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Quality of life metrics in LVAD patients after hemocompatibility-related adverse events

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Abstract

Background: Hemocompatibility-related adverse events (HRAE) negatively influence survival. However, no study has examined the impact of these events on health-related quality of life (HRQOL) and functional outcomes following continuous-flow left ventricular assist device implantation (CF-LVAD). We assessed the impact of HRAE events on HRQOL and hypothesized that HRAE's adversely impact HRQOL and functional outcomes.

Methods: INTERMACS database identified patients undergoing primary CF-LVAD implantation from 2008 to 2017. HRAEs included stroke, non-surgical bleeding, hemolysis, and pump thrombosis and were identified as defined in the literature. HRAEs were further stratified as Tier 1–2 and disabling stroke events. Time-series analysis was executed for HRAE patients with values pre-HRAE, post-HRAE, and closest to 12 months follow up. Local polynomial regression curves modeling individual patients were superimposed into “spaghetti” plots.

Results: All HRQOL and functional metrics improved in patients over time, despite HRAE complications. However, these patient metrics were significantly reduced compared to the non-HRAE cohort. Advanced data visualization techniques noted a decline after experiencing an HRAE with a subsequent recovery to baseline levels or higher. Six-minute walk test (6MWT) was noted to be most affected in the post-HRAE period but recovered similar to other metrics.

Conclusions: The burden of HRAE following CF-LVAD implantation did not negatively impact the quality of life. However, the 6MWT did not increase in the post-HRAE period in all HRAE patients. Improvement of heart failure symptoms after CF-LVAD coupled with optimal management following the HRAE act to preserve the enhanced quality of life.

KEYWORDS

adverse events, heart failure, HRAE, left ventricular assist device, quality of life

1 | INTRODUCTION

With 6.5 million Americans currently diagnosed with heart failure, it is a major source of morbidity and mortality in the United States. Exacerbation of heart failure-related symptoms has been shown to be a burden to our patients and the healthcare system.¹ For end-stage heart failure, heart transplant remains the gold standard. However, with an ever-increasing mismatch between organ need and donor heart supply, alternative treatment modalities are required.² With the improving durability and efficacy of left ventricular assist devices (LVADs), mechanical circulatory support has become a vital component of the care of heart failure patients as bridge-to-transplant and destination therapy.

As device functionality has advanced, treatment goals for VAD patients have grown ambitious. However, works like Anwer et al. have posed the question: How do we define successful implantations?³ This is a multi-level response as a successful outcome is much more than improvement in clinical status. With the newly placed alterations to patients' daily activities of living, VAD-related adverse events, and further dependence on the healthcare system, there is a complex burden to both patient and caregiver health-related quality of life (HRQoL).^{4,5}

HRQoL has been studied in depth within the CF-LVAD population. The Kansas City Cardiomyopathy Questionnaire (KCCQ) quality of life score (KCCQ QoL), physical limitation score (KCCQ PLS) the Euro-QoL EQ-5D, and the six-minute walk test (6MWT) are validated measures of patient QoL and functional status that have been studied extensively in the CF-LVAD population.⁶⁻⁸ Now widely used, these metrics provide snapshots to patient outcomes post-implant. As a whole, CF-LVAD patients have been shown to have a relatively poor quality of life but these scores do tend to improve on support overall.^{9,10} However, perceived QoL and status improvements may not be the experience in all CF-LVAD patients across the board. It is documented that patients with a self-reported poor QoL pre-implant are more likely to experience QoL improvements compared to those who identify with having an acceptable QoL.¹¹ This finding adds a layer of complexity to clinical decision making when categorizing appropriate candidates for VAD implants.

A particularly notable aspect of mechanical circulatory support and the impact on HRQoL is the propensity of adverse events and the resulting potential for worsening clinical status, increasing interaction with the health system, and exacerbating psychosocial challenges. With recent landmark clinical trials like MOMENTUM 3, a new paradigm to classify and better understand a subset of these events has been formed. Labeled Hemocompatibility-Related Adverse Events (HRAEs), these events are defined

as neurologic events, thromboembolic events, or non-surgical bleeding occurring within 6 months of the implant. Paired with a tiered hemocompatibility score (HCS) system, clinicians are developing a risk-stratification methodology to better understand etiologies of HRAEs and their impact on short-term and long-term outcomes.¹²

HRQoL and patient functional status have been well studied after adverse events. Particularly, Cowger et al. has reviewed MOMENTUM 3 data noting improvement in patient HRQoL status after implant but attenuated improvement, particularly in 6MWT distance, after serious adverse events.¹³ However, no work has yet analyzed the effect on the quality of life and functional status in patients after events now classified as an HRAE.¹⁴ As such, the aim of this study was to understand the impact of HRAEs on patient quality of life and functional status.

2 | METHODOLOGY

2.1 | Study population

This retrospective study utilized the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database to query patients undergoing continuous-flow left ventricular assist device (CF-LVAD) placement between 2008 and 2017. Unique operation and patient IDs were identified. Patients were selected for continuous flow, durable, surgically implanted devices. Only adult patients were included in the analysis. Furthermore, this cohort was partitioned by stratifying patients based on reported HRAEs. Time series data from the time of device implant to the most recent follow-up were selected.

2.2 | Identification of hemocompatibility-related adverse events

HRAEs were defined using criteria put forth by the work of Uriel and Mehra.^{12,15} This definition includes nonsurgical bleeding, neurologic events such as: stroke, TIA, or seizure, or thromboembolic events including suspected pump thrombosis or arterial thromboembolism. These events must occur within 6 months postoperatively, as per the HRAE definition (Page 6 par 2). In the context of this database analysis, HRAEs were identified in the INTERMACS data by including etiologies of adverse events most closely resembling the HRAE definition. Events of major bleeding 30 days postoperatively, neurologic events, and thromboembolic events were then combined into a composite event.

The burden of HRAEs on this cohort was further stratified using the hemocompatibility score proposed by



Mehra et al.¹⁵ Due to a lack of granularity in this data, we could only achieve a partial stratification. Patients with a disabling stroke were substituted for tier 3–4 burden, while all remaining HRAEs were considered tier 1–2.

2.3 | Quality of life metrics

Quality of life data was obtained throughout the clinical course (1) preimplant, (2) pre-HRAE, and (3) post-HRAE within a period of 12 months post-operatively. QoL was measured using the KCCQ QoL and KCCQ PLS, as well as the Euro-qol EQ-5D score. Functional status pertaining to the quality of life was assessed via 6MWT.

2.4 | Summary statistics

Demographic and clinical data were obtained and analyzed using summary statistics. Numeric variables were reported using median and interquartile ranges. Categorical variables were reported in percentages. Numeric variables were analyzed with Wilcoxon rank-sum test. Categorical variables were compared using the Chi-square test. Statistical outliers were removed from individual variables to prevent skewed results.

2.5 | Data imputation

Missing data were found in many of the functional statuses and QoL metrics noted in the database. These metric-specific variables were considered to be missing at random. Patient demographics and descriptive clinical characteristics were left as is to demonstrate the overall cohort size present in the database. Specifically, follow-up QoL and functional status variables were imputed to maintain a more robust time-series analysis for each patient in an effort to increase statistical power. Data imputation was executed using the creation of a Bayesian Network. This supervised machine learning allows for efficient creation of a network, evaluation of network structure, and subsequent imputation.

2.6 | Quality of lifetime series analysis

Quality of life variables was analyzed by selecting for values at predefined time points: score pre-HRAE, first score post-HRAE, and score closest to one-year post-op. Time from the first HRAE was the designed time point used. HRAE groups were compared at values closest to one-year post-op using aggregate data and compared via

Friedman's test. To assess individual patient changes over time between the three time points, a post hoc analysis of statistically significant Friedman's test was executed using Wilcoxon rank-sum test to compare time points individually. The use of time points associated with the timing of HRAE limits comparability to non-HRAE patients. However, in an effort to evaluate the overall progression of HRAE and non-HRAE patients, scores were compared at the time closest to one-year post-op to assess for statistical difference. p -value <0.05 was considered statistically significant.

2.7 | Visualization of time series

Data imputation allowed for a more robust quantitative analysis however, there is nuance in the existing data that is more appropriately viewed over a continuous timeline instead of specific time points. To assess these aggregate cohort changes over time, local polynomial regression curves were fitted to model individual patients. These curves were then superimposed into spaghetti plots. This process was executed using an open-source R function for visually weighted regressions.¹⁶ Automated information criterion testing was utilized to assure the most appropriate fit of the regression. Similar to the quantitative analysis, data were normalized to a time "0" being the time of HRAE. This allowed for a more accurate demonstration of the cumulative effect of an HRAE, however, this limited direct visual comparison to the non-HRAE cohort.

2.8 | Statistical software

All data organization and statistical analysis were completed using R Statistical Software version 3.6.2 (packages: "bnlearn" "data table," "dplyr," "plyr," "reshape2," "ggplot2," "RColorBrewer," "publish").

3 | RESULTS

3.1 | Demographics

A total of 21 552 patients were identified in the INTERMACs database. 3509 Patients were determined as having one or more HRAEs. A total of 18 043 were considered non-HRAE. As per protocol, all patients received support from durable, surgically implanted continuous flow VADs. The median age for the cohort was 59 [49, 66] and 78.5% male. Median height and weight were 85.5 kg [72.6, 100.9] and 175.3 cm [168.0, 182.0], respectively. 82.0% of patients underwent support with an axial device,

the remaining 18% were implanted with a centrifugal device. 76.1% of the cohort were documented NYHA Class IV with 16.9% as Class III.

3.2 | HRAEs

The HRAE group had a significantly greater percentage of centrifugal flow VADs (21.5%) compared to the non-HRAE group (17.3%) ($p < 0.001$). Patients in the HRAE group were older ($p = 0.04$), less likely to be male, and had a shorter median height ($p < 0.001$). Systolic blood pressure was also statistically higher in the HRAE group ($p = 0.03$), and HRAE patients were more likely to hold a preoperative NYHA Stage 4 designation (0.01). The remaining demographic and clinical data can be found in Table 1.

3.3 | Aggregate data visualization

Data visualization of aggregate quality of life and functional status metrics can be seen on a normalized x -axis with time zero allowing for pre and post HRAE values to be observed relative to the event. All plots demonstrated a decrease in KCCQ QoL (Figure 1), KCCQ PLS (Figure 2), 6MWT distance in feet (Figure 3), and Euro-QoL EQ-5D

(Figure 4) near the time of HRAE. However, a recovery of these metrics is observed in the post-HRAE period, with almost all groups achieving near or exceeding pre-HRAE values.

3.4 | HRAE vs. non-HRAE follow up analysis

Despite the uniform trend of improvement in reported metrics in the following months post-HRAE, when comparing the broad HRAE and non-HRAE cohorts at 12-month follow-up post-operatively, all scores were reduced in HRAE patients compared to the non-HRAE cohort at 12-month follow up (Table 2).

3.5 | Time series analysis

In the paired time-series analysis, all groups represented an improvement in the change of quality of life or functional status metrics over time. Most often pre- and post-HRAE change was limited, but by 12-month follow-up significant improvements were demonstrated (Table 2). For the KCCQ quality of life data, the entire HRAE cohort and the HRAE Tier 1–2 group showed a significantly increasing trend over time before and after HRAE

TABLE 1 Demographic and clinical data

Variable	Non-HRAE (<i>n</i> = 18 043)	HRAE (<i>n</i> = 3509)	Total (<i>n</i> = 21 552)	<i>p</i> -value
Age, median [IQR]	59 [49, 66]	60 [50, 66]	59 [49, 66]	0.04
Male, <i>n</i> (%)	12 870 (79.2)	2238 (74.5)	15 108 (78.5)	<0.001
Weight, median [IQR]	85.5 [72.7, 101.0]	85.2 [72.0, 100.2]	85.5 [72.6, 100.9]	0.26
Height, median [IQR]	175.3 [170.0, 182.9]	175 [167.6, 180.3]	175.3 [168.0, 182.9]	<0.001
Severely reduced left ventricular ejection fraction, <i>n</i> (%)	10 507 (67.1)	1918 (65.9)	12 425 (66.9)	0.34
NYHA, <i>n</i> (%)				0.01
Stage 1	22 (0.1)	2 (0.1)	24 (0.1)	
Stage 2	133 (0.8)	13 (0.4)	146 (0.8)	
Stage 3	2793 (17.2)	462 (15.4)	3255 (16.9)	
Stage 4	12 307 (75.7)	2337 (77.8)	14 644 (76.1)	
Unknown	995 (6.1)	191 (6.4)	1186 (6.2)	
VAD type				<0.001
Axial	14 925 (82.7)	2756 (78.5)	17 681 (82.0)	
Centrifugal	3118 (17.3)	753 (21.5)	3871 (18.0)	
Platelet ($\times 10^3 \mu\text{l}$), median [IQR]	187 [143, 239]	185 [137, 240]	186 [142, 239]	0.13
Hemoglobin A1c (%), median [IQR]	6.1 [5.6, 7.0]	6.2 [5.5, 7.0]	6.1 [5.6, 7.0]	0.73
Creatinine (mg/dl), median [IQR]	1.3 [1.0, 1.6]	1.3 [1.0, 1.6]	1.3 [1.0, 1.6]	0.82
Use of thrombin inhibitors, <i>n</i> (%)	16 252 (100.0)	3005 (100.0)	19 257 (100.0)	1.00

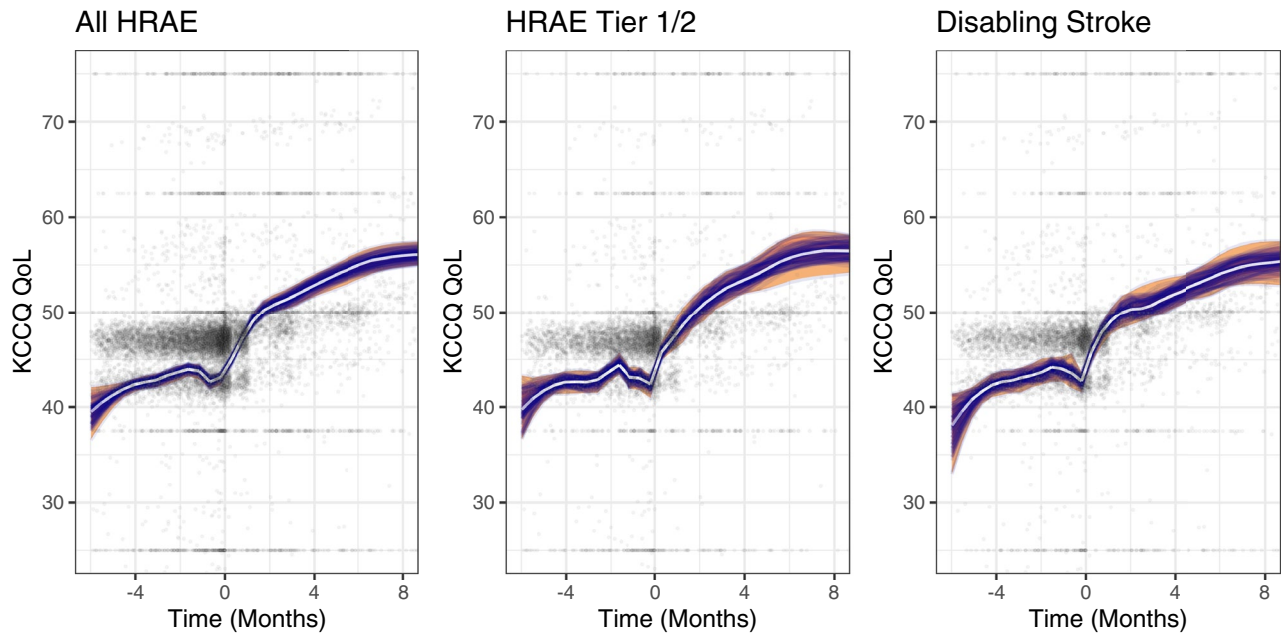


FIGURE 1 Data visualization of patient Kansas City cardiomyopathy questionnaire quality of life score in relation to HRAE. Can be appreciated that there is a distinct drop in quality of life at the moment of HRAE, however, has adequate recovery in the following time period. For this particular score, improvement post-VAD implant is quite steep and this trajectory continues after HRAE recovery

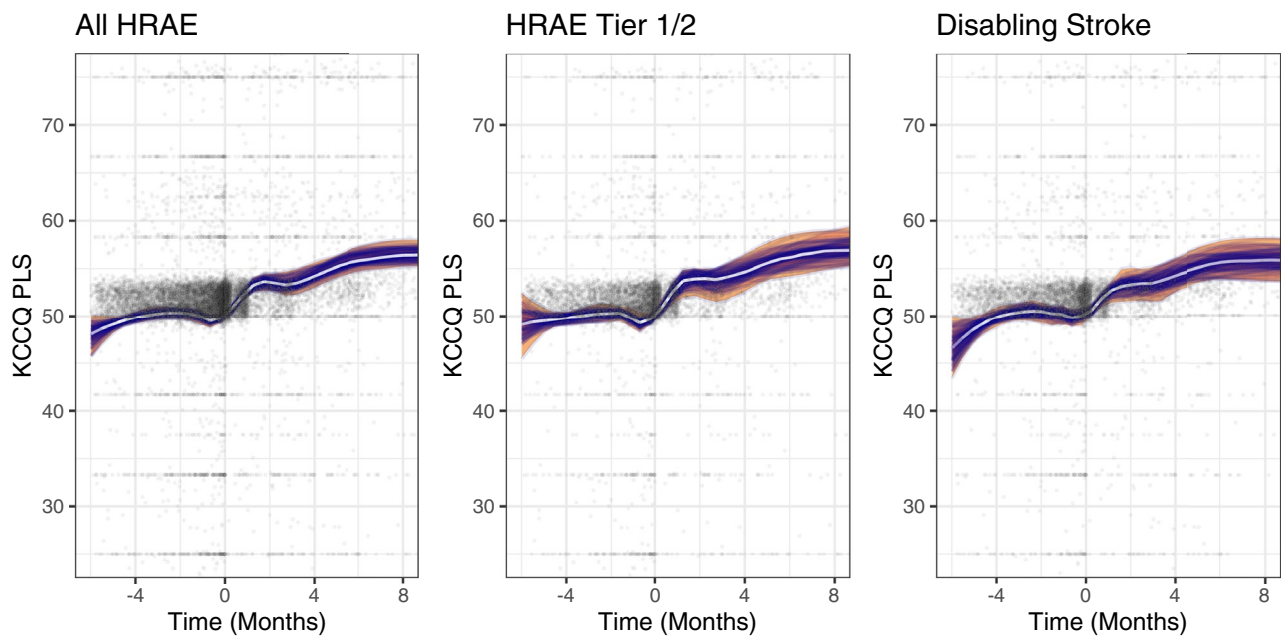


FIGURE 2 Data visualization of patient Kansas City cardiomyopathy questionnaire physical limitation score in relation to HRAE. Similar to Figure 2, a distinct decrease in cumulative limitation score is appreciated in the peri-event period. However, patients are able to recover to baseline immediately post-event and continue to trend with improvement

(Table 2). Patients suffering from disabling stroke also had a statistically significant increase in QoL score over time ($p < 0.001$). Post hoc analysis demonstrated a significant increase in QoL score when comparing pre and post-HRAE time-points ($p \leq 0.001$) as well as pre-HRAE and up to 12-month post-operative time-points ($p \leq 0.001$). This

trend was replicated by both the KCCQ PLS and Euro-qol EQ-5D metrics (Table 2).

6MWT also significantly increased over time in the all HRAE ($p < 0.001$), HRAE Tier 1–2 ($p < 0.001$), and disabling stroke cohorts ($p < 0.001$). However, post hoc analysis did reveal a stall in functional status progression

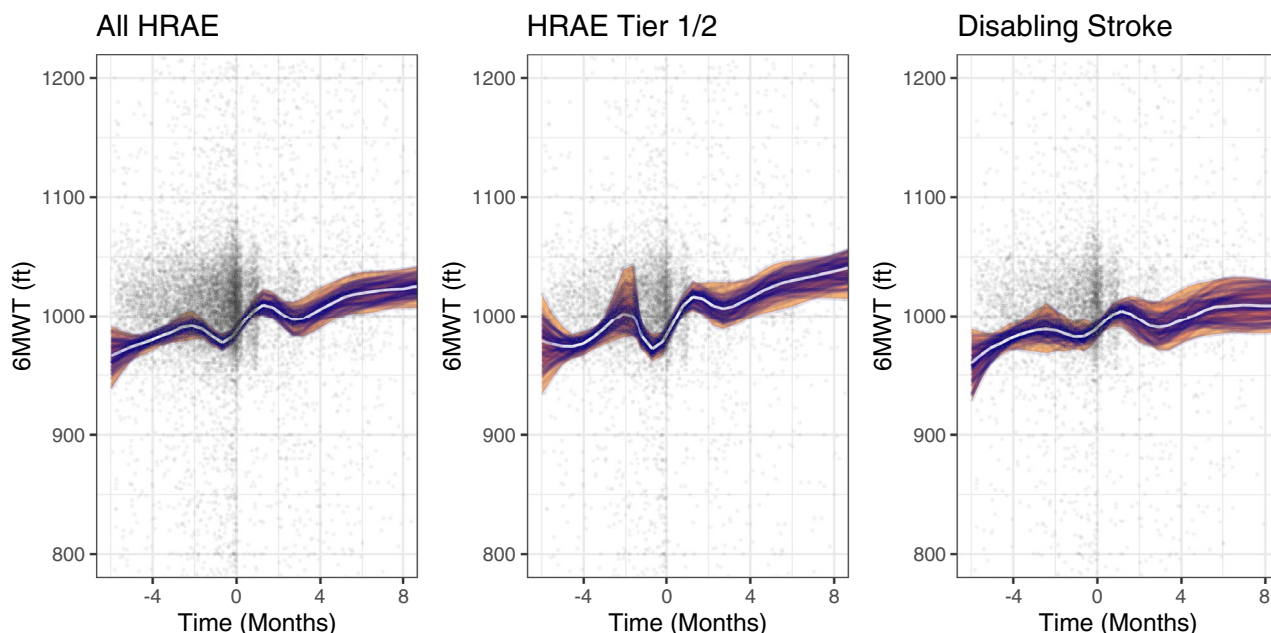


FIGURE 3 Data visualization of six-minute walk distance (in feet) in relation to HRAE. Drop in walk distance is noted after HRAE. However, it can be appreciated after disabling stroke the slope in improvement is not as substantial as after less severe events

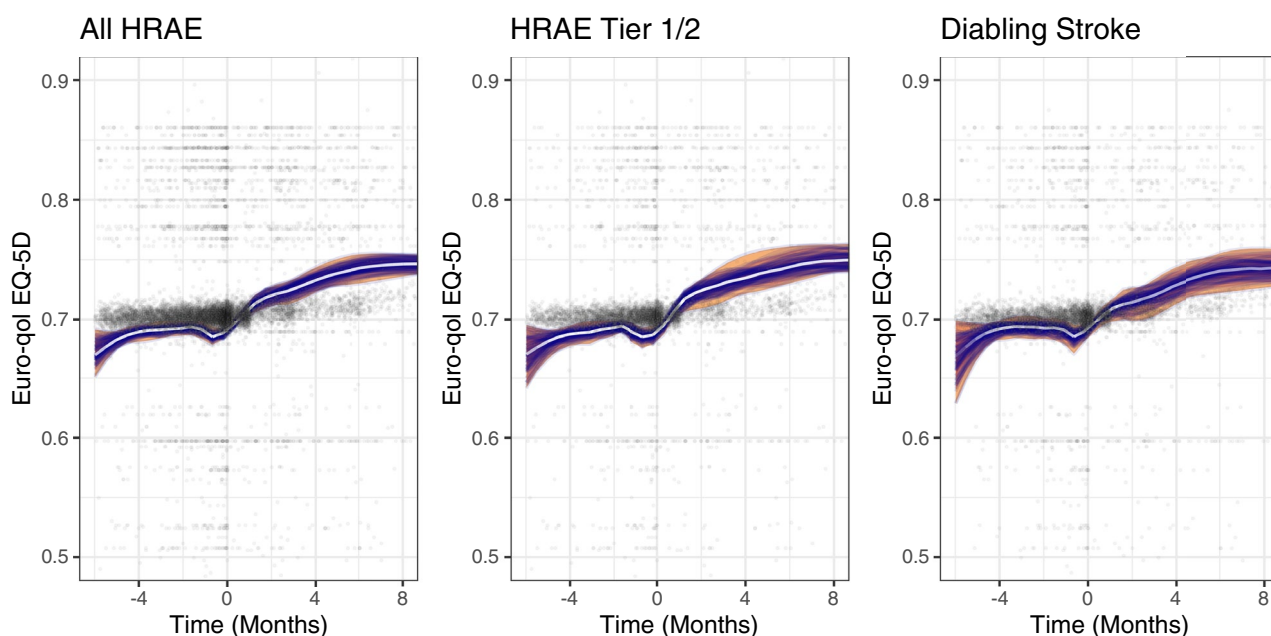


FIGURE 4 Data visualization of patient euro-qol EQ-5D score in relation to HRAE. A noticeable decrease in quality of life score after HRAE with an immediate recovery after the event

when comparing pre- and post-HRAE values in the all HRAE (1010.6 [987.6, 1034.0] vs. 1009.1 [977.9, 1039.5], $p = 0.87$), HRAE tier 1/2 (1008.1 [985.9, 1031.1] vs. 1009.0 [979.6, 1043.2], $p = 0.87$) and the disabling stroke group (1012.2 [989.5, 1035.5] vs. 1008.6 [977.8, 1036.9], $p = 0.46$). However, these patients significantly recovered and improved by 12-month follow up (Table 2). It should be

noted that there are minor discrepancies between Tables 2 and 3 in terms of the HRAE cohort at 12-month follow up. This is due to very slight differences in the cohorts used for these two analyses. In the time-series analysis, complete cases were only included (Table 3). For the overall HRAE vs non-HRAE (Table 2), all patients were included resulting in minimal differences in summary statistics.



4 | DISCUSSION

Despite substantial improvements to CF-LVAD functionality and efficacy, patient quality of life and functional status is still a complex aspect of mechanical circulatory support care. Multiple factors lead to a unique interplay between clinical and psychosocial factors that ultimately result in a patient's quality of life. Adverse events are a major obstacle in CF-LVAD care, and the new HRAE classification helps elucidate that process. Therefore, knowing the impact of HRAE on QoL and status metrics is vital moving forward.

The natural evolution of LVAD device mechanisms and modalities must be initially referenced. The ventricular device space is ever-changing with the near-full adoption of centrifugal flow devices. This study does not serve to compare the nature of axial vs. centrifugal devices and their rates of HRAE. However, interestingly, there was an increased percentage of centrifugal

LVADs in the HRAE group compared to axial devices. Despite this finding, the benefit of centrifugal LVADs in outcomes and reduction of adverse events is known, and this finding may be one related to the timeframe with which this cohort is drawn. This is further amplified given the demonstrated improvement in HRAE outcomes in the new VAD devices as referenced previously. Nevertheless, despite differences in device modality, it is apparent that HRAE does have a short time effect. Yet these events can be overcome with the overall benefit of ventricular support. As such, it is believed these findings can be attributable to the broad LVAD field with the knowledge that modern LVADs and advancements in the field can help to reduce adverse events and overcome the short-term disability associated.

In our pairwise analysis, overall, patients had a trending increase in all four metrics in both the total HRAE and sub-stratified HRAE groups. However, the results of the 6MWT data were particularly notable as patient functional status failed to significantly improve from the pre- to post-HRAE timepoints, unlike the other three metrics. This effect was most extreme in the disabling stroke group (pre-HRAE median distance = 1012.2 vs. post-HRAE median distance = 1008.6 (Table 2). Taken together, these results are similar to those presented in Cowger et al. in a cohort of patients suffering adverse events, without using HRAE designations.¹³ QoL metrics did not change after adverse events, and immediate improvement in 6MWT distance may be attenuated after severe adverse events such as disabling stroke.

TABLE 2 Quality of life and physical status data at 12-month follow up

	HRAE (3327)	Non-HRAE (18043)	
KCCQ QOL	53.7 [37.5, 75]	62.5 [37.5, 75]	$p = 0.05$
KCCQ PLS	50 [37.5, 75]	58.3 [33.3, 83.3]	$p = 0.08$
Euro-qol EQ-5D	0.80 [0.68, 0.74]	0.81 [0.69, 0.76]	$p < 0.01$
Six min walk	1027 [711.2, 1290.0]	1082 [800, 1300]	$p < 0.01$

TABLE 3 Quality of life and physical status data at 12-month follow up

	Pre-HRAE	Post-HRAE	12 month follow up	p value
KCCQ QOL, median [IQR]				
HRAE	47.4 [46.1, 48.4]	48.4 [46.5, 50.2]	54.7 [50.3, 55.9]	<0.001
HRAE-tier 1–2	47.5 [46.2, 48.5]	48.3 [46.5, 50.3]	54.8 [50.8, 55.8]	<0.001
HRAE—disabling stroke	47.3 [46.0, 48.3]	48.4 [46.4, 50.1]	54.7 [50.1, 56.0]	<0.001
Six minute walk, median [IQR]				
HRAE	1010.6 [987.6, 1034.0]	1009.6 [977.9, 1039.5]	1039.0 [1011.0, 1068.0]	<0.001
HRAE-tier 1	1008.1 [985.9, 1031.1]	1009.0 [979.6, 1043.2]	1039.0 [1012.0, 1066.0]	<0.001
HRAE—disabling stroke	1012.2 [989.5, 1035.5]	1008.6 [977.8, 1036.9]	1041.0 [1014.0, 1069.0]	<0.001
KCCQ PLS, median [IQR]				
HRAE	52.3 [51.4, 53.1]	52.7 [51.2, 53.9]	56.8 [53.9, 57.7]	<0.001
HRAE-tier 1–2	52.3 [51.1, 53.1]	52.6 [51.2, 54.4]	56.8 [54.1, 57.7]	<0.001
HRAE—disabling stroke	52.3 [51.2, 53.2]	52.7 [51.2, 53.7]	56.8 [53.7, 57.9]	<0.001
Euro-qol EQ-5D, median [IQR]				
HRAE	0.703 [0.698, 0.709]	0.707 [0.700, 0.719]	0.758 [0.729, 0.767]	<0.001
HRAE-tier 1–2	0.703 [0.698, 0.708]	0.707 [0.700, 0.721]	0.758 [0.732, 0.765]	<0.001
HRAE—disabling stroke	0.703 [0.697, 0.708]	0.706 [0.700, 0.714]	0.759 [0.747, 0.766]	<0.001

Contrastingly, aggregate data analysis and visualization techniques revealed a more intuitive impact on these metrics after confirming HRAE. QoL and functional status data were significantly decreased in all groups compared to the non-HRAE cohort (Table 3). With the addition of the distinct drop and recovery appreciated with the aggregate time-series curves, it can be interpreted that HRAEs do have a more subtle impact on patient QoL and functional status.

Comprehending these three distinct findings in context can result in a few related interpretations. Primarily, patients as a whole will typically improve their status and QoL during CF-LVAD support. Resolution of heart failure symptoms, in addition to knowledge of improving prognosis, may drive this progress. Therefore, when reviewing individualized complete patient data, it is expected patient metrics will improve, or at very least, stabilize after HRAE. It is not until broad aggregate data would be used that it could be appreciated that, although patient metrics improve post-HRAE, they may not improve at the same expected rate of event-free patients.

Additionally, inherent qualities of these very metrics may be able to capture the broad trends spoken of above, however, more subtle patterns may not be reflected. Our analysis of 6MWT data may have further demonstrated this metric as potentially the most representative and responsive metric to indicate changes in status after HRAEs, particularly after the more serious events such as disabling stroke. This is consistent with prior findings as 6MWT distance has been shown to be a viable metric demonstrating patient status improvement, as well as a strong predictor of patient mortality.^{6,17} QoL scales have been less successful. McIlvennan et al. reported stable QoL scores even in the months leading up to death.¹⁸ In this analysis, these potential limitations are particularly noted as disabling stroke minimally affected scores. Development and validation of new or improved metrics would greatly serve clinicians to better improve patient experience and outcomes.

The use of less representative indices for QoL and status particularly reviewed using three distinct pre- and post-HRAE time points will likely limit any quantitative analysis. It appears the use of aggregate data without the limitations of complete patient cases and specific time points represents a more granular view of patient response to HRAE. The benefit of using normalized QoL scales allows for use of individual data points to paint a broader picture of the impact of these adverse events. Noticeable dips after the event with strong recovery may be due to the majority of HRAEs resulting in short-term inconvenience and morbidity to patients. Coupled with high-quality care and device management, patients can overcome these obstacles and start again on the path to

improvement, although that path is blunted compared to non-HRAE patients.

Ultimately, this analysis of the patient response to HRAEs can help put into context the impact of these events and further clinicians' understanding of the role of HRAEs in CF-LVAD care. However, more analyses are needed with similar approaches to review longer-term data to review the impact of these events on quality of life. In particular, this study hopes to place into context the limitations of current standards and approaches of quantifying functional status and QoL.

The primary shortcoming naturally involves the measures themselves. 6MW has been validated in terms of functional status, however, quality of life measures are limited due to the same barriers of all subjective, qualitative analyses. Although measures need to be further validated, perhaps a more real-time solution is not just the data, but the frequency with which it is obtained. One of the primary limitations in this study is missing data, particularly short-term and long-term longitudinal QoL data in patients, particularly with an HRAE. As this clinical information is unique in that can be obtained at home on a regular basis. The use of mobile applications could help generate a more regular stream of information for these patients to help identify how LVAD support does impact their QoL, particularly in the face of an adverse event. This data source would allow for a better understanding of this proposed attenuation of improvement after an HRAE and how multiple events may affect these scores. Ultimately, more effective collection can help unlock how socio-economic, geographic, and institutional differences can affect these patients QoL at baseline and overtime—helping clinicians make more informed clinical decisions.

4.1 | Limitations

This project was not without limitations. As is the nature of retrospective database analyses, a lack of data granularity played a role in the review of the data. Specifically, this limitation did not allow for complete stratification of the cohort based on the hemocompatibility score tiers. Additionally, although a significant number of HRAE and non-HRAE patients were identified in the INTERMACs database, there was a limited number of patients with complete cases within the criteria of the predefined pre-HRAE, post-HRAE, and close to 12-month follow up time points used for the paired analysis. This limitation was partially addressed using the imputation of missing data. Although this is a statistically valid methodology, it cannot completely replicate complete original data.



5 | CONCLUSION

This represents the first study to analyze the quality of life and functional status metrics after HRAEs. Patients likely experience a sharp decrease after HRAE but are able to recover relatively quickly. Overall, patient metrics improve over time after HRAE, however, this improvement may be blunted compared to event-free patients. 6MWT distance is likely the most responsive and representative metric of patient status, particularly after severe events such as disabling stroke. However, improvement of current QoL scales and development of new metrics are needed moving forward. Finally, visualization of continuous time-series appears to accurately represent patient QoL and functional status after HRAE. Studies viewing longer-term data are needed to further understand the impact of these events throughout the entirety of CF-LVAD support.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Matthew P. Weber: concept design, data analysis, and manuscript preparation. John Stulak: hypothesis formation and data interpretation. Simon Maltais: data collection and data interpretation. Francis D. Pagani: manuscript approval, hypothesis formation, and data interpretation. Jennifer Cowger: data interpretation and study design. Vakhtang Tchanchaleishvili: principle investigator, study design, data interpretation, and manuscript preparation.

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