. Intermacs profiles of advanced heart failure: The current picture. *J Heart Lung Transplant*. 2009; 28:535–41. [PubMed: 19481012]
 17. Lietz K, Long JW, Kfoury AG, et al. Outcomes of left ventricular assist device implantation as destination therapy in the post-rematch era: Implications for patient selection. *Circulation*. 2007; 116:497–505. [PubMed: 17638928]
 18. Andersen PK, Gill RD. Cox's regression model for counting processes: A large sample study. *Ann Stat*. 1982; 10:1100–20.
 19. Lund LH, Matthews J, Aaronson K. Patient selection for left ventricular assist devices. *Eur J Heart Fail*. 2010; 12:434–43. [PubMed: 20172939]
 20. Alba AC, Rao V, Ivanov J, Ross HJ, Delgado DH. Usefulness of the intermacs scale to predict outcomes after mechanical assist device implantation. *J Heart Lung Transplant*. 2009; 28:827–33. [PubMed: 19632580]
 21. Rogers JG, Bostic RR, Tong KB, Adamson R, Russo M, Slaughter MS. Cost-effectiveness analysis of continuous-flow left ventricular assist devices as destination therapy. *Circ Heart Fail*. 2012; 5:10–16. [PubMed: 22052901]
 22. Slaughter MS, Meyer AL, Birks EJ. Destination therapy with left ventricular assist devices: Patient selection and outcomes. *Curr Opin Cardiol*. 2011; 26:232–6. [PubMed: 21430527]
 23. McNallan SM, Singh S, AC, Kane RL, et al. Frailty and healthcare utilization among patients with heart failure in the community. *JACC: Heart Fail*. 2013; 1:135–41. [PubMed: 23956958]
 24. Hasin T, Topilsky Y, Schirger JA, et al. Changes in renal function after implantation of continuous-flow left ventricular assist devices. *J Am Coll Cardiol*. 2012; 59:26–36. [PubMed: 22192665]
 25. Fairhall N, Aggar C, Kurrle SE, et al. Frailty intervention trial (fit). *BMC Geriatr*. 2008; 8:27. [PubMed: 18851754]

Figure 1. One-Year Mortality According to Tertiles of the Frailty Deficit Index

Fig 2a

Not Frail	28	24	27	17
Int Frail	26	24	17	14
Frail	22	19	14	11

Fig 2b

Not Frail	28	24	27	17
Int Frail	26	24	17	14
Frail	22	19	14	11

Figure 2. Risk of Death and Rehospitalization by Frailty Tertiles

The Kaplan Meier curves for death are shown by tertiles of the frailty Deficit Index (lowest= not frail, middle= intermediate frail, highest= frail, panel A). The mean number of hospitalizations over time are shown by frailty tertiles (panel B).

Table 1**Deficit Index**

Cumulative Deficit Index	Cut-points
1. Need help preparing meals	Yes=1, No=0
2. Need help feeding yourself	Yes=1, No=0
3. Need help dressing yourself	Yes=1, No=0
4. Need help using the toilet	Yes=1, No=0
5. Need help with housekeeping	Yes=1, No=0
6. Need help climbing stairs	Yes=1, No=0
7. Need help bathing	Yes=1, No=0
8. Need help walking	Yes=1, No=0
9. Need help using transportation	Yes=1, No=0
10. Need help getting in and out of bed	Yes=1, No=0
11. Need help managing medications	Yes=1, No=0
12. Depend on assistive devices (walker, cane, etc) or other people to perform activities of daily life	Yes=1, No=0
13. Dependent on a device for normal breathing	Yes=1, No=0
14. Climb 2 flights of stairs without rest	No, can't do at all=1 Yes, with difficulty=0.5 Yes with no difficulty=0
15. Myocardial infarction	Yes=1, No=0
16. Diabetes	Yes=1, No=0
17. Peripheral Vascular Disease	Yes=1, No=0
18. Cerebrovascular Disease	Yes=1, No=0
19. COPD	Yes=1, No=0
20. Ulcer	Yes=1, No=0
21. Hemiplegia	Yes=1, No=0
22. Moderate/severe renal insufficiency	Yes=1, No=0
23. History of liver disease	Yes=1, No=0
24. Rheumatologic disease	Yes=1, No=0
25. History of malignancy	Yes=1, No=0
26. History of dementia	Yes=1, No=0
27. Hypertension	Yes=1, No=0
28. Hyperlipidemia	Yes=1, No=0
29. BMI	Underweight or obese=1, overweight=0.5 normal=0
30. Depression	Yes=1, No=0
31. Anemia	Yes=1, No=0

Table 2

Baseline Characteristics.

	Total (N=99)	Frailty Deficit Index Tertile*			P for trend
		Not Frail (N=32)	Intermediate Frail (N=33)	Frail (n=34)	
Age, mean $\pm$ SD, y	65.1 (9.4)	63.6 (11.0)	66.3 (9.5)	65.4 (7.5)	0.46
Men	81 (81.8)	28 (87.5)	26 (78.8)	27 (79.4)	0.41
EF, mean $\pm$ SD, %	18.5 (6.8)	18.5 (8.1)	17.9 (6.0)	18.9 (6.1)	0.82
Ischemic HF	55 (55.6)	11 (34.4)	20 (60.6)	24 (70.6)	0.004
Prior sternotomy	58 (58.6)	18 (56.3)	20 (60.6)	20 (58.8)	0.84
INTERMACS profile, median (interquartile range)	4 (3, 5)	4 (3, 5)	4 (4, 5.5)	4 (3, 5)	0.26
Leitz-Miller Score, median (interquartile range)	11 (6, 13)	12.5 (6, 13)	9 (4, 13)	11 (6, 13)	0.84
Comorbidity Deficits					
Prior myocardial infarction	62 (62.6)	15 (46.9)	22 (66.7)	25 (73.5)	0.027
Diabetes	37 (37.4)	2 (6.3)	11 (33.3)	24 (70.6)	<0.001
Peripheral vascular disease	29 (29.3)	6 (18.9)	10 (30.3)	13 (38.2)	0.085
Cerebrovascular disease	33 (33.3)	4 (12.5)	11 (33.3)	18 (52.9)	<0.001
COPD	15 (15.2)	3 (9.4)	4 (12.1)	8 (23.5)	0.11
Moderate/severe renal insufficiency	59 (59.6)	15 (46.9)	17 (51.5)	27 (79.4)	0.007
History of malignancy	22 (22.2)	5 (15.6)	11 (33.3)	6 (17.6)	0.88
Depression	37 (37.4)	6 (18.8)	12 (36.4)	19 (55.9)	0.002
Anemia	72 (72.7)	22 (68.8)	22 (66.7)	28 (82.4)	0.21
Activity of Daily Living Deficits					
Need help walking	34 (34.3)	4 (12.5)	11 (33.3)	19 (55.9)	<0.001
Uses a cane or wheelchair for ambulation	29 (29.3)	5 (15.6)	7 (21.2)	17 (50.0)	0.002
Need help housekeeping	23 (23.2)	1 (3.1)	9 (27.3)	13 (38.2)	<0.001
Need help climbing stairs	58 (58.6)	11 (34.4)	17 (51.5)	30 (88.2)	<0.001
Need help managing medications	11 (11.1)	1 (3.1)	2 (6.1)	8 (23.5)	0.008
Need help getting dressed	8 (8.1)	1 (3.1)	2 (6.1)	5 (14.7)	0.084

* Tertiles of the frailty deficit index are <0.23= not frail, 0.23–0.32=intermediate frail, >0.32=frail

COPD= chronic obstructive pulmonary disease, EF= ejection fraction, HF= heart failure, SD= standard deviation

All values shown are N(%) unless otherwise indicated

Table 3**Risk of Mortality and Rehospitalization by Frailty**

* Frailty Deficit Index Tertile				
	Not Frail	Intermediate Frail	Frail	P for Trend
Mortality				
Unadjusted	1 (referent)	1.78 (0.75–4.50)	3.32 (1.53–7.96)	0.002
[†] Adjusted	1	1.70 (0.71–4.31)	3.08 (1.40–7.48)	0.004
Rehospitalization				
Unadjusted	1	1.71 (1.25–2.33)	1.31 (0.92–1.85)	0.096
[†] Adjusted	1	1.70 (1.23–2.34)	1.42 (0.98–2.06)	0.024

* Tertiles of the frailty deficit index are <0.23= not frail, 0.23–0.32=intermediate frail, >0.32=frail

[†] Adjusted for age and sex and INTERMACS profile