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Title: Self-reported quality of life in children on ventricular assist devices

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Running title: Quality of life in children with VADs

List of non-standard abbreviations: quality of life (QOL), ventricular assist device (VAD), Pediatric Quality of Life Inventory (PedsQL), Society of Thoracic Surgeons Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs), interquartile range (IQR), Advanced Cardiac Therapies Improving Outcomes Network (ACTION)

ABSTRACT

Background: We sought to describe quality of life (QOL) in children on ventricular assist device (VAD) and to identify factors associated with impaired QOL.

Methods: There were 82 children (6-19 y) in the Pediatric Interagency Registry for Mechanical Circulatory Support who completed the Pediatric Quality of Life Inventory (PedsQL) +/- a VAD-specific QOL assessment pre-VAD implant (n=18), 3 months post-VAD (n=63) and/or 6 months post-VAD (n=38). Significantly impaired QOL is a score >1 SD below norms.

Results: Study patients were 59% male, 67% Caucasian, with cardiomyopathy diagnosis in 82%, and median age at implant of 14 y (IQR 11-17). PedsQL scores were lower than norms for physical ($p<.0001$) and psychosocial ($p<.01$) QOL in pre- and post-VAD groups. Compared to chronic health condition and complex or severe heart disease groups, PedsQL scores were lower for physical and psychosocial QOL in the pre-VAD group ($p<.0001$), however psychosocial QOL was not significantly different in post-VAD groups. Psychosocial QOL was impaired in 67%, 40%, and 24% in pre-VAD, 3-month, and 6-month post-VAD groups respectively. Total and psychosocial QOL scores were significantly higher in the 3-month and 6-month post-VAD group than pre-VAD (all $p\leq0.02$). VAD patients were most bothered by their inability to participate in usual play activities. Impaired QOL 3 months post-VAD was associated with inotropic support >2 weeks/ongoing post-VAD ($p=.04$).

Conclusion: Physical QOL is significantly impaired in most children pre- and post-VAD. However, psychosocial QOL is not significantly impaired in most children post-VAD suggesting VAD implantation may improve psychosocial QOL in children. **INTRODUCTION**

Over the past decade, ventricular assist devices (VADs) have been increasingly utilized in children with end-stage heart failure[1, 2] and have led to significantly improved survival in this population.[3, 4] It is important, however, that success not be measured by mortality and morbidity alone. Quality of life (QOL) is a multidimensional construct which includes physical, psychological, and social functioning. When effective, a VAD augments circulation, increases functional capacity, and decreases heart failure symptoms and these effects should be reflected in the assessment of the patient's QOL. Thus, QOL has emerged as an important outcome of VAD therapy.

The positive impact that VADs have on QOL in adults is well-established.[5] QOL has been examined in children with heart disease,[6] children with heart failure[7], and pediatric heart transplant

recipients.[8, 9] The one previous analysis of QOL of children while on VAD support was limited by its small, single-center sample and variable and unclear timing of QOL evaluations after VAD.[10] In light of the ever-present donor shortage, increasing waitlist times and consideration of VADs as chronic therapy in pediatrics,[4, 11] there is a need for data on QOL in children while on VAD support.[12]

The Society of Thoracic Surgeons Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs), a National Institutes of Health-sponsored United States database, provides a unique multicenter source of data to answer important questions about QOL in pediatric VAD recipients. We sought (1) to describe self-reported QOL in children on VAD support and (2) to identify potential factors associated with impaired QOL. We hypothesized that pediatric patients who survive after VAD implant would have improved total, psychosocial and physical QOL.

METHODS

Patient population

Patients enrolled in Pedimacs, aged 6 to 19 years of age, who completed the Pediatric Quality of Life Inventory (PedsQL) +/- a VAD-specific QOL measure developed for the study at any of 3 time-points (pre-VAD implant, 3months post-VAD implant, or 6 months post-VAD implant) from 2012-2019 were included in the study. Patients who died or were transplanted prior to 3-month questionnaire completions were excluded. Patients who did not have completed measurements (intubated and/or sedated, "too sick", administrative/coordinator issues) were also excluded. The documented reasons for why the PedsQL was not completed at certain time points for the study cohort are displayed in Supplemental Table 1. The study was designated by the Institutional Review Board as not regulated.

Procedures and Measures

To assess health-related QOL, patients completed the Pediatric Quality of Life Inventory.[13] The 23-item PedsQL 4.0 Generic Core Scales (Total PedsQL) encompass Physical Functioning (Physical PedsQL), Emotional Functioning, Social Functioning, and School Functioning. Items are reverse-scored and linearly transformed to a 0 – 100 scale, so that higher scores indicate better QOL. To create a Psychosocial Health Summary (Psychosocial PedsQL) score, the mean is computed as the sum of the items divided by the number of items in the Emotional, Social, and School functioning scales. The reliability and validity of the PedsQL Generic Core Scales has been demonstrated in healthy and patient populations.[13, 14] Published self-report internal consistency reliabilities exceed the minimum alpha coefficient standard of .70 for group comparisons in 8-18 year olds (range .75-.91). Across the ages, the Generic Core Scales Total Score for child self-report approached or exceeded an alpha of .90,

recommended for individual patient analysis.[13] Significantly impaired QOL is defined as a score >1 SD below norms as previously described.[13]

An investigator-designed VAD-specific QOL questionnaire was also administered to patients who were supported by VAD at 3-months and 6-months following initial VAD implant. Discussions with VAD health care providers and focused-interviews with parents of children on VADs formed the basis for the VAD-specific QOL item generation. The resultant VAD-specific QOL measure has 12 items, including two overall ratings of worry and level of happiness. The remaining 10 items inquire about specific physical or psychosocial concerns, including noise, limited mobility, sleep difficulty, discomfort, play restrictions, social isolation, appearance, and worry about the VAD breaking/malfunctioning. Items were scored as above for the PedsQL.

The VAD-specific scale internal consistency reliability was determined by calculating Cronbach's coefficient alpha. The reliability of the VAD-specific QOL child self-report measure exceeded the reliability standard of 0.70 for group comparison, α coefficients ranging from 0.72 to 0.79. The VAD-specific score was significantly correlated with the total PedsQL QOL score at 3-months post-VAD (Pearson correlation coefficient r=0.50, p=0.0003) and 6-months post-VAD (r =0.54, p=0.002) supporting the validity. All patient characteristics data were obtained through Pedimacs.

Statistical analyses

Descriptive statistics were reported as mean ± standard deviation or median with interquartile range (IQR) for continuous variables, depending on distributional assumptions, and frequency with percentage for categorical variables. Mean PedsQL scale and summary scores were calculated at pre-implant, 3 months and 6 months post-VAD implant. Significant impaired QOL was reported as frequency (percentage) at each time point. Differences in PedsQL scores between pre-implant group and 3- and 6-month post-VAD implant groups were examined using two-sample t-test. Cohen's d effect size for difference was calculated as mean difference between the two time points divided by the pooled standard deviation of the two time points, indicating small (.20), medium (.50), and large (.80).[15] Additionally, paired t-test was used to assess for changes in individual patients' PedsQL scores between pre-implant and 3- and 6-month post-VAD implant. PedsQL scores for the VAD patients were compared to children with a chronic health condition (asthma, diabetes, attention deficit hyperactivity disorder, depression, or other),[13] complex or severe heart disease non-VAD children (which includes ambulatory patients with uncorrectable or palliated heart disease including single ventricles),[16] and a healthy pediatric population of the same age[13] using two-sample t-tests. Similarly, effect sizes for the differences were also reported. Univariate associations of patient and clinical characteristics with impaired Total PedsQL at 3-month follow-up since

device implant were evaluated using Chi-square test or Fisher's exact test for categorical variables and Wilcoxon rank sum test (if not normally distributed) or two-sample t-test for continuous variables, as appropriate. Similar comparisons were made for (continuous) VAD-specific QOL scores at 3-month follow-up since device implant using two-sample t-test or Wilcoxon rank sum test for categorical variables and Spearman correlation coefficient for continuous variables. All analyses were performed using SAS Version 9.4 (SAS Institute Inc, Cary, NC). A p-value < 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

There were a total of 482 new patients, age 6-19 years, enrolled in Pedimacs during the study period of which 191 and 105 were alive on device at 3 and 6 months post-implant respectively. A total of 82 patients completed surveys at one or more time points (18 patients pre-implant, 63 patients at 3 months post-implant, and 38 patients at 6 months post-implant). Of the 82 patients included, 13 patients had both pre-implant and 3-month follow-up PedsQL scores and 10 patients had both pre-implant and 6-month follow-up scores. Patient characteristics are shown in Table 1. Median age at VAD implant was 14 years (IQR 11-17 years). Of the 82 study patients, 55 (67%) were Caucasian/white, 67 (82%) had a primary diagnosis of cardiomyopathy, 78 (95%) were on intravenous inotrope infusion pre-VAD, 58 (71%) were NYHA Functional Class IV, and 49 (60%) had a patient profile of 2 ("progressive decline on inotropic support"). A minority of patients (24%) had a patient profile of 1 ("critical cardiogenic shock"), were intubated at the time of implant (29%) and had a history of extracorporeal membrane oxygenation (10%). Most study patients received an implantable continuous flow device (85%). Device strategy was mostly bridge to transplant (39%) or bridge to candidacy (54%). At 3 and 6 months post-VAD, 63% and 81% were outpatient.

Mean PedsQL scores before VAD implant, at 3 months post-implant and at 6 months post-implant are presented in Table 2. As reported by pediatric VAD recipients, 78% had scores more than 1 standard deviation below the population mean for total QOL in the pre-VAD group, 60% in the 3-month post-VAD group, and 50% in the 6-month post VAD group (Table 2). Impaired Psychosocial PedsQL scores were observed in 67% of the pre-VAD group, 40% of the 3-month post-VAD group, and 24% of the 6-month post-VAD group.

Differences in PedsQL scores by group

Mean Total Peds QL scores were significantly higher in the 3-month (64.5, p=0.02) and 6-month (69.5, p=0.003) post-VAD groups than the pre-VAD group (54.0, Tables 2-3). Psychosocial PedsQL

scores were higher in the 3-month and 6- month post-VAD groups than the pre-VAD group (mean 69.7 and 75.4 vs. 56.5, p=0.004 and 0.0003 respectively, Table 3). There was no significant difference in Physical PedsQL scores across the three groups.

Changes in PedsQL scores within-patient

For the patients with repeated measures, within-patient comparisons on the PedsQL scores did not reach statistical significance with the small sample size. However, Total and Psychosocial PedsQL scores at 6-month follow-up increased by a mean of 14.3 ± 25.6 (p=0.11) and 20.1 ± 29.0 (p=0.06) respectively compared with pre-implant scores.

Comparison of QOL Scores across VAD, heart disease and healthy groups

Comparisons of PedsQL mean scores for children supported with VAD, children with complex or severe heart disease, children with a chronic health condition, and healthy pediatric norms are shown in Table 4.[13, 16] Total, Physical, and Psychosocial PedsQL mean scores were significantly lower in children pre-VAD implant and at 3 and 6 month post-VAD follow-up as compared with healthy peers (all $p<0.01$). In comparison with children with a chronic health condition and children with complex or severe heart disease specifically, Physical PedsQL mean scores were significantly lower in children pre-VAD implant, at 3 months post-VAD, and at 6 months post-VAD (all $p<.0001$) and Psychosocial PedsQL mean scores were lower in children pre-VAD implant ($p<0.001$). However, at 3 month and 6 month follow-up post-VAD, Psychosocial PedsQL, including emotional, social, and school functioning, was not significantly different when compared with children with a chronic health condition and with complex or severe heart disease.

Specific concerns in children on VADs

The VAD-specific QOL questionnaire was completed by 52 patients at the 3-month follow-up and the results are shown in Table 5. Being unable to "participate in usual play activities with the VAD" was noted by 42% of the patients as occurring "always" or "very often." Additionally, 27% of respondents reported "always" or "very often" being unable to "visit family or friends outside the home or hospital with the VAD" and 23% not being able to "move easily from place to place with the VAD." Of note, 42% of the patients had "low" "day-to-day level of worry with the VAD" and 42% also described "day-to-day level of happiness with the VAD" to be "high."

Correlates of Quality of Life Scores in VAD Recipients

Three months after VAD implant, univariate analysis revealed impaired Total Peds QL was associated with prolonged inotropic support greater than 2 weeks (or ongoing) post-implant (p=0.04). Impaired Total Peds QL was not associated with demographic characteristics including patient sex, race, age at implant, primary diagnosis, patient profile, device class, intensive care or overall hospital length of stay, adverse events, patient status (inpatient vs. outpatient) at 3-month follow-up, or re-hospitalizations after discharge (Table 6). There were no patient and clinical characteristics associated with VAD-specific QOL score.

DISCUSSION

In this study, we found that overall QOL was significantly impaired in the majority of children before and after VAD implant compared to healthy peers and children with chronic conditions including complex or severe heart disease. In patients following VAD implantation, however, Total PedsQL scores were higher and there was less impairment in Psychosocial PedsQL, with scores that were similar when compared with children with a chronic health condition and with complex or severe heart disease. At the three-month follow-up, patients who received inotropic support for more than 2 weeks post-implant were more likely to have impaired Total PedsQL scores.

This analysis is the first multi-center study of self-reported QOL in children while on VAD support to date. Several studies have shown that QOL after heart transplant for children bridged to transplant with VADs is favorable and comparable to the QOL of pediatric heart transplant recipients who were not bridged with VADs.[9, 17, 18] However, these studies did not assess the QOL while on VAD. Our study builds upon important qualitative work that has sought to capture the experience and impact of VAD support in a small sample of children through direct interviews.[19, 20] Many of the limitations and emotions articulately described by these individual patients likely represent shared experiences as they were consistent with the impaired PedsQL scores that we found across a larger cohort of patients.

One earlier, single-center study by Miller et al evaluated the self-reported PedsQL in 13 pediatric patients (10 on paracorporeal pulsatile devices and 3 on implantable continuous flow devices).[10] Similar to our study, they found that mean PedsQL scores of children supported on VAD were significantly lower than healthy controls, outpatients with complex or severe heart disease, and children after heart transplant. They also found that psychosocial function after VAD was better, with scores that were comparable to these latter two comparison groups. We found it encouraging that Psychosocial PedsQL scores were higher in patients after VAD and similar to the scores of ambulatory children with a chronic health condition, including complex heart disease. Likewise, in the small group with scores before and after VAD implant, we saw a clear trend towards improved psychosocial QOL in those individuals. These data

support that VADs can not only increase survival for children with severe, life-threatening heart failure but may also improve emotional, social, and school functioning in children. Nevertheless, 40% of children at 3 months and 24% of children at 6 months continue to have impaired Psychosocial PedsQL scores. These data add to what is known about the mental health complexities of children on VADs, as Diaz and colleagues found that 40% (105/264) of children ≥8 years old requiring VAD support at time of transplant were diagnosed with a psychiatric disorder.[21] As recommended by the recently published guidelines, comprehensive psychosocial evaluation is an essential part of the pre-implant assessment process.[22, 23] Additionally, ongoing psychosocial and mental health screening, assessment, and intervention to address the many psychosocial challenges that our children face on VADs must be prioritized.[12] This study also highlights the ongoing impairments in physical QOL for children supported with VADs. Despite the progress made in this field, these Physical PedsQL data show that many children have difficulty with walking, play/activity, lifting, fatigue, aches/pains, and bathing post-implant.

We found that prolonged inotropic support (≥2 weeks) after implant was a factor associated with impaired Total PedsQL. This was not completely unexpected as prolonged use of inotropes after VAD implant is generally for right heart failure or may reflect suboptimal circulatory support. Right heart failure is directly correlated with more critical pre-implant status and often results in refractory heart failure symptoms, end-organ dysfunction, and higher mortality which all may directly impact QOL.[24, 25] There were more outpatients (compared with inpatients) with normal PedsQL scores at 3 months however this association did not reach statistical significance. This result, along with other negative findings, may reflect the low numbers and insufficient power to detect differences. Nevertheless, our study lends support to the idea that most patient and device characteristics, pre-implant severity, and post-implant disposition were not directly correlated with self-reported QOL and that there is universal risk of impaired QOL. QOL must be explicitly assessed in all patients to better understand and improve their experience.

As mortality and serious adverse event rates have decreased, we must focus greater attention on the QOL for children living with VADs. To do so, our results show that we must improve the physical functioning of these patients. A recent study has shown that there is great variability in the functional assessment and rehabilitation of children on VADs due in large part to the providers' lack of experience and knowledge.[26] In an effort to promote greater physical function and rehabilitation in children on VADs, Advanced Cardiac Therapies Improving Outcomes Network (ACTION), a large quality improvement collaborative focused on improving pediatric heart failure care, is actively working on the development and implementation of standardized pediatric VAD rehabilitation protocols to address this area of need.[27] The VAD-specific QOL questionnaire was important because it identified some concerns and struggles in patients that we would typically not necessarily ask about. In the VAD-specific QOL

questionnaire, patients were quite frequently bothered by not being able to participate in "usual play activities" This finding highlights the importance of child-life, physical, and occupational therapists to closely collaborate with the bedside providers in facilitating and accommodating as much age-appropriate play as possible. Children were also bothered by not being able to visit with loved ones. Care teams need to advocate for more visitation opportunities and outings when possible and utilize virtual connections to overcome limitations. ACTION is also working on increasing the discharge rate for children on VADs and sharing best practices for ways to normalize, as best we can, the lives of these children and to directly address these reported concerns.[28] We noted that unlike in previous eras, the noise of the VADs was rarely a concern. We hope that future technological advancement, such as smaller drivers, peripherals, and pumps, can allow children to be more mobile, confident, and comfortable with their hardware. It was noteworthy that most children did not endorse high day-to-day levels of worry in this questionnaire.

Many potentially eligible patients did not complete the QOL surveys which limits the generalizability and power of the study. The main reason for not completing the survey pre-implant was that the patient was "too sick" and thus the PedsQL instrument could not be applied. In a previous survey of VAD coordinators from Pedimacs centers regarding QOL forms, over 70% felt that the primary reason for incomplete pre-implant forms was "inappropriate time to ask families/patients given the severity of illness and that the questions did not feel applicable at the time."[29] Post-implant, the main reasons cited for incomplete forms were administrative constraints (likely staffing and time constraints). Since many patients did not complete assessments at each time point (no longer on VAD or assessment not completed), the sample size at the three time points varied and there was limited data for analysis of changes in scores within patients over time. We also acknowledge that there is likely response and participant bias in a registry study such as this one. Nevertheless, this study is still, by far, the largest, multi-center study of QOL in children on VADs. These results are important as they highlight specific targets for intervention in this at-risk population. The limitations of our study are an important call to the field to develop more reliable methods of collecting QOL and other patient reported outcomes and be able to evaluate for changes in specific patients' QOL over time. Future work should also study longitudinal changes in the QOL in children on longer-term, chronic VAD therapy as this population was inadequately addressed in this study and is likely to have unique challenges. ACTION has subsequently designed and launched mobile apps and direct text messaging to collect patient reported outcomes more consistently from patients and families. An early pilot experience across six ACTION centers demonstrated high clinician satisfaction with this data collection approach as well as excellent completion rates of measures by eligible parents and patients.[30] Careful attention must be paid to ensure diverse and underrepresented groups are reached in these efforts.

Despite tremendous advancement and improved survival with VADs in children, children on VAD support have significant impairments in QOL, particularly in the physical domain. Greater focus and innovation must be directed towards physical rehabilitation in this population. Total and psychosocial PedsQL scores were higher in children after VAD implant. Our data also suggest that VADs in children with severe heart failure may improve their psychosocial QOL while on support. Efforts to capture QOL more reliably and identify more areas for targeted intervention in children with VADs should be prioritized.

Author contributions

DP, SY, RL, JS, EB, KU were involved in the design of this project. SY, RL performed the data analysis. DP, SY, CV, MC, JS, EB, KU contributed to the interpretation of results, writing the manuscript, revision of the manuscript, and approval of the final version.

Conflicts

None of the authors have relevant disclosures to report.

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TABLES

Table 1. Patient characteristics prior to implant and at time of implant (N=82)

Age at VAD implant, years	14 (11-17)
Weight at VAD implant, kg	56.3 ± 28.7
Male sex	48 (58.5)
Caucasian race	55 (67.1)
Diagnosis	
Congenital heart disease	10 (12.2)
Cardiomyopathy	67 (81.7)
Other	4 (4.9)
Unknown	1 (1.2)
Patient profile	
1. Critical Cardiogenic Shock	20 (24.4)
2. Progressive Decline	49 (59.8)
3. Stable but Inotrope Dependent	10 (12.2)
4. Resting Symptoms	2 (2.4)
Not Specified	1 (1.2)
Device type	
LVAD	70 (85.4)
RVAD	3 (3.7)

	BiVAD	8 (9.8)
	Total Artificial Heart	1 (1.2)
Device class		
	Paracorporeal Pulsatile	7/79 (8.9)
	Paracorporeal Continuous	2/79 (2.5)
	Implantable Continuous	67/79 (84.8)
	TAH	1/79 (1.3)
	Percutaneous	2/79 (2.5)
Device strategy		
	Bridge to Transplant (listed)	32 (39.0)
	Bridge to Candidacy – Likely to be eligible	44 (53.7)
	Destination Therapy (patient definitely not eligible transplant	2 (2.4)
	Bridge to Recovery	3 (3.7)
Genetic syndrome		3 (3.7)
Previous cardiac operation		29 (35.4)
ECMO history		8 (9.8)
Stroke history		1 (1.2)
Sedated prior to implant		19 (23.2)
Paralyzed prior to implant		8 (9.8)
Intubated prior to implant		24 (29.3)
Ambulating prior to implant		36 (43.9)
IV inotrope support at implant		78 (95.1)
NYHA class		
	I/II	0 (0.0)
	III	13 (15.9)
	IV	58 (70.7)
	Unknown	11 (13.4)

* Data are presented as N (%) for categorical variables and median (interquartile range) or mean ± standard deviation for continuous variables.

Table 2. PedsQL by self-report for children before VAD implant and 3 and 6 months after device implant

	Pre-implant (N=17-18)[¥]	**3-month F/U** (N=54-63)[¥]	**6-month F/U** (N=34-38)[¥]
PedsQL (core) Total score	54.0 ± 15.7	64.5 ± 17.3	69.5 ± 17.8
Physical functioning score	49.5 ± 18.7	55.9 ± 26.5	59.0 ± 26.5
Psychosocial Summary score	56.5 ± 19.6	69.7 ± 15.6	75.4 ± 15.6
Emotional functioning score	53.9 ± 29.5	68.4 ± 19.6	75.5 ± 19.6
Social functioning score	65.6 ± 21.7	75.2 ± 15.4	78.5 ± 15.1
School functioning score	50.3 ± 21.4	65.1 ± 24.6	71.2 ± 20.6
Impaired Total (< 69.71)	14/18 (77.8)	37/62 (59.7)	19/38 (50.0)
Impaired Physical functioning (< 72.98)	16/18 (88.9)	45/63 (71.4)	25/38 (65.8)
Impaired Psychosocial Summary (< 66.03)	12/18 (66.7)	25/62 (40.3)	9/38 (23.7)
Impaired Emotional functioning (< 59.57)	9/18 (50.0)	17/62 (27.4)	8/38 (21.1)
Impaired Social functioning (< 66.61)	10/18 (55.6)	18/60 (30.0)	9/38 (23.7)
Impaired School functioning (< 62.99)	12/17 (70.6)	26/54 (48.1)	12/34 (35.3)

[*] Data are presented as N (%) for categorical variables and Mean ± Standard deviation for continuous variables.

[¥] N is a range because certain patients did not complete all the scales. N for each scale is noted in the denominator under the lower part of the table ('Impaired').

Table 3. Differences in PedsQL by groups

	Pre-implant to 3-month F/U (N=17-18)¥			Pre-implant to 6-month F/U (N=54-63)¥			3-month to 6-month F/U (N=34-38)¥		
	Difference	P-value	Effect size	Difference	P-value	Effect size	Difference	P-value	Effect size
PedsQL (core) Total score	10.5 ± 17.0	0.02	0.62	15.5 ± 17.1	0.003	0.90	5.0 ± 17.5	0.17	0.28
Physical functioning score	6.4 ± 25.0	0.34	0.26	9.5 ± 24.3	0.18	0.39	3.1 ± 26.5	0.57	0.12
Psychosocial Summary score	13.2 ± 16.5	0.004	0.80	18.8 ± 17.0	0.0003	1.11	5.7 ± 15.6	0.08	0.36
Emotional functioning score	14.5 ± 22.2	0.06	0.66	21.6 ± 23.2	0.01	0.93	7.1 ± 19.6	0.08	0.36
Social functioning score	9.6 ± 17.0	0.04	0.56	13.0 ± 17.5	0.01	0.74	3.4 ± 15.3	0.29	0.22
School functioning score	14.8 ± 23.9	0.03	0.62	20.9 ± 20.9	0.001	1.00	6.1 ± 23.1	0.23	0.26

* Data are presented as Mean ± Standard deviation.

‡ P-value from two-sample t-test.

δ Effect size is calculated as mean difference between the two time points divided by the pooled standard deviation of the two time points; small (.20), medium (.50), and large (.80).

¥ N is a range because certain patients did not complete all the scales. N for each scale is noted in the denominator under the lower part of the Table 2 ('Impaired').

Table 4. Comparison of PedsQL by VAD patient report to Healthy pediatric population, Children with a chronic health condition, and Children with complex or severe heart disease without VAD

	Comparison	Pre-implant	P-value	Effect size	3-month F/U	P-value	Effect size	6-month F/U	P-value	Effect size
Healthy pediatric population[1]	N=5,026-5,079	N=17-18			N=54-63			N=34-38		
PedsQL (core) Total score	83.9 ± 12.5	54.0 ± 15.7	<.0001	2.39	64.5 ± 17.3	<.0001	1.54	69.5 ± 17.8	<.0001	1.15
Physical functioning score	87.8 ± 13.1	49.5 ± 18.7	<.0001	2.91	55.9 ± 26.5	<.0001	2.39	59.0 ± 26.5	<.0001	2.17
Psychosocial Summary score	81.8 ± 14.0	56.5 ± 19.6	<.0001	1.81	69.7 ± 15.6	<.0001	0.87	75.4 ± 15.6	0.005	0.46
Emotional functioning score	79.2 ± 18.0	53.9 ± 29.5	<.0001	1.40	68.4 ± 19.6	<.0001	0.60	75.5 ± 19.6	0.21	0.20
Social functioning score	85.0 ± 16.7	65.6 ± 21.7	<.0001	1.16	75.2 ± 15.4	<.0001	0.59	78.5 ± 15.1	0.02	0.39
School functioning score	81.3 ± 16.1	50.3 ± 21.4	<.0001	1.93	65.1 ± 24.6	<.0001	1.00	71.2 ± 20.6	0.0003	0.63
Children with a chronic health condition[1]	N=568-574	N=17-18			N=54-63			N=34-38		
PedsQL (core) Total score	74.2 ± 15.4	54.0 ± 15.7	<.0001	1.31	64.5 ± 17.3	<.0001	0.62	69.5 ± 17.8	0.07	0.30
Physical functioning score	79.5 ± 17.1	49.5 ± 18.7	<.0001	1.75	55.9 ± 26.5	<.0001	1.30	59.0 ± 26.5	<.0001	1.15
Psychosocial Summary score	71.3 ± 17.1	56.5 ± 19.6	0.0004	0.86	69.7 ± 15.6	0.48	0.09	75.4 ± 15.6	0.16	0.24
Emotional functioning score	69.3 ± 21.4	53.9 ± 29.5	0.003	0.71	68.4 ± 19.6	0.75	0.04	75.5 ± 19.6	0.08	0.29
Social functioning score	76.4 ± 21.6	65.6 ± 21.7	0.04	0.50	75.2 ± 15.4	0.68	0.06	78.5 ± 15.1	0.54	0.10
School functioning score	68.3 ± 19.1	50.3 ± 21.4	0.0001	0.94	65.1 ± 24.6	0.26	0.16	71.2 ± 20.6	0.38	0.15
Children with complex or severe heart disease[2]	N=78	N=17-18			N=54-63			N=34-38		
PedsQL (core) Total score	75.8 ± 13.9	54.0 ± 15.7	<.0001	1.53	64.5 ± 17.3	<.0001	0.73	69.5 ± 17.8	0.04	0.41

Physical functioning score	78.4 ± 17.7	49.5 ± 18.7	<.0001	1.62	55.9 ± 26.5	<.0001	1.02	59.0 ± 26.5	<.0001	0.93
Psychosocial Summary score	74.4 ± 15.0	56.5 ± 19.6	<.0001	1.12	69.7 ± 15.6	0.07	0.30	75.4 ± 15.6	0.75	0.06
Emotional functioning score	74.7 ± 21.0	53.9 ± 29.5	0.001	0.91	68.4 ± 19.6	0.07	0.31	75.5 ± 19.6	0.84	0.04
Social functioning score	77.7 ± 19.0	65.6 ± 21.7	0.02	0.62	75.2 ± 15.4	0.41	0.14	78.5 ± 15.1	0.81	0.05
School functioning score	71.0 ± 18.2	50.3 ± 21.4	<.0001	1.10	65.1 ± 24.6	0.12	0.28	71.2 ± 20.6	0.95	0.01

[*] Data are presented as Mean ± Standard deviation. N is a range because certain patients did not complete all the scales.

[1] Varni JW, Burwinkle TM, Seid M, Skarr D. The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. Ambul Pediatr 2003;3:329-41 (Table 2).

[2] Varni JW, Limbers CA, Burwinkle TM. Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. Health Qual Life Outcomes 2007;5:43 (Table 4).

[δ] Effect size is calculated as mean difference between the study cohort and the comparison population divided by the pooled standard deviation of the two groups at each time point; small (.20), medium (.50), and large (.80).

Table 5. VAD-specific QOL questionnaire by patient report at 3-month follow-up since device implant (N=52)

	Always	Very Often	Sometimes	Rarely	Never
1. The VAD noise bothers me when I am awake	2 (3.8)	3 (5.8)	2 (3.8)	13 (25.0)	32 (61.5)
2. The VAD noise bothers me when I am trying to sleep	3 (5.8)	2 (3.8)	7 (13.5)	5 (9.6)	35 (67.3)
3. I have pain or discomfort at the driveline or tubing pump exit site	2 (3.8)	2 (3.8)	20 (38.5)	13 (25.0)	15 (28.8)
4. I have difficulty sleeping due to the position of the driveline or tubing pump exit site	2 (3.8)	2 (3.8)	16 (30.8)	10 (19.2)	22 (42.3)
5. I am bothered by how I look with the VAD	5 (9.6)	6 (11.5)	12 (23.1)	6 (11.5)	23 (44.2)
6. I worry about the VAD breaking or malfunctioning	6 (11.5)	5 (9.6)	18 (34.6)	10 (19.2)	13 (25.0)
7. I am bothered that I cannot visit family or friends outside the home or hospital with the VAD	10 (19.2)	4 (7.7)	7 (13.5)	11 (21.2)	20 (38.5)
8. I am bothered that I cannot move easily from place to place with the VAD	7 (13.5)	5 (9.6)	14 (26.9)	8 (15.4)	18 (34.6)
9. I cannot participate in usual play activities with the VAD	10 (19.2)	12 (23.1)	16 (30.8)	9 (17.3)	5 (9.6)
10. I find it difficult to express feelings and talk to others about the VAD	5 (7.7)	2 (3.8)	13 (25.0)	9 (17.3)	24 (46.2)
	High	**Medium-High**	**Medium**	**Low-Medium**	**Low**
11. Overall, I would describe my day-to-day level of worry with the VAD to be	1 (1.9)	0 (0.0)	17 (32.7)	12 (23.1)	22 (42.3)
12. Overall, I would describe my day-to-day level of happiness with the VAD to be	22 (42.3)	9 (17.3)	16 (30.8)	3 (5.8)	2 (3.8)

* Data are presented as N (%).

Table 6. (Univariate) Associations of Patient and clinical characteristics with Impaired Total PedsQL at 3-month follow-up after device implant (N=62)

Characteristics	All (N=62)	Impaired (Total) PedsQL		P-value
		Yes (N=37)	No (N=25)	
Male sex	33 (53.2)	22 (59.5)	11 (44.0)	0.19
Age at implant, years	13 (10-16)	12 (9-16)	13 (11-16)	0.44
Weight at implant, kg	55.8 ± 29.4	56.1 ± 32.5	55.3 ± 24.7	0.92
Caucasian race	40 (64.5)	27 (73.0)	13 (52.0)	0.09
Primary diagnosis				0.73†
CHD	6 (9.7)	4 (10.8)	2 (8.0)	
Cardiomyopathy	52 (83.9)	32 (86.5)	20 (80.0)	
Other	3 (4.8)	1 (2.7)	2 (8.0)	
Unknown	1 (1.6)	0 (0.0)	1 (4.0)	
Patient profile				0.79‡
1. Critical Cardiogenic Shock	16 (25.8)	10 (27.0)	6 (24.0)	
2. Progressive Decline	36 (58.1)	20 (54.1)	16 (64.0)	
3. Stable but Inotrope Dependent	8 (12.9)	5 (13.5)	3 (12.0)	
4. Resting Symptoms	1 (1.6)	1 (2.7)	0 (0.0)	
Not Specified	1 (1.6)	1 (2.7)	0 (0.0)	
Device class				0.11¥
Paracorporeal Pulsatile	7/61 (11.5)	6/36 (16.7)	1/25 (4.0)	
Paracorporeal Continuous	1/61 (1.6)	1/36 (2.8)	0/25 (0.0)	
Implantable Continuous	50/61 (82.0)	27/36 (75.0)	23/25 (92.0)	
TAH	1/61 (1.6)	0/36 (0.0)	1/25 (4.0)	
Percutaneous	2/61 (3.3)	2/36 (5.6)	0/25 (0.0)	
Genetic syndrome	2 (3.2)	1 (2.7)	1 (4.0)	1.00
Neurological/developmental abnormalities	2 (3.2)	1 (2.7)	1 (4.0)	1.00
Previous (any) cardiac surgery	23 (37.1)	13 (35.1)	10 (40.0)	0.70
Previous congenital cardiac surgery	8 (12.9)	3 (8.1)	5 (20.0)	0.25
ECMO history	7 (11.3)	5 (13.5)	2 (8.0)	0.69
Sedated prior to implant	15 (24.2)	11 (29.7)	4 (16.0)	0.26
Paralyzed prior to implant	5 (8.1)	4 (10.8)	1 (4.0)	0.64

Intubated prior to implant		18 (29.0)	14 (37.8)	4 (16.0)	0.06
Ambulating prior to implant		26 (41.9)	13 (35.1)	13 (52.0)	0.15
Acute care (ICU/CCU) LOS since implant, days	(N=54)	17 (12-38)	20 (11-42)	17 (12-26)	0.43
Immediate/step-down care LOS since implant, days	(N=54)	12 (0-19)	12.5 (0-20.5)	11.5 (3-18)	0.88
Approximate time patient was extubated					
< 1 week		41 (66.1)	23 (62.2)	18 (72.0)	0.59
≥ 1 week		14 (22.6)	9 (24.3)	5 (20.0)	
Not specified		7 (11.3)	5 (13.5)	2 (8.0)	
Approximate time for discontinuation of inotropes					
< 2 weeks		32 (51.6)	15 (40.5)	17 (68.0)	0.04
> 2 weeks/Ongoing		23 (37.1)	17 (45.9)	6 (24.0)	
Not specified		7 (11.3)	5 (13.5)	2 (8.0)	
Hospital LOS since implant, months	(N=55)	1.1 (0.8-1.8)	1.2 (0.8-2.3)	0.9 (0.7-1.6)	0.18
Patient status at 3-month follow-up					
Inpatient		22 (35.5)	15 (40.5)	7 (38.0)	0.37
Outpatient		39 (62.9)	22 (59.5)	17 (68.0)	
Other facility		1 (1.6)	0 (0.0)	1 (4.0)	
Adverse event within 3-month follow-up since implant		45 (72.6)	28 (75.7)	17 (68.0)	0.51
Re-hospitalization within 3-month follow-up since implant		44 (71.0)	24 (64.9)	20 (80.0)	0.20

* Data are presented as N (%) for categorical variables and Median (interquartile range) or Mean ± Standard deviation for continuous variable.

§ P-value from Chi-square test or Fisher's exact test for categorical variables and Wilcoxon rank sum test or two-sample –t-test for continuous variable.

† Comparison was made as Cardiomyopathy vs. CHD or other and p-value came from Fisher's exact test.

‡ Comparison was made as Critical Cardiogenic Shock vs. Progressive Decline vs. others and p-value came from Chi-square test.

¥ Comparison was made as Implantable Continuous vs. all other and p-value came from Fisher's exact test.