10-1-2022

Health-related quality of life in older patients with heart failure from before to early after advanced surgical therapies: Findings from the SUSTAIN-IT study

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Circulation: Heart Failure

ORIGINAL ARTICLE

Health-Related Quality of Life in Older Patients With Heart Failure From Before to Early After Advanced Surgical Therapies: Findings From the SUSTAIN-IT Study

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BACKGROUND: Restoring health-related quality of life (HRQOL) is a therapeutic goal for older patients with advanced heart failure. We aimed to describe change in HRQOL in older patients (60–80 years) awaiting heart transplantation (HT) with or without pretransplant mechanical circulatory support (MCS) or scheduled for long-term MCS, if ineligible for HT, from before to 6 months after these surgeries and identify factors associated with change.

METHODS: Patients from 13 US sites completed the EuroQol 5-dimension 3L questionnaire and Kansas City Cardiomyopathy Questionnaire-12 at baseline and 3 and 6 months after HT or long-term MCS. Analyses included univariate comparisons and multivariable linear regression.

RESULTS: Among 305 participants (cohort mean age=66.2±4.7 years, 78% male, 84% White, 55% New York Heart Association class IV), 161 underwent HT (n=68 with and n=93 without pretransplant MCS), and 144 received long-term MCS. From baseline to 3 months, EuroQol 5-dimension visual analog scale scores improved in HT patients without pretransplant MCS (54.5±24.3 versus 75.9±16.0, $P<0.001$) and long-term MCS patients (45.7±22.9 versus 66.2±20.9, $P<0.001$); while Kansas City Cardiomyopathy Questionnaire-12 overall summary scores improved in all 3 groups (HT without pretransplant MCS: 47.2±20.9 versus 77.4±20.1, $P<0.001$; long-term MCS: 35.3±20.2 versus 58.6±22.0, $P<0.001$; and HT with pretransplant MCS: 58.3±23.6 versus 72.1±23.5, $P=0.002$). No further HRQOL improvement was found from 3 to 6 months. Factors most significantly associated with change in HRQOL, baseline 3 months, were right heart failure and 3-month New York Heart Association class, and 3 to 6 months, were 6-month New York Heart Association class and major bleeding.

CONCLUSIONS: In older heart failure patients, HRQOL improved from before to early after HT and long-term MCS. At 6 postoperative months, HRQOL of long-term MCS patients was lower than one or both HT groups. Understanding change in HRQOL from before to early after these surgeries may enhance decision-making and guide patient care.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT02568930.

Key Words: decision-making ■ heart failure ■ heart transplantation ■ mechanical circulatory support ■ quality of life

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Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCHEARTFAILURE.122.009579.

For Sources of Funding and Disclosures, see page 955.

Circulation: Heart Failure is available at www.ahajournals.org/journal/circheartfailure

WHAT IS NEW?

- In older (60–80 years) patients with advanced heart failure, health-related quality of life (HRQOL) improves from before to 3 months after heart transplantation (HT) and long-term mechanical circulatory support (MCS) if ineligible for HT, with no change in HRQOL between 3 and 6 postoperative months.
- Patients who undergo long-term MCS and HT without MCS as a pretransplant management strategy experience the greatest improvement in HRQOL; yet HRQOL of long-term MCS patients is lower than HT patients at 6 postoperative months.
- Demographics, preoperative HRQOL, anxiety, postoperative adverse events, 6-minute walk distance, and New York Heart Association class are associated with changes in HRQOL across time.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Findings from our head-to-head study comparing HRQOL among patients who undergo alternative advanced surgical therapies (ie, heart transplantation [HT] and long-term mechanical circulatory support [MCS]) may inform shared decision-making when older patients with heart failure consider these treatment options and guide more targeted treatment to enhance HRQOL.
- It is important to convey to patients that improvement in HRQOL from before to early after these advanced surgical therapies, differs based on surgical strategy (ie, HT or long-term MCS).
- Adverse events, such as major bleeding and right heart failure, experienced primarily by long-term MCS patients, negatively impact HRQOL early after surgery.

Nonstandard Abbreviations and Acronyms

6MWT	6-minute walk test
EQ-5D-3L	EuroQol 5-dimension 3 L questionnaire
HF	heart failure
HRQOL	health-related quality of life
HT	heart transplantation
KCCQ-12	Kansas City Cardiomyopathy Questionnaire-12
MCS	mechanical circulatory support
OSS	overall summary score
STAI	State-Trait Anxiety Inventory
SUSTAIN-IT	Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support
UNOS	United Network for Organ Sharing
VAS	visual analog scale

Heart transplantation (HT) and long-term (ie, destination therapy) mechanical circulatory support (MCS) are therapeutic options for patients with advanced heart failure (HF). Outcomes, including survival and health-related quality of life (HRQOL), improve early after HT and MCS.[1-8] During the first several months after these surgical therapies, patients adjust to living with a donor heart or MCS[9-13] and may experience adverse events.[1,2]

Prospective, longitudinal research examining HRQOL early after MCS and HT is limited and typically includes patients of all ages.[4,5,14-17] Notably, more older patients with advanced HF undergo HT and MCS than in previous eras,[18] despite often having high rates of comorbidities and postoperative adverse events.[19-24] To our knowledge, there are no contemporary, prospective, longitudinal studies comparing HRQOL in older patients with HF who undergo HT or long-term MCS, which may inform shared decision-making when patients consider these treatment options.

Therefore, we aimed to describe change in HRQOL over time (before to 3 months and 3 to 6 months after surgery) among older (60–80 years) HF patients who undergo (1) HT with MCS as a pretransplant management strategy (referred to as HT MCS), (2) HT without pretransplant MCS (referred to as HT non-MCS), or (3) long-term MCS if ineligible for HT. We hypothesized that overall HRQOL and dimensions/domains will increase significantly in all 3 groups for both time periods. We also aimed to examine cross-sectional differences in HRQOL among the 3 groups at baseline and 3 and 6 months postoperatively, hypothesizing that patients who undergo long-term MCS will have lower HRQOL scores overall and for dimensions/domains at all 3 time points, compared with both HT groups. Lastly, we aimed to identify factors associated with change in overall HRQOL across time (baseline to 3 months and 3 to 6 months). We hypothesized that factors associated with change in HRQOL will include comorbidities, patient group, and postoperative adverse events. We divided HT patients into 2 groups, with and without pretransplant MCS because we identified differences in HRQOL by HT group at enrollment[25,26] and wanted to determine if these differences persist early after HT. Examination of 3 time points (baseline, 3 months, and 6 months) is supported in the MCS HRQOL literature.[5,14] HRQOL was defined as "the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient."[27] Our study was guided by Spilker and Revicki's[27] theoretical framework that models the effect of disease and its treatment on HRQOL.

METHODS

Data supporting findings of this study are available from the corresponding author upon reasonable request. Our data were

from the SUSTAIN-IT study (Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support).[26] Dr Andrei had full access to all data in the study and takes responsibility for its integrity and data analysis. For this report, we used a prospective, longitudinal, multi-site, observational design.

Sites and Cohort

Our cohort was recruited from 13 US sites with HT and MCS programs. Inclusion criteria were advanced HF, 60 to 80 years of age, English speaking, awaiting HT (listed with the United Network for Organ Sharing [UNOS]) or being evaluated/scheduled for primary long-term MCS implantation, and able to provide written informed consent. HT candidates who required MCS after enrollment (n=9) remained in the HT candidate group without MCS, per intention to treat principles. Long-term MCS candidates were included if they had a high likelihood of remaining on long-term MCS, per opinion of the site investigator or designate. Patients with MCS had second or third-generation Food and Drug Administration–approved or investigational left ventricular assist devices. For patients who crossed over from long-term MCS to being an HT candidate (n=1), data collection ended at time of cross-over. No HT candidates were deemed ineligible for HT and moved to a long-term MCS strategy. Patients listed with UNOS for retransplant or multiorgan transplant and long-term MCS patients scheduled for implant of a subsequent device were excluded from participation. All sites received Institutional Review Board approval, and all patients provided written informed consent.

Data Collection and Procedures

Patients completed self-report HRQOL questionnaires: the EuroQol (EuroQol 5-dimension 3 L questionnaire [EQ-5D-3L]),[28] and Kansas City Cardiomyopathy Questionnaire-12 (KCCQ-12),[29], and other assessments (Table S1). Minimal clinically important differences for the KCCQ-12[29] and EQ-5D visual analog scale (VAS)[8,30] are 5 and 10 points, respectively. HRQOL using the KCCQ-12 is represented by the following ranges: 0 to 24=very poor to poor, 25 to 49=poor to fair, 50 to 74=fair to good, and 75 to 100=good to excellent.[31]

Baseline assessments were administered as follows: (1) in the HT MCS group: after listing with UNOS while on MCS, (2) in the HT non-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. We used baseline data closest to HT surgery and long-term MCS implant. For HT candidates, data were collected every 6 months until HT and immediately pre-HT, if possible. Post-HT and long-term MCS data were collected at 3 months and 6 months after these surgeries.

Demographic data (eg, age, sex, and race) and medical records data (eg, medical history, New York Heart Association [NYHA] class, hospitalizations, and postoperative adverse events) were collected by research coordinators from patient medical records or downloaded securely from the Society of Thoracic Surgeons Interagency Registry for Mechanically Assisted Circulatory Support database.

Statistical Analyses

Demographics, clinical variables, and assessments were summarized using means and SD, medians and first/third quartile (Q1/Q3), or counts and percentage, as appropriate. Item-level missing data for HRQOL assessments were imputed via the within-group respondent's mean (if continuous) and mode (if categorical).[32] Imputation was used if <15% of item-level data were missing, except for the KCCQ-12, wherein scoring that accommodates missing data was performed per scoring instructions. When 6-minute walk test (6MWT) was not available due to patients being unable or too sick to walk, the value was set to 0. Changes in HRQOL (baseline versus 3 months or 3 versus 6 months) were compared with paired *t* tests for each domain. Between-group pairwise comparisons of these changes relied upon 2-sample *t* tests. Overall survival since surgery was summarized using Kaplan-Meier curves and compared among the 3 groups using hazard ratios derived via Cox Regression.

Univariable least squares regression models with change in EQ-5D VAS score and change in KCCQ-12 overall summary score (OSS) as dependent variables were created. The 3-month change from baseline was modeled as the outcome, adjusting for the corresponding baseline value. Then, the 6-month change from 3 months was modeled as the outcome, adjusting for the corresponding 3-month value. Similar to landmark analyses, this approach reduces the potential for selection bias postbaseline and permits one to adjust for postbaseline information.[33] Variables significant univariately at the 0.3 level constituted the pool from which multivariable models were created using stepwise selection procedures. The following independent variables were first screened univariately: patient group (ie, 3 groups); demographics (age, sex, race, marital status, education level, work status, insurance type, and presence of a caregiver); number and type of comorbidities (arrhythmias, chronic kidney disease, diabetes, and pulmonary hypertension); NYHA class; assessments of functional capacity (6MWT),[34] depressive symptoms (Personal Health Questionnaire-8),[35] anxiety (State-Trait Anxiety Inventory state),[36] and cognitive function (Montreal Cognitive Assessment)[37]; baseline or 3-month VAS score or KCCQ-12 OSS (depending on whether the outcome was 3- or 6-month corresponding value); and postoperative adverse events (rehospitalization, arrhythmias, major bleeding, major infection, stroke, psychiatric episode, renal dysfunction, respiratory failure, and right heart failure), within 3 months or 3 to 6 months after surgery.

Between-center differences for outcomes (EQ-5D VAS and KCCQ-12 OSS) and multicollinearity were assessed. Statistical significance was established at a 2-sided 5% level; no adjustments were made for multiplicity. Statistical analyses were performed using SAS v 9.4 (SAS Institute, Cary, NC) and R v 3.6.1 (R Foundation, 2020).

RESULTS

Between 10/1/15 and 12/31/18, of 635 patients with advanced HF approached (n=369 HT candidates and n=266 long-term MCS candidates), we enrolled 396 patients: 241 awaiting HT (118 with MCS, 121 without MCS, and 2 who were ineligible and withdrawn) and 155 before long-term MCS, including 1 who was ineligible and withdrawn (Figure 1). Reasons for not approaching patients included being too sick, timing of surgery, administrative reasons (eg, staffing issues), and other

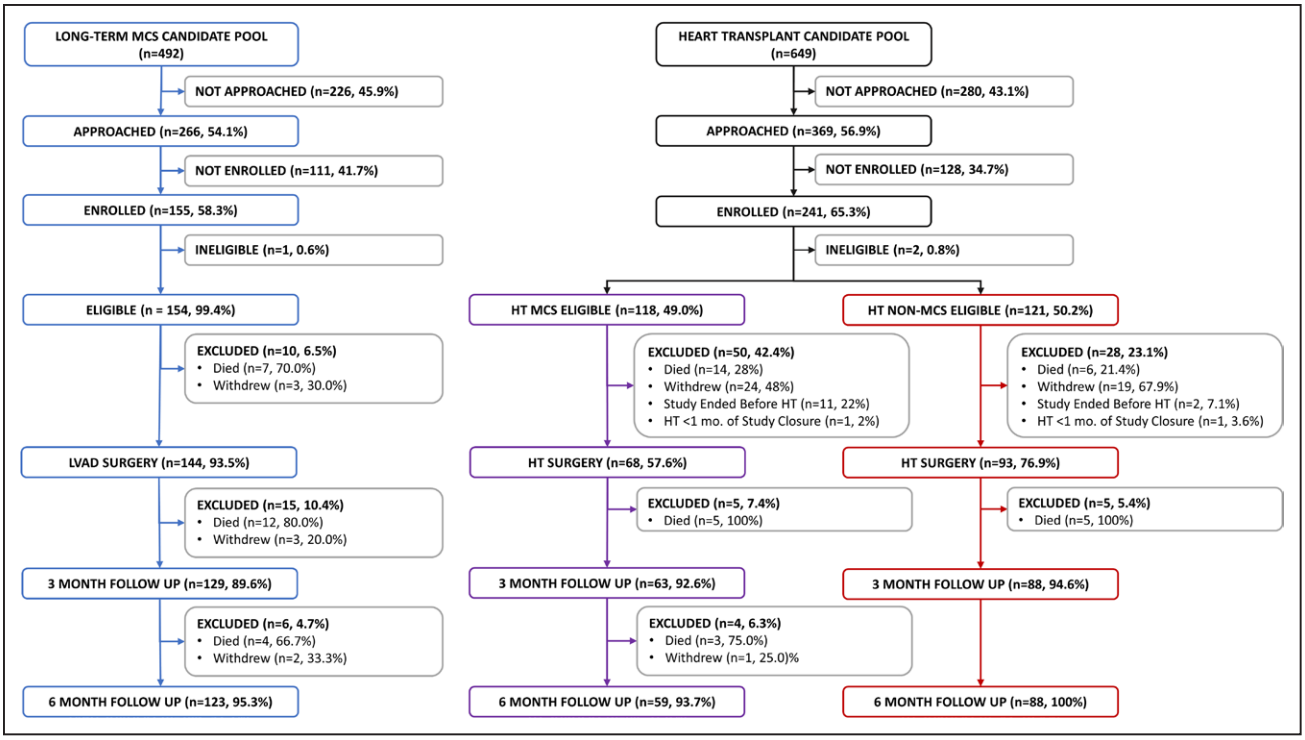

Figure 1. Consort flow diagram for patients who underwent long-term mechanical circulatory support (MCS) or heart transplantation (HT) with or without MCS before transplant.
LVAD indicates left ventricular assist device.

reasons.[26] Of 393 eligible enrollees, those who underwent surgery and had complete data at baseline, 3 months, or 6 months for either of the 2 outcomes (EQ-5D VAS or KCCQ-12) comprised the sample for this report (n=305): 68 HT MCS, 93 HT non-MCS, and 144 long-term MCS. Reasons for not undergoing HT or long-term MCS implant are listed in Figure 1. Participants were included in linear regression modeling if they completed HRQOL at 2 time points to compare change in HRQOL over time.

The majority of patients were male, White, married, and 71% were educated beyond high school. The long-term MCS group was, on average, significantly older and had more comorbidities than the 2 HT groups (Table 1). At baseline, the majority of the entire cohort were NYHA class III to IV and had a left ventricular ejection fraction <30% (Table 1). More long-term MCS patients were NYHA class IV than both HT patient groups (Table 1). Index hospital length of stay differed significantly among groups; rehospitalization within 6 months of discharge occurred more frequently in the long-term MCS group than in both HT groups (Table 2). The most frequent adverse events after surgery for the entire cohort were major infection, major bleeding, and cardiac arrhythmias; significant differences in adverse events were detected among groups (Table 2). For example, from surgery to 3 months, the long-term MCS group had a higher likelihood of bleeding and right HF and lower likelihood of renal dysfunction. Kaplan-Meier survival curves revealed no significant differences in mortality rates among the 3 groups from surgery to 6 postoperative months (Figure 2). Furthermore, no significant differences in baseline demographic and clinical characteristics, including comorbidities, were found between 6-month survivors and nonsurvivors, except for HF cause and HT candidate UNOS status at enrollment (Table S2).

Rates of completion of assessments at each time point ranged from 80% to 99% for all groups. There were no significant systematic differences in EQ-5D VAS scores and KCCQ-12 OSSs between patients with complete data and those without data at baseline and 3 months. The 6MWT completion rate lagged at baseline (overall=46%–85%), primarily due to patients being too sick; the rate at 3 months (overall=58%–60%) and 6 months (overall=66%–68%) after HT or long-term MCS lagged primarily due to patient study withdrawal and refusal (Table S3).

Within-Group Change in HRQOL Across Time

By 3 months after surgery, EQ-5D VAS mean scores improved significantly only in the HT non-MCS and long-term MCS groups; from 3 to 6 months after surgery, no significant change was found for any of the 3 groups (Figure 3). VAS mean scores for all groups ranged from 46 to 68 at baseline and 66 to 80 at 3 and 6 months (Tables S4 through S6). Regarding EQ-5D dimensions,

Table 1. Patient Demographics and Clinical Characteristics at Baseline

Variable	N available cohort (per group)	Entire cohort (n=305)	Patients with long-term MCS (n=144)	Patients with MCS before HT (n=68)	Patients without MCS before HT (n=93)	*P* value
Demographic characteristics						
Age at enrollment, y (mean±SD)	305 (144, 68, 93)	66.2±4.7	68.6±5.1	64.1±3.2	64.0±2.8	<0.001
Age at surgery, y (mean±SD)	305 (144, 68, 93)	66.9±4.6	69.1±5.2	65.3±3.2	64.8±2.8	<0.001
Sex (male), N (%)	305 (144, 68, 93)	238 (78%)	113 (78%)	55 (81%)	70 (75%)	0.69
Race (White), N (%)	304 (144, 68, 92)	254 (84%)	117 (81%)	56 (82%)	81 (88%)	0.37
Ethnicity: Hispanic or Latino, N (%)	299 (140, 68, 91)	5 (2%)	3 (2%)	2 (3%)	0 (0%)	0.30
Marital status: married/domestic partner, N (%)	303 (142, 68, 93)	236 (78%)	109 (77%)	52 (76%)	75 (81%)	0.74
Education (> high school), N (%)	278 (125, 60, 93)	197 (71%)	88 (70%)	44 (73%)	65 (70%)	0.89
Currently working, N (%)	294 (133, 68, 93)	51 (17%)	19 (14%)	12 (18%)	20 (22%)	0.37
Primary insurance type, N (%)	305 (144, 68, 93)					<0.001
Medicare/Medicaid		186 (61%)	105 (73%)	37 (54%)	44 (47%)	
Private insurance		119 (39%)	39 (27%)	31 (46%)	49 (53%)	
Body mass index, kg/m^2, at study enrollment	280 (142, 45, 93)	28.2±5.5	28.5±6.4	29.2±4.3	27±4.2	0.12
Baseline clinical characteristics						
Heart failure cause, N (%)	305 (144, 68, 93)					0.09
Ischemic cardiomyopathy		137 (45%)	74 (51%)	29 (43%)	34 (37%)	
Dilated cardiomyopathy		153 (50%)	63 (44%)	38 (56%)	52 (56%)	
Other		15 (5%)	7 (5%)	1 (1%)	7 (8%)	
NYHA class at study enrollment, N (%)	296 (140, 64, 92)					<0.001
I		9 (3%)	0 (0%)	8 (13%)	1 (1%)	
II		39 (13%)	1 (1%)	29 (45%)	9 (10%)	
III		84 (28%)	14 (10%)	20 (31%)	50 (54%)	
IV		164 (55%)	125 (89%)	7 (11%)	32 (35%)	
INTERMACS profile at enrollment, N (%)	209 (144, 65, NA)					0.004
Profile 1		23 (11%)	11 (8%)	12 (18%)	NA	
Profiles 2–3		156 (75%)	(81%)	39 (60%)	NA	
Profiles 4–7		30 (14%)	16 (11%)	14 (22%)	NA	
UNOS status at enrollment, N (%)	161 (NA, 68, 93)					<0.001
1A		40 (25%)	NA	13 (19%)	27 (29%)	
1B		92 (57%)	NA	51 (75%)	41 (44%)	
2		25 (16%)	NA	1 (1%)	24 (26%)	
7		4 (2%)	NA	3 (4%)	1 (1%)	
Length of time on UNOS waitlist at enrollment, d, median (Q1, Q3)	161 (0, 68, 93)	255 [61, 643]	NA	514 [256, 825]	94 [43, 330]	<0.001
Length of time on VAD from implant to enrollment, d, median (Q1, Q3)	68 (NA, 68, NA)	386 [189, 694]	NA	386 [189, 694]	NA	.
Length of time from completion of baseline assessment closest to HT (with and without MCS) or long-term MCS, d, median (Q1, Q3)	305 (144, 68, 93)	9 [1, 59]	2 [1, 4)]	79.5 [33, 130]	39 [15, 87]	<0.001
LVEF (closest to date of surgery), N (%)	238 (143, 42, 53)					0.009
>50 (normal)		3 (1%)	0 (0%)	1 (2%)	2 (4%)	
40–49 (mild)		4 (2%)	0 (0%)	1 (2%)	3 (6%)	
30–39 (moderate)		13 (5%)	6 (4%)	1 (2%)	6 (11%)	
20–29 (moderate/ severe)		75 (32%)	45 (31%)	12 (29%)	18 (34%)	
<20 (severe)		130 (55%)	86 (60%)	22 (52%)	22 (42%)	
Not recorded/documented in medical record		13 (5%)	6 (4%)	5 (12%)	2 (4%)	
Inotropes within 48 h of surgery, N (%)	303 (143, 67, 93)	190 (63%)	116 (81%)	12 (18%)	62 (67%)	<0.001
Temporary MCS at enrollment, N (%)	305 (144, 68, 93)	7 (2%)	3 (2%)	2 (3%)	2 (2%)	0.92

(*Continued*)

Table 1. Continued

Variable	N available cohort (per group)	Entire cohort (n=305)	Patients with long-term MCS (n=144)	Patients with MCS before HT (n=68)	Patients without MCS before HT (n=93)	*P* value
ICD device at study enrollment, N (%)	282 (143, 46, 93)	246 (87%)	125 (87%)	38 (83%)	83 (89%)	0.54
CRT at study enrollment, N (%)	272 (134, 46, 92)	115 (42%)	56 (42%)	16 (35%)	43 (47%)	0.40
No. of comorbidities (mean±SD)	305 (144, 68, 93)	4.4±2.1	5.0±2.2	4.0±1.7	3.7±1.8	<0.001
No. of comorbidities (binned)	305 (144, 68, 93)					<0.001
1		24 (8%)	7 (5%)	5 (7%)	12 (13%)	
2		35 (11%)	14 (10%)	7 (10%)	14 (15%)	
3		53 (17%)	15 (10%)	16 (24%)	22 (24%)	
4		57 (19%)	26 (18%)	16 (24%)	15 (16%)	
5		46 (15%)	21 (15%)	11 (16%)	14 (15%)	
6+		90 (30%)	61 (42%)	13 (19%)	16 (17%)	
Chronic kidney disease, N (%)	305 (144, 68, 93)	114 (37%)	65 (45%)	23 (34%)	26 (28%)	0.022
Hypertension, N (%)	305 (144, 68, 93)	182 (60%)	94 (65%)	37 (54%)	51 (55%)	0.17
Arrhythmia, N (%)	305 (144, 68, 93)	185 (61%)	93 (65%)	42 (62%)	50 (54%)	0.25
Hyperlipidemia, N (%)	305 (144, 68, 93)	180 (59%)	90 (63%)	40 (59%)	50 (54%)	0.41
Diabetes, N (%)	305 (144, 68, 93)	137 (45%)	80 (56%)	28 (41%)	29 (31%)	<0.001
Myocardial infarction, N (%)	305 (144, 68, 93)	99 (32%)	55 (38%)	19 (28%)	25 (27%)	0.13
History of smoking, N (%)	293 (134, 66, 93)	87 (30%)	23 (17%)	22 (33%)	42 (45%)	<0.001
Pulmonary hypertension, N (%)	305 (144, 68, 93)	63 (21%)	32 (22%)	20 (29%)	11 (12%)	0.020
Stroke, N (%)	305 (144, 68, 93)	44 (14%)	23 (16%)	11 (16%)	10 (11%)	0.48
History of cancer, N (%)	305 (144, 68, 93)	44 (14%)	26 (18%)	6 (9%)	12 (13%)	0.19
Coronary artery diseases, N (%)	305 (144, 68, 93)	34 (11%)	21 (15%)	3 (4%)	10 (11%)	0.09

CRT indicates cardiac resynchronization therapy; 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 classification; Q, quartile; and UNOS, United Network for Organ Sharing.

by 3 months after surgery, the long-term MCS group reported significantly fewer problems with self-care, usual activities, and anxiety/depression, the HT MCS group reported fewer problems with pain/discomfort, and the HT non-MCS group reported fewer problems with self-care (Figures S1 and S2). From 3 to 6 months, the long-term MCS group reported even fewer problems with usual activities (Figure S1). Frequency of problems regarding usual activities, mobility, and pain/discomfort were >50% for some groups at 3 and 6 months (Tables S5 and S6).

Findings using the KCCQ-12 were somewhat similar to the EQ-5D VAS. All 3 groups improved their KCCQ-12 OSS by 3 postoperative months; no significant within-group changes were found from 3 to 6 months (Figure 3). KCCQ-12 OSS for all groups ranged from 35 to 58 at baseline and 59 to 83 at 3 and 6 months (Tables S4 through S6). For KCCQ-12 domain scores, by 3 months, all 3 groups had fewer physical limitations and better quality of life (Figure S3). The HT non-MCS and long-term MCS groups also had a decrease in symptom frequency and social limitations scores (Figure S3). No significant changes were identified for any group from 3 to 6 months. Domain mean scores for all groups ranged from 52 to 84 at 3 and 6 months, varying by domain (Tables S5 and S6).

Cross-Sectional Differences in HRQOL Between Groups at Each Time Period

Although significant baseline differences were detected among all groups for EQ-5D VAS scores, with the long-term MCS group having the lowest score, significant differences in scores were found only between the long-term MCS group, wherein the score was lower, and HT non-MCS group at 3 and 6 postoperative months (Figure 3). The long-term MCS group also reported more problems with self-care compared to both HT groups at 3 and 6 months (Figure S1).

Significant differences in the KCCQ-12 OSS were identified among all groups at baseline; the long-term MCS group had the lowest scores. At 3 and 6 months, the long-term MCS group had lower scores than both HT groups (which had similar scores; Figure 3). Regarding domains, long-term MCS patients had more physical limitations and worse quality of life than both HT groups at 3 and 6 months (Figure S3). Symptom frequency and social limitations of long-term MCS patients were worse than both HT groups at 6 months (Figure S3).

Factors Associated With Change in HRQOL Across Time

There was minimal variability among centers for outcomes; therefore, we did not control for center effects.

Table 2. Patient Clinical Characteristics Early After HT or Long-Term MCS

Variable	N available cohort (per group)	Entire cohort (n=305)	Patients with long-term MCS (n=144)	Patients with MCS before HT (n=68)	Patients without MCS before HT (n=93)	*P* value
Post-HT or long-term MCS clinical characteristics						
Index hospital length of stay, d, median (Q1, Q3)	285 (135, 62, 88)	17 (12, 26)	19 (14, 32)	18 (15, 28)	13 (10, 17)	<0.001
Discharge to home, N (%)	285 (135, 62, 88)	197 (69%)	79 (59%)	43 (69%)	75 (85%)	<0.001
Rehospitalization within 6 mo of discharge from index hospitalization, N (%)	305 (144, 68, 93)	156 (51%)	83 (58%)	35 (51%)	38 (41%)	0.041
Adverse events: day of surgery to 3 mo post-HT or long-term MCS surgery, N (%)						
Adverse events (mean±SD)	305 (144, 68, 93)	2.1±3.2	2.3±3.4	2.4±3.4	1.5±2.9	0.13
Major infection, N (%)	305 (144, 68, 93)	58 (19%)	30 (21%)	19 (28%)	9 (10%)	0.011
Major bleeding, N (%)	305 (144, 68, 93)	53 (17%)	38 (26%)	8 (12%)	7 (8%)	<0.001
Cardiac arrhythmia, N (%)	305 (144, 68, 93)	47 (15%)	27 (19%)	11 (16%)	9 (10%)	0.17
Renal dysfunction, N (%)	305 (144, 68, 93)	39 (13%)	10 (7%)	15 (22%)	14 (15%)	0.006
Respiratory failure, N (%)	305 (144, 68, 93)	35 (11%)	19 (13%)	12 (18%)	4 (4%)	0.021
Rejection, N (%)	161 (NA, 68, 93)	15 (9%)	NA	6 (9%)	9 (10%)	0.85
Major hemolysis, N (%)	144 (144, NA, NA)	11 (8%)	11 (8%)	NA	NA	.
Right heart failure, N (%)	305 (144, 68, 93)	21 (7%)	15 (10%)	2 (3%)	4 (4%)	0.07
Venous thromboembolic event, N (%)	305 (144, 68, 93)	20 (7%)	0 (0%)	7 (10%)	13 (14%)	<0.001
MCS device malfunction, N (%)	144 (144, NA, NA)	9 (6%)	9 (6%)	NA	NA	.
Neuro dysfunction–stroke, N (%)	305 (144, 68, 93)	14 (5%)	11 (8%)	3 (4%)	0 (0%)	0.023
Pneumonia, N (%)	305 (144, 68, 93)	12 (4%)	8 (6%)	2 (3%)	2 (2%)	0.38
Neuro dysfunction–nonstroke, N (%)	305 (144, 68, 93)	10 (3%)	7 (5%)	2 (3%)	1 (1%)	0.28
Psychiatric episode/suicide, N (%)	305 (144, 68, 93)	10 (3%)	8 (6%)	1 (1%)	1 (1%)	0.11
Adverse events: 3 to 6 mo post-HT or long-term MCS surgery, N (%)						
Adverse events (mean±SD)	305 (144, 68, 93)	0.5±1.2	0.5±1.0	0.6±1.4	0.6±1.4	0.71
Major infection, N (%)	305 (144, 68, 93)	33 (11%)	14 (10%)	7 (10%)	12 (13%)	0.73
Rejection, N (%)	161 (NA, 68, 93)	9 (6%)	NA	2 (3%)	7 (8%)	0.21
Major bleeding, N (%)	305 (144, 68, 93)	15 (5%)	15 (10%)	0 (0%)	0 (0%)	<0.001
Renal dysfunction, N (%)	305 (144, 68, 93)	8 (3%)	2 (1%)	4 (6%)	2 (2%)	0.15
Cardiac arrhythmia, N (%)	305 (144, 68, 93)	6 (2%)	4 (3%)	1 (1%)	1 (1%)	0.62
Pneumonia, N (%)	305 (144, 68, 93)	5 (2%)	3 (2%)	1 (1%)	1 (1%)	0.83
Neuro dysfunction–stroke, N (%)	305 (144, 68, 93)	4 (1%)	3 (2%)	0 (0%)	1 (1%)	0.45
Respiratory failure, N (%)	305 (144, 68, 93)	3 (1%)	2 (1%)	0 (0%)	1 (1%)	0.63
MCS device malfunction, N (%)	144 (144, NA, NA)	2 (1%)	2 (1%)	NA	NA	.
Neuro dysfunction–nonstroke, N (%)	305 (144, 68, 93)	2 (1%)	2 (1%)	0 (0%)	0 (0%)	0.33
Psychiatric episode/suicide, N (%)	305 (144, 68, 93)	2 (1%)	1 (1%)	1 (1%)	0 (0%)	0.52
Right heart failure, N (%)	305 (144, 68, 93)	1 (0%)	1 (1%)	0 (0%)	0 (0%)	0.57

HT indicates heart transplantation; MCS, mechanical circulatory support; NA, not applicable; and Q, quartile.

Multicollinearity among independent variables was minimal at baseline; correlations between NYHA class and outcome variables were low (univariable regression model $R^2<0.1$ for both outcomes). Variables significant at $P<0.3$ from the univariable models (Tables S7 and S8) were included in multivariable modeling. By 3 months after surgery, for the EQ-5D VAS, male sex was significantly associated with an increase in the VAS score; baseline VAS score, 3-month State-Trait Anxiety Inventory state score, and right HF were significantly associated with a decrease in the VAS score (total $R^2=0.77$; Table 3). Longer distance walked on the 6MWT at 3 months was significantly associated with an increase in the KCCQ-12 OSS. Baseline KCCQ-12 OSS, 3-month NYHA class III and IV, 3-month State-Trait Anxiety Inventory state score, and right HF were significantly associated with a decrement in the KCCQ-12 OSS (total $R^2=0.73$; Table 3).

From 3 to 6 months, longer distance on the 6MWT at 6 months was significantly associated with an increase in the EQ-5D VAS score, whereas the 3-month EQ-5D VAS score and major bleeding between 3 and 6 months were significantly associated with a decrease in the EQ-5D VAS score (total $R^2=0.38$; Table 4). From 3 to

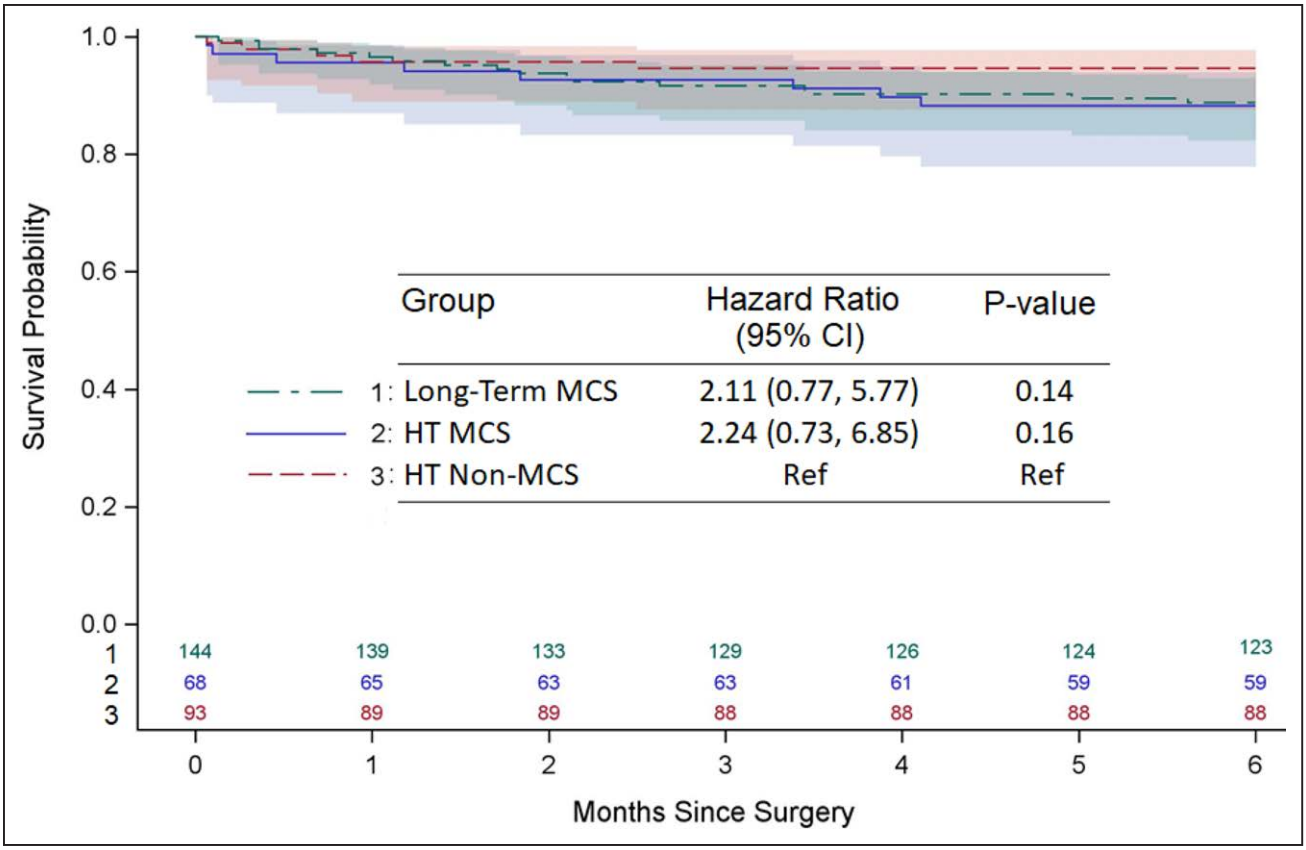

Figure 2. Kaplan-Meier survival curves from baseline to 6 months after long-term mechanical circulatory support (MCS) or heart transplantation (HT) with or without MCS before transplant.
Ref indicates reference.

6 months, using the KCCQ-12 OSS as the dependent variable, distance walked on the 6MWT at 6 months was significantly associated with an increase in the KCCQ-12 OSS; the 3-month KCCQ-12 OSS, NYHA classes III, and IV at 6 months, and major bleeding between 3 and 6 months were significantly associated with a decrement in the KCCQ-12 OSS (total R^2=0.44; Table 4).

DISCUSSION

Our contemporary head-to-head comparison of HRQOL in older HF patients by type of advanced surgical therapy is novel and adds to existing literature with several noteworthy findings. First, we found that overall HRQOL improved in all 3 groups by 3 months postoperatively, except for the HT MCS group, using the EQ-5D VAS, whereas no significant changes occurred for any group between 3 and 6 months, using both the EQ-5D VAS and KCCQ-12 OSS. Most improvement in dimension/domain scores (eg, physical function, daily activities, social limitations, and HF symptoms) occurred in the long-term MCS and HT non-MCS groups through 3 months, with minimal additional improvement from 3 to 6 months. These clinically important changes highlight the early and dramatic benefit of these surgeries on HRQOL. These findings partially support our first hypothesis, as HRQOL increased significantly by 3 months after surgery in all 3 groups; however, our hypothesis was not supported from 3 to 6 months, wherein no significant change occurred. Second, while significant differences in overall HRQOL were found among all 3 groups at baseline, significant differences at 3 and 6 months were found only between the long-term MCS group and one or both HT groups (depending on the measure used), with the long-term MCS group having lower scores. The 2 HT groups had similar HRQOL, overall and for dimension/domain scores, at 3 and 6 months. These findings disprove our second hypothesis, as while baseline scores were lower for the long-term MCS group compared to both HT groups, 3- and 6-month scores were not lower than both HT groups for both HRQOL measures. Lastly, factors associated with change in HRQOL after HT or MCS included demographic characteristics, baseline overall HRQOL score, anxiety, postoperative adverse events, 6MWT distance, and NYHA class, partially supporting our third hypothesis. Notably, factors associated with change in HRQOL did not include comorbidities and patient group, as hypothesized. The strongest associations for HRQOL through 3 months were right HF and 3-month NYHA class and from 3 to 6 months, were 6-month NYHA class and major bleeding.

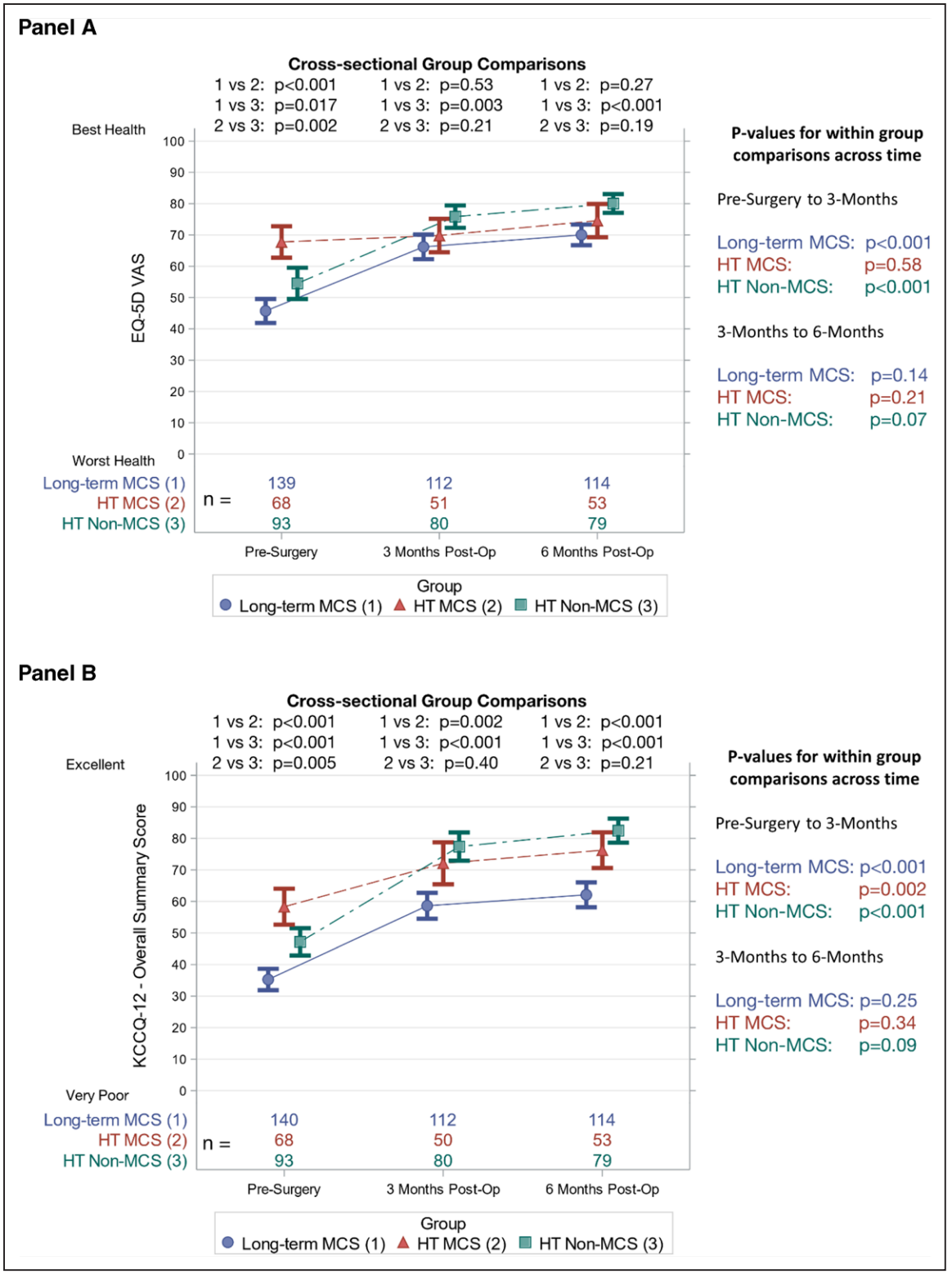

Figure 3. Cross-sectional and across time group comparisons for the EuroQol 5-dimension (EQ-5D) visual analog scale score and Kansas City Cardiomyopathy Questionnaire (KCCQ)-12 overall summary score.
A, EuroQol 5-dimension 3L questionnaire (EQ-5D-3L). **B**, KCCQ-12. HT indicates heart transplantation; and MCS, mechanical circulatory support.

Contemporary literature examining change in HRQOL early after advanced surgical therapies has focused primarily on MCS implantation, without comparison to HT.[4,5,14] Furthermore, studies have included patients of all ages, while SUSTAIN-IT focuses on older patients. Cowger et al.[5] reported significant improvement in overall HRQOL in adults (age range=19–81 with >50% on long-term MCS) at 3 months and 6

Table 3. Factors Associated With Change in Health-Related Quality of Life for Heart Transplantation or Long-Term Mechanical Circulatory Support for Patients, From Baseline to 3 Months, Using Multivariable Linear Regression

Covariates	Beta coefficient	95% confidence limit		*P* value
Change in EQ-5D VAS score, R^2: 0.771, n=201				
Intercept	89.0	55.6	122.4	<0.001
Patient group				
Long-term MCS candidates	−4.2	−9.1	0.7	0.09
HT candidates with MCS	−4.9	−10.4	0.5	0.07
HT candidates without MCS	REF	REF	REF	REF
Patient age at surgery	−0.0	−0.5	0.5	0.99
Patient sex (male)	5.6	0.7	10.4	0.025
Patient baseline EQ-5D VAS score	−0.9	−0.9	−0.8	<0.001
Patient 3-mo STAI-state score	−0.8	−1.0	−0.6	<0.001
Patient 3-mo, 6-min walk distance (per 100 m)	0.9	−0.4	2.2	0.16
Patient right heart failure, between surgery and 3 mo	−26.9	−36.9	−16.9	<0.001
Patient major infection, between surgery and 3 mo	−4.9	−10.5	0.6	0.08
Change in KCCQ-12 overall summary score, R^2: 0.731, n=161				
Intercept	87.8	49.2	126.4	<0.001
Patient group				
Long-term MCS candidates	−3.5	−10.0	3.0	0.29
HT candidates with MCS	−4.7	−11.2	1.8	0.15
HT candidates without MCS	REF	REF	REF	REF
Patient age at surgery	0.0	−0.5	0.6	0.88
Patient sex (male)	−0.1	−5.5	5.4	0.99
Patient baseline KCCQ-12 OSS	−0.8	−0.9	−0.7	<0.001
Patient 3-mo NYHA class				
I	REF	REF	REF	REF
II	−1.2	−7.4	5.0	0.69
III	−15.0	−22.4	−7.6	<0.001
IV	−18.4	−33.8	−3.0	0.020
Patient 3-mo STAI-state total score	−1.0	−1.2	−0.7	<0.001
Patient 3-mo, 6-minute walk distance, m	2.7	1.1	4.2	<0.001
Patient right heart failure, between surgery and 3 mo	−17.5	−28.1	−6.9	0.001

EQ-5D VAS indicates EuroQol 5-dimension visual analog scale; HT, heart transplantation; KCCQ-12, Kansas City Cardiomyopathy Questionnaire; MCS, mechanical circulatory support; NYHA, New York Heart Association; OSS, overall summary score; REF, reference; and STAI-state, State-Trait Anxiety Inventory, range 20=less to 80=worse anxiety.

months after implantation of a HeartMate II versus HeartMate 3 with no between-group differences across time. Bidwell et al[14] also reported improved HRQOL in predominantly HT candidates with MCS (n=50, mean age=55 years) at 1 month and 6 months after implant, with more gradual improvement from 1 to 6 months. We described improved HRQOL through 6 months after implant in a cohort including HT candidates with MCS and patients with long-term MCS.[4] We are aware of only 2 older studies that compared HRQOL between HT and MCS groups. In cohorts of on average middle-aged HT and MCS patients, our research team[16] and Kugler et al[17] demonstrated differences in overall HRQOL, physical function, and mental health through <6 months after HT or MCS, finding better HRQOL in the HT group.

Despite improvement over time, lower HRQOL scores observed in the long-term MCS group at 3 and 6 months, compared with one or both HT groups, may be related to their higher burden of comorbidities (eg, diabetes) and greater frequency of postoperative adverse events. Nonetheless, the long-term MCS group experienced improved HRQOL from baseline to early after surgery. For example, baseline KCCQ-12 scores were poor to fair, and 6-month scores were fair to good.[31]

Similarity in HRQOL between the 2 HT groups early after transplant demonstrates the benefits of HT, regardless of pretransplant management strategy. Specifically, KCCQ-12 scores in both HT patient groups at 6 months after transplant were good to excellent.[31] Notably, higher overall HRQOL at baseline in the HT MCS group and

Table 4. Factors Associated With Change in Health-Related Quality of Life for HT or Long-Term MCS Patients, From 3 to 6 Months Using Multivariable Linear Regression Models

Covariates	Beta coefficients	95% confidence limits		*P* value
Change in EQ-5D VAS score, R^2: 0.377, n=212				
Intercept	54.5	25.3	83.7	<0.001
Patient group				
Long-term MCS candidates	−0.5	−5.4	4.4	0.83
HT candidates with MCS	−1.3	−6.4	3.8	0.62
HT candidates without MCS	REF	REF	REF	REF
Patient age at surgery	−0.3	−0.7	0.2	0.24
Patient sex (male)	−2.0	−6.5	2.5	0.38
Patient 3-mo EQ-5D VAS score	−0.5	−0.6	−0.4	<0.001
Patient 6-mo, 6-min walk distance (per 100 m)	2.4	1.2	3.6	<0.001
Patient major bleeding, between 3 mo and 6 mo	−11.7	−19.8	−3.5	0.005
Change in KCCQ-12 overall summary score, R^2: 0.435, n=173				
Intercept	56.0	23.5	88.5	<0.001
Patient group				
Long-term MCS candidates	1.4	−4.9	7.7	0.66
HT candidates with MCS	−0.1	−6.1	5.8	0.96
HT candidates without MCS	REF	REF	REF	REF
Patient age at surgery	−0.3	−0.8	0.2	0.19
Patient sex (male)	−0.4	−5.4	4.6	0.87
Patient 3-mo KCCQ-12 OSS	−0.5	−0.6	−0.4	<0.001
Patient 6-mo NYHA class				
I	REF	REF	REF	REF
II	−4.0	−9.7	1.7	0.16
III	−12.9	−19.5	−6.2	<0.001
IV	−19.1	−33.7	−4.4	0.011
Patient 6-mo, 6-min walk distance (per 100 m)	3.0	1.5	4.5	<0.001
Patient major bleeding, between 3 mo and 6 mo	−9.0	−17.7	−0.4	0.040

EQ-5D VAS indicates EuroQol 5-dimension visual analog scale; HT, heart transplantation; KCCQ, Kansas City Cardiomyopathy Questionnaire; MCS, mechanical circulatory support; NYHA, New York Heart Association; and OSS, overall summary score.

lack of a clinically important change in score from baseline to 3 months, using the EQ-5D VAS, reflects the benefits of MCS as a pretransplant management strategy.

Some of the factors associated with change in HRQOL in our study were supported by the literature, including baseline HRQOL score, 6MWT distance, adverse events, and higher NYHA class.[4,5] The association of male sex with an increased VAS score has not been previously reported but is consistent with our report from the Interagency Registry for Mechanically Assisted Circulatory Support that men had significantly fewer problems with usual activities, pain/discomfort, and anxiety/depression than women at 3 and 6 months after MCS implantation.[4] Patient group (ie, HT MCS, HT non-MCS, and long-term MCS) was not significant in any of the multivariable models, although there was a trend for the VAS model from baseline to 3 months.

Findings from this SUSTAIN-IT report may inform shared decision-making when older patients consider these surgical strategies and guide more targeted treatment to enhance HRQOL. We recommend informing older HF patients who are considering HT or long-term MCS of the improvement in HRQOL early after surgery. Additionally, it is important to convey to patients that awaiting HT with pretransplant MCS is associated with higher HRQOL than awaiting HT without MCS, although further improvement early after HT may be less. These findings are supported by our previous report that HT MCS candidates had higher HRQOL over time while on the UNOS waiting list compared to HT non-MCS candidates.[25] Lastly, informing patients that adverse events, such as major bleeding and right HF, experienced primarily by long-term MCS patients, negatively impact HRQOL.

Factors associated with change in HRQOL across time and dimension/domain scores may guide treatment strategies. For example, anxiety scores, as measured by the State-Trait Anxiety Inventory state, while similar to older male and female adults under nonstressful conditions (mean score range, 32–35),[36] were nonetheless associated with a

decrement in HRQOL, which provides a potential target for psychological intervention by psychologists or social workers. Also, while problems with self-care, usual activities, mobility, pain/discomfort, and anxiety/depression were less frequent over time for some groups, we recommend assessment of these dimensions early after surgery for all groups, as some problems (ie, usual activities, mobility, and pain/discomfort) were moderate or higher early postoperatively. Physical therapy and occupational therapy consultation early after surgery is highly recommended. Lastly, differences in improvement in HRQOL by sex provide an opportunity for targeted interventions.

Limitations of our study include survivorship bias, although there were no differences in survival among the 3 groups of patients across time and very few differences when comparing baseline characteristics between survivors and nonsurvivors. Also, patient groups were fairly homogeneous regarding sex, race, marital status, and education, but these demographic characteristics are similar to the Interagency Registry for Mechanically Assisted Circulatory Support,[4] except education, which is lower in the Interagency Registry for Mechanically Assisted Circulatory Support.

CONCLUSIONS

HRQOL improved through 3 postoperative months and was sustained through 6 months in older patients after HT and long-term MCS; patients undergoing long-term MCS and HT without pretransplant MCS experienced the largest change in HRQOL. Nonetheless, at 6 postoperative months, HRQOL of long-term MCS patients was lower than one or both HT groups. Understanding differences in HRQOL among these groups and factors associated with change in HRQOL over time may contribute to better patient-centered care by informing decision-making and guiding HRQOL-related therapies.

ARTICLE INFORMATION

Received February 2, 2022; accepted July 27, 2022.

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Sources of Funding

This work was sponsored by the National Institutes of Health, National Institute on Aging, SUSTAIN-IT study (Sustaining Quality of Life of the Aged: Heart Transplant or Mechanical Support; R01AG047416, Dr Grady [Principal Investigator]).

Disclosures

Dr Grady is a consultant for Amgen Inc; paid lecturer for American Heart Association; and received grant support from the National Institutes of Health (National Institute on Aging and National Heart, Lung, and Blood Institute). Dr Kao is a member of Advisory Board for CareDx and Bioventrix. Dr Spertus is a consultant for Amgen, Novartis, Bayer, Myokardia, and Janssen; Scientific Advisory Board, United HealthCare; Board of Directors, Blue Cross Blue Shield, Kansas City; and is a copyright holder to Kansas City Cardiomyopathy Questionnaire. Dr Pagani is a noncompensated scientific advisor for FineHeart Inc; member of Data Safety Board Member for Carmat and the National Heart, Lung, and Blood Institute PumpKIN Clinical Study; and grant support from the National Heart, Lung, and Blood Institute and Agency for Healthcare Research and Quality. Dr Petty receives speaking honorarium from Abbott Inc. M. Murray is a consultant on a research project at GE Healthcare. Dr Silvestry is a consultant for Abiomed, Medtronic, Syncardia, and Abbott. Dr Kirklin is a director of the Data and Clinical Consulting Center of the Society of Thoracic Surgeons Interagency Registry for Mechanically Assisted Circulatory Support and receives grant support from the National Institutes of Health/National Institute on Aging. Dr Yancy reports spousal employment at Abbott Labs Inc. The other authors report no conflicts.

Supplemental Material

Tables S1–S8
Figures S1–S3

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