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ORIGINAL ARTICLE

Validity of Patient-Reported Outcomes Measurement Information System Physical, Mental, and Social Health Measures After Left Ventricular Assist Device Implantation and Implications for Patient Care

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BACKGROUND: A better understanding is needed of the burdens and benefits of left ventricular assist device (LVAD) implantation on patients' physical, mental, and social well-being. The purpose of this report was to evaluate the validity of Patient-Reported Outcomes Measurement Information System (PROMIS) measures for LVAD patients and to estimate clinically important score differences likely to have implications for patient treatment or care.

METHODS: Adults from 12 sites across all US geographic regions completed PROMIS measures ≥3 months post-LVAD implantation. Other patient-reported outcomes (eg, Kansas City Cardiomyopathy Questionnaire-12 item), clinician ratings, performance tests, and clinical adverse events were used as validity indicators. Criterion and construct validity and clinically important differences were estimated with Pearson correlations, ANOVA methods, and Cohen d effect sizes.

RESULTS: Participants' (n=648) mean age was 58 years, and the majority were men (78%), non-Hispanic White people (68%), with dilated cardiomyopathy (55%), long-term implantation strategy (57%), and New York Heart Association classes I and II (54%). Most correlations between validity indicators and PROMIS measures were medium to large (≥0.3; $p<0.01$). Most validity analyses demonstrated medium-to-large effect sizes (≥0.5) and clinically important differences in mean PROMIS scores (up to 14.8 points). Ranges of minimally important differences for 4 PROMIS measures were as follows: fatigue (3–5 points), physical function (2–3), ability to participate in social roles and activities (3), and satisfaction with social roles and activities (3–5).

CONCLUSIONS: The findings provide convincing evidence for the relevance and validity of PROMIS physical, mental, and social health measures in patients from early-to-late post-LVAD implantation. Findings may inform shared decision-making when patients consider treatment options. Patients with an LVAD, their caregivers, and their clinicians should find it useful to interpret the meaning of their PROMIS scores in relation to the general population, that is, PROMIS may help to monitor a return to normalcy in everyday life.

REGISTRATION: URL: https://clinicaltrials.gov; Unique: identifier: NCT03044535.

Key Words: adult ■ fatigue ■ female ■ heart failure ■ humans ■ patient reported outcome measures

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For Sources of Funding and Disclosures, see page 154.

WHAT IS KNOWN

- Patient-reported outcomes capture important elements of patient experiences after left ventricular assist device implantation.
- A few measures from the Patient-Reported Outcomes Measurement Information System (PROMIS) were shown to demonstrate reliability, validity, and responsiveness to change in heart transplant patients, but only 1 previous study examined PROMIS in a left ventricular assist device population.

WHAT THE STUDY ADDS

- This study (MCS A-QOL; Mechanical Circulatory Support: Measures of Adjustment and Quality of Life) provided convincing evidence for the relevance and validity of PROMIS physical, mental, and social health measures in a left ventricular assist device population.
- Patients with a left ventricular assist device, their caregivers, and their clinicians should find it useful to be able to interpret the meaning of their PROMIS scores in relation to the general population, that is, PROMIS may help to monitor a return to normalcy in everyday life.

Nonstandard Abbreviations and Acronyms

EQ-5D-3L	EuroQOL 5 dimension, 3 level
HRQOL	health-related quality of life
KCCQ-12	Kansas City Cardiomyopathy Questionnaire-12 item
LVAD	left ventricular assist device
MCS A-QOL	Mechanical Circulatory Support: Measures of Adjustment and Quality of Life
MID	minimally important difference
PRO	patient-reported outcome
PROMIS	Patient-Reported Outcomes Measurement Information System

Patient-reported outcomes (PROs), including health-related quality of life (HRQOL), in combination with clinical measures, are important to evaluate in patients with cardiovascular disease.[1] In order to improve patient centeredness of care, clinical trials of left ventricular assist devices (LVADs)[2,3] and device registry reports[4–9] have moved away from analyses that include only survival free of adverse events, to inclusion of PROs, which capture important elements of patient experiences after LVAD implant. Patients must adapt to lifestyle changes (eg, modifications in showering) and learn self-care (eg, connecting to power sources, monitoring device function, and changing driveline dressings) that may impact HRQOL. Findings from a systematic review of 16 studies assessing PROs in LVAD populations[10] and later studies[2–9,11] revealed that LVADs were associated with improvement in physical and mental domains of HRQOL.

Measures frequently used to assess HRQOL of patients undergoing LVAD implantation include the EuroQOL 5 dimension, 3 level (EQ-5D-3L)[12,13] and Kansas City Cardiomyopathy Questionnaire-12 item (KCCQ-12),[14,15] generic and heart failure–specific measures, respectively. These measures have strengths and limitations. The EQ-5D-3L is a brief generic HRQOL measure, which supports its use in large registries, including the Society of Thoracic Surgeons Interagency Registry for Mechanically Assisted Circulatory Support (STS Intermacs) database.[11] However, the EQ-5D-3L does not include domains such as social functioning, sleep, and cognitive function, which may be potentially relevant to understanding HRQOL after LVAD implantation. Furthermore, some concepts (eg, anxiety/depression) are combined into one item, thus reducing clarity in findings. The KCCQ-12 is clinically sensitive and responsive to understanding the impact of heart failure on HRQOL[16] but does not address the impact of treatment (eg, an LVAD) on HRQOL. Additionally, some relevant mental health HRQOL subdomains (eg, anxiety and depression) are not well addressed in KCCQ-12. Lastly, since it is a disease-specific measure, comparison of KCCQ-12 findings with other chronic diseases is not possible.

Recommended areas for future LVAD research include psychometric evaluation of existing PRO measures, development of new LVAD-specific measures, and inclusion of additional HRQOL domains in routine assessments.[10] The aims of the MCS A-QOL study (Mechanical Circulatory Support: Measures of Adjustment and Quality of Life) addressed some of these recommendations. This report describes findings from an MCS A-QOL study aim to conduct a psychometric evaluation of existing PRO measures administered post-LVAD implant. The Patient-Reported Outcomes Measurement Information System (PROMIS)[17–21] measures of physical, mental, and social health were selected for this study based on a conceptual model and their relevance to patients with advanced heart failure who have undergone LVAD implementation.[22] PROMIS measures assess common, generic symptoms and experiences that apply to people in a variety of contexts or with a variety of diseases without needing to make attributions to a specific condition.[20] The ability of a measure to capture the burden of disease or treatment relies on the psychometric strength of its performance in the target population.[23–26] The purpose of this report was to evaluate indicators of criterion and construct validity[24,27] of the PROMIS measures, and estimates of clinically important differences in PROMIS scores, that is, clinically significant score differences likely to have implications for patient treatment or care.[28–30]

METHODS

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

Sites and Sample

Two groups of patients with continuous-flow LVADs were recruited in the hospital or outpatient clinic before implant (group 1; pre and postimplant longitudinal assessments) or at least 3 months post-implant (group 2; 1-time assessment) at 12 US sites from October 2016 through February 2020. Study inclusion criteria were as follows: (1) age ≥19 years of age, (2) scheduled for, or implanted with, a primary or subsequent (eg, second) continuous-flow LVAD, (3) goal of LVAD therapy as follows: (a) short term (heart transplant candidate listed with the United Network for Organ Sharing), (b) uncertain heart transplant candidacy (possible heart transplant candidate but not listed with United Network for Organ Sharing), or (c) long term (ineligible for heart transplantation, ie, destination therapy) and (4) able to speak and understand English and provide self-report data on a computer touchscreen, standard computer, or paper-based forms with minimal assistance. The study was approved by all site institutional review boards, and patients provided written informed consent before study participation. This report only used postimplant data from MCS A-QOL (all group 2 participants and only 1 postimplant assessment for group 1 participants) and also included a small group of participants recruited via the MyLVAD online resource and support website (https://www.mylvad.com) to boost enrollment numbers. The Northwestern University Institutional Review Board approved online consent and self-report of eligibility criteria for MyLVAD participants.

Procedures

Participants completed a set of PROMIS and other PRO measures by their preferred mode, method, and location of completion: self-administration (iPad in the clinic, home computer using a personalized link sent by email, or paper questionnaires distributed in person or sent by mail) or in-person interview administration by the study coordinator. Participants were encouraged to complete PROs on site; however, some chose to complete them at home. All participants were enrolled in person before the March 11, 2020, declaration of COVID-19 as a pandemic. A small number of participants who were scheduled to complete questionnaires after this date were encouraged to complete them at home. All MyLVAD participants completed PROs on their own computer. Windows for PRO completion were ±30 days at 3 months post-implant and ±60 days at 6 months or later. The set of PROs took ≈1 hour to complete, and participants received a $20 gift card in person or by mail; MyLVAD participants were mailed a $10 gift card. PROMIS measures were completed as computer-adaptive tests (questions are tailored to that person) when administered by computer or as fixed-length short forms when administered on paper.[18,20] All other PROs were administered as fixed-length forms whether completed electronically or on paper. Sociodemographic data were collected directly from study participants, while clinical data were either securely downloaded from the North American STS Intermacs registry database[11] or collected from electronic medical records by research coordinators for participants not enrolled in the registry (17%). MyLVAD participants (n=25; 4%) self-reported selected clinical information. Research Electronic Data Capture was used for data collection and management.[31]

PROs, Clinician Ratings, Performance Tests, and Adverse Events

Table 1 summarizes information about instruments administered in this study. The 12 PROMIS measures evaluated for validity included physical health (Fatigue,[32,33] Physical Function,[34,35] Sleep Disturbance,[36,37] Sleep-Related Impairment[36,37]), mental health (Depression,[38,39] Anxiety,[38] Cognitive Function[40,41]), and social health (Social Function: Ability to Participate in Social Roles,[42] Satisfaction With Social Roles and Activities[42]; Social Relationships: Emotional, Informational, and Instrumental Social Support[42]). The PROs, clinician ratings, performance tests, and clinical adverse events that were used as validity indicators included KCCQ-12,[14,15] EQ-5D-3L,[12,13] Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being 12-item scale,[43,44] PROMIS Overall Quality of Life item,[20] New York Heart Association functional classification,[45] Health Literacy Assessment Using Touchscreen Technology,[46,47] 6-minute walk test,[48–51] trail making test, part B,[52–54] and neurological dysfunction.[11]

Statistical Methods

All PROs and performance tests were scored according to the published guidelines. PROMIS scores are reported as T scores (mean, 50; SD, 10), standardized to the US general population. Two types of validity were evaluated for the PROMIS instruments: criterion and construct.[24,27] Criterion validity refers to the extent to which scores of the instrument are related to a criterion or gold standard or legacy measure (see Table 1 for information on the legacy measures). Construct validity was evaluated in multiple ways: by examining the extent to which the measure is (or is not) associated with measures of similar (or dissimilar) traits (convergent or divergent validity) and by evaluating known-groups validity (how well the measure distinguishes between groups that are expected to differ). The MCS A-QOL coprincipal investigators (E.A.H. and K.L.G.) selected validity indicators for each PROMIS measure based on recommended methods including a literature review, clinical judgment, and theoretical implications.[24] Pearson correlations and ANOVA methods were implemented with the SAS/STAT software, version 9.4, of the SAS System for Windows.[55] To control for multiple comparisons,[56] a nominal significance level of 0.01 was used to interpret the significance of Pearson correlation coefficients. Cohen guidelines were used to interpret the size of criterion and construct validity correlations: 0.1 is considered small, 0.3 is medium, and 0.5 is large.[57] For the known-groups validity analyses, mean score differences between clinically distinct categories were calculated; the Tukey-Kramer method[58,59] was used to adjust p values for pairwise comparisons when there were >2 groups to be compared and the overall p value was <0.05. For the construct validity analyses Cohen d effect sizes[57] were computed by dividing the category score difference by the overall SD for the sample.[60,61] An effect size of 0.2 (ie, one-fifth SD) is considered small, 0.5 is medium, and 0.8 is large.[57] Effect sizes are a useful way to describe the magnitude of differences.[62]

Table 1. Instruments Administered in the Study of LVAD Patients

Type of measure	Instrument	Description	Score metric*	Meaning of a higher score
PROMIS measures evaluated for validity				
Physical health				
	PROMIS Fatigue v1.0	Assesses fatigue from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that is likely to decrease one's ability to carry out daily activities, including the ability to work effectively and to function at one's usual level in family or social roles.	IRT T score	More fatigue
	PROMIS Physical Function v1.2	Assesses ability to carry out activities that require physical actions, ranging from self-care (activities of daily living) to more complex activities that require a combination of skills, often within a social context.	IRT T score	Better physical function
	PROMIS Sleep Disturbance v1.0	Assesses perceptions of sleep quality, sleep depth, and restoration associated with sleep; perceived difficulties and concerns with getting to sleep or staying asleep; and perceptions of the adequacy of and satisfaction with sleep	IRT T score	Greater sleep disturbance
	PROMIS Sleep-Related Impairment v1.0	Assesses perceptions of alertness, sleepiness, and tiredness during usual waking hours and the perceived functional impairments during wakefulness associated with sleep problems or impaired alertness	IRT T score	Greater sleep-related impairment
Mental health				
	PROMIS Depression v1.0	Assesses negative mood, negative views of self, negative social cognition, and decreased positive affect and engagement	IRT T score	More depression
	PROMIS Anxiety v1.0	Assesses fear (eg, fearfulness, feelings of panic), anxious misery (eg, worry, dread), hyperarousal (eg, tension, nervousness, restlessness), and somatic symptoms related to arousal (eg, racing or pounding heart, dizziness).	IRT T score	More anxiety
	PROMIS Cognitive Function v1.0/v2.0†	Assesses perception of functional abilities with regard to cognitive tasks in areas such as concentration, memory, and mental acuity, including perceptions regarding change in one's cognitive ability.	IRT T score	Better cognitive function
Social health				
Social function				
	PROMIS Ability to Participate in Social Roles and Activities v2.0	Assesses the perceived ability to perform one's usual social roles and activities.	IRT T score	Fewer limitations (better ability to participate in social roles)
	PROMIS Satisfaction With Social Roles and Activities v2.0	Assesses satisfaction with performing one's usual social roles and activities.	IRT T score	Greater satisfaction
Social relationships				
	PROMIS Social Support v2.0: Emotional Support, Informational Support, Instrumental Support	3 measures that assess functional aspects of supportive relationships: emotional (perceived feelings of being cared for and valued as a person; having confidant relationships), informational (perceived availability of helpful information or advice), instrumental (perceived availability of assistance with material, cognitive, or task performance)	IRT T score	More support
Measures used as validity indicators				
Patient-reported outcomes				
	KCCQ-12‡	Assesses heart failure–specific HRQOL; 4 subscales/domains, an overall summary score, and 1 single sleep item: physical limitation, symptom frequency, quality of life, social limitation, overall, sleep siting up	Sum score: 0–100; ordinal scale for sleep item: every night–never	Greater HRQOL
	EQ-5D-3L‡	Assesses generic health status: 5 dimensions: mobility, self-care, usual activities, pain/discomfort, anxiety/depression, VAS of overall health	Ordinal scale for each dimension: no problems, some problems, extreme problems. VAS: 0–100	Each dimension: extreme problems. VAS: best imaginable health
	FACIT-Sp-12	Brief assessment of spiritual well-being, defined as the degree to which patients' spirituality can help them make sense of their lives and feel whole, hopeful, and peaceful even in the midst of a serious illness; not limited to any religious or spiritual tradition	Sum score, 4–48	Better spiritual well-being

(*Continued*)

Table 1. Continued

Type of measure	Instrument	Description	Score metric*	Meaning of a higher score
	PROMIS Overall Quality of Life	Single item	Ordinal scale: poor, fair, good, very good, excellent	Excellent quality of life
Clinician rating				
	NYHA functional classification‡	Clinician rating of how severely symptoms of heart failure limit physical activity	Ordinal scale: no limitation, slight limitation, marked limitation, unable to carry on any physical activity without discomfort	Worse heart failure–related functional status
Performance tests				
	Health LiTT	Self-administered multimedia test of health literacy	IRT T score. Categories	T score: better health literacy. Categories: low vs adequate
	6-min walk test‡	Assessment of functional capacity during a 6-min walk in an enclosed hallway, which is free of traffic and distractions	Meters walked	Greater functional capacity
	TMT-B‡	Assessment of cognitive dysfunction	Seconds	Greater cognitive dysfunction
Clinical adverse events				
	Neurological dysfunction‡	A transient ischemic attack or an ischemic stroke that occurred at any time from date of implant to time of the PRO assessment	Yes vs no	Dysfunction

IRT T score: mean, 50; SD, 10. Sum score: aggregated item responses. EQ-5D-3L indicates EuroQOL 5 dimension, 3 level; FACIT-Sp-12, Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being 12-item; Health LiTT, Health Literacy Assessment Using Touchscreen Technology; HRQOL, health-related quality of life; IRT, item response theory; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12 item; NYHA, New York Heart Association; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; and TMT-B, trail making test, part B.

*Score metric: information about how the instrument is scored.

†Although 2 versions of this measure were used, the scoring was recalibrated to be comparable.

‡Gold standard or legacy measure used for criterion validity.

Known-groups construct validity analyses also provided estimates of clinically important differences.[30] When individuals can be classified into distinct, clinically relevant categories, then score differences between any 2 categories can be considered clinically important. Minimally important differences (MIDs) were estimated by significant (adjusted $p<0.05$) differences between adjacent, minimally different categories.[61]

Pairwise deletion was used for missing data, that is, available data were used for each analysis. The amount of missing data varied. Most sociodemographic and clinical characteristics had little-to-no missing data. Missing data for the PROMIS measures ranged from 2% to 7%. The amount of missing data was fairly large (25%–29%) for some of the validity indicator variables, for example, KCCQ-12 and EQ-5D-3L, primarily because of historically high missing data in the STS Intermacs national registry.[63] Over half of the study participants (52%) did not complete the 6-minute walk test due to site concerns about mobility.

RESULTS

Participant Characteristics and PROs

Table 2 summarizes sociodemographic, clinical, and questionnaire completion characteristics of the 648 participants included in this report. Participant mean age was 58 years, and the majority were men (78%), non-Hispanic White people (68%), with a long-term implant strategy (57%), with dilated cardiomyopathy (55%), and with New York Heart Association classes I and II (54%). Nearly half (48%) of the participants completed the questionnaires at home on their own computer. The majority (84%) reported no difficulty completing questionnaires.

Descriptive statistics for the PROMIS physical, mental, and social health measures are summarized in Table 3 (PROMIS measures evaluated for validity). PROMIS T scores are standardized to a mean of 50, based on large samples of people with and without any chronic conditions. For this post-LVAD implant sample, PROMIS scores were comparable to the general population mean of 50 for fatigue, sleep disturbance, sleep-related impairment, depression, anxiety, and cognitive function. Scores were lower (worse) than the general population for Physical function, ability to participate in social roles and activities, and satisfaction with social roles and activities. Scores were higher (better) for emotional, informational, and instrumental support. Table 3 (PROs, performance tests, and adverse events used as validity indicators) summarizes descriptive statistics for the measures used for criterion and construct validity. The 4 KCCQ-12 domain scores were fair to good[16] (mean scores, 58–76). Many participants reported no problems (45%–74%) with EQ-5D-3L mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, while the remainder reported some/extreme problems. The majority (72%) reported good-to-excellent overall quality of life. Regarding performance-based tests, only 31% had low health literacy; the mean 6-minute walk distance of 354 m was

Table 2. Characteristics of LVAD Study Participants (n=648)

Sociodemographic characteristics	
Age, y; mean (SD)	57.5 (14.0)
Women	140 (22%)
Married/committed partner	385 (64%)
Ethnicity, race	
Hispanic, any race	55 (9%)
Non-Hispanic, White people	434 (68%)
Non-Hispanic, Black people	118 (18%)
Non-Hispanic, other	35 (5%)
Highest education	
HS or less	248 (39%)
Attended college/Tech school	178 (28%)
Associate/bachelor's degree	151 (24%)
Graduate degree	55 (9%)
Financial difficulties	
Not at all	137 (22%)
A little bit	230 (37%)
Quite a bit	122 (20%)
Very much	131 (21%)
Clinical characteristics	
LVAD implant strategy	
Short-term MCS	157 (25%)
Possible short-term MCS	118 (18%)
Long-term MCS	362 (57%)
Time since implant, mo	
3–12	391 (60%)
>12 to <36	155 (24%)
≥36	102 (16%)
Etiology of heart failure	
Dilated cardiomyopathy	353 (55%)
Ischemic cardiomyopathy	230 (36%)
Other	59 (9%)
NYHA class closest to assessment date	
Class I (no limitation of physical activity)	81 (14%)
Class II (slight limitation of physical activity)	238 (40%)
Class III (marked limitation of physical activity)	168 (28%)
Class IV (unable to carry on any physical activity without discomfort)	68 (12%)
	35 (6%)
Unknown	…
Questionnaire completion	
Mode, method, and location of administration	
Self-administration, iPad, clinic	75 (12%)
Self-administration, home computer	305 (48%)
Self-administration, paper, home or clinic	210 (33%)
Interviewer administration, iPad, clinic	19 (3%)
Interviewer administration, paper, clinic	10 (2%)
Multiple modes/methods/locations	12 (2%)
Any difficulty completing the questionnaires?	
Not at all	489 (84%)
A little bit	63 (11%)
Somewhat	20 (3%)
Quite a bit	8 (1%)

(*Continued*)

Table 2. Continued

Entries in the table represent the number of participants (%), unless otherwise specified. Missing data were excluded. HS indicates high school; LVAD, left ventricular assist device; MCS, mechanical circulatory support; NYHA, New York Heart Association; and Tech, technical.

below the mean distance walked for healthy people (571 m);[64] cognitive dysfunction was high compared with normative data[65] as measured by the trail making test; and only 7% had a stroke or transient ischemic attack since LVAD implantation. Some measures in Table 2 were also used for validity analyses (New York Heart Association and marital status).

Criterion and Construct Validity: Correlations

Pearson correlations for interval-level criterion and construct validity indicators are shown in Table 4 for each PROMIS measure. Correlations were in the expected direction, for example, Fatigue was negatively correlated with the 6-minute walk test (−0.255); Physical Function was positively correlated with KCCQ-12 Physical Limitations (0.576); Depression was negatively correlated with KCCQ-12 Quality of Life (−0.370); and Ability to Participate was positively correlated with KCCQ-12 Social Limitations (0.513). Most correlations for PROMIS Physical Health measures were medium to large (|0.380| to |0.579|) and statistically significant ($p<0.01$). Most correlations for PROMIS Depression and Anxiety measures were medium (|0.333| to |0.370|) and statistically significant ($p<0.01$). The PROMIS Cognition measure was not significantly correlated with either validity indicator, although correlations were in the expected directions. All correlations with validity indicators for PROMIS Social Function measures (Ability to Participate and Satisfaction With Participation) were medium to large (|0.357| to |0.519|) and statistically significant ($p<0.01$). Correlations for PROMIS Social Support measures were low (0.033–0.167). The only indicator of divergent validity (Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being 12-item scale) demonstrated mixed results, that is, medium correlation for PROMIS Fatigue (−0.353) and low correlation for PROMIS Physical Function (0.151).

Known-Groups Construct Validity: Clinically Important Differences

Known-groups validity results are shown in Table 5. Clinically important differences were detected for all PROMIS measures (range of statistically significant mean differences: |1.7| to |14.8|), except for Cognitive Function. Most (69%) paired comparisons for

Table 3. Descriptive Statistics for Patient-Reported Outcome Measures, Performance Tests, and Adverse Events, Among LVAD Study Participants

	n	Mean	SD	Range	n (%)
PROMIS measures evaluated for validity					
Physical health					
PROMIS Fatigue	637	50.9	9.5	24.3–77.8	…
PROMIS Physical Function	612	39.1	6.8	20.0–73.3	…
PROMIS Sleep Disturbance	612	50.5	8.8	26.3–83.8	…
PROMIS Sleep-Related Impairment	619	49.5	10.5	26.2–83.1	…
Mental health					
PROMIS Depression	611	49.5	9.5	34.2–76.9	…
PROMIS Anxiety	615	50.5	10.0	32.9–84.9	…
PROMIS Cognitive Function	615	50.7	9.3	21.3–68.0	
Social health					
Social function					
PROMIS Ability to Participate in Social Roles and Activities	609	47.2	8.1	21.5–67.5	…
PROMIS Satisfaction With Social Roles and Activities	604	46.7	9.3	22.0–68.7	…
Social relationships					
PROMIS Emotional Support	622	55.2	8.8	20.2–66.2	…
PROMIS Informational Support	621	58.4	9.1	23.2–69.8	…
PROMIS Instrumental Support	623	59.2	7.9	25.4–66.2	…
PROs, performance tests, and adverse events used as validity indicators					
PROs					
KCCQ-12					
Physical Limitation	479	59.1	26.6	0–100	…
Symptom Frequency	485	75.7	21.3	4.2–100	…
Quality of Life	480	57.7	26.3	0–100	…
Social Limitation	471	60.1	27.8	0–100	…
Fatigue Limitation	…	…	…	…	
All of the time					19 (4%)
Several times per day					52 (11%)
At least once a day					59 (12%)
≥3× per week					54 (11%)
1–2× per week					93 (19%)
Less than once a week					95 (20%)
Never					110 (23%)
Shortness of breath: forced to sleep sitting/propped up	…	…	…	…	
Every night					32 (7%)
≥3× per week					11 (2%)
1–2× per week					10 (2%)
Less than once a week					61 (13%)
Never over past 2 weeks					369 (76%)
EQ-5D-3L					
Mobility	…	…	…	…	
No problems					269 (57%)
Some problems					204 (43%)
Extreme problems					2 (0%)
Self-care	…	…	…	…	
No problems					352 (74%)
Some problems					115 (24%)
Extreme problems					7 (1%)

(*Continued*)

Table 3. Continued

	n	Mean	SD	Range	n (%)
Usual activities	…	…	…	…	
No problems					211 (45%)
Some problems					237 (50%)
Extreme problems					26 (5%)
Pain/discomfort	…	…	…	…	
No problems					248 (52%)
Some problems					200 (42%)
Extreme problems					25 (5%)
Anxiety/depression	…	…	…	…	
No problems					297 (63%)
Some problems					166 (35%)
Extreme problems					11 (2%)
VAS	460	71.3	18.3	7.0–100.0	…
FACIT Spirituality total score	609	36.4	9.5	4.0–48.0	…
PROMIS Overall Quality of Life	…	…	…	…	
Poor					26 (4%)
Fair					142 (23%)
Good					240 (39%)
Very good					151 (25%)
Excellent					50 (8%)
Performance tests					
Health literacy (Health LiTT)					
Low health literacy (<55)	…	…	…	…	155 (31%)
T score	507	57.7	6.4	38.4–64.8	…
6-min walk test, m	299	354.4	112.1	5.5–719.9	…
Trail making test (part B), s	180	102.3	54.6	35.0–497.0	…
Clinical adverse events					
Neurological dysfunction (stroke or TIA since LVAD implant)	…	…	…	…	40 (7%)

Missing data were excluded. EQ-5D-3L indicates EuroQOL 5 dimension, 3 level; FACIT, Functional Assessment of Chronic Illness Therapy; Health LiTT, Health Literacy Assessment Using Touchscreen Technology; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12 item; LVAD, left ventricular assist device; PRO, patient-reported outcome; PROMIS, Patient-Reported Outcomes Measurement Information System; TIA, transient ischemic attack; and VAS, Visual Analog Scale. Range: Observed range in this sample.

PROMIS Fatigue had medium-to-large effect sizes (Cohen d, 0.44–1.13) and were statistically significant. Most (62%) paired comparisons for PROMIS Physical Function had medium-to-large effect sizes (0.44–1.09) and were statistically significant. All paired comparisons for PROMIS Sleep Disturbance and Sleep-Related Impairment had medium effect sizes (0.52–0.60) and were statistically significant. Paired comparisons for PROMIS Depression and Anxiety had large effect sizes (0.99–1.10) and were statistically significant. Many of the paired comparisons for PROMIS Social Function (Ability [50%] and Satisfaction [62%]) had medium-to-large effect sizes (0.47–0.80) and were statistically significant. Some of the paired comparisons for PROMIS Social Relationships (Emotional [50%], Informational [0%], and Instrumental [33%] Support) had medium effect sizes (0.47–0.50) and were statistically significant.

Minimally Important Differences

MIDs, that is, significant (adjusted $p<0.05$) differences between adjacent, minimally different categories, are shown in Table 5. For PROMIS Fatigue, MIDs were ≈3 to 5 points. For PROMIS Physical Function, MIDs were 2 to 3 points. For PROMIS Ability to Participate in Social Roles and Activities, the MID was ≈3 points. For PROMIS Satisfaction With Social Roles and Activities, the MIDs were ≈3 to 5 points. For the remaining PROMIS measures (Sleep Disturbance, Sleep-Related Impairment, Depression, Anxiety, and Emotional, Informational, and Instrumental Support), although there were large, clinically important differences between many categories (eg, having no sleep problems versus any problems), these represent categories that are more than minimally different. In other words, these categories represent very broad ways to dichotomize groups.

Table 4. Correlations Between PROMIS Measures and Validity Indicators in LVAD Study Participants

PROMIS measure	Validity indicator							
	KCCQ-12 Physical Limitation	KCCQ-12 Quality of Life	KCCQ-12 Social Limitation	EQ VAS (overall health)	FACIT Spirituality	Health LiTT	6-min walk, m	Trail making time, s
PROMIS physical health								
Fatigue					−0.353		−0.255	
					p<0.001		*p*<0.001	
					n=598		n=298	
Physical Function	0.576*		0.579		0.151		0.420*	
	p<0.001		*p*<0.001		*p*<0.001		*p*<0.001	
	n=459		n=451		n=601		n=286	
Sleep Disturbance		−0.288						
		p<0.001						
		−n=458						
Sleep-Related Impairment		−0.380						
		p<0.001						
		n=464						
PROMIS mental health								
Depression	−0.284	−0.370	−0.353					
	p<0.001	*p*<0.001	*p*<0.001					
	n=459	n=458	n=451					
Anxiety	−0.279	−0.351	−0.333					
	p<0.001	*p*<0.001	*p*<0.001					
	n=462	n=461	n=454					
Cognitive Function						0.079		−0.078*
						p=0.076		*p*=0.300
						n=505		n=177
PROMIS social health								
Social function								
Ability to Participate	0.357		0.513*					
	p<0.001		*p*<0.001					
	n=459		n=452					
Satisfaction With Roles	0.364		0.519					
	p<0.001		*p*<0.001					
	n=456		n=449					
Social relationships								
Emotional Support		0.167						
		p<0.001						
		n=466						
Informational Support		0.142		0.132				
		p=0.002		*p*=0.005				
		n=467		n=449				
Instrumental Support	0.033	0.078						
	p=0.471	*p*=0.092						
	n=467	n=467						

Empty cells: no associations between variables were expected or evaluated. FACIT indicates Functional Assessment of Chronic Illness Therapy; Health LiTT, Health Literacy Assessment Using Touchscreen Technology; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12 item; PROMIS, Patient-Reported Outcomes Measurement Information System; and VAS, visual analogue scale.

*Correlation with a gold standard or legacy measure.

Table 5. Known Groups Validity for PROMIS Measures in LVAD Study Participants

PROMIS measure	Measure to assess validity	n	Mean PROMIS score	Paired comparison	Mean difference*	*p* value†	Effect size‡
Physical health							
PROMIS Fatigue							
	NYHA						
	1	80	46.8	1-2	−3.4*	0.019	0.36
				1-3	−6.9	<0.001	0.73
				1-4	−4.9	0.007	0.51
	2	236	50.2	2-3	−3.4*	0.001	0.36
				2-4	−1.4	0.659	0.01
	3	161	53.7	3-4	2.0	0.435	0.21
	4	67	51.7				
	EQ-5D Usual Activities						
	No problems (0)	211	46.7				
	Any problems (1)	261	54.3	1-0	7.6	<0.001	0.79
	KCCQ-12 Fatigue						
	Once per day or more (1)	129	57.9	1-2	5.3*	<0.001	0.56
				1-3	10.7	<0.001	1.13
				1-4	14.8	<0.001	1.56
	At least once per week (2)	146	52.6	2-3	5.4*	<0.001	0.57
				2-4	9.6	<0.001	1.01
	Less than once per week (3)	95	47.2	3-4	4.2*	<0.001	0.44
	Never (4)	110	43.1				
PROMIS Physical Function							
	NYHA						
	1	77	42.1	1-2	2.3*	0.039	0.34
				1-3	5.4	<0.001	0.79
				1-4	3.0	0.042	0.44
	2	230	39.7	2-3	3.0*	<0.001	0.45
				2-4	0.6	0.906	0.09
	3	157	36.7	3-4	−2.4	0.069	0.35
	4	64	39.1				
	EQ-5D Usual Activities						
	No problems (0)	200	42.6				
	Any problems (1)	253	36.5	1-0	−6.1	<0.001	0.90
	EQ-5D Mobility						
	No problems (0)	256	42.5				
	Any problems (1)	198	35.1	1-0	−7.4	<0.001	1.09
PROMIS Sleep Disturbance							
	EQ-5D Usual Activities						
	No problems (0)	201	47.8				
	Any problems (1)	252	52.4	1-0	4.7	<0.001	0.53
	KCCQ-12 Sleep Sitting Up or With Pillows						
	Never (0)	350	49.1				
	Ever (1)	111	53.7	1-0	4.6	<0.001	0.52
PROMIS Sleep-Related Impairment							
	EQ-5D Usual Activities						
	No problems (0)	204	46.2				

(*Continued*)

Table 5. Continued

PROMIS measure	Measure to assess validity	n	Mean PROMIS score	Paired comparison	Mean difference*	*p* value†	Effect size‡
	Any problems (1)	255	52.5	1-0	6.3	<0.001	0.60
	KCCQ-12 Sleep						
	Never (0)	356	48.3				
	Ever (1)	111	54.2	1-0	5.9	<0.001	0.56
Mental health							
PROMIS Depression							
	EQ-5D Anxiety						
	No problems (0)	285	45.6				
	Any problems (1)	167	56.0	1-0	10.4	<0.001	1.10
PROMIS Anxiety							
	EQ-5D Anxiety						
	No problems (0)	284	46.9				
	Any problems (1)	170	56.8	1-0	9.9	<0.001	0.99
PROMIS Cognitive Function							
	Neurological dysfunction						
	No (0)	506	51.1				
	Yes (1)	36	48.1	1-0	−3.0	0.061	0.32
	Health LiTT						
	55+ (1)	352	51.0	1-0	1.3	0.153	0.14
	<55 (0)	153	49.7				
Social health							
Social function							
PROMIS Ability to Participate in Social Roles and Activities							
	NYHA						
	1	78	50.0	1-2	3.2*	0.015	0.39
				1-3	3.8	0.004	0.47
				1-4	3.9	0.022	0.48
	2	228	46.9	2-3	0.7	0.857	0.08
				2-4	0.8	0.913	0.09
	3	159	46.2	3-4	0.1	1.000	0.01
	4	62	46.1				
	EQ-5D Usual Activities						
	No problems (0)	203	50.5				
	Any problems (1)	249	44.5	1-0	−6.0	<0.001	0.74
	EQ-5D Mobility						
	No problems (0)	257	49.9				
	Any problems (1)	196	43.8	1-0	−6.1	<0.001	0.75
PROMIS Satisfaction With Social Roles and Activities							
	NYHA						
	1	78	51.5	1-2	4.8*	<0.001	0.52
				1-3	7.4	<0.001	0.80
				1-4	6.2	<0.001	0.67
	2	225	46.7	2-3	2.6*	0.037	0.28
				2-4	1.4	0.712	0.15
	3	155	44.1	3-4	−1.2	0.825	0.13
	4	63	45.3				
	EQ-5D Usual Activities						

(*Continued*)

Table 5. Continued

PROMIS measure	Measure to assess validity	n	Mean PROMIS score	Paired comparison	Mean difference*	*p* value†	Effect size‡
	No problems (0)	202	50.6				
	Any problems (1)	247	43.8	1-0	−6.8	<0.001	0.73
	EQ-5D Mobility						
	No problems (0)	256	49.5				
	Any problems (1)	194	43.4	1-0	−6.1	<0.001	0.65
Social relationships							
PROMIS Emotional Support							
	EQ-5D Anxiety						
	No problems (0)	289	56.5				
	Any problems (1)	171	52.4	1-0	−4.1	<0.001	0.47
	Marital status						
	Married/domestic partner (0)	370	55.9	0-1	2.0	0.009	0.23
	Not married/domestic partner (1)	210	53.9				
PROMIS Informational Support							
	Marital status						
	Married/domestic partner (0)	369	58.9	0-1	1.7	0.032	0.18
	Not married/domestic partner (1)	210	57.3				
PROMIS Instrumental Support							
	EQ-5D Usual Activities						
	No problems (0)	206	59.3				
	Any problems (1)	255	58.8	1-0	−0.5	0.469	0.07
	EQ-5D Self-Care						
	No problems (0)	342	59.1				
	Any problems (1)	119	58.7	1-0	−0.4	0.653	0.05
	Marital status						
	Married/domestic partner (0)	370	60.6	0-1	3.9	<0.001	0.50
	Not married/domestic partner (1)	211	56.7				

EQ-5D indicates EuroQOL 5 dimension; Health LiTT, Health Literacy Assessment Using Touchscreen Technology; KCCQ-12, Kansas City Cardiomyopathy Questionnaire-12 item; MID, minimally important difference; NYHA, New York Heart Association; and PROMIS, Patient-Reported Outcomes Measurement Information System.

*MID: significant (adjusted $p<0.05$) difference between adjacent, minimally different categories.

†*p* value for paired comparison.

‡Effect size: mean difference divided by the overall SD for the sample.

DISCUSSION

Findings from this study provide convincing evidence for the relevance and validity of PROMIS physical, mental, and social health measures in patients from early-to-late post-LVAD implantation. Validity is not a property of a measure itself but rather a process of evaluating evidence for the intended interpretation of scores and their relevance for a particular use.[66,67] The more the evidence about the psychometric strength of an instrument, the more confidence one has in its usefulness for that population. Strong relationships were demonstrated between validity indicators and many PROMIS measures, and large, clinically important differences were detected. MIDs were estimated for 4 PROMIS measures: Fatigue (3–5 points), Physical Function (2–3 points), Ability to Participate in Social Roles and Activities (3 points), and Satisfaction With Social Roles and Activities (3–5 points). These estimates can be useful for interpreting differences in PROMIS measures for LVAD patients and for use in power calculations.

PROMIS measures have been used in diverse populations, but only a few studies evaluated their validity in heart failure populations, including those on medical therapy and those who undergo advanced surgical therapies such as heart transplantation and LVAD implantation.[68,69] Among patients with heart failure assessed pre- and post-heart transplantation, 4 PROMIS measures (Physical Function, Fatigue, Depression, and Satisfaction With Discretionary Social Activities) were found to be reliable, valid, and responsive to change.[68] PROMIS Satisfaction With Discretionary Social Activities also demonstrated improvement after heart transplantation

among participants with congestive heart failure.[70] In a study of 132 patients up to 8 years post-LVAD implantation, they experienced worse PROMIS Physical Function and similar Pain and Depression compared with the general population and a significant positive correlation between PROMIS measures and the KCCQ-12.[69] Among 60 patients with chronic heart failure, the PROMIS Fatigue measure demonstrated improvement in symptoms after treatment and responsiveness to change in symptoms;[32] and the PROMIS Physical Function, Depression, and Anxiety measures demonstrated responsiveness to change over time following heart transplant.[71] Among 158 patients with heart failure and major depressive disorder,[72,73] the PROMIS Depression measure was moderately associated with a legacy measure of depressive symptoms at baseline and strongly associated at the 6-month follow-up visit.[74,75] Results from MCS A-QOL can be added to this growing body of evidence about the usefulness of PROMIS measures in heart failure populations who undergo durable mechanical circulatory support.

MCS A-QOL findings build upon the only other study to use PROMIS measures in an LVAD population[69]; however, that study was limited by lack of psychometric evaluation of the measures, use of only 3 PROMIS measures, and nonstandardized data collection relative to implant date. This MCS A-QOL report psychometrically evaluated the use of 12 PROMIS measures (4 physical health, 3 mental health, and 5 social health) in an LVAD population; the findings strongly support clinical use of these measures in device patients. For example, understanding differences (either better or worse) in HRQOL domains (eg, physical function and satisfaction with social roles) after LVAD implantation, as compared with a general US population, may inform shared decision-making. On an individual level, identifying sleep disturbances and sleep-related impairment during waking hours may provide targets for treatment after implant, while assessment of support may provide clinicians (eg, ventricular assist device coordinators, social workers, and psychologists) with an opportunity to discuss challenges in receiving support with patients and their caregivers to enhance support. Importantly, per a survey regarding patient perspectives on completion and use of PRO measures in routine clinical care, overall, patients reported that PRO measures (including PROMIS measures) were useful in identifying concerns but also indicated that their value was reduced by lack of discussion with clinicians.[76]

There are some limitations to this study. The sample lacked diversity, as the majority were men, non-Hispanic White people, well-educated, and married; however, this is similar to LVAD recipients in the United States. Specifically, participants in this study were similar to LVAD recipients in the United States in terms of sociodemographic and clinical characteristics[77] and KCCQ-12 HRQL scores.[78] The data were cross-sectional, not longitudinal. Some of the validity indicator variables had a large amount of missing data. Additional validity indicator variables, estimates of MIDs, and responsiveness to change should be examined.

Conclusions

The use of PROMIS PROs in combination with condition-specific measures may contribute to enhanced shared decision-making as patients consider the options of advanced surgical therapies and may provide guidance for therapeutic interventions after implant. The PROMIS measures are advantageous for use in populations with multiple chronic illnesses, which allows comparability of experiences across diseases. Thus, patients with an LVAD, their caregivers, and their clinicians should find it useful to be able to interpret the meaning of their PROMIS scores in relation to the general population, that is, PROMIS may help to monitor a return to normalcy in everyday life.

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Dr Adler is a consultant to Abiomed, Sana Biotechnology, NovartisMedtronic, Abbott Lexeo Pharmaceuticals, and Ionis Pharmaceuticals Cytokinetics; provided expert testimony for AstraZeneca; and is in a leadership role with Papillion Therapeutics and ResQ Pharmaceuticals. Dr Allen is a consultant to ACI Clinical, Amgen, Boston Scientific, Cytokinetics, and Novartis and is an Associate Editor for *Circulation: Heart Failure*. Dr Grady received honoraria from the American Heart Association (AHA); received travel support from International Society for Heart and Lung Transplantation and AHA; and is on the Board of Directors for International Society for Heart and Lung Transplantation. Dr Lee is a Chair of the Data and Safety Monitoring Board for a Patient-Centered Outcomes Research Institute study. Dr Lindenfeld is a consultant to Abbott, AstraZeneca, Alleviant, Boston Scientific, Merck, CVRx, VWave, and Edwards. Dr Ruo received honoraria from Society of General Internal Medicine. Dr Stehlik is a consultant to Medtronic. Dr Teuteberg received honoraria from CareDx, Medtronic, and Paragonix and is on the Data and Safety Monitoring Board for CareDx, Medtronic, Abiomed, Takeda, and Abbott. The other authors report no conflicts.

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