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PROMIS fatigue scores are moderately correlated with heart failure severity in pediatrics

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BACKGROUND: Patient-reported outcome measures (PROMs) correlate with heart failure (HF) severity among adults and are adjunct tools in clinical care. Limited data exist regarding the validity of PROMs in pediatric HF. *Hypothesis:* Patient-Reported Outcome Measurement Information System (PROMIS) Pediatric Fatigue correlates with HF severity, measured by the New York University Pediatric Heart Failure Index (NYU PHFI).

METHODS: Children ≥8 and < 18 years old were enrolled prospectively at 4 hospitals, from September 2019 to February 2023, while receiving inpatient HF care. NYU PHFI and pediatric self-report PROMIS measures were administered to inpatient and outpatient patients. PROMIS measures: Mobility, Anxiety, Depressive symptoms, Peer relationships, and Fatigue (primary outcome). Paired *t*-tests compared PROMIS and NYU PHFI scores across time. A mixed-effects model generated correlation coefficients.

RESULTS: In the 41-patient cohort, 20 (48.8%) were discharged without ventricular assist device/transplant, 18 completed inpatient and outpatient assessments. Mean PROMIS Fatigue *t*-scores improved: 58.1 ± 12.9 to 48.9 ± 16.9; $p = 0.007$. Clinically meaningful improvements were observed in other PROMIS *t*-scores, except Peer relationships. NYU PHFI scores improved: 13.3 ± 2.6 to 7.8 ± 3.4; $p < 0.001$. PROMIS Fatigue and NYU PHFI moderately correlated (r = 0.5; 95% confidence interval 0.3, 0.6).

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CONCLUSIONS: PROMIS Fatigue *t*-scores moderately correlated with HF severity in children suggesting that Fatigue could be useful in longitudinal monitoring and clinical trials.
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Background

Pediatric heart failure (HF) is a chronic illness associated with high morbidity and mortality.[1-4] Among children discharged home from an HF hospitalization, readmission rates are high.[5,6] The current clinical practice is to bring children to the clinic for frequent follow-up visits, hopefully averting rehospitalization. Despite close follow-up, HF severity and progression are difficult to assess, as symptoms may be vague affecting multiple systems.[7] HF severity scoring systems exist but cannot be used remotely as they require in-person patient data or have been developed for use in the inpatient environment.[8,9] (These scoring systems do not include patient-reported data, which may be an important source of information.) When assessing geographically remote outpatients for whom physical exam information is not available, evaluation of HF severity is increasingly difficult. Given the high hospital readmission rates among children with HF, additional tools to help assess and track HF severity in the outpatient setting would be valuable.[1,10]

In adults, patient-reported outcome measures (PROMs) are well-established adjunct tools in the management of HF. Patient-reported outcomes are "report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else."[11] Among adults, PROMs are sensitive to changes in HF severity and predictive of cardiovascular morbidity and mortality.[12,13] This allows tracking of patient status and potential for early intervention for patients experiencing health declines between clinic visits. PROMs may have similar value in pediatric HF but have not been rigorously tested. The ability to assess children's HF status over time, with or without a clinic visit, could allow more timely outpatient medical intervention and potentially improve children's functional status and quality of life. Validated PROMs exist in pediatrics and include Patient-Reported Outcome Measurement Information System (PROMIS).[14]

PROMIS measures are particularly well-suited for use in pediatric HF. Pediatric PROMIS measures can assess physical, social, and mental well-being in chronic illnesses characterized by exacerbations and remissions. PROMIS scores accurately reflect disease severity among children with asthma, cancer, cerebral palsy, chronic kidney disease, and sickle cell disease,[15-20] but have not been studied in pediatric HF. For PROMIS to have value in assessing pediatric HF clinical status, measures must be validated in this population. In this study, we describe the correlation between PROMIS scores and a Clinician Reported Outcome of HF severity, the New York University Pediatric Heart Failure Index (NYU PHFI) scores,[9] among children with HF. We hypothesize PROMIS and NYU PHFI scores will improve from the time of HF hospitalization to the time of outpatient follow-up, and that PROMIS Fatigue and NYU PHFI scores will correlate.

Materials and methods

In this prospective cohort, patients with systolic and/or diastolic HF were recruited while receiving inpatient HF treatment at 4 advanced pediatric HF centers: Primary Children's Hospital, Lucille Packard Children's Hospital at Stanford, University of Florida Health Shands Children's Hospital, and Lurie Children's Hospital of Chicago. Patients were enrolled sequentially from September 2019 to February 2023. Active recruitment periods varied across study sites due to COVID-19 pandemic research restrictions. Institutional review board approval was obtained at each site. Parents and children provided informed consent and assent. The authors agree with and confirm that this study adheres to the principles of the World Medical Association Statement on Organ and Tissue Donation, the Declaration of Helsinki, and the Declaration of Istanbul.

Patients ≥8 and < 18 years, receiving intravenous diuretics, intravascular vasoactive medications, or positive pressure ventilation, including high flow nasal cannula to treat HF, were identified by the site principal investigator (PI). PIs applied standard definitions of HF: "a clinical and pathophysiologic syndrome resulting from ventricular dysfunction, volume, or pressure overload, alone or in combination."[21,22] Exclusion criteria: traumatic injury/major surgery ≤2 weeks prior; unable to complete PROMIS (including patients with significant developmental delays); not fluent in English or Spanish.

HF severity

HF severity was defined using a Clinician Reported Outcome,[23] the NYU PHFI score. The NYU PHFI is a validated, objective scoring method for HF severity in pediatric patients (Supplementary Materials; Table S1).[9] Higher scores (on a scale of 0-30) reflect more severe HF. Scores correlate well with echocardiographic and biochemical markers of HF (left ventricular end-diastolic dimension and N-terminal pro b-type natriuretic peptide)[24]

with high predictive value.[25] For consistency across sites, standardized definitions for NYU PHFI scoring are outlined in Supplementary Materials; Table S1. The NYU PHFI was chosen instead of the New York Heart Association Class[26] because the New York Heart Association Class is subjective, poorly reproducible even among skilled providers, and lacks sensitivity to change.[27] Alternative HF severity measures, such as the Treatment Intensity Score[28] and Stanford Acute Heart Failure Index,[8] were considered but chosen because unlike the NYU PHFI, as these measures have not been validated for use in outpatients.

PROMIS measures

English or Spanish pediatric-bank v.2.0 self-report PROMIS domain tools were administered at 3 time points as described in "Data collection." Tools included: Mobility (Domain: Physical Function); Fatigue (Domain: Fatigue); Anxiety (Domain: Anxiety/Fear); Depressive symptoms (Domain: Depression/Sadness); and Peer Relationships (Domain: Relationships/Social Support). PROMIS instruments were delivered via computer-adaptive tests (CATs) through a Research Electronic Data Capture (REDCap) platform.

PROMIS measures were chosen for this study because they correlate well with legacy measures of pediatric fatigue, anxiety, and quality of life while decreasing participant burden.[18,29,30] PROMIS measures use CAT which frequently decreases the number of questions that participants are required to answer. For example, if a patient's response is that they are unable to get out of bed, they will not be asked the question as to whether they can run a mile. Additionally, PROMIS measures are available in Spanish and English, are available in an electronic format allowing them to be delivered remotely via email, and link both to a REDCap database and to HealthMeasures scoring. PROMIS measures are known to be responsive to changes in disease status in other pediatric populations.[18,31] PROMIS measures have been used in pediatric cardiac populations in the past, including transplant recipients with a history of HF[32] and ventricular assist device (VAD) recipients,[33] and in other pediatric chronic illnesses.[16-18,31] While legacy PROMs exist in pediatrics, there are specific advantages to PROMIS. PROMIS is readily accessible in electronic format which facilitates administration before a clinic visit. PROMIS uniquely connects directly to RedCAP which not only provides standardized scoring through the HealthMeasures system but also enables ease of export of data without transcribing from paper forms. Also unlike the legacy PROMs, the CAT versions of PROMIS also allow very good differentiation of quality of life at the highest and lowest ends of the functional status spectrum. CATs also enable greater efficiency of data collection. For example, if a patient's response is that they are unable to get out of bed, they will not be asked the question as to whether they can run a mile. This approach reduces administration time for the measures and burden for the patient; additional advantages of PROMIS.

PROMIS scoring

PROMIS responses were scored via the HealthMeasures Scoring Service. Raw PROMIS scores were converted into *t*-scores.[34] For PROMIS, the *t*-score distributions are standardized. A *t*-score of 50 represents the mean for the US population, and 10 points represents 1 standard deviation (SD). A higher score indicates more of the measured quantity; a high mobility score indicates better mobility, and a high fatigue score indicates greater fatigue.

In addition to the standard scores, we compared changes in *t*-score to the "minimally important difference" (MID) in *t*-score, defined as the "...smallest difference in score that patients perceive as important…and which would lead the clinician to consider a change in…management."[35] This provides context about the potential clinical importance of a change in score at the patient level. For PROMIS, a half SD (5 points) of change in *t*-score is likely to be clinically important.[36] For pediatric PROMIS Mobility, Fatigue, and Depression, the MID is generally considered a change in score of 3 points.[35]

Data collection

Data were collected at the time of hospitalization, within 48 hours of initiating HF treatment (time 1, T1); within 1 month of discharge (time 2, T2); and within 3 to 6 months of discharge (time 3, T3).

At T1, parents completed a family demographics survey. Children completed self-report PROMIS Pediatric measures on an iPad and were encouraged to complete the measures without parental input. PROMIS measures were administered within 48 hours of the NYU PHFI scoring. No parent-proxy PROMIS measures were used.

If discharged from hospital following their index admission (T1), children completed follow-up PROMIS measures at T2 and T3 either on a personal electronic device via a secure email link or on an iPad in clinic. Site PIs calculated the NYU PHFI score at each encounter.

PROMIS Fatigue was the primary outcome, based on a high burden of reported fatigue among this population and responsiveness of the fatigue measure among adults with HF.[37] PROMIS pediatric Fatigue item banks and CATs have sound psychometric properties,[38,39] good test-retest reliability (correlation of 0.8 using CATs), and internal consistency (reliability coefficient 0.87).[40]

Statistical approach

Continuous demographics and clinical outcomes were summarized: mean and SD, median and interquartile range (IQR). Paired *t*-tests compared baseline (T1) inpatient scores to outpatient scores for NYU PHFI and PROMIS. Because only a subset of children had both T2 and T3, we compared T1 to the next available outpatient score (T2 or T3).

To evaluate the correlation between PROMIS *t*-scores and NYU PHFI scores in the longitudinal data set, we obtained a marginal correlation coefficient from a univariable linear mixed-effects model[41] fitted to the 3 time points (T1-T3), using the R function r.squaredGLMM in package "MuMIn" with an unstructured covariance matrix. This correlation coefficient (r) measured the relationship between PROMIS and NYU PHFI over time. We calculated the corresponding 95% confidence interval (CI) from 1,000 subject-level bootstrap samples.

To assess whether change in PROMIS Fatigue score was responsive to change in the NYU PHFI, we took the difference for each measure (T2 or T3 − T1), and fit a linear regression model, as described in Husted et al.[42] Statistical significance was assessed at the 0.05 level, using R v. 4.1.2 (R Foundation).[43]

Results

Forty-three patients were enrolled and 2 were later withdrawn: 1 patient became too sick to participate, and 1 was found to have developmental delays that limited PROMIS completion. Thus, the cohort is comprised of 41 patients with data collected at T1. The flow of patients through the study is shown in Figure 1.

Demographics

Most enrolled were male (58.5%), non-Hispanic (73.2%), and Caucasian (65.9%; Table 1). The most common diagnosis was cardiomyopathy (48.8%), with predominantly systolic HF (51.2%). Among those with congenital heart disease, 14/17 (82.4%) had single ventricle heart disease. Of the 20 patients discharged from hospital during the study period, outpatient data at either T2 or T3 were available for 18. Seventeen patients were hospitalized for cardiac reasons < 6 months before the enrollment hospitalization. Five (29.4%) of these were hospitalized ≥3 times in the 6 months preceding the enrollment hospitalization. Median days from prior discharge to the enrollment hospitalization were 35 days (IQR 18, 135).

Most participants were English-speaking (80.5%) and had public insurance (56.1%). Among family demographic data available, 32/38 (84.2%) had a parent with at least high school education, 17/32 (53.1%) had a combined income over $50,000 per year, and 9/27 (33.3%) were classified as below the federal poverty level.[44]

Clinical outcomes

Twenty-one (51.2%) patients were not discharged from hospital during the study period (Figure 1). Most of these

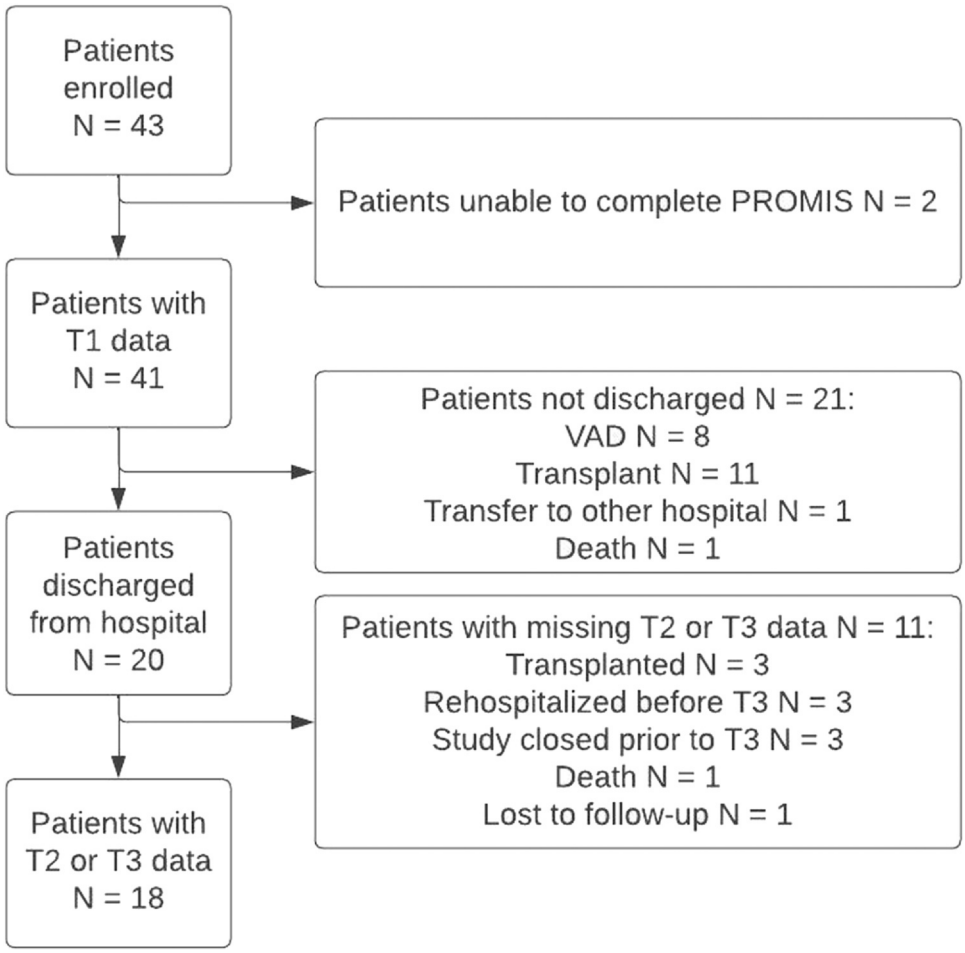

Figure 1 Cohort diagram. PROMIS, Patient-Reported Outcome Measurement Information System; T1, time 1, T2, time 2; T3, time 3; VAD, ventricular assist device.

Table 1 Demographics of the Study Cohort; N = 41

Characteristic	N (%)
Child demographics	
Sex	
Female	17 (41.5%)
Male	24 (58.5%)
Race	
White/Caucasian	27 (65.9%)
Black/African American	7 (17.1%)
Asian	1 (2.4%)
Not specified	6 (14.6%)
Ethnicity	
Hispanic or Latino	10 (24.4%)
Not Hispanic or Latino	30 (73.2%)
Not specified	1 (2.4%)
Underlying diagnosis	
Cardiomyopathy	20 (48.8%)
Congenital heart disease	17 (41.5%)
Other	4 (9.7%)
Type of heart failure	
Systolic	21 (51.2%)
Diastolic	13 (31.7%)
Both systolic and diastolic	7 (17.1%)
Median age (years) at HF diagnosis	
Cohort	14.6 (IQR 12.7, 16.3)
Cardiomyopathy	14.8 (IQR 13.4, 16.3)
Congenital heart disease	13.9 (IQR 12.7, 14.8)
HF diagnosis	
New diagnosis of HF at enrollment	23 (56.1%)
Established HF diagnosis	18 (43.9%)
Cardiac hospitalization within 6 months of enrollment	17/41 (41.5%)
One recent hospitalization	11/17 (64.7%)
Two recent hospitalizations	1/17 (5.9%)
≥3 recent hospitalizations	5/17 (29.4%)
Family demographics	
Language spoken at home	
English	33 (80.5%)
Spanish	7 (17.1%)
Other	1 (2.4%)
Insurance	
Public	23 (56.1%)
Private	17 (41.5%)
No insurance	1 (2.4%)
Household annual income	
< $25,000	3 (7.3%)
$25,000-$49,999	12 (29.3%)
$50,000-$99,999	6 (14.6%)
$100,000-$149,999	4 (9.8%)
$150,000 or greater	7 (17.1%)
Not specified	9 (21.9%)
Highest parental level of education	
None to 8th grade	4 (9.8%)
9th-11th grade	2 (4.9%)
High school graduate or equivalent	10 (24.4%)
Some college, 2-year degree, trade school	10 (24.4%)
3- or 4-year college or university degree	4 (9.8%)
Graduate degree	8 (19.5%)
Not specified	3 (7.3%)

Abbreviation: HF, heart failure.

patients received a heart transplant (11/21; 52.4%) or VAD (8/21; 38.1%) during their hospitalization. Six patients (14.6%) were on the heart transplant waitlist at enrollment. Therapies during the enrollment hospitalization included intravenous diuretics (35/41,85.4%), vasoactive medications (28/41, 68.3%), and noninvasive positive pressure ventilation (9/41, 22.0%).

Among the 20 patients discharged from the hospital, the median length of stay was 7 days (IQR 4.0, 13.0). Outpatient data (T2 and/or T3) were available for 18 of 20 of the discharged patients. After T2 data were collected, 3 patients were readmitted to hospital before T3; median time to readmission was 31 days (IQR 26.5, 38.3).

NYU PHFI and PROMIS domain *t*-scores

A total of 345 PROMIS CATs were administered to the study cohort. Responses were incomplete or missing for 5/345 (1.4%). NYU PHFI scores and PROMIS *t*-scores for the entire cohort at enrollment (T1), and for patients with at least 1 outpatient assessment, are shown in Table 2. At T1, mean PROMIS Fatigue and PROMIS Mobility scores (61.2 ± 12.9, and 39.3 ± 8.2, respectively) in children in the study cohort were > 1 SD (10 points) from the population mean of 50. Mean PROMIS Peer relationships and PROMIS Anxiety scores (41.2 ± 9.2 and 55.1 ± 11.2, respectively) were > 0.5 SD from the population mean, while the mean *t*-score for PROMIS Depressive symptoms (51.0 ± 9.8) was within 0.5 SD of the population mean. The expected responses to items in the Fatigue and Mobility measures are available online.[45]

The median enrollment (T1) PROMIS Fatigue *t*-score for the subset of patients who had prior HF admissions was not significantly different from the enrollment score of the patients without a recent prior hospital admission (median *t*-scores 57.0 vs 61.1, respectively; $p = 0.13$).

Correlation of NYU PHFI scores and PROMIS domain *t*-scores across time

For the subset of patients with inpatient and outpatient data (N = 18), the mean NYU PHFI improved from 13.3 ± 2.6 to 7.8 ± 3.4 from enrollment to outpatient ($p < 0.001$). In comparison to PROMIS *t*-scores at enrollment, mean outpatient *t*-scores improved in each domain except Peer relationships, although the improvement was only statistically significant for Fatigue. The greatest improvement was observed in the Fatigue *t*-score, in which the mean score

Table 2 Mean PROMIS *t*-Scores and Mean NYU PHFI Scores for the Full Study Cohort and Comparison of Scores for the Subset of Patients With at Least 1 Follow-Up Outpatient Assessment After Hospital Discharge (T2 or T3)

Variable	Full study cohort N = 41 Mean (SD)	Subset of patients with outpatient data N = 18 Mean (SD)		*p*-value[a]
	Enrollment (T1)	Enrollment (T1)	Outpatient (T2 or T3)	
NYU PHFI	13.4 (2.8)	13.3 (2.6)	7.8 (3.4)	< 0.001
PROMIS Fatigue	61.2 (12.9)	58.1 (13.5)	48.9 (16.9)[b]	0.007
PROMIS Anxiety	55.1 (11.2)	54.6 (12.9)	48.8 (11.0)[b]	0.06
PROMIS Depression	51.0 (9.8)	49.1 (10.6)	45.9 (11.9)[b]	0.21
PROMIS Peer relationships	41.2 (9.2)	41.9 (6.9)	44.0 (6.8)	0.26
PROMIS Mobility	39.3 (8.2)	38.8 (8.9)	39.9 (6.4)	0.46

Abbreviations: HF, heart failure; PROMIS, Patient-Reported Outcome Measurement Information System; T1, time 1, T2, time 2; T3, time 3.

For all PROMIS tools, the *t*-score distributions are standardized such that a score of 50 represents the mean for the US general population, and 10 points represents 1 standard deviation (SD). A higher score indicates more of the measured quantity. The minimally important difference (MID) is the smallest difference in score that patients perceive as important. For pediatric PROMIS Mobility, Fatigue, and Depression, the MID is generally considered a change in score of 3 points.[35] The New York University Pediatric Heart Failure Index (NYU PHFI) is a Clinician Reported Outcome, with a higher score indicating greater HF severity.

[a]Enrollment vs outpatient scores for the subset of patients with outpatient data.

[b]Denotes a change that exceeds the minimally important difference of 3 points for Fatigue, Depression, or clinically important change of at least 5 points for Anxiety.

improved by nearly a full SD (61.2-48.9). Change in mean PROMIS *t*-scores and NYU PHFI scores is shown in Figure 2, with individual-level data shown in Figure 3.

Both the mean NYU PHFI score and mean PROMIS Fatigue *t*-score improved from enrollment to first outpatient follow-up (NYU PHFI: 13.3-7.8, $p < 0.001$ and PROMIS: 58.1-48.9; $p = 0.007$, respectively). This improvement exceeded the MID, suggesting this was also a clinically important improvement.[35] The improvement in Anxiety *t*-scores did not reach statistical significance ($p = 0.06$) but did exceed a 5-point change so was likely clinically important. Clinically significant improvement (a change exceeding the MID) in Depression was also noted, but this was not statistically significant ($p = 0.2$). The mean *t*-score for Peer relationships at the enrollment and outpatient time points was low and remained nearly 1 SD lower than the population mean (mean *t*-score 41.9 vs 44.0, respectively; $p = 0.26$). The slight improvement in Peer relationship score was not statistically significant nor did it exceed the 5-point change to suggest clinical importance. Similarly, the mean *t*-score for Mobility at enrollment was < 1.2 SD from the population mean and did not statistically or clinically improve at the outpatient assessment ($p = 0.46$).

The PROMIS Fatigue *t*-score and NYU PHFI score were moderately correlated across time (r = 0.5; 95% confidence interval 0.3, 0.6; Table 3). The correlation between other PROMIS measures and the NYU PHFI was weak, and the change in PROMIS *t*-scores was not responsive to the change in NYU PHFI (Table 3).

Among the 3 patients who were readmitted to hospital after their enrollment hospitalization, PROMIS Fatigue *t*-scores improved from enrollment (T1) to outpatient (T2 or T3), then worsened by the time of readmission (Table 4). Small sample size for this subgroup precludes statistical comparison to the overall cohort or those without a readmission.

Discussion

This study describes the trajectory of HF severity and patient-reported outcome scores for a cohort of hospitalized children with HF. Based on PROMIS results, the burden of fatigue and poor mobility at the time of hospital admission are very high in this population, with worse *t*-scores than observed in most other pediatric chronic illnesses.[18,46] Children with HF are at risk of important functional limitations[47] which impact quality of life, and this study is the first to describe the specifics of these limitations using longitudinal self-report measures.

As patients' HF improved and they were discharged, both the HF severity and Fatigue scores improved. Both the PROMIS Anxiety and Depression scores improved and while these improvements were not statistically significant, the magnitude of improvement was likely of clinical importance and would be relevant to the patient based on the concept of MID. Mobility and Peer relationships did not improve, with Peer relationships remaining very poor across all time points. In addition, we found a moderate correlation of r = 0.5 between children's PROMIS Fatigue scores and their HF severity as measured by NYU PHFI. However, any correlation r > 0.3 demonstrates acceptable concurrent validity between the measures.[48]

The burden of fatigue among this patient cohort was very high at the time of hospitalization, with a mean enrollment PROMIS Fatigue *t*-score of 61.2. This is among the highest reported population *t*-scores in the pediatric chronic illness literature. For context, this level of fatigue is similar to that of children experiencing a sickle cell exacerbation, higher than children undergoing chemotherapy for cancer (*t*-scores 48.4-53.8)[46] and higher than children with nephrotic syndrome (*t*-scores 50).[18] Among adults with HF, assessed before VAD implant, the mean PROMIS

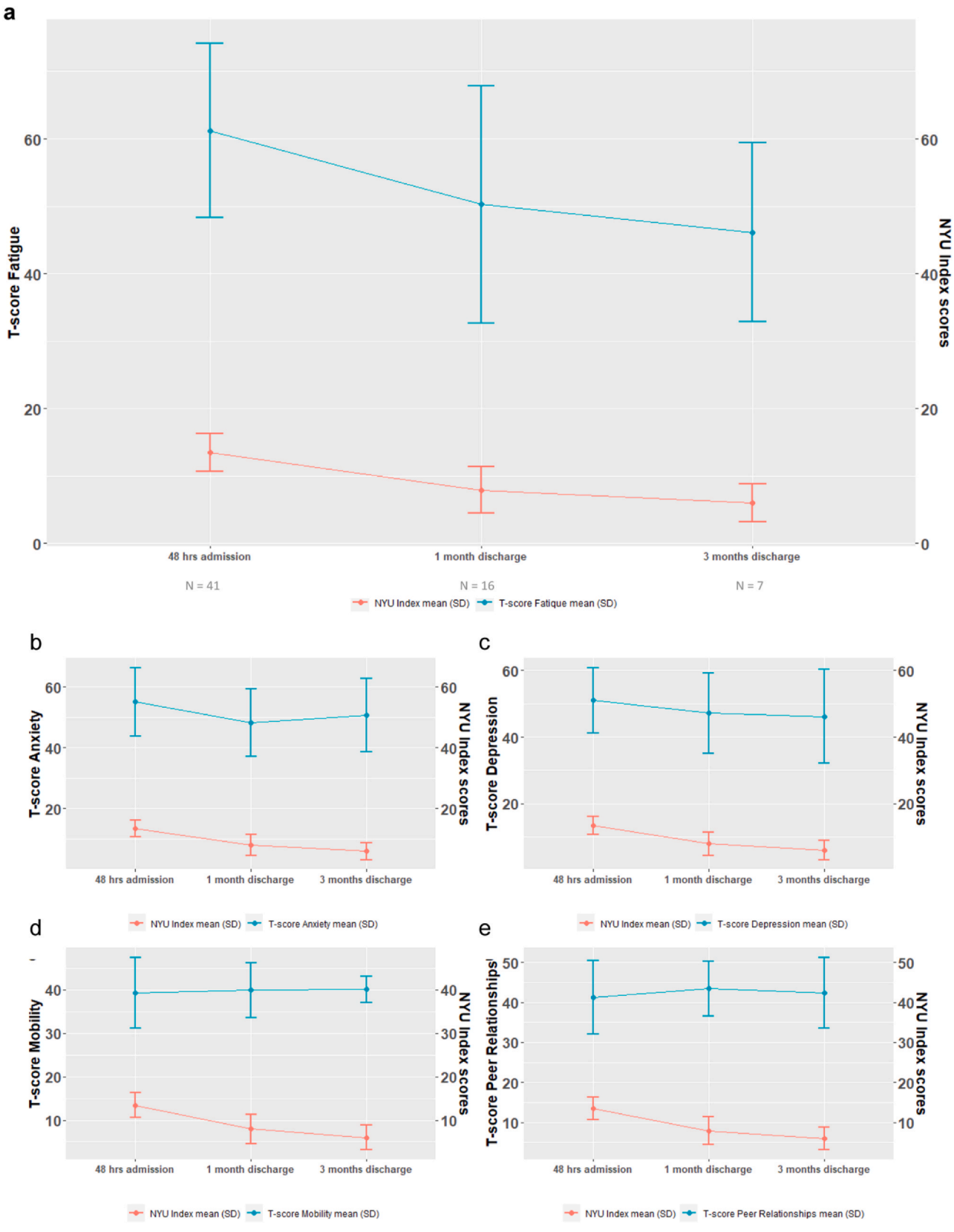

Figure 2 (a) Mean (±SD) PROMIS fatigue *t*-scores and NYU PHFI scores across all 3 time points: within 48 hours of hospital admission (T1; N = 41), within 1 month of hospital discharge (T2; N = 16), and within 3 to 6 months of hospital discharge (T3; N = 7). For the subset of patients with inpatient and outpatient data, changes in NYU PHFI score and PROMIS Fatigue score from admission to first follow-up were significantly improved ($p < 0.001$ and $p = 0.007$, respectively) (Table 2). (b-e) Mean (±SD) PROMIS Anxiety (b), Depression (c), Mobility (d), and Peer relationships (e) *t*-scores and NYU PHFI scores across all 3 time points: within 48 hours of hospital admission (T1), within 1 month of hospital discharge (T2), and within 3 to 6 months of hospital discharge (T3). NYU PHFI, New York University Pediatric Heart Failure Index; PROMIS, Patient-Reported Outcome Measurement Information System; SD, standard deviation; T1, time 1, T2, time 2; T3, time 3.

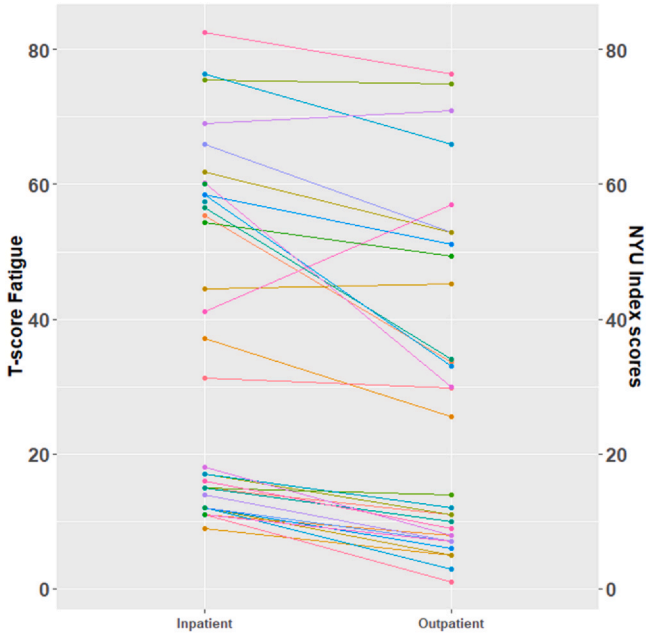

Figure 3 Spaghetti plot representing the individual-level data (PROMIS Fatigue *t*-scores and NYU PHFI scores) for the 18 patients with both inpatient and outpatient data. Each straight line connecting 2 dots represents a unique subject. NYU PHFI, New York University Pediatric Heart Failure Index; PROMIS, Patient-Reported Outcome Measurement Information System.

t-score for Fatigue was similar to our population (mean 58.4 ± 11.2).[37] Thus, children hospitalized for HF face a substantial burden of fatigue.

Similarly, enrollment Mobility scores for the cohort were worse than those for patients actively receiving chemotherapy and worse than patients experiencing an exacerbation of sickle cell disease.[18] Such poor Fatigue and Mobility scores suggest a high degree of functional impairment. The PROMIS Mobility scores failed to improve significantly from enrollment to outpatient. Although the reason for this is unclear, Mobility scores may not have improved due to deconditioning during the acute HF period.

Peer relationship scores were poor at both enrollment and follow-up. This is somewhat unexpected and inconsistent with prior literature in which Peer relationship scores in pediatric chronic illness are similar to the US population norms.[16,18] It is likely that poor Peer relationship scores were related to social isolation associated with restrictions during the COVID-19 pandemic,[49] which may have especially impacted children with chronic illnesses. As a result, it remains unclear whether the poor Peer relationship scores were HF-specific or circumstantial.

Table 4 PROMIS Fatigue *t*-Scores Among Patients Readmitted to Hospital During the Study Period (N = 3)

Patient ID	Enrollment (T1)	Outpatient (T2 or T3)	Readmission (T1R)
1	55.3	33.7	48.6
2	54.4	49.3	49.9
3	65.9	52.9	62.6

Abbreviations: PROMIS, Patient-Reported Outcome Measurement Information System; T1, time 1, T2, time 2; T3, time 3.

Children with HF had a low burden of depression, with scores similar to that of the US population. Anxiety scores were elevated at hospital admission but were near population norms after hospital discharge; based on the degree of change this was likely of clinical significance. While it was anticipated that the burden of HF may lead to high levels of anxiety and depression,[50] children with other chronic health conditions (such as nephrotic syndrome and sickle cell disease) also have PROMIS *t*-scores for depression and anxiety that are similar to the US population.[18,46]

Longitudinally our cohort had an improvement in fatigue *t*-score of 9.2 points as HF status improved, which was both statistically and clinically important, exceeding the published MID in adults.[35] Furthermore, children's reported fatigue was positively correlated with HF severity over time. This suggests that PROMIS fatigue may have a role in the routine clinical assessment of pediatric HF patients. In the adult HF literature, the use of PROMs in routine assessment improves the accuracy of HF assessment and improves patient experience.[51] PROMIS could also be helpful for monitoring children with HF who live long distances from their HF center. A rising PROMIS fatigue score could prompt a more expedited clinical assessment, to potentially avoid hospital readmission. In addition, our findings suggest that PROMIS fatigue may be an adjunct tool for pediatric HF medication and device trials, as in adult HF.[52-54]

Table 3 Correlation Between PROMIS Measure and NYU Index Score, and Responsiveness to Change

PROMIS domain	Correlation with NYU Index Score		Responsiveness	
	R (95% CI)		Coefficient (95% CI)	*p*-value
Fatigue	0.5 (0.3, 0.6)	Moderate	0.1 (0.0, 0.2)	0.22
Anxiety	0.3 (0.1, 0.4)	Weak	0.0 (−0.1, 0.2)	0.61
Depression	0.2 (0.0, 0.4)	Weak to none	0.1 (0.0, 0.1)	0.21
Mobility	−0.3 (−0.4, −0.1)	Weak	−0.1 (0.0, 0.1)	0.41
Peer relationships	−0.1 (−0.2, 0.0)	Weak to none	−0.18 (−0.4, 0.1)	0.15

Abbreviations: CI, confidence interval, NYU PHFI, New York University Pediatric Heart Failure Index; PROMIS, Patient-Reported Outcome Measurement Information System.

This prospective study represents a unique contribution to the literature as it includes a contemporary population of children with symptomatic HF, using self-reported PROMIS measures. Prior studies using PROMs among children with HF included patients with cardiomyopathy, but HF status was unclear at the time of PROM collection, and largely focused on parent-reported proxy measures[24,47] which are known to differ from patient-reported functional status.[55] Some PROM data among children on VADs have suggested improvement in functional status after VAD implant[56] but these so far have relied mainly on parent-proxy data, and no studies to date have evaluated a PROM responsiveness to changes in HF status. While we did not demonstrate the responsiveness of the measures to HF severity, this may be related to small sample size.

One limitation of this study is that enrollment patterns and PROMs (especially measures of peer relationships) may have been influenced by the COVID-19 pandemic. Another potential limitation is the small sample size at follow-up; many patients were too unwell to be discharged from the hospital or were readmitted to the hospital before the next assessment. By enrolling hospitalized patients at major referral centers, this may represent a smaller, sicker population of HF patients than children with HF managed as outpatients; however, use of a sicker population allowed us to measure change over time. Despite the small sample size, generalizability of our findings is supported by the multicenter nature of this work, the inclusion of non–English speaking patients, and economic diversity of the patient population.

The utility of PROMIS in children cared for solely as outpatients deserves further study. Given the predictive value of NT-proBNP in the cardiomyopathy population,[56] there may be benefit in prospective PROMIS data collection in conjunction with NT-proBNP or other clinical data to inform longitudinal clinical care.

In conclusion, PROMIS Fatigue measure is moderately correlated with a Clinician Reported Outcome assessment of children's HF severity (NYU PHFI). Results suggest that PROMIS Fatigue could help improve care delivery in this high-risk HF patient population and our findings provide a critical platform for future larger-scale study.

Author contributions

Dr May participated in all aspects of the work (conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision; validation; visualization; roles/writing – original draft; and writing – review and editing). Dr Stehlik, Dr Ou, Dr Presson, Dr Rosenthal, and Dr Keenan contributed to study design (conceptualization), funding acquisition, data analysis (methodology), and writing of manuscript. Ms Lambert, Dr Chen, Dr Machado, Ms Lopez-Colon, Dr Shih, Ms Gibbons, Mr Madden, and Dr Watanabe contributed to study design (conceptualization) and writing of manuscript. Dr Cizik contributed to data analysis (methodology) and writing of manuscript.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author(s) did not use any generative AI and AI-assisted technologies.

Disclosure statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2024.100144.

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