





ORIGINAL RESEARCH

# Health-Related Quality of Life in Older Patients With Advanced Heart Failure: Findings From the SUSTAIN-IT Study

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**BACKGROUND:** There is a paucity of research describing health-related quality of life (HRQOL) in older adults considered for advanced heart failure surgical therapies. Using data from our SUSTAIN-IT (Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support) study, we aimed to compare HRQOL among 3 groups of older (60–80 years) patients with heart failure before heart transplantation (HT) or long-term mechanical circulatory support (MCS) and identify factors associated with HRQOL: (1) HT candidates with MCS, (2) HT candidates without MCS, or (3) candidates ineligible for HT and scheduled for long-term MCS.

**METHODS AND RESULTS:** Patients from 13 US sites completed assessments, including self-reported measures of HRQOL (EuroQol-5 Dimension Questionnaire, Kansas City Cardiomyopathy Questionnaire–12), depressive symptoms (Personal Health Questionnaire–8), anxiety (State-Trait Anxiety Inventory–state form), cognitive status (Montreal Cognitive Assessment), and performance-based measures (6-minute walk test and 5-m gait speed). Analyses included ANOVA,  $\chi^2$  tests, Fisher's exact tests, and linear regression. The sample included 393 patients; the majority of patients were White men and married. Long-term MCS candidates ( $n=154$ ) were significantly older and had more comorbidities and a higher New York Heart Association class than HT candidates with MCS ( $n=118$ ) and HT candidates without MCS ( $n=121$ ). Long-term MCS candidates had worse HRQOL than HT candidates with and without MCS (EQ-5D visual analog scale scores,  $46\pm 23$  versus  $68\pm 18$  versus  $54\pm 23$  [ $P<0.001$ ] and Kansas City Cardiomyopathy Questionnaire–12 overall summary scores,  $35\pm 21$  versus  $60\pm 21$  versus  $49\pm 22$  [ $P<0.001$ ], respectively). In multivariable analyses, lower 6-minute walk distance, higher New York Heart Association class, depressive symptoms, and not being an HT candidate with MCS were significantly associated with worse overall HRQOL.

**CONCLUSIONS:** Our findings demonstrate important differences in overall and domain-specific HRQOL of older patients with heart failure before HT or long-term MCS. Understanding HRQOL differences may guide decisions toward more appropriate and personalized advanced heart failure therapies.

**Key Words:** advanced heart failure ■ quality of life ■ older age

Approximately 6.2 million US adults have heart failure (HF), with an incidence approaching 21 per 1000 population after 65 years of age.<sup>1</sup> Many HF

subgroups have poor survival. Among Medicare beneficiaries with HF, the 1-year mortality rate is 29.6%.<sup>2</sup> Patients with advanced HF have even worse survival,

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## CLINICAL PERSPECTIVE

### What Is New?

- In a cohort of older patients with advanced heart failure, health-related quality of life (HRQOL) was poor to fair; patients who were ineligible for heart transplantation and scheduled for implantation of long-term mechanical circulatory support had worse HRQOL than patients awaiting heart transplantation with or without mechanical circulatory support.
- Being a heart transplant candidate with mechanical circulatory support was associated with better HRQOL compared with being a heart transplant candidate without mechanical circulatory support, whereas a decreased 6-minute walk test distance, higher New York Heart Association class, and depressive symptoms were associated with worse HRQOL in these older patients with heart failure.

### What Are the Clinical Implications?

- Understanding differences in HRQOL before alternative advanced surgical therapies (ie, heart transplantation and long-term mechanical circulatory support) contributes to more informed shared decision-making discussions for older patients with heart failure considering these treatment options.
- Differences in domain-specific HRQOL (eg, problems with mobility, usual activities, social functioning, anxiety/depression, and pain/discomfort and potentially worsening heart failure symptoms) in older patients before heart transplantation and long-term mechanical circulatory support provide important individualized targets for treatment, especially for those awaiting long-term mechanical circulatory support as they reported more problems than heart transplant candidates.

## Nonstandard Abbreviations and Acronyms

<b>6MWT</b>	6-minute walk test
<b>BTC</b>	bridge to candidacy
<b>BTT</b>	bridge to transplantation
<b>DT</b>	destination therapy
<b>EQ-5D-3L</b>	EuroQol-5 Dimension Questionnaire
<b>HT</b>	heart transplantation
<b>KCCQ-12</b>	Kansas City Cardiomyopathy Questionnaire-12

**MOMENTUM 3** Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3

**OSS** overall summary score  
**SUSTAIN-IT** Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support

with 1-year mortality rates of 75% to 89%.<sup>3</sup> Treatment goals for these patients are focused not only on improving survival but also on improving health-related quality of life (HRQOL).

Studies demonstrate a range of HRQOL outcomes in adult patients with advanced HF, varying by disease severity,<sup>4–12</sup> but have rarely exclusively focused on older patients (ie, ≥60 years), despite the prevalence of HF being greatest in the elderly. In patients with ambulatory advanced HF, REVIVAL (Registry Evaluation of Vital Information for VADs in Ambulatory Life) investigators reported on outcomes in patients with a median of 60 years of age (interquartile range [IQR], 54–68 years of age),<sup>5</sup> whereas MedaMACS (Medical Arm of Mechanically Assisted Circulatory Support) investigators examined outcomes in patients who were on average 59 years of age (mean±SD, 59±11 years of age).<sup>4</sup> Studies of cohorts of patients who were more severely ill with advanced HF also included adult patients of all ages. Patients enrolled in the MOMENTUM 3 (Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3) trial were a median of 64 years of age (range, 19–81 years of age; HeartMate 3) and a median of 61 years of age (range, 24–78 years of age; HeartMate II).<sup>9</sup> A European cross-sectional study of patients undergoing heart transplantation (HT) by Emin et al<sup>8</sup> included patients whose median age in years for HT candidates with MCS was 49.6 (IQR, 39.1–55.3 years of age) and for HT candidates on medical therapy was 47.1 (IQR, 40.6–56.7 years of age). Thus, we lack an understanding of HRQOL outcomes in older patients with advanced HF, including those who may be eligible for advanced surgical therapies.

As HT and mechanical circulatory support (MCS) implantation, advanced surgical treatment options for patients with HF, are being offered more frequently to the elderly,<sup>13,14</sup> gaps in the literature also exist regarding HRQOL benefits, based on intended goal of therapy, which may inform how much these patients may benefit and which therapies may provide more HRQOL-related benefit. White-Williams and colleagues<sup>15</sup> compared baseline HRQOL in adult patients with advanced HF before left ventricular assist device (LVAD) implantation

enrolled in the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) database by implant strategy (bridge to transplantation [BTT], bridge to candidacy [BTC], and destination therapy [DT]), which did not include patients awaiting HT without MCS. Similarly, in the MOMENTUM 3 trial, investigators identified baseline differences in HRQOL in adult patients with BTT and BTC versus DT implant strategies that also did not include a group of patients who were being medically treated and awaiting HT.<sup>12</sup> Groups in the study of HRQOL by Emin et al<sup>8</sup> included adult patients evaluated for HT, listed for HT on medical therapy, listed for HT on LVAD therapy, and after HT, but did not include a DT MCS group. Although these studies compared HRQOL in patients with either MCS and/or HT as an intended goal of therapy, none included all of the following 3 groups: HT (with or without MCS as a pre-HT management strategy) and DT MCS. We examined baseline differences in HRQOL by age in 3 separate articles focused on patients undergoing HT, DT MCS, or MCS (combining patients with BTT and DT MCS), yet we did not include comparative analyses by intended goal of therapy.<sup>7,16,17</sup> Thus, a “head-to-head” comparison of baseline HRQOL in a contemporary cohort of older patients with advanced HF who are candidates for HT (with or without MCS while awaiting HT) or DT MCS remains to be elucidated. To address this gap in knowledge, as optimizing HRQOL is often a primary goal of therapy for older patients, we present findings from the SUSTAIN-IT (Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support) study, whose primary aim is to compare HRQOL outcomes in older patients (60–80 years of age) with advanced HF who undergo HT or DT MCS from before to 2 years after these surgeries.

In this report from the SUSTAIN-IT study, we compared HRQOL in older patients with advanced HF at baseline (ie, before undergoing HT or DT [long-term] MCS). HT candidates were divided into 2 groups (ie, those awaiting HT with MCS and those awaiting HT without MCS) to provide insight into differences in HRQOL between these 2 alternative pre-HT management strategies. Thus, we aimed to compare HRQOL among the following 3 groups of patients: (1) HT candidates with MCS, (2) HT candidates without MCS, and (3) those deemed ineligible for HT and therefore candidates for long-term MCS. We also aimed to identify patient factors associated with HRQOL. We hypothesized that (1) baseline overall and domain-specific HRQOL of long-term MCS candidates would be different from baseline HRQOL of the HT candidate groups, and (2) factors associated with overall HRQOL would include patient group, indicators of HF severity (eg, New York Heart Association [NYHA] class and functional capacity), and psychological variables (ie, anxiety and depressive symptoms).

Our nomenclature regarding the 3 groups of patients in this article is based on the recent Centers for

Medicare and Medicaid National Coverage Decision to remove intent-to-treat criteria of BTT and DT by removing the requirement that patients with BTT MCS must be active on the United Network for Organ Sharing (UNOS) waiting list for HT. Thus, instead of BTT, we use the phrase “HT candidate with MCS,” and instead of DT, we use the phrase “long-term MCS.” We defined HRQOL as “the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient”<sup>18</sup> and used the theoretical framework by Spilker and Revicki<sup>18</sup> (modified to include caregivers) to guide our research as it is focused on the influence of disease and treatment on HRQOL outcomes.

## METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Design, Settings, and Sample

We used an observational, cross-sectional, multisite design to compare HRQOL in patients with HF before HT or long-term MCS. Patients were recruited from 13 US medical centers with HT and MCS programs that participated in the SUSTAIN-IT study. Study inclusion criteria were presence of advanced HF; 60 to 80 years of age; able to speak, read, and understand English; and listed with the UNOS for HT or being considered or scheduled for long-term primary MCS, specifically LVAD implantation. Second-generation and third-generation US Food and Drug Administration–approved and investigational LVADs were permissible. HT candidates with MCS could have had 1 or more LVADs. Long-term MCS candidates were recruited only if they had a low probability of becoming HT candidates (<35% chance at 2 years), per opinions of site investigators. We identified this enrollment cutoff to ensure, as best as possible, that patients in the long-term MCS group would remain in this group for the duration of the study and not cross over to HT candidacy, at which time they would be censored. HT candidates listed for retransplant, multiple organ transplant, and/or those with right or bi-ventricular assist devices were excluded from the study. Long-term MCS candidates with prior ventricular assist devices were also excluded. The study was approved by all site institutional review boards, and participants provided written informed consent.

### Instruments, Data Collection, and Procedures

Patients completed the following self-reported assessments of HRQOL: EuroQoL-5 Dimension Questionnaire

(EQ-5D-3L<sup>19</sup>; a 6-item generic measure of HRQOL) and Kansas City Cardiomyopathy Questionnaire–12 (KCCQ-12<sup>20</sup>; a 12-item, HF-specific measure of HRQOL; Table S1). The EQ-5D-3L includes 5 dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a visual analog scale (VAS; 0 [worst]–100 [best] imaginable health state). The KCCQ-12 has 4 domains (physical limitations, symptom frequency, social limitations, and quality of life) and an overall summary score (OSS) created from the domain scores. Clinically important differences for the EQ-5D-3L<sup>17,21</sup> and the KCCQ-12<sup>20</sup> are 10 and 5 points, respectively. Patients also completed an 8-item screen for depressive symptoms (Personal Health Questionnaire–8),<sup>22</sup> a 20-item measure of current anxiety (State-Trait Anxiety Inventory–state form),<sup>23</sup> an interviewer-administered screen of cognitive function (Montreal Cognitive Assessment),<sup>24</sup> and the following 2 researcher-monitored, performance-based measures as surrogate markers of functional capacity and frailty, respectively (Table S1): 6-minute walk test (6MWT)<sup>25</sup> and 5-m gait speed.<sup>26</sup>

Assessments were administered as follows: (1) in the HT candidate with MCS group after listing with UNOS while on MCS, (2) in the HT candidate without MCS group after listing with UNOS while on medical therapy, and (3) in the long-term MCS group after being considered and/or scheduled for long-term MCS.

Sociodemographic characteristics (eg, age, sex, race, marital status, work status, and insurance) and clinical variables (eg, etiology of HF, medical/surgical history, NYHA class, INTERMACS profile, and UNOS status) were collected by sites from patient medical records and/or directly from the Society of Thoracic Surgeons INTERMACS database via secure monthly data downloads.

## Statistical Analysis

Demographic characteristics, clinical variables, and assessments were summarized using mean±SD, median (first quartile, third quartile), or count (percentage) as appropriate. Group comparisons (ie, analysis of variance [ANOVA],  $\chi^2$  tests, or Fisher's exact test) were used to test the hypothesis that baseline HRQOL of long-term MCS candidates is different from baseline HRQOL of HT candidate groups.

Item-level missing data on the HRQOL assessments were imputed via the within-group respondent mean (if continuous) and mode (if categorical) to avoid group cross-contamination.<sup>27</sup> This imputation method was used if <15% of item-level data were missing, except for the KCCQ-12, wherein imputation was not used per scoring instructions. For 58 patients with 6MWT data missing for reasons other than inability to walk or patient being too sick or too tired to walk (for whom we

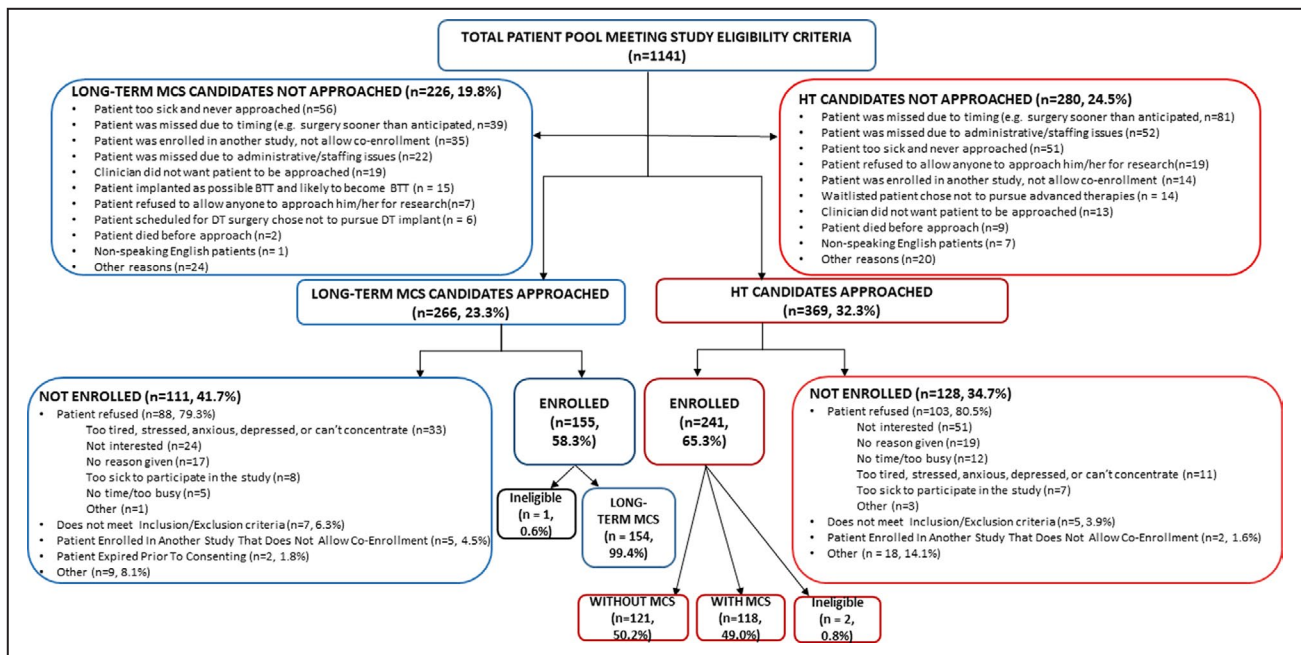
imputed a value of 0), we used model-predicted single imputation based on a least squares regression model with NYHA class at enrollment and KCCQ-12 symptom frequency as explanatory variables. We also conducted sensitivity analyses by fitting separate models for each outcome using solely observed 6MWT values (no imputation).

The second hypothesis (factors associated with overall HRQOL would include patient group, indicators of HF severity, and psychological variables) was tested using univariable and multivariable linear least squares regression models. We modeled separately overall HRQOL scores (EQ-5D-3L VAS and KCCQ-12 OSS). In the univariable models, the initial pool of baseline variables included age, sex, race, marital status, working status, highest level of education more than high school, insurance type, Personal Health Questionnaire–8, State-Trait Anxiety Inventory–state form, patient group (ie, HT candidate with MCS, HT candidate without MCS, and long-term MCS), method of payment for medical care, history of smoking, comorbidities (myocardial infarction, diabetes, hypertension, kidney disease, arrhythmia, hyperlipidemia), Montreal Cognitive Assessment, and 6MWT. We used an entry point of  $\alpha=0.3$  in the univariable models to define the candidate pool for multivariable model building. Multivariable models were created by including each variable significant univariately at the 0.3  $\alpha$  level, excluding variables that were collinear with the outcome or poorly reported.

Between-center differences for patient demographic and clinical characteristics and outcomes were assessed. Statistical significance was established at a 2-sided  $\alpha=0.05$ , and no adjustments were made for multiplicity. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). Dr Andrei had full access to all data in the study and takes responsibility for its integrity and the data analysis.

## RESULTS

Between October 1, 2015 and December 31, 2018, from a pool of 1141 patients with advanced HF (649 HT candidates and 492 long-term MCS candidates), 635 patients were approached (n=369 HT candidates and n=266 long-term MCS candidates), and 396 (n=241 HT candidates and n=155 long-term MCS candidates) were recruited to participate in the SUSTAIN-IT study (Figure). A total of 2 HT candidates and 1 long-term MCS candidate who were enrolled were deemed ineligible and immediately withdrawn, leaving a final sample size of 393 patients (239 HT candidates and 154 long-term MCS candidates). Among those patients listed for



**Figure 1. Timeline and consort flow diagram for patients before long-term MCS or HT.**

BTT indicates bridge to transplantation; DT, destination therapy; HT, heart transplantation; and MCS, mechanical circulatory support.

HT, there were 118 with MCS and 121 without MCS. Reasons for not approaching candidates included timing of surgery and administrative issues (eg, staffing issues), being too sick, and other reasons. Reasons for refusal to participate for those approached included lack of interest, too sick, and other (Figure).

The majority of patients were White men and married, and 67% had more than a high school education (Table 1). Long-term MCS candidates were older, on average, than HT candidates with and without MCS, although substantial overlap was observed between groups (Figure S1). Long-term MCS candidates also had significantly more comorbidities and a higher NYHA class at enrollment (Table 1).

### Rates of Assessment Completion and Psychometrics

Baseline completion of assessments varied based on type of assessment and group. Rates of patient completion of self-report assessments and the interview were excellent (ranges, 92%–99% and 91%–92%, respectively), whereas completion rates for the performance-based measures (6MWT and 5-m gait speed) were lower (range, 24%–66%) and lowest for patients awaiting long-term MCS (Table S2). The most frequently reported reason for incomplete performance-based measures was that the participant was too sick, which varied by site (1%–22%; Table S3). Sensitivity analyses based on observed (unimputed) 6MWT data show that, for each outcome, model coefficients are not impacted substantially; their directionality and statistical

significance remaining unchanged. Cronbach's  $\alpha$  were acceptable for the outcome variables (EQ-5D-3L, 0.72; KCCQ-12 OSS, 0.90) in our SUSTAIN-IT study cohort.

### Baseline Comparisons of HRQOL Among Groups

Baseline overall HRQOL for the entire sample was poor to fair (EQ-5D-3L mean $\pm$ SD VAS score, 55 $\pm$ 23; KCCQ-12 mean $\pm$ SD OSS, 47 $\pm$ 23; Table 2). Significant differences were found among groups. Long-term MCS candidates had worse HRQOL than HT candidates with and without MCS (EQ-5D-3L mean $\pm$ SD VAS score, 46 $\pm$ 23 versus 68 $\pm$ 18 versus 54 $\pm$ 23 [ $P$ <0.001]; KCCQ-12 mean $\pm$ SD OSS, 35 $\pm$ 21 versus 60 $\pm$ 21 versus 49 $\pm$ 22 [ $P$ <0.001], respectively), whereas HT candidates with MCS had the highest scores. Regarding EQ-5D-3L dimensions, >50% of the total sample reported problems with mobility, usual activities, and pain/discomfort. Long-term MCS candidates had significantly more problems with mobility, self-care, usual activities, and anxiety/depression than HT candidates with and without MCS (Table 2). No group differences were detected for pain/discomfort. Although reports of “extreme problems” were generally low for the aforementioned dimensions, long-term MCS candidates reported more extreme problems regarding mobility, self-care, and usual activities than both groups of HT candidates (Table S4). KCCQ-12 domain scores also differed significantly among groups. Long-term MCS candidates reported more physical and social limitations, higher symptom frequency, and worse quality

**Table 1. Patient Demographic and Clinical Characteristics at Baseline**

Variable	Available sample total, by group*	Total sample, n=393†	Long-term MCS candidates, n=154†	HT candidates with MCS, n=118†	HT candidates without MCS, n=121†	P value
<b>Demographic characteristics</b>						
Age, y	393 (154, 118, 121)	66.0±4.6	68.6±5.2	64.4±3.3	64.0±2.9	<0.001
Male sex	393 (154, 118, 121)	315 (80)	122 (79)	99 (84)	94 (78)	0.45
White race	390 (154, 118, 118)	323 (83)	126 (82)	94 (80)	103 (87)	0.27
Ethnicity: Hispanic or Latino	386 (150, 118, 118)	6 (2)	3 (2)	2 (2)	1 (1)	0.88
Marital status: married/domestic partners	388 (151, 116, 121)	302 (78)	118 (78)	89 (77)	95 (79)	0.94
Education, more than high school	363 (133, 109, 121)	245 (67)	93 (70)	69 (63)	83 (69)	0.52
Currently working	382 (143, 118, 121)	67 (18)	21 (15)	23 (19)	23 (19)	0.52
Working part-time vs full-time	49 (15, 13, 21)					0.45
Part-time		19 (39)	7 (47)	6 (46)	6 (29)	
Full-time		30 (61)	8 (53)	7 (54)	15 (71)	
Insurance type	393 (154, 118, 121)					<0.001
Medicare/Medicaid		243 (62)	113 (73)	69 (58)	61 (50)	
Private insurance		150 (38)	41 (27)	49 (42)	60 (50)	
BMI at time of study enrollment, kg/m <sup>2</sup>	346 (148, 78, 120)	28.4±5.5	28.4±6.5	29.9±4.7	27.5±4.3	0.008
<b>Clinical characteristics</b>						
Heart failure etiology	393 (154, 118, 121)					0.17
Ischemic cardiomyopathy		182 (46)	81 (53)	55 (47)	46 (38)	
Dilated cardiomyopathy		187 (48)	65 (42)	57 (48)	65 (54)	
Other		24 (6)	8 (5)	6 (5)	10 (8)	
NYHA class at study enrollment	382 (149, 113, 120)					<0.001
I		18 (5)	0 (0)	16 (14)	2 (2)	
II		57 (15)	1 (1)	43 (38)	13 (11)	
III		128 (34)	17 (11)	39 (35)	72 (60)	
IV		179 (47)	131 (88)	15 (13)	33 (28)	
INTERMACS profile at enrollment	259 (146, 113, NA)					0.005
Profile 1		33 (13)	12 (8)	21 (19)	NA	
Profiles 2 to 3		189 (73)	118 (81)	71 (63)	NA	
Profiles 4 to 7		37 (14)	16 (11)	21 (19)	NA	

(Continued)

**Table 1. Continued**

Variable	Available sample total, by group*	Total sample, n=993†	Long-term MCS candidates, n=154†	HT candidates with MCS, n=118†	HT candidates without MCS, n=121†	P value
UNOS status at enrollment	239 (NA, 118, 121)					<0.001
1A		44 (18)	NA	16 (14)	28 (23)	
1B		138 (58)	NA	87 (74)	51 (42)	
2		44 (18)	NA	5 (4)	39 (32)	
7		13 (5)	NA	10 (8)	3 (2)	
Length of time on UNOS waiting list at enrollment, d	160 (NA, 67, 93)	252 (61, 629)	NA	507 (255, 825)	94 (43, 330)	<0.001
Length of time on VAD from implant to enrollment, d	118 (NA, 118, NA)	352 (171, 692)	NA	352 (171, 692)	NA	
LVEF closest to date of surgery	238 (143, 42, 53)					0.009
>50, normal		3 (1)	0 (0)	1 (2)	2 (4)	
.40 to 49, mild		4 (2)	0 (0)	1 (2)	3 (6)	
30 to 39, moderate		13 (5)	6 (4)	1 (2)	6 (11)	
20 to 29, moderate/severe		75 (32)	45 (31)	12 (29)	18 (34)	
<20, severe		130 (55)	86 (60)	22 (52)	22 (42)	
Not recorded/documentated		13 (5)	6 (4)	5 (12)	2 (4)	
Temporary MCS at enrollment	393 (154, 118, 121)	10 (3)	4 (3)	4 (3)	2 (2)	0.69
ICD device in place at enrollment	352 (150, 81, 121)	303 (86)	129 (86)	64 (79)	110 (91)	<0.001
History of smoking	390 (153, 116, 121)	116 (30)	25 (16)	37 (32)	54 (45)	<0.001
Number of comorbidities	393 (154, 118, 121)	4.4±2.1	5.0±2.2	4.2±2.1	3.9±1.8	<0.001
Hypertension	393 (154, 118, 121)	239 (61)	102 (66)	67 (57)	70 (58)	0.21
Hyperlipidemia	393 (154, 118, 121)	234 (60)	95 (62)	68 (58)	71 (59)	0.77
Arrhythmia	393 (154, 118, 121)	229 (58)	99 (64)	69 (58)	61 (50)	0.07
Diabetes	393 (154, 118, 121)	181 (46)	85 (55)	53 (45)	43 (36)	0.005
Chronic kidney disease	393 (154, 118, 121)	145 (37)	71 (46)	39 (33)	35 (29)	0.008
Myocardial infarction	393 (154, 118, 121)	136 (35)	56 (36)	40 (34)	40 (33)	0.83
Pulmonary hypertension	393 (154, 118, 121)	79 (20)	35 (23)	28 (24)	16 (13)	0.08

BMI indicates body mass index; HT, heart transplantation; ICD, implantable cardioverter defibrillator; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; NA, not applicable; NYHA, New York Heart Association; UNOS, United Network for Organ Sharing; VAD, ventricular assist device.

\*Data are expressed as total number (total number of HT candidates with MCS; total number of HT candidates without MCS; total number of candidates ineligible for HT and scheduled for long-term MCS).

†Data are expressed as mean±SD, number (percentage), or median (quartile 1, quartile 3).

**Table 2. Patient Questionnaires, Interview, and Performance-Based Assessments Completed at Baseline**

Variable	Available sample total (by group)*	Total sample, n=393†	Long-term MCS candidates, n=154†	HT candidates with MCS, n=118†	HT candidates without MCS, n=121†	P value
EQ-5D-3L VAS score	382 (144, 118, 120)	55±23	46±23	68±18	54±23	<0.001
EQ-5D-3L VAS score, by 25-point ranges	382 (144, 118, 120)					<0.001
0 to 24		35 (9)	22 (15)	2 (2)	11 (9)	
25 to 49		99 (26)	52 (36)	9 (8)	38 (32)	
50 to 74		150 (39)	51 (35)	57 (48)	42 (35)	
75 to 100		98 (26)	19 (13)	50 (42)	29 (24)	
EQ-5D-3L mobility, percent with problems	380 (143, 118, 119)	210 (55)	92 (64)	54 (46)	64 (54)	0.010
EQ-5D-3L self-care, percent with problems	380 (143, 118, 119)	124 (33)	67 (47)	32 (27)	25 (21)	<0.001
EQ-5D-3L usual activities, percent with problems	381 (143, 118, 120)	262 (69)	113 (79)	71 (60)	78 (65)	0.003
EQ-5D-3L pain/discomfort, percent with problems	380 (143, 118, 119)	194 (51)	74 (52)	54 (46)	66 (55)	0.32
EQ-5D-3L anxiety/depression, percent with problems	380 (143, 118, 119)	135 (36)	62 (43)	41 (35)	32 (27)	0.021
KCCQ-12 physical limitation	370 (137, 117, 116)	49±28	38±27	59±26	53±26	<0.001
KCCQ-12 symptom frequency	383 (145, 118, 120)	58±26	46±24	71±22	61±26	<0.001
KCCQ-12 quality of life	383 (145, 118, 120)	35±27	23±23	51±27	35±25	<0.001
KCCQ-12 social limitation	364 (132, 115, 117)	46±30	34±28	60±26	47±30	<0.001
KCCQ-12 overall summary score	383 (145, 118, 120)	47±23	35±21	60±21	49±22	<0.001
KCCQ-12 overall summary score, by 25-point ranges	383 (145, 118, 120)					<0.001
0 to 24		81 (21)	58 (40)	7 (6)	16 (13)	
25 to 49		128 (33)	49 (34)	30 (25)	49 (41)	
50 to 74		123 (32)	34 (23)	53 (45)	36 (30)	
75 to 100		51 (13)	4 (3)	28 (24)	19 (16)	
PHQ-8 total score	382 (147, 115, 120)	88 (23)	49 (33)	16 (14)	23 (19)	<0.001
PHQ-8 total score	382 (147, 115, 120)	6.4±5.2	8.2±5.9	4.7±4.5	5.9±4.1	<0.001
STAI-state total score	382 (147, 115, 120)	37±11	39±11	35±12	34±10	<0.001
MoCA total score	359 (141, 108, 110)	25.0±3.3	23.8±3.6	25.4±2.9	26.3±2.7	<0.001
Six-min walk, m	209 (51, 89, 69)	309±121	204±115	348±106	336±96	<0.001
Gait speed, m/s	183 (37, 78, 68)	1.1±0.3	0.9±0.3	1.1±0.3	1.1±0.3	<0.001

EQ-5D-3L VAS score indicates EuroQol-5 Dimension Questionnaire Visual Analog Scale (score range 0=worst to 100=best imaginable health state); HT, heart transplantation; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12 (score range: 0=worst to 100=best health status); MCS, mechanical circulatory support; MoCA, Montreal Cognitive Assessment (score range: 0=worst to 30=best score; cognitive dysfunction is defined as a MoCA score<26); PHQ-8, Personal Health Questionnaire-8 (depression screen; score range 0=less to 24=worse depression); and STAI-state, State-Trait Anxiety Inventory-state form (score range 20=less to 80=worse anxiety).

\*Data are expressed as total number (total number of HT candidates with MCS, total number of HT candidates without MCS, total number of candidates ineligible for HT and scheduled for long-term MCS).

†Data are expressed as mean±SD or number (percentage).



of life than the 2 HT candidate groups, whereas HT candidates with MCS had the highest domain scores among the 3 groups (Table 2).

### Factors Associated With HRQOL in Patients Awaiting HT and Long-Term MCS

We identified minimal variability among centers and therefore chose not to control for center effects. Multicollinearity among independent variables was minimal. Significant variables from the univariable models (Table S5) were included in the multivariable models. In the multivariable model for the EQ-5D-3L VAS score, being an HT candidate with MCS was associated with an 8.6-point increase (95% CI, 2.7–14.4;  $P=0.004$ ) in the VAS score compared with HT candidates without MCS. Decreased 6MWT distance and more depressive symptoms were associated with a decreased EQ-5D-3L VAS score and along with patient group explained 33% of the variance (Table 3). Patient group was not significantly associated with the KCCQ-12 OSS in the multivariable model. Increased depressive symptoms, decreased 6MWT distance, and higher NYHA class were associated with decreased HRQOL using the KCCQ-12 OSS, explaining 58% of variance (Table 3).

## DISCUSSION

Guided by our theoretical framework, we have extended knowledge of HRQOL in adult patients to those who are 60 to 80 years of age before advanced surgical therapies. In addition, we have expanded on baseline findings from studies regarding intended goal of therapy (ie, INTERMACS, MOMENTUM 3 trial, and the European study by Emin et al)<sup>8,12,15</sup> by comparing HRQOL among older patients who were awaiting HT with or without MCS or long-term MCS if ineligible for HT. Key baseline findings in this older cohort of patients with HF from the SUSTAIN-IT study were that overall HRQOL was poor to fair, and along with domains of HRQOL, important differences were detected among groups (ie, worse before long-term MCS), thus supporting our first hypothesis that baseline overall and domain-specific HRQOL of long-term MCS candidates would be different from baseline HRQOL of the 2 HT candidate groups. Furthermore, we identified factors (ie, patient group, indicators of HF severity, and psychological factors) associated with worse baseline HRQOL for older patients with advanced HF, which supported our second hypothesis.

Notably, long-term MCS candidates who had worse HRQOL, compared with both HT candidate groups, were older and had more comorbidities (including diabetes and chronic kidney disease) and also had a higher

NYHA class, lower left ventricular ejection fraction, and lower 6MWT and gait speed, which suggest a higher severity of HF. Thus, it is perhaps not unexpected that compared with older HT candidates, older long-term MCS candidates had significantly worse overall generic and HF-specific HRQOL, which are clinically important differences.<sup>17,20,21</sup> Our findings are partially supported by findings from the observational ROADMAP (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management) study (overall mean±SD age, 63±13 years), which enrolled 2 groups of patients with advanced HF who were ambulatory: those scheduled for long-term MCS and those who remained on optimal medical management. ROADMAP investigators reported that HRQOL was lower at baseline in patients with long-term MCS compared with those on optimal medical management (45±20 versus 58±20, respectively).<sup>11</sup> In contradistinction, INTERMACS investigators and MOMENTUM 3 trial investigators detected no clinically important differences in baseline overall HRQOL between adult HT candidates with MCS (which included patients with BTC MCS in the MOMENTUM 3 trial) and those awaiting long-term MCS.<sup>12,15</sup> Differences in findings between these 2 studies and our study are unclear but may be attributed to age differences in groups among studies. For example, the mean±SD ages of candidates for DT MCS and candidates for BTT/BTC MCS in the MOMENTUM 3 trial were 63±12 years of age and 55±12 years of age, respectively, whereas the mean±SD ages for long-term MCS (ie, DT) candidates and HT candidates with MCS (BTT) in the SUSTAIN-IT study were 69±5 years of age and 64±3 years of age, respectively. Also, MOMENTUM 3 trial investigators combined patients with BTT and BTC MCS (including those who were likely, moderately likely, and unlikely to become transplant eligible) into 1 group,<sup>12</sup> which may have influenced their findings, as moderately likely and unlikely patients with BTC MCS may have been more similar to DT candidates than HT candidates.

In addition, older patients awaiting HT with MCS had the highest HRQOL scores, which most likely represents the positive impact of MCS on reducing HF symptoms and improving functional capacity. Emin et al<sup>8</sup> also reported clinically important differences in overall HRQOL in their younger cohort of patients, favoring HT candidates with MCS compared with those on medical therapy (KCCQ-12 OSS, 52.6±22.0 versus 33.3±21.1, respectively).

Few studies have identified factors associated with HRQOL in older patients with HF awaiting advanced surgical therapies. The association between being an HT candidate with MCS and better HRQOL may be attributed to improved health on MCS and the anticipation of HT. We previously reported that patients awaiting HT with MCS commented that the device

**Table 3. Factors Associated With Health-Related Quality of Life in Patients Awaiting HT and Long-Term MCS Using Multivariable Linear Regression Models**

Effect	Effect size	95% Confidence limits		P value
EQ-5D VAS score ( $R^2=0.33$ )				
Intercept	63.7	27.8	99.7	<0.001
Patient group				
Long-term MCS candidates	-1.3	-8.0	5.4	0.71
HT candidates with MCS	8.6	2.7	14.4	0.004
HT candidates without MCS	Reference	Reference	Reference	Reference
Patient White race	-2.2	-8.1	3.7	0.50
Patient PHQ-8 total score	-1.4	-1.9	-0.8	<0.001
Patient 6-min walk, m				
0	-9.8	-17.7	-2.0	0.015
1 to 183	-6.9	-15.0	1.1	0.09
184 to 300	-2.2	-9.9	5.6	0.58
301 to 378	0.9	-6.3	8.1	0.81
>378	Reference	Reference	Reference	Reference
Patient history of arrhythmia	-3.4	-7.6	0.8	0.11
Patient history of chronic kidney disease	-3.3	-7.7	1.2	0.15
Patient history of diabetes	-2.6	-6.8	1.7	0.23
Patient history of hypertension	-1.6	-5.9	2.8	0.48
Patient NYHA class at enrollment				
1	Reference	Reference	Reference	Reference
2	-2.6	-13.4	8.2	0.63
3	-8.0	-18.7	2.7	0.14
4	-6.2	-17.8	5.3	0.29
Patient history of smoking	2.9	-1.8	7.6	0.23
Patient STAI-state total score	-0.03	-0.3	0.2	0.82
Patient male sex	-3.3	-8.8	2.2	0.24
Patient age	0.3	-0.2	0.8	0.30
KCCQ-12 overall summary score ( $R^2=0.58$ )				
Intercept	65.4	36.4	94.3	<0.001
Patient group				
Long-term MCS candidates	-0.5	-5.8	4.7	0.84
HT candidates with MCS	3.7	-0.9	8.3	0.11
HT candidates without MCS	Reference	Reference	Reference	Reference
Patient PHQ-8 total score	-2.2	-2.6	-1.8	<0.001
Patient 6-min walk, m				
0	-15.9	-22.1	-9.7	<0.001
1 to 183	-16.3	-22.6	-10.0	<0.001
184 to 300	-7.3	-13.4	-1.2	0.019
301 to 378	-3.8	-9.5	1.9	0.19
>378	Reference	Reference	Reference	Reference
Patient insurance type				
Medicare/Medicaid	-1.8	-5.4	1.8	0.32
Private insurance	Reference	Reference	Reference	Reference
Patient history of diabetes	-1.4	-4.7	1.9	0.41
Patient NYHA class at enrollment				
1	Reference	Reference	Reference	Reference

(Continued)

**Table 3. Continued**

Effect	Effect size	95% Confidence limits		P value
2	-2.7	-11.2	5.8	0.53
3	-8.9	-17.2	-0.5	0.039
4	-12.1	-21.2	-3.1	0.009
Patient history of smoking	1.4	-2.2	5.1	0.45
Patient STAI-state total score	-0.03	-0.2	0.2	0.75
Patient age	0.3	-0.2	0.7	0.26

EQ-5D VAS indicates EuroQol Visual Analog Scale; HT, heart transplantation; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12; MCS, mechanical circulatory support; NYHA, New York Heart Association; PHQ-8, Personal Health Questionnaire-8; and STAI, State-Trait Anxiety Inventory.

reduced HF symptoms and improved participation in usual activities, yet patients were also anxious to undergo HT and “get on with life.”<sup>28</sup> Less distance walked on the 6MWT and its association with worse HRQOL is also logical, as it reflects impaired functional capacity, which was also found by Stehlik and colleagues<sup>5</sup> in their report from the REVIVAL study. Similar to our findings, Stehlik et al<sup>5</sup> also reported that a higher NYHA class was associated with worse HRQOL at baseline. Notably, significantly more long-term MCS candidates in our study were NYHA class IV than both HT candidate groups. Given the strength of the association of a higher NYHA class with a decrease in HRQOL, monitoring NYHA class in long-term MCS candidates is especially warranted. The association between depressive symptoms and HRQOL in patients with HF is well supported in the literature in, on average, middle-aged and older-aged cohorts.<sup>11,29,30</sup> Rutledge and colleagues<sup>31</sup> reported that depression was more prevalent in patients with HF with higher NYHA class, also providing support for our findings.

This baseline report from the SUSTAIN-IT study provides valuable information for shared decision-making discussions with older patients with advanced HF when considering surgical treatment options and regarding targets for HRQOL-related treatment. It is well known that HRQOL influences preferences for treatment.<sup>32</sup> A critical question is the following: Will older patients with advanced HF incur more HRQOL-related benefit from HT or long-term MCS? The answer to this question is complex, as symptom burden, functional capacity, comorbidities, other outcomes (eg, survival), and postoperative risks and benefits must be considered. Our “head-to-head” comparison of baseline HRQOL among older patients before these surgical therapies partially addresses this question. Understanding differences in baseline HRQOL in our 3 groups of older patients provides critical information that may be useful to gauge the amount of improvement in HRQOL after HT or long-term MCS that may ultimately contribute to identifying which therapy conveys more HRQOL-related benefit. In support of this notion, findings from our INTERMACS study of HRQOL by severity of HF

from before through 1 year after MCS implant (patient mean±SD age, 53±12 years of age) revealed greater gains in HRQOL by patients with lower INTERMACS profiles (ie, more-severe HF) than patients with higher INTERMACS profiles (ie, less-severe HF) despite postimplant adverse events.<sup>10</sup> Thus, sharing baseline HRQOL with older patients regarding potential surgical treatment options, that in the opinion of the clinician may provide benefit, contributes to a more informed shared decision-making process, which has been well described in the literature,<sup>33</sup> and importantly is iterative, as patient preferences for survival versus HRQOL can change over time, often based on symptom burden and functional capacity.<sup>34</sup>

Our study also contributes to a better understanding of differences in HRQOL in older patients before HT and long-term MCS, especially domain-specific HRQOL (eg, problems with mobility, usual activities, social functioning, anxiety/depression, and pain/discomfort and potentially worsening HF symptoms), which provides important individualized targets for treatment. We and others recommend assessment of baseline HRQOL by self-report, rather than proxy (eg, physicians and family members), which can be discrepant, either overestimating or underestimating HRQOL.<sup>18,35</sup> These data can be captured and scored electronically in real time. Careful and frequent monitoring of older patients’ HF trajectory, NYHA class, symptoms, HRQOL (both overall and domains), functional capacity,<sup>33,36</sup> and subsequent development of a treatment plan, including consultation with the palliative care team and allied health team members, especially physical therapists, psychologists, and social workers, may contribute to enhanced HRQOL and improved health while awaiting HT or long-term MCS. Notably, older long-term MCS candidates in our study reported more problems with physical function (ie, mobility, self-care, and usual activities) and mood (ie, anxiety and depression) than both groups of older HT candidates. Assessment of these HRQOL domains in this group of patients with advanced HF and the development of a treatment plan is especially warranted. Our recommendations are partially supported by Dew et al,<sup>37</sup>

who identified key domains for evaluation of candidacy for cardiothoracic transplantation and MCS, including evaluations of patients' current mental and social histories and understanding of their current illness, impact on daily functioning, symptoms, and treatment. Ultimately, understanding and subsequently treating HRQOL-focused problems while older patients with advanced HF await HT or long-term MCS may contribute to better outcomes after these surgical therapies.

Subsequent analyses from the SUSTAIN-IT study will compare changes over time in overall and domain-specific HRQOL early (baseline to 6 months) and later (baseline to 2 years) after HT (with or without MCS as a pretransplant management strategy) versus long-term MCS and identify factors related to change in HRQOL. Future findings from our study may increase knowledge of this patient-centric outcome so that clinicians may better inform older patients with advanced HF considering these treatment options as to which option may convey more HRQOL-related benefit and initiate postoperative HRQOL-focused treatment, especially regarding domain-specific findings.

A limitation of our study is that older patients enrolled in the SUSTAIN-IT study were prescreened and deemed eligible/awaiting advanced surgical therapies; thus, their HRQOL may not be reflective of the broader population with advanced HF. Also, a substantial number of patients in our total patient pool were not approached as a result of being too sick or were approached and refused participation for similar reasons, which may have resulted in an overestimation of HRQOL. In addition, our sample was fairly homogeneous, and more patients had more than a high school education than samples from other studies, which may limit generalizability. Lastly, lower completion rates of performance-based measures, which varied by site, may also have influenced our findings, although we used a robust method to impute data for the 6MWT.

## CONCLUSIONS

These findings demonstrate important differences in overall and domain-specific HRQOL of older patients with advanced HF before HT or long-term MCS. Understanding differences in HRQOL may guide decisions toward more personalized, advanced HF therapies. Older patients before long-term MCS are an especially appropriate target for these therapies given their worse HRQOL compared with both HT candidate groups.

## ARTICLE INFORMATION

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## Supplemental Material

Table S1–S5  
Figure S1

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# **SUPPLEMENTAL MATERIAL**

**Table S1. Assessments Completed by Patients at Baseline.**

Measure	Description of Measure
<b>Self-report Measures</b>	
<b>EQ-5D-3L</b> <sup>19</sup>	<p><b>Generic Overall Health-related Quality of Life (HRQOL) and dimensions:</b></p> <ul style="list-style-type: none"> <li>• Single item rating current health status uses a vertical graduated (0-100) 20cm visual analog scale (VAS). Mean VAS scores are calculated.</li> <li>• 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/ depression with 3 levels of response (no problems, some/moderate problems, and extreme problems).</li> </ul>
<b>Kansas City Cardiomyopathy Questionnaire (KCCQ-12)</b> <sup>20</sup>	<p><b>Heart failure-specific Overall HRQOL and domains:</b></p> <ul style="list-style-type: none"> <li>• 12-item disease specific questionnaire that measures HRQOL in patients with heart failure.</li> <li>• Four domains: physical limitations, symptom frequency, social limitations, and quality of life, and an overall summary score, combining the domains. Responses are set up as Likert scales. Scale scores are transformed to 0-100; higher scores = better health-related quality of life.</li> </ul>
<b>Personal Health Questionnaire (PHQ-8)</b> <sup>22</sup>	<p><b>Mental HRQOL domain:</b></p> <ul style="list-style-type: none"> <li>• 8-item screen for depression, based on the first eight criteria on which the diagnosis of DSM-IV depressive disorder is based.</li> <li>• Subjects indicate how often they have been bothered by depressive symptoms over the previous two weeks on a scale of 0=not at all to 3=nearly every day.</li> <li>• A summary score is calculated, with possible scores ranging from 0 to 24. Higher scores indicate higher levels of depressive symptoms. Scores <math>\geq 10</math> indicate the need for clinical assessment and management.</li> </ul>
<b>State-Trait Anxiety Inventory -State form (STAI-State)</b> <sup>23</sup>	<p><b>Mental HRQOL domain:</b></p> <ul style="list-style-type: none"> <li>• 20 self-report items assessing current levels of anxiety.</li> <li>• Subjects use a four-point Likert scale ranging from (1) not at all to (4) very much so. Higher scores = greater state anxiety.</li> </ul>
<b>Performance-based Measures</b>	
<b>Six minute walk test (6MWT)</b> <sup>25</sup>	<p><b>Physical domain:</b></p> <ul style="list-style-type: none"> <li>• Measure of physical functional capacity, consists of having a patient walk for 6 minutes in an enclosed hallway, free of traffic and distractions, with distance measured in meters.</li> </ul>

	<ul style="list-style-type: none"> <li>Patients are instructed to walk steadily to cover as much distance as possible during the 6 minutes. At the end of the walk, the total time (if less than 6 minutes) and distance covered is recorded. If a patient is bed-bound, a score of "0" may be assigned.<sup>36</sup></li> </ul>
<b>5-meter gait speed<sup>26</sup></b>	<b>Frailty:</b> <ul style="list-style-type: none"> <li>Clinical marker of frailty, used in an elderly cardiac surgical population.<sup>26</sup></li> <li>Conducted in a well-lit, unobstructed hallway with markings at 0 and 5 meters.</li> <li>Patients are instructed to walk at a comfortable pace; canes and walkers are allowed. If a patient cannot walk, data are considered missing. This test is performed three times and averaged. Slower gait speed = longer walk time over 5 meters (m/sec).</li> </ul>
<b>Interview Administered Measure</b>	
<b>Montreal Cognitive Assessment (MoCA)<sup>24</sup></b>	<b>Cognitive dysfunction:</b> <ul style="list-style-type: none"> <li>10-minute screening instrument (worst-to-best total score range=0-30), includes 7 cognitive domains.</li> <li>Cognitive dysfunction: (MoCA total score less than 26).</li> </ul>



**Table S2. Completion of Assessments at Baseline.**

<b>Patient Baseline Forms</b>	<b>HT* Candidates (with and without MCS) Completed/Expected (%)</b>	<b>Long-term MCS† Candidates Completed/Expected (%)</b>	<b>Total Completed/Expected (%)</b>
<b>Self-report Assessments</b>			
EQ-5D-3L‡	237/239 (99%)	142/154 (92%)	379/393 (96%)
KCCQ-12§	237/239 (99%)	143/154 (93%)	380/393 (97%)
PHQ-8¶	235/239 (98%)	147/154 (95%)	382/393 (97%)
STAI-state#	235/239 (98%)	147/154 (95%)	382/393 (97%)
<b>Interviewer-administered Assessment</b>			
MoCA**	218/239 (91%)	141/154 (92%)	359/393 (91%)
<b>Performance-based Assessments</b>			
Five Meter Gait Speed	146/239 (61%)	37/154 (24%)	183/393 (47%)
Six Minute Walk Test	158/239 (66%)	51/154 (33%)	209/393 (53%)

\* HT = heart transplantation

† MCS = mechanical circulatory support

‡ EQ-5D-3L = EuroQol-5 dimension-3L

§ KCCQ-12 = Kansas City Cardiomyopathy Questionnaire-12

¶ PHQ-8 = Personal Health Questionnaire

# STAI-state = State-Trait Anxiety Inventory-state form

\*\* MoCA = Montreal Cognitive Assessment.

**Table S3. Patient Baseline Reasons for Missing Data for Performance-based Measures.**

Variable	Available sample total (by group)	Total sample (n=393)	Long-term MCS* candidates (n=154)	HT† candidates with MCS (n=118)	HT candidates without MCS (n=121)	p-value
<u>Six Minute Walk Missing Status, No. (%)</u>	184(103,29,52)					0.67
. Form Incomplete/Reason Not Provided		1 (1%)	1 (1%)	0 (0%)	0 (0%)	
. Test Not Done (Reason Provided)		183 (99%)	102 (99%)	29 (100%)	52 (100%)	
<u>Reason Six Minute Walk Not Done, No. (%)</u>	183(102,29,52)					0.030
. Patient Refused, Unable to Walk		30 (16%)	22 (22%)	3 (10%)	5 (10%)	
. Patient Refused, Too Tired/Sick		89 (49%)	50 (49%)	13 (45%)	26 (50%)	
. Patient Refused, No Time/Too Busy		6 (3%)	1 (1%)	1 (3%)	4 (8%)	
. Patient Refused, No Reason Given		1 (1%)	1 (1%)	0 (0%)	0 (0%)	
. Did Not Approach Due to Patient Health Status		26 (14%)	17 (17%)	2 (7%)	7 (13%)	
. Coordinator Forgot/No Time		2 (1%)	1 (1%)	0 (0%)	1 (2%)	
. Collected For INTERMACS‡ Within Visit Window		5 (3%)	4 (4%)	1 (3%)	0 (0%)	
. Other		24 (13%)	6 (6%)	9 (31%)	9 (17%)	
<u>Five Meter Gait Speed Missing Status, No. (%)</u>	210(117,40,53)					0.67
. Form Incomplete/Reason Not Provided		1 (0%)	1 (1%)	0 (0%)	0 (0%)	
. Test Not Done (Reason Provided)		209 (100%)	116 (99%)	40 (100%)	53 (100%)	
<u>Reason Five Meter Gait Speed Not Done, No. (%)</u>	209(116,40,53)					0.002
. Patient Refused, Unable to Walk		32 (15%)	25 (22%)	3 (8%)	4 (8%)	
. Patient Refused, Too Tired/Sick		101 (48%)	59 (51%)	16 (40%)	26 (49%)	
. Patient Refused, No Time/Too Busy		8 (4%)	1 (1%)	3 (8%)	4 (8%)	
. Patient Refused, No Reason Given		2 (1%)	2 (2%)	0 (0%)	0 (0%)	
. Did Not Approach Due to Patient Health Status		31 (15%)	20 (17%)	4 (10%)	7 (13%)	
. Coordinator Forgot/No Time		5 (2%)	2 (2%)	2 (5%)	1 (2%)	
. Other		30 (14%)	7 (6%)	12 (30%)	11 (21%)	

\* MCS = mechanical circulatory support

† HT = heart transplantation

‡ INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support

**Table S4. Patient Baseline EQ-5D-3L Dimension Scores by 3 Levels of Problems.**

Variable	Available sample total (by group)	Total sample (n=393)	Long-term MCS* candidates (n=154)	HT <sup>†</sup> candidates with MCS (n=118)	HT candidates without MCS (n=121)	p-value
EQ-5D-3L <sup>‡</sup> Mobility, No. (%)	380(143,118,119)					<0.001
. No Problems in Walking About		170 (45%)	51 (36%)	64 (54%)	55 (46%)	
. Some Problems in Walking About		179 (47%)	68 (48%)	54 (46%)	57 (48%)	
. Confined to Bed		31 (8%)	24 (17%)	0 (0%)	7 (6%)	
EQ-5D-3L Self-Care, No. (%)	380(143,118,119)					<0.001
. No Problems with Self-Care		256 (67%)	76 (53%)	86 (73%)	94 (79%)	
. Some Problems Washing or Dressing Myself		101 (27%)	46 (32%)	32 (27%)	23 (19%)	
. Unable to Wash or Dress Myself		23 (6%)	21 (15%)	0 (0%)	2 (2%)	
EQ-5D-3L Usual Activities, No. (%)	381(143,118,120)					<0.001
. No Problems with Performing My Usual Activities		119 (31%)	30 (21%)	47 (40%)	42 (35%)	
. Some Problems with Performing My Usual Activities		193 (51%)	65 (45%)	66 (56%)	62 (52%)	
. Unable to Perform My Usual Activities		69 (18%)	48 (34%)	5 (4%)	16 (13%)	
EQ-5D-3L Pain/Discomfort, No. (%)	380(143,118,119)					0.23
. No Pain or Discomfort		186 (49%)	69 (48%)	64 (54%)	53 (45%)	
. Moderate Pain or Discomfort		183 (48%)	67 (47%)	52 (44%)	64 (54%)	
. Extreme Pain or Discomfort		11 (3%)	7 (5%)	2 (2%)	2 (2%)	
EQ-5D-3L Anxiety/Depression, No. (%)	380(143,118,119)					0.08
. Not Anxious or Depressed		245 (64%)	81 (57%)	77 (65%)	87 (73%)	
. Moderately Anxious or Depressed		126 (33%)	57 (40%)	38 (32%)	31 (26%)	
. Extremely Anxious or Depressed		9 (2%)	5 (3%)	3 (3%)	1 (1%)	

- \* MCS = mechanical circulatory support
- † HT = heart transplantation
- ‡ EQ-5D-3L = EuroQol -5D-3L Questionnaire

**Table S5. Factors Associated with Health-related Quality of Life in Patients Awaiting Heart Transplantation and Long-term Mechanical Circulatory Support using Univariable Linear Regression Models.**

Effect	n Available	Effect Size	95% Confidence Interval		p-value
<b>Outcome: EQ-5D* VAS Score</b>					
Sample (Reference = HT <sup>+</sup> candidates without MCS)					
• Long-term MCS <sup>+</sup> candidates	382	-8.5	-13.8	-3.3	0.001
• HT candidates with MCS		13.7	8.2	19.1	<0.001
Age, years	382	-0.6	-1.2	-0.1	0.014
Male	382	-4.0	-9.8	1.9	0.18
Race (White)	380	-4.9	-11.2	1.3	0.12
Education > High School	357	-2.9	-8.0	2.2	0.27
History of Smoking	379	4.1	-1.0	9.2	0.11
Arrhythmia	382	-5.3	-10.0	-0.5	0.030
Kidney Disease	382	-5.4	-10.2	-0.5	0.030
Diabetes	382	-5.5	-10.2	-0.8	0.021
Hypertension	382	-3.7	-8.5	1.1	0.12
NYHA Class at Enrollment (Reference = 1)					
• 2	371	-8.3	-19.9	3.2	0.16
• 3		-21.4	-32.2	-10.6	<0.001
• 4		-28.7	-39.3	-18.2	<0.001
Patient Six Minute Walk (meters) (Reference is >378)					

• 0	381	-23.1	-30.0	-16.4	<0.001
• 1 - 183		-18.6	-26.0	-11.3	<0.001
• 184 - 300		-9.6	-17.4	-1.8	0.016
• 301 - 378		-2.5	-10.0	4.9	0.50
PHQ-8 <sup>§</sup> Total Score	378	-2.0	-2.4	-1.5	<0.001
STAI <sup>  </sup> Total Score	378	-0.6	-0.8	-0.4	<0.001
MoCA <sup>#</sup> Total Score	351	0.9	0.1	1.6	0.022
<b>Outcome: KCCQ-12** Overall Summary Score</b>					
Sample (Reference = HT candidates without MCS)					
• Long-term MCS candidates	383	-13.6	-18.7	-8.5	<0.001
• HT candidates with MCS		11.0	5.6	16.4	<0.001
Age, years	383	-1.0	-1.5	-0.4	<0.001
Education > High School	358	-3.4	-8.5	1.8	0.20
Insurance Type: Private Insurance vs Medicare/Medicaid	383	5.6	0.8	10.4	0.021
Currently Working	359	8.4	1.9	14.8	0.011
History of Smoking	380	5.1	-0.01	10.2	0.050
Diabetes	383	-5.7	-10.3	-1.0	0.018
NYHA Class at Enrollment (Reference = 1)					
• 2	372	-11.1	-21.9	-0.3	0.043
• 3		-25.2	-35.2	-15.1	<0.001
• 4		-38.3	-48.2	-28.5	<0.001
Patient Six Minute Walk (meters) (Reference is >378)					
• 0	382	2.8	-2.8	8.3	0.32
• 1 - 183		17.6	11.6	23.6	<0.001

• 184 - 300		26.1	20.5	31.8	<0.001
• 301 - 378		35.2	29.2	41.2	<0.001
PHQ-8 Total Score	379	-2.9	-3.3	-2.6	<0.001
STAI Total Score	379	-0.8	-1.0	-0.7	<0.001
MoCA Total Score	352	1.77	1.0	2.4	<0.001

\* EQ-5D VAS = EuroQol visual analog scale

† HT = heart transplantation

‡ MCS = mechanical circulatory support

§ PHQ-8 = Personal Health Questionnaire-8

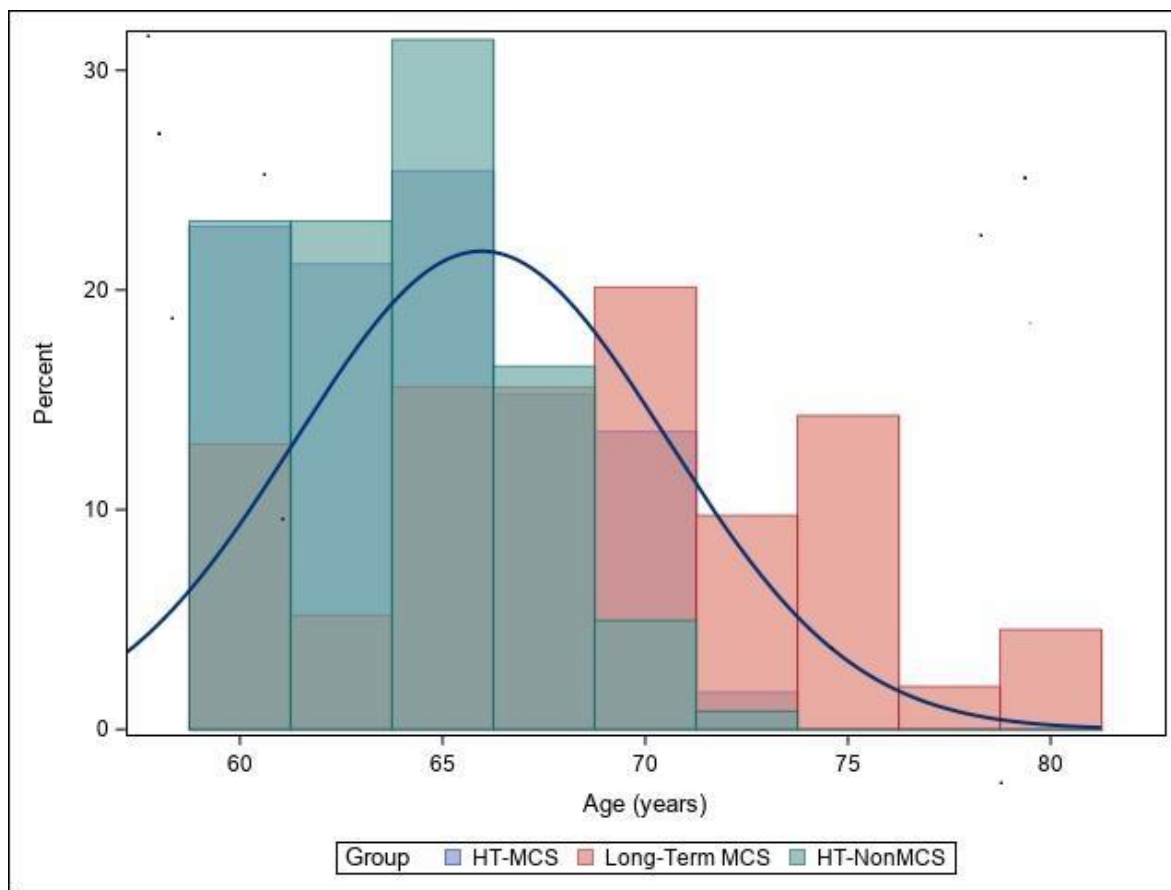
|| STAI-state = State-Trait Anxiety Inventory-state form

# MoCA = Montreal Cognitive Assessment

\*\* KCCQ-12 = Kansas City Cardiomyopathy Questionnaire



**Figure S1. Histogram for the three groups of candidates as individual overlays, with a density curve that represents the entire cohort.**



HT-MCS = heart transplant candidate with mechanical circulatory support prior to transplantation, Long-term MCS = advanced heart failure patient prior to long-term mechanical circulatory support, and HT-NonMCS = heart transplant candidate without mechanical circulatory support prior to transplantation.