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Primary Disease, Sex, and Racial Differences in Health-Related Quality of Life in Adolescents and Young Adults with Heart Failure

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Abstract

Health-related quality of life (HRQOL) is an important clinical and research trial endpoint in adult heart failure and has been shown to predict mortality and hospitalizations in adult heart failure populations. HRQOL has not been adequately studied in the growing pediatric and young adult heart failure population. This study described HRQOL in adolescents and young adults (AYAs) with heart failure and examined primary disease, sex, race, and other correlates of HRQOL in this sample. Participants in this cross-sectional, single-center study included adolescent and young adults with heart failure and a parent/guardian. Patients and their parent/proxies completed the PedsQL, a well-established measure of HRQOL in pediatric chronic illness populations. HRQOL is impaired in AYAs with heart failure resulting from dilated, hypertrophic, or other cardiomyopathy, congenital heart disease, or post-transplant with rejection/complications. Patients identifying as white endorsed poorer total HRQOL than non-white patients ($p = 0.002$). Subscale analysis revealed significant correlations between female sex ($p = 0.01$) and white race ($p = 0.01$) with poorer self-reported physical functioning. Family income was unrelated to HRQOL. Functional status was strongly associated with total ($p = 0.0003$) and physical HRQOL ($p < 0.0001$). Sociodemographic and disease-specific risk and resilience factors specific to HRQOL in AYAs with heart failure include primary cardiac disease, race, sex, and functional status. Building upon extensive work in adult heart failure, utilization, and study of HRQOL as a clinical and research trial outcome is necessary in pediatric heart failure. Developing targeted interventions for those at greatest risk of impaired HRQOL is an important next step.

Keywords Heart failure · Quality of life · Adolescents · Young adults

Introduction

High morbidity, mortality, and resource utilization in pediatric heart failure has prompted calls for action to improve outcomes for patients and families impacted by this complex disease [1, 2]. Resulting from various etiologies, such as primary cardiomyopathy, congenital heart disease (CHD), and acquired heart disease, it is estimated that approximately 14,000 children are hospitalized with heart failure annually in the USA [3]. Hospital-based mortality for children with heart failure is estimated at 7%, which is more than double the in-hospital mortality of adults with heart failure [4]. Advanced cardiac therapies, including ventricular assist devices (VAD) and heart transplantation, are often used in the treatment of pediatric heart failure with improving outcomes observed in recent years [5, 6]. With all chronic diseases and advanced therapies, attention to patient health-related quality of life (HRQOL) is critically important.

In adult heart failure, patient-reported HRQOL detected more meaningful changes in health status and outcomes, including mortality and heart failure hospitalization, than clinician-assigned functional status [7]. While some have described HRQOL in pediatric heart failure [8, 9], most pediatric cardiology literature has focused on HRQOL in CHD [10–12] and heart transplant [13] populations. Given a growing population of pediatric and young adult patients with heart failure [1, 14], as well as the recognized importance

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of patient-reported outcomes in pediatric cardiology, this study aimed to describe self- and proxy-reported HRQOL in adolescent and young adult (AYA) patients with heart failure. Group comparisons based on primary cardiac diagnosis leading to heart failure were conducted, as this has not previously been examined. Patient sociodemographic and disease characteristics, including sex, race, and functional status, were also examined as correlates of HRQOL. Consistent with previous research [8], it was hypothesized that worse functional status would be associated with poorer HRQOL.

Materials and Methods

Study Design and Measures

This cross-sectional study was approved by the local IRB. Participants completed electronic (tablet or emailed) self- or proxy (parent)-reported versions of the 23-item Likert scale PedsQL 4.0 Generic Core which assesses HRQOL across four domains: Physical, Emotional, Social, and School functioning [15]. Scores are transformed to a 0–100 scale with higher scores representing more positive HRQOL. Impaired HRQOL was defined as a score > 1 SD below norms as previously described [16]. Self-reported sociodemographic characteristics were collected (e.g., race, parental education, income level) from adult participants. Additional demographic and disease characteristics were obtained via medical chart review, including patient sex, age at survey, cardiac diagnosis, age at diagnosis, cardiac device (e.g., VAD, implantable cardiac device) and surgical history, hospitalizations, New York Heart Association (NYHA) functional class, and palliative care involvement.

Participants and Recruitment

As part of a larger, federally funded study on communication, decision-making, and psychosocial outcomes in AYA heart failure, patient–parent dyads were recruited from a single-center heart failure service at a Midwestern U.S. children's hospital. Both inpatients and outpatients were medically eligible if they met criteria for any of the following: (1) American Heart Association ≥ Stage C Heart Failure, (2) receiving chronic medical therapy for heart failure, (3) listed for heart transplantation, or (4) post-heart transplantation with life-limiting complication (e.g., cardiac allograft vasculopathy, refractory rejection). Eligibility was similar to previous research in this area [8], but was expanded to include those patients who are post-transplant with heart failure due to transplant-related complications. Exclusion criteria, defined by the larger study, included (1) suicidality, homicidality, or psychosis in past 6 months, (2) intubated, unable to respond verbally, or with active delirium, (3) intellectual impairment or significant developmental delay that precludes patient from completing survey measures, even with assistance, and (4) non-English speaking youth. Participant recruitment occurred July 2018–April 2021, with an extended period of pause in recruitment as a result of the COVID-19 pandemic.

Eligible participants were identified by multidisciplinary heart failure team members. After verbal consent to be contacted was obtained, a research nurse coordinator met with eligible patients' in-person or by phone to describe study procedures and obtain informed consent/assent. Due to the COVID-19 pandemic, study procedures were adapted to include both in-person and virtual study completion. Participating patient–parent dyads completed survey measures electronically via REDCap.

Statistical Analysis

A total sample size of 46 AYA–parent dyads was determined necessary to detect a medium effect size (correlation coefficient, $r = 0.40$) of the hypothesized associations to achieve an 80% power based on a two-sided 0.05 significance level. Standard descriptive statistics were reported as frequency with percentage for categorical variables and median with interquartile range (IQR) or mean ± standard deviation (SD) for continuous variables. Group comparisons of self- and proxy-reported HRQOL total, physical functioning, and psychosocial functioning scores were made by cardiac diagnosis using analysis of variance (ANOVA) or two-sample t test. Univariate associations of patient sociodemographic and disease characteristics with HRQOL total, physical functioning, and psychosocial functioning scores were examined using ANOVA or two-sample t test for categorical variables and Spearman correlation coefficient for continuous variables, as appropriate. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA), with a statistical significance level of 0.05 using two-sided tests.

Results

Participant Characteristics

Participant characteristics are reported in Table 1; 100 participants were identified as meeting medical eligibility. Of these, 37 were ineligible due to cognitive/neurodevelopmental status of patient prohibiting survey completion ($N = 26$), non-English speaking patient or caregiver ($N = 3$), recent suicidality or homicidality ($N = 3$), or cardiologist did not support approaching patient/family ($N = 2$). Three eligible participants were transplanted or died before being approached for study participation.

Of 63 eligible patients, 56 patient–parent/caregiver dyads enrolled in the study (89% enrollment rate). Among the 7 who

Table 1 Sociodemographic and disease characteristics (N = 53)

Male patient	34 (64.2)
Patient age at survey, years	17.8 (15.8–19.0)
Patient race/ethnicity	
White/Caucasian	40 (75.5)
Black/African American	7 (13.2)
Hispanic or Latino	2 (3.8)
Native American	1 (1.9)
Bi-Racial/Multiracial	3 (5.7)
Patient's cardiac diagnosis	
Dilated cardiomyopathy	9 (17.0)
Restrictive cardiomyopathy	0 (0.0)
Hypertrophic cardiomyopathy	2 (3.8)
Anthracycline cardiomyopathy	11 (20.8)
Other cardiomyopathy	2 (3.8)
CHD—single ventricle	12 (22.6)
CHD—not single ventricle	3 (5.7)
Post-transplant with complications	14 (26.4)
Age at cardiac diagnosis, years	7.7 (0.0–14.3)
ECMO history	5 (9.4)
Cardiac device history	12 (22.6)
Cardiac arrest history	4 (7.5)
Extra-cardiac disease	22 (41.5)
Cardiac surgery (not including Heart transplant)	21 (39.6)
Catheterization interventions within the last 5 years	18 (34.0)
Hospitalizations within the last 5 years	40 (75.5)
NYHA class	
I or II	20 (37.7)
III or IV	15 (28.3)
Unknown	18 (34.0)
Heart transplant recipient	14 (26.4)
Resuscitation	53 (100.0)
Referral to Palliative Care team	8 (15.1)
Family type	
Single-parent home	12 (22.6)
Married, both parents live at home	31 (58.5)
Mixed family home	9 (17.0)
Other	1 (1.9)
Family's annual income	
< $25,000	6 (11.3)
$25,000–$50,000	13 (24.5)
$50,000–$75,000	2 (3.8)
$75,000–$100,000	10 (18.9)
> $100,000	21 (39.6)
Not reported	1 (1.9)
Highest level of education completed by the patient's mother	
Some high school	2 (3.8)
High school	7 (13.2)
Some college	24 (45.3)
Bachelor's Degree	12 (22.6)
Professional Degree (Master's, Doctorate Degree)	8 (15.1)

Table 1 (continued)

Male patient	34 (64.2)
Highest level of education completed by the patient's father	
Some high school	4 (7.5)
High school	14 (26.4)
Some college	16 (30.2)
Bachelor's Degree	14 (26.4)
Professional Degree (Master's, Doctorate Degree)	5 (9.4)

*Data are presented as N (%) for categorical variables and Median (interquartile range) for continuous variables

did not enroll, lack of time or desire were cited as reasons for non-participation. The final study cohort was composed of 53 dyads as three consented participants were lost to follow-up and could not be reached to complete study surveys. Median patient age was 17.8 years (IQR 15.8–19.0) and 64% of patient participants were male. While most patient participants identified as white (75%), 25% identified as unrepresented minority race or bi/multi-racial. Primary cardiac diagnosis varied across the sample and included post-transplant with rejection/life-threatening complications (26%), single-ventricle CHD (23%), anthracycline-induced cardiomyopathy (21%), and dilated cardiomyopathy (17%). Disease burden was high among the sample with 42% with other comorbidities (e.g., renal disease, liver disease, diabetes) and 34% experiencing greater than 11 hospitalizations.

Quality of Life (HRQOL) in AYA Heart Failure by Cardiac Diagnosis

Self- and proxy-reported HRQOL total, physical functioning, and psychosocial functioning mean scores are presented in Figs. 1a and 1b. Per patient self-report (Fig. 1a), AYAs with heart failure, and (a) dilated, hypertrophic, or other cardiomyopathy, (b) CHD, or (c) post-transplant with rejection/ complications diagnoses endorsed significantly lower total (mean $67.4 \pm$ SD 16.9 vs. 81.4 ± 20.5, $p = 0.02$) and physical (66.3 ± 23.4 vs. 85.8 ± 18.5, $p = 0.01$) HRQOL than patients with anthracycline-induced cardiomyopathy resulting in heart failure, which reported mean total and physical HRQOL within normal limits. All group mean scores for psychosocial HRQOL fell within the normative range.

Similarly, via proxy-reported measures (Fig. 1b), significantly lower total HRQOL was endorsed by parents of AYAs with heart failure and (a) dilated, hypertrophic, or other cardiomyopathy, (b) CHD, or (c) post-transplant with rejection/complications. Parents of youth with CHD or post-heart transplant with rejection/complications noted physical functioning to be impaired. Parents of youth with dilated, hypertrophic or other cardiomyopathy, or post-heart transplant with rejection/complications endorsed impaired psychosocial functioning. Parents of children with heart failure and CHD reported psychosocial functioning approaching clinically impaired. Parents of children with heart failure from/caused by anthracycline-induced

cardiomyopathy reported overall normative mean HRQOL, with total HRQOL ($p = 0.04$) and physical functioning ($p = 0.01$) that was significantly better than other cardiac groups.

Sociodemographic Correlates of Quality of Life (HRQOL) in AYAs with Heart Failure

Patient sociodemographic and disease factors were examined as potential correlates of HRQOL (Tables 2). Patient
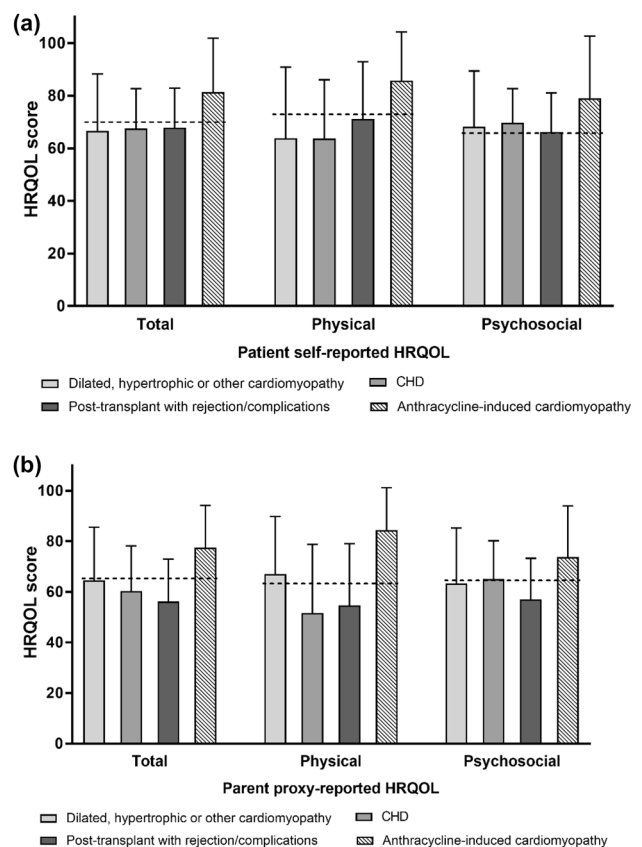

Fig. 1 Self- **a** and proxy-reported **b** HRQOL total, physical functioning, and psychosocial functioning by cardiac diagnosis. A bar represents a mean HRQOL score and an upper error bar on each bar indicates a standard deviation of a mean HRQOL score. A horizontal dot line on each HRQOL domain represents an impaired HRQOL cutoff and below the line indicates clinically impaired

Table 2 Associations of Sociodemographic and disease characteristics with Patient PedsQL score (N = 53)

Characteristics	Patient PedsQL score					
	Total	p	Physical functioning	p	Psychosocial functioning	p
Patient sex		0.12		**0.01**		0.59
Male	73.0 ± 18.0		76.9 ± 19.8		71.4 ± 19.3	
Female	65.0 ± 18.4		58.6 ± 25.9		68.5 ± 16.7	
Patient age at survey, years	$r = -0.01$	0.94	$r = -0.04$	0.78	$r = -0.02$	0.88
Race		**0.002**		**0.01**		0.053
White/Caucasian	66.8 ± 19.1		65.5 ± 24.1		67.6 ± 18.7	
Others	81.1 ± 11.1		85.3 ± 14.5		78.8 ± 14.6	
Patient's cardiac diagnosis		0.17		0.07		0.34
Dilated, hypertrophic, or other Cardiomyopathy	66.7 ± 21.6	0.50^{α}	63.9 ± 27.0	0.21^{β}	68.2 ± 21.2	0.87^{γ}
Anthracycline cardiomyopathy	81.4 ± 20.5		85.8 ± 18.5		79.1 ± 23.6	
CHD	67.6 ± 15.1		63.8 ± 22.3		69.7 ± 13.0	
Post-transplant with complications	67.9 ± 15.0		71.2 ± 21.7		66.2 ± 14.9	
Age at cardiac diagnosis, years	$r = 0.12$	0.38	$r = 0.18$	0.19	$r = 0.07$	0.59
ECMO history		0.50		0.28		0.77
Yes	65.0 ± 22.2		59.4 ± 24.9		68.0 ± 22.7	
No	70.9 ± 18.2		71.5 ± 23.5		70.6 ± 18.1	
Cardiac device history		0.07		**0.02**		0.23
Yes	61.8 ± 20.6		56.3 ± 29.3		64.7 ± 16.9	
No	72.9 ± 17.2		74.5 ± 20.3		72.0 ± 18.6	
Cardiac arrest history		0.16		0.31		0.15
Yes	57.9 ± 20.9		58.6 ± 28.5		57.5 ± 16.9	
No	71.4 ± 18.1		71.3 ± 23.3		71.4 ± 18.2	
Extra-cardiac disease		0.41		0.95		0.18
Yes	67.8 ± 16.9		70.6 ± 20.4		66.4 ± 19.0	
No	72.1 ± 19.5		70.2 ± 26.0		73.2 ± 17.5	
Cardiac surgery (not including Heart transplant)		0.19		**0.0496**		0.49
Yes	66.2 ± 17.3		62.5 ± 23.6		68.2 ± 15.2	
No	73.1 ± 18.9		75.5 ± 22.6		71.8 ± 20.2	
Catheterization interventions within the last 5 years		0.61		0.80		0.34
Yes	68.5 ± 13.5		71.5 ± 19.3		66.9 ± 13.9	
No	71.3 ± 20.6		69.7 ± 25.9		72.1 ± 20.1	
Hospitalizations within the last 5 years		0.65		0.88		0.65
Yes	71.0 ± 16.2		70.6 ± 22.0		71.2 ± 15.4	
No	68.3 ± 24.8		69.5 ± 29.1		67.7 ± 25.8	
NYHA class (N = 35)		**0.0003**		**< .0001**		**0.01**
I or II	79.5 ± 15.1		83.0 ± 18.2		77.7 ± 15.4	
III or IV	57.7 ± 17.2		49.8 ± 23.7		61.9 ± 16.7	
Heart transplant recipient		0.57		0.88		0.33
Yes	67.9 ± 15.0		71.2 ± 21.7		66.2 ± 14.9	
No	71.2 ± 19.6		70.0 ± 24.6		71.8 ± 19.3	
Referral to Palliative Care team		0.80		0.34		0.79
Yes	71.9 ± 20.2		77.7 ± 23.9		68.8 ± 20.3	
No	70.1 ± 18.3		69.0 ± 23.6		70.6 ± 18.5	
Family type		0.39		0.49		0.42
Single-parent home	73.8 ± 14.2		72.9 ± 19.6		74.3 ± 14.5	
Married, both parents live at home	71.2 ± 18.4		72.0 ± 23.2		70.9 ± 18.8	
Mixed family home or Other	63.4 ± 22.7		62.2 ± 29.6		64.0 ± 20.9	

Table 2 (continued)

Characteristics	Patient PedsQL score					
	Total	p	Physical functioning	p	Psychosocial functioning	p
Family's annual income		0.11		0.28		0.08
< $75,000	65.3 ± 17.6		65.9 ± 24.0		65.0 ± 17.1	
≥ $75,000	73.8 ± 18.7		73.3 ± 23.7		74.1 ± 18.7	
Highest level of education completed by the patient's mother		0.08		0.37		**0.04**
High school or some college	73.7 ± 18.0		72.6 ± 24.4		74.3 ± 17.0	
Bachelor's or professional degree	64.7 ± 18.1		66.6 ± 22.4		63.8 ± 18.9	
Highest level of education completed by the patient's father		0.66		0.72		0.66
High school or some college	71.2 ± 18.3		71.2 ± 23.2		71.2 ± 17.6	
Bachelor's or professional degree	68.8 ± 19.1		68.8 ± 25.0		68.9 ± 19.8	

Bold values denote statistical significance at the $p < 0.05$

sex and age at survey were unrelated to total HRQOL. While not a clinically significant difference, the female mean HRQOL total score was in the impaired range ($65.0 ± 18.4$), whereas the male mean HRQOL total score was in the normative range ($73.0 ± 18.0$). Patients identifying as white endorsed poorer total HRQOL (with a mean score in the clinically impaired range) than non-white patients ($p = 0.002$).

PedsQL subscale analysis revealed significant correlations between female sex ($p = 0.01$) and white race ($p = 0.01$) with poorer physical functioning. Patient sex was unrelated to self-reported psychosocial functioning, while white race trended toward association with poorer psychosocial functioning when compared to all other races ($p = 0.053$).

Family income was not correlated with patient-reported total and physical HRQOL scores. Patients with a family income of $75,000 or greater had a higher mean psychosocial HRQOL score than those with family income less than $75,000, although this did not reach a statistical significance ($p = 0.08$). Patients with a mother who obtained a college degree had lower patient-reported psychosocial HRQOL scores compared to those with a mother without a college degree ($p = 0.04$).

Disease-Related Correlates of Quality of Life (HRQOL) in AYAs with Heart Failure

Age at initial cardiac diagnosis was unrelated to patient-reported HRQOL (Table 2). More severe functional impairment (NYHA III or IV) was associated with poorer patient-reported total HRQOL ($p = 0.0003$). A trend toward significance ($p = 0.07$) was detected between lifetime cardiac device history (e.g., VAD, ICD) and poorer total HRQOL, but lifetime ECMO, cardiac arrest, surgical history, and hospitalization history were unrelated to patient-reported total HRQOL.

Cardiac device history ($p = 0.02$), non-transplant cardiac surgery history ($p = 0.05$), and worse functional status per NYHA class ($p < 0.0001$) correlated with poorer patient-reported physical functioning. Similarly, worse functional status correlated with poorer patient-reported psychosocial functioning ($p = 0.01$).

Discussion

Although the study of HRQOL in pediatric cardiomyopathy and heart failure has been identified as a research priority [17], it has been inadequately described to date. In adult heart failure care, HRQOL is increasingly being used as a critical clinical and research trial endpoint [18, 19]. With growing emphasis on advanced cardiac therapies in pediatric heart failure, it is necessary to understand the impact of the disease course and the interventions offered on patient HRQOL. The current study expands upon earlier work in this field [8, 9] by examining group differences by cardiac diagnosis in self- and proxy-reported HRQOL, in addition to sociodemographic and disease correlates of HRQOL.

Overall, per self- and proxy report total HRQOL and physical functioning were below expected or normative level in the study's sample of AYAs with heart failure resulting from dilated, hypertrophic or other cardiomyopathy, CHD, or post-transplant rejection/complications. Self-reported HRQOL findings in the current study were consistent with previous research by Wilmot and colleagues [8], with poorer total HRQOL and physical functioning being reported by patients themselves when compared to healthy children. Consistent with past research [8], proxy-reported physical functioning was in the normative range for those with primary cardiomyopathy; however, parents of children with heart failure resulting from CHD or post-transplant complications indicated significantly impaired physical functioning.

Diagnostic group comparisons yielded interesting findings. In AYAs with heart failure resulting from anthracycline-induced cardiomyopathy, total HRQOL and physical functioning were in the normative range per self- and proxy report, with significantly higher proxy-reported HRQOL observed in this group when compared to all other diagnostic groups. In fact, the anthracycline-induced cardiomyopathy group was the only diagnostic group in the current study with normative scores across all self- and proxy-reported scales, including total, physical, and psychosocial HRQOL. While all study patients were recruited from the same multidisciplinary heart failure service, there are a few possible explanations for this group difference. First, the Children's Oncology Group guidelines recommend regular cardiac screening for those with exposure to anthracyclines [20], which is likely to result in earlier identification and treatment of heart failure symptoms. Thus, this group likely represents patients with less severe heart failure or those with less impact of heart failure on HRQOL due to earlier comprehensive heart failure management. This differs from the CHD population, for example, as many cardiologists have expressed concern that patients with CHD are referred too late for heart failure therapies [2].

Moreover, many have documented the presence of post-traumatic growth (i.e., positive changes, perspective, and/ or meaning following a traumatic event) in AYA cancer survivors [21, 22], particularly for those with greater perceived treatment severity, life threat, and fear of death [21, 23]. It is possible that resilience derived from *overcoming* or *surviving* the pediatric cancer experience serves as a protective factor in terms of maintaining HRQOL despite future long-term sequalae of cancer treatment, such as heart failure. On the contrary, other cardiomyopathies, CHD, and post-heart transplant status are viewed as chronic, life-long conditions, without periods akin to being in "remission" or "cancer-free." Engagement in psychosocial care and supports throughout the cancer journey has also been shown to be associated with greater post-traumatic growth [23], among other positive outcomes. Standardized guidelines for psychosocial care in pediatric cancer have been established since 2015 [24], whereas only recently has the field of pediatric cardiology began to emphasize such supports [25].

Similar to previous adult [19, 26] and pediatric studies [8], functional status as described by NYHA class, was strongly associated with HRQOL in the study sample. Lifetime cardiac device history, including VAD and ICD, also emerged as a correlate of HRQOL, particularly for physical functioning, which is consistent with past research [8, 27]. It is possible that cardiac device history served as another indicator of disease severity or life threat at time of survey. In a recent study of HRQOL within the Pedimacs multi-center pediatric VAD registry, physical and psychosocial HRQOL were poorer in children pre-VAD implant when compared

to children with other severe forms of heart disease or non-cardiac chronic illnesses [28].

Differing from the work of Wilmot et al. [8], the current study results indicated some differences in HRQOL by sex and race. Patients identifying as female-reported poorer physical functioning than males. This sex-based risk in HRQOL is consistent with research in adult failure [19]. In adult heart failure clinical trials, women were found to have more symptoms and signs of heart failure, received suboptimal medical treatment and device therapies, and reported worse HRQOL when compared to male counterparts [29]. Our data provide some evidence for the extension of this gender disparity in HRQOL to pediatric heart failure and underscore a critical need for additional study in this area. Among the study sample, patients identifying as non-white (25% of the sample) reported significantly better HRQOL across total, physical, and psychosocial subscales. In a large adult heart failure sample, HRQOL was rated more positively by Hispanic patients than by non-Hispanic white patients [30]. Others have documented ethnic differences in HRQOL in adult heart failure, with HRQOL being lowest in Malay and Chinese patients, moderate in black and Indian patients, and highest in white, Japanese, and Korean patients. Disease self-efficacy was noted to be highest in white and black patients [31]. Current study findings must be replicated before major takeaways can be made, but it is possible that some racial and cultural experiences of underrepresented minority groups, such as "rising" above hardships and inequities [32], extended family and community supports [33], and greater spirituality[33] provide some buffering against the negative impact of pediatric heart failure on HRQOL.

Although others have documented associations between HRQOL and family income in pediatric CHD [26, 34, 35], study findings are most consistent with recent results reported by the Pediatric Heart Network [36] with no significant associations detected in the current study between family income and patient-reported total and physical HRQOL. Patients with family-reported income in the middle to upper class range ($75,000 or greater) endorsed higher mean psychosocial HRQOL score than those with family income less than $75,000, but this did not reach statistical significance. While it is encouraging that no strong associations were detected between HRQOL and family income in this single-center experience, findings highlight the value of screening for social determinants of health and the significance of integrated support services for patients and families in pediatric heart failure care, including social work, financial/transportation coordinators, and education/school liaisons. Parental educational level was also examined as a potential correlate of HRQOL, but only maternal education was found to be significant. Patient-reported psychosocial functioning was lower in those with a mother with a college degree compared to those with a mother without a college degree. It is likely that another covariate

not captured by the current study, such as parental anxiety or illness expectations, may better explain this association. Much like our null findings between parental education, total HRQOL, and physical functioning, maternal education was unrelated to HRQOL in the recent Pediatric Heart Network study of young children with single-ventricle CHD [36].

Findings should be interpreted with consideration of study limitations. First, this was a single-center study with patients recruited from a single heart failure clinic/inpatient service. Thus, it is possible that some eligible patients at the study center were not approached for participation. Despite our single-center sample, recruitment efforts were very successful, surpassing sample size power estimates and capturing a diverse representation of participants. Second, for analyses purposes, race as a correlate was defined as white vs non-white. As shown in Table 1, participants identified across diverse racial groups. The sample size did not allow for further analysis based on race, but we acknowledge the distinct and unique experiences that occur across racial and ethnic groups. Additionally, non-English-speaking participants were not included, further limiting our study of important racial and ethnic factors. The cross-sectional study design also limited detection of causal patterns. Further, although by design the inclusion criteria was broad to capture the heterogeneity of pediatric heart failure, we recognize the differing presentations, disease courses, therapies, and impairments among the study sample. This is a heterogeneous sample representing patients at difference phases in heart failure course. Lastly, although much of the data were collected prior to the COVID-19 pandemic, some study data were collected beyond March 2020. It is possible that the COVID-19 pandemic, much like other non-health-related stressors that may occur in an AYA's life, impacted HRQOL reporting. For example, among an international sample of young people and caregivers with heart disease, general stress was found to be very high during the initial months of the first wave of the pandemic [37].

Results of the current study elucidate important future directions for research and practice. First, similar to adult heart failure, HRQOL assessments should become a standard component of pediatric heart failure clinical care and research trial endpoints. ACTION (Advanced Cardiac Therapies Improving Outcomes Network) has demonstrated the feasibility of collecting patient-reported outcomes (PROs), including HRQOL, in pediatric and young adult patients pre-VAD implant and throughout the VAD course. Continued study of the utility of PROs to inform clinical practice and predict outcomes is needed [38, 39]. This can be accomplished through multi-center learning network collaborations and registries, such as those hosted by ACTION and Pedimacs. Further, multi-center studies would allow for larger, racially, and ethnically diverse samples, increasing our understanding of these important factors. As this study demonstrates, discrepancies in patient and proxy/parent report exist, thus, we must continue to engage AYAs themselves in research to better understand their healthcare needs and outcomes [39, 40]. With advanced statistics, such as machine learning, we may be able to better understand risk and resilience factors, including sex and race, smaller samples of pediatric heart failure patients with regards to HRQOL, physical, and psychosocial outcomes. Importantly, results point to the potential benefits of resiliency-focused interventions in pediatric-advanced heart disease. Such interventions have been trialed in other pediatric chronic illness conditions, such as cancer, with demonstrated success. Lastly, another opportunity for bolstering HRQOL includes the enhancement of physical activity in pediatric and young adult patients with heart failure. Associations between physical activity and HRQOL have been shown in Fontan [41] populations. As larger datasets are cumulated to inform science and practice in pediatric and young adult heart failure, efforts to provide targeted interventions to those at greatest risk of impaired HRQOL will be necessary.

In summary, sociodemographic and disease-specific risk and resilience factors specific to HRQOL in AYAs with heart failure include primary cardiac disease, race, sex, and functional status. Building upon extensive work in adult heart failure, utilization and study of HRQOL as a clinical and research trial outcome are necessary in pediatric heart failure. Developing targeted interventions for those at greatest risk of impaired HRQOL is an important next step.

Declarations

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