

Health-related quality of life in left ventricular assist device-supported patients

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Abstract

Aims This study aimed to evaluate the different health-related quality of life (HR-QoL) aspects in patients with both short-term and long-term duration LVAD support at pre-specified time intervals.

Methods and results We performed a single-centre HR-QoL analysis of short-term and long-term LVAD-supported patients using the short version of the Kansas City Cardiomyopathy Questionnaire (KCCQ-12) and the Changes in Sexual Functioning Questionnaire along with a survey to evaluate patients' social and driving routines. Data were collected at baseline and at 6 or 12 month follow-up. Included were 46 patients with a median time from LVAD implantation of 1.1 [inter-quartile range (IQR) 0.5, 2.6] years. The median KCCQ-12 summary score was 56 (IQR 29, 74) with most favourable scores in the symptom frequency domain [75 (IQR 50, 92)] and worse scores in the physical limitation [42 (IQR 25, 75)] and QoL [44 (IQR 25, 75)] domains. No significant changes were apparent during study follow-up [KCCQ-12 summary score 56 (IQR 35, 80)], and no significant correlation between the KCCQ-12 summary score and ventricular assist device-support duration was detected ($r = -0.036$, $P = 0.812$). Sexual dysfunction was noted across all domains with a cumulative score of 31 (IQR 22, 42). Seventy-six per cent of patients resumed driving after LVAD implantation, and 43% of patients reported they socialize with family and friends more frequently since surgery.

Conclusions Short-term and long-term LVAD-supported patients had impaired HR-QoL and sexual function at baseline and at follow-up yet reported an improvement in social interactions and independency. A broader spectrum of patient's reported HR-QoL measures should be integrated into the pre-LVAD implantation assessment and preparation.

Keywords Quality of life; Sexual dysfunction; Left ventricular assist devices; Heart failure

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Introduction

Left ventricular assist devices (LVADs) are the mainstay of treatment nowadays for patients with advanced heart failure (HF) either as a bridge to heart transplantation (HTx) or as a destination therapy.^{1–3} While the impact of LVAD implantation on longevity has been repeatedly demonstrated,^{4,5} contemporary data describing its effect on patients' health-related quality of life (HR-QoL) are limited.^{6–8} HR-QoL is a multidimensional concept with different aspects,

which encompass independency, impact on daily activities, social interaction, and sexual function.^{9–11} Published LVAD HR-QoL studies included newly and short-duration LVAD-supported patients and were designed to compare between patients' perception of health pre-LVAD vs. post-LVAD implantation.^{6–8} Moreover, methodology was based on non-LVAD-specific questionnaires, which were either developed for HF [i.e. Kansas City Cardiomyopathy Questionnaire (KCCQ)] or used in the evaluation of the general population (i.e. the European Quality of Life EQ-5D-3L tool).^{6–8} These

studies disregarded other important well-being aspects such as social interactions, sexual function, and driving—all of which are of specific relevance for LVAD-supported patients. Recently, a call for new metrics in LVAD-supported patients was made because of failure in capturing LVAD-specific adverse effects using common HF instruments.⁶ Indeed, an integrative evaluation of HR-QoL in LVAD-supported patients is vital both in order to improve their well-being on LVAD support and in order to optimize pre-LVAD implantation decision making.

Therefore, we sought to evaluate the different HR-QoL aspects (including HF symptoms, daily activities, driving, and social and sexual function) in a cohort of patients with both short-term and long-term duration LVAD support at pre-specified time intervals.

Materials and methods

Study population and design

All alive patients who underwent LVAD implantation between 1 January 2012 and 31 December 2019 ($n = 108$) at the Rabin Medical Center, Israel, and have not undergone HTx by the time of study initiation were approached ($n = 51$), regardless of ventricular assist device (VAD) support duration (Supporting Information, *Figure S1*). Patients who consented were handed the study questionnaire and were asked to fill it privately either at the clinic or at their home. Questionnaires were handed in non-acute clinical states and in the ambulatory setting. Following this baseline evaluation, patients were asked to repeat the same questionnaire at 6 month interval (in the newly implanted patients) or at 1 year interval (in all the others). Patients who were physically unable to complete the survey were excluded.

Demographic and baseline clinical parameters

Clinical and demographic data were extracted retrospectively from patients' electronic records. LVAD-related complications [gastrointestinal (GI) bleeding events, non-GI bleeding events, thrombotic events and cerebrovascular accidents or transient ischaemic events, LVAD-related infections, non-LVAD-related infections, and the occurrence of malignant ventricular arrhythmias] were based on the Interagency Registry for Mechanically Assisted Circulatory Support definitions¹² and as previously described.⁵ HF-related admissions were also reported. Mortality during follow-up was determined for all patients using the Israeli National Population Registry.

Measurement instruments

In this study, we used several instruments, each designated to capture a different aspect of patient's HR-QoL.

- i The Kansas City Cardiomyopathy Questionnaire including its short version (KCCQ-12) is a self-administered questionnaire that was designed to capture a subjective perception of general health in patients with HF and includes physical limitation, symptom frequency, and QoL domains. It is a validated questionnaire for assessing HF-specific QoL¹³ and prognosis.^{13–15} Items are scored from 0 to 100 with 0 representing the worst and 100 the best possible functional status. The KCCQ-12 summary scores are divided to quartiles defined as follows: score range 1–24 reflects a very poor to poor HR-QoL, score range 25–49 reflects a poor to fair HR-QoL, score range 50–74 reflects fair to good HR-QoL, and score range 75–100 reflects a good to excellent HR-QoL.^{16,17} The questionnaire has undergone linguistic validation into Hebrew by the Mapi (<https://mapi-trust.org/>) research institute.
- ii The Changes in Sexual Functioning Questionnaire (CSFQ) focuses on patient's sexual desire and function. This questionnaire consists of five domains, which investigate patient's pleasure, desire (frequency and interest), arousal, and orgasm and was previously used in LVAD-supported patients.¹⁸ Patients were asked to grade their interest in sexual activity, pleasure or satisfaction with sex, problems with frequency of sexual activity, and disturbance to sexual performance, particularly those related to the device itself. Female and male patients are evaluated separately using a different scoring algorithm. The following are the stated cut-off scores for male patients for each domain, which are indicative of sexual dysfunction and the domain's theoretical score range: pleasure 4 (range 1–5), desire frequency 8 (2–10), desire interest 11 (3–15), arousal 13 (3–15), orgasm 13 (3–15), and CSFQ total score 47 (14–70). We also added three-item section designed by our centre VAD team, which aimed to further characterize sexual function among LVAD-supported patients (Supporting Information, *Data S1*). The CSFQ questionnaire was translated to Hebrew and back-translated to English and checked to ensure consistency.
- iii Driving instrument is a five-item section designed by our centre VAD team to evaluate patient's driving patterns (Supporting Information, *Data S1*). Our aim was to characterize the LVAD-supported driver and his inherent difficulties.
- iv Social and travelling instrument is a five-item section designed by our centre VAD team, which aimed to evaluate patient's social interactions and domestic and international travelling patterns (Supporting Information, *Data S1*). To note, questionnaires were handed to patients

before the social and travelling restrictions of the corona virus 2019 pandemic.

The study protocol was approved by the Institutional Review Board of the Rabin Medical Center, Israel, and patients' approval has been obtained (RMC-18-0742).

Statistical analysis

The statistical analysis for this paper was performed using SAS Software, Version 9.4 (SAS Institute Inc., Cary, NC). Continuous variables were presented by median and inter-quartile range (IQR) 25th, 75th. Categorical variables were presented by (*n*, %).

We stratified our cohort based on LVAD support duration (<1 vs. ≥1 year) and on the device implanted (HeartMate 3 vs. HeartMate II/HeartWare LVADs). For between-group comparisons of categorical variables, we used Fisher's exact test, and for continuous variables, we used the Wilcoxon signed-rank test due to skewed distributions. We also used the Wilcoxon signed-rank test to assess statistical significance of paired differences in the KCCQ and CSFQ scores ('baseline cohort' vs. 'follow-up cohort'). The Pearson correlation coefficient was used to assess associations between continuous variables (the correlation between the KCCQ-12 summary score/CSFQ score and LVAD support duration).

Two-sided *P* values less than 0.05 were considered statistically significant.

Results

The study 'baseline cohort' included 46 LVAD-supported patients following the exclusion of three patients who suffered from significant neurological co-morbidities and two patients who refused to participate in the study. During the study follow-up period, three patients died, five patients underwent HTx, three patients refused to continue participating in the study, and two patients did not complete their follow-up period. Thus, the study 'follow-up cohort' consisted of 33 patients (Supporting Information, *Figure S1*).

At the time of study initiation, the median VAD support duration was 1.1 (IQR 25th, 75th 0.5, 2.6) years, and 44% of the study cohort had ≥2 year VAD support (Supporting Information, *Figure S1*). The median patient's age was 66 (59, 72) years, and most of the study patients were men with ischaemic cardiomyopathy. The most frequently implanted VAD was HeartMate 3 (*n* = 35, 76%). [Correction added on 07 April 2021, after first online publication: In the preceding sentence, the data associated with HeartMate 3 has been corrected from "(*n* = 31, 69%)" to "(*n* = 35, 76%)" to accord with the data in Table 1 in this current version.] The most common LVAD-related complication occurring prior to study initiation was non-GI-related bleeding (*n* = 11, 24%), and 6

Table 1 Baseline characteristics of patients supported with LVADs

	Baseline cohort (<i>n</i> = 46)
Age at time of questionnaire (years)	66 (59, 72)
Gender (female), %	5 (11)
Ischaemic cardiomyopathy (%)	33 (72)
Hypertension (%)	20 (43)
Atrial fibrillation (%)	22 (48)
Diabetes mellitus	24 (52)
Chronic renal failure (estimated glomerular filtration rate <60) (%)	15 (33)
CVA/TIA prior to implantation (%)	3 (7)
INTERMACS profile	3 (3, 3)
Destination therapy	18 (39)
Bridge to transplantation	19 (41)
Bridge to decision	1 (2)
Bridge to candidacy	8 (17)
VAD type	
HeartMate II	6 (13)
HeartWare	5 (11)
HeartMate 3	35 (76)
Caregiver identity	
Spouse/life partner	37 (80)
Family member	5 (11)
Professional caregiver	2 (4)
Self-care only	2 (4)
Prior LVAD-related complications	
Heart failure-related admission	4 (9)
LVAD-related infection	8 (17)
Non-LVAD-related infection	8 (17)
CVA/TIA after implantation	6 (13)
Thrombotic events	4 (9)
Malignant ventricular arrhythmias	7 (15)
Gastrointestinal bleeding	9 (20)
Non-gastrointestinal bleeding	11 (24)

CVA, cerebrovascular accident; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; TIA, transient ischaemic attack; VAD, ventricular assist device.

Data are presented as median (25th, 75th quartiles) or as percentages, as appropriate.

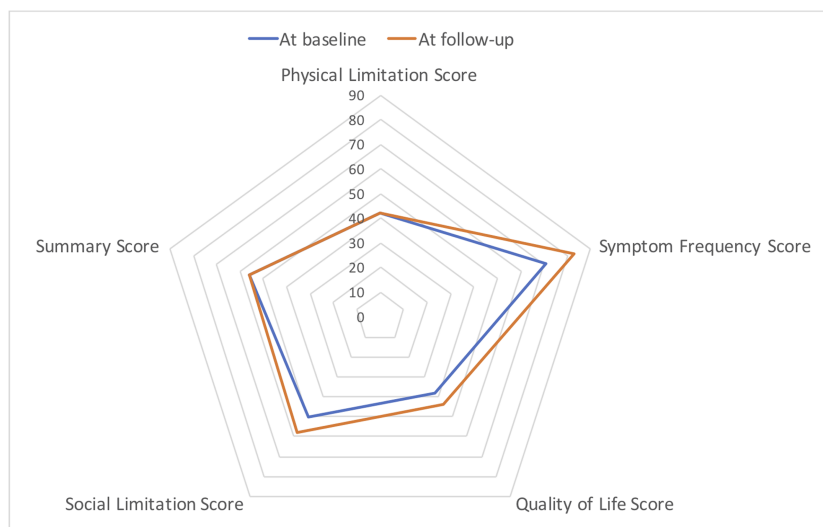
(13%) patients had a cerebrovascular accident/transient ischaemic attack episode since LVAD implantation. Other patients' baseline clinical parameters are presented in *Table 1*.

Short version of the Kansas City Cardiomyopathy Questionnaire in left ventricular assist device-supported patients

The median KCCQ-12 baseline summary score was 56 (IQR 29, 74). Median scores calculated for the different KCCQ-12 domains are presented in *Figure 1* and Supporting Information, *Table S1* showing most favourable scores in the symptom frequency domain yet worse scores in the physical limitation and QoL domains.

We further analysed our patient population according to VAD support duration (Supporting Information, *Table S1*). We found that the KCCQ-12 scores were similar among patients implanted <1 or ≥1 year, and no correlation was detected between LVAD support duration and the KCCQ-12

Figure 1 Short version of the Kansas City Cardiomyopathy Questionnaire scores of left ventricular assist device-supported patients at baseline and at study follow-up. Baseline and follow-up short version of the Kansas City Cardiomyopathy Questionnaire summary and domains' (symptom frequency, social limitation, quality of life, and physical limitation) scores.



scores (Pearson correlation coefficient -0.036 , $P = 0.812$). Importantly, no association was found between the prior occurrence of LVAD-related complication, including cerebrovascular accident/transient ischaemic attack, and the median KCCQ-12 summary score [median KCCQ-12 summary score in patients with prior LVAD-related complications 51 (25, 72) vs. 62 (35, 74) in patients with no prior LVAD-related complications, $P = 0.266$]. We also investigated the long-term changes in patient's HR-QoL as reflected by the KCCQ-12 scores, defining each patient as its own baseline control. During the study follow-up, no significant changes were apparent in the median KCCQ-12 summary score [median 56 (IQR 35, 80)] and its various domains (Figure 1).

Furthermore, although the number of patients in the cohort with non-HearMate 3 LVAD was low ($n = 11$, 24%), we sought to investigate whether the type of the device implanted affects patient's KCCQ-12 scores. In patients implanted with HearMate 3 LVADs vs. HeartMate II/HeartWare LVADs, no significant changes were apparent in the median KCCQ-12 summary score [median 54 (IQR 29, 68) vs. median 57 (IQR 23, 84), $P = 0.625$] and its various domains.

Sexual function with left ventricular assist devices

Sexual function-related items are presented in Figure 2. Because our cohort included only five female patients, out of which only two consented to complete the sexual function instrument, the herein presented analysis only included LVAD-supported male patients. To note, the two LVAD-supported female patients reported poor sexual

function. We used the CSFQ to evaluate the sexual desire and sexual function of our study patients. Baseline CSFQ scores stratified by the different domains are presented in Figure 2. The median CFSQ summary score was 31 (IQR 22, 42) indicating sexual dysfunction, which was observed across all domains. In patients implanted with HearMate 3 LVADs vs. HeartMate II/HeartWare LVADs, no significant changes were apparent in the median CFSQ summary score [median 32 (IQR 24, 41) vs. median 22 (IQR 21, 46), $P = 0.501$].

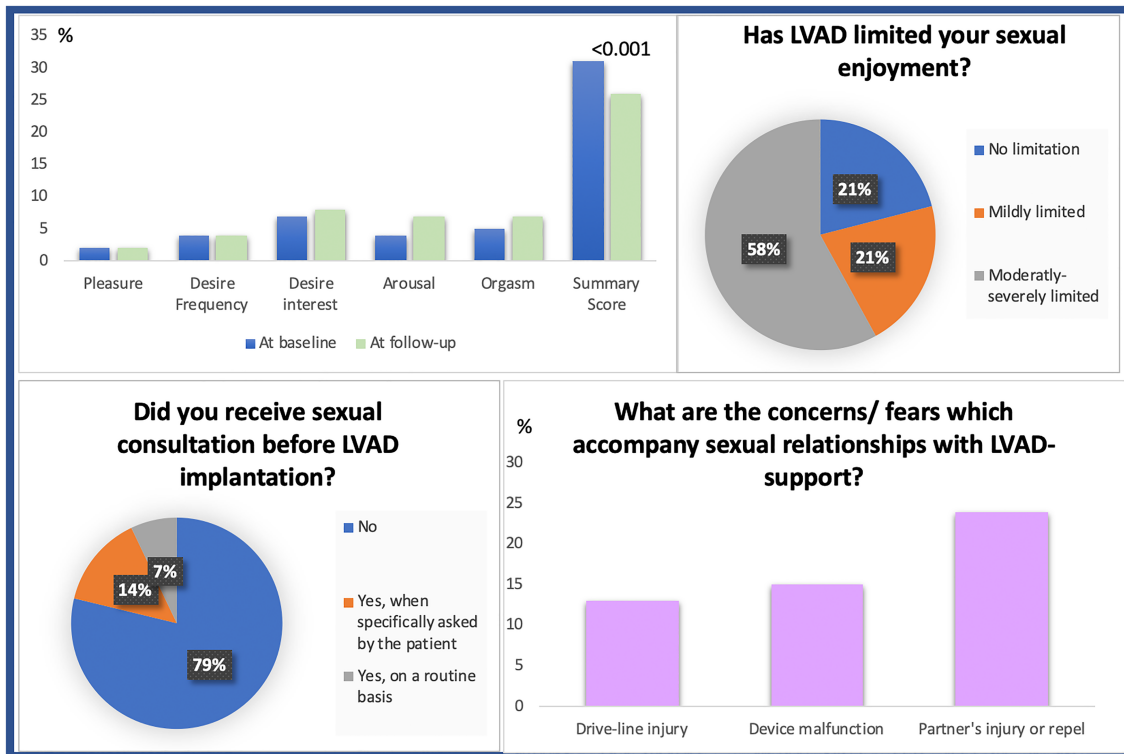
We found that the CSFQ scores were similar among patients implanted <1 or ≥ 1 year (Supporting Information, Table S2), and no correlation was detected between LVAD support duration and sexual dysfunction (Pearson correlation coefficient -0.165 , $P = 0.328$). We also investigated the changes in patient's sexual function as reflected by the CSFQ scores, defining each patient as its own baseline control. During study follow-up, we found a decline in the CSFQ summary score [median 26 (IQR 21, 31), $P < 0.001$].

Most of the patients (58%) answered that the device severely affected their sexual enjoyment. Seventy-seven per cent of the cohort denied receiving sexual consult prior to LVAD implantation, and 15% only did upon their specific request. Major concerns regarding sexual relationships were partner's reaction or partner's possible LVAD-related injury.

Driving with left ventricular assist devices

Driving-related items are presented in Figure 3. Seventy-six per cent of patients who were active drivers before LVAD implantation resumed driving, of which 89% did so during their first year after surgery. The majority of patients (87%) felt

Figure 2 Sexual function of left ventricular assist device (LVAD)-supported patients at baseline and at study follow-up. Upper right: baseline and study follow-up Changes in Sexual Functioning Questionnaire summary and domains' (pleasure, desire frequency, desire interest, arousal, and orgasm) scores. Upper left and lower panels display patients' questionnaire responses.



that driving with an LVAD does not pose a limitation. Patients who reported the cessation of driving most frequently admitted to act upon their family or physician's advice. Three patients (9%) self-reported to be involved in a car accident as drivers.

Social, work, and travelling with left ventricular assist devices

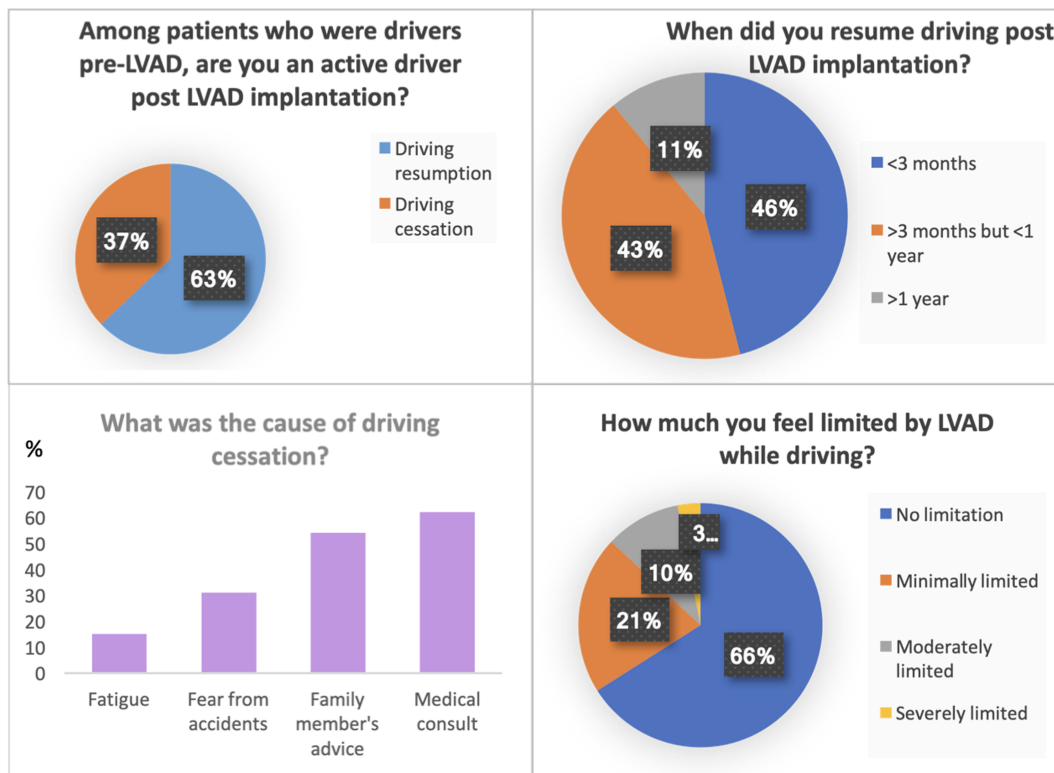
Travelling, work, and social-related items are presented in *Figure 4*. Most patients reported to domestically travel with an LVAD (business or pleasure) around the country (57%) yet refrained from travelling abroad (27%). When asked about their comfort while travelling with LVADs, the majority of patients reported that the device did not or only minimally posed a limitation on their travelling experience (78%). When asked about their social lifestyle habits, 43% of patients reported they socialize with family and friends more frequently since LVAD implantation, and 41% of patients described visiting the theatre, cinema, or restaurants at least once a month. Only 6 (14%) LVAD-supported patients report holding a steady job. However, it should be noted that 86% of the cohort did not work as part of their daily life routines even before LVAD implantation.

Integrative health-related quality of life

We performed several statistical analyses to further define the interactions between the HF-QoL instrument KCCQ-12 and other HR-QoL aspects investigated in this LVAD-supported cohort. There was a moderate association between CSFQ summary score and KCCQ summary score ($r = 0.278$, $P = 0.096$). Resuming driving post-LVAD implantation was associated with a higher KCCQ score (Wilcoxon two-sample test, $P = 0.009$). Both the increased frequencies of social interactions and domestic travelling were associated with higher KCCQ scores (Wilcoxon two-sample test $P = 0.005$ and $P = 0.005$, respectively).

Discussion

This study provides new insights into the HR-QoL of patients supported with LVADs. The novelty of this study is in its integrative approach aiming to capture the various HR-QoL aspects at different time intervals after implantation. LVAD-supported patients, regardless of their VAD support duration, reported impaired HR-QoL and sexual dysfunction, findings that persisted and even mildly deteriorated during

Figure 3 Driving in left ventricular assist device (LVAD)-supported patients. Patients' questionnaire responses to the five-item driving instrument.

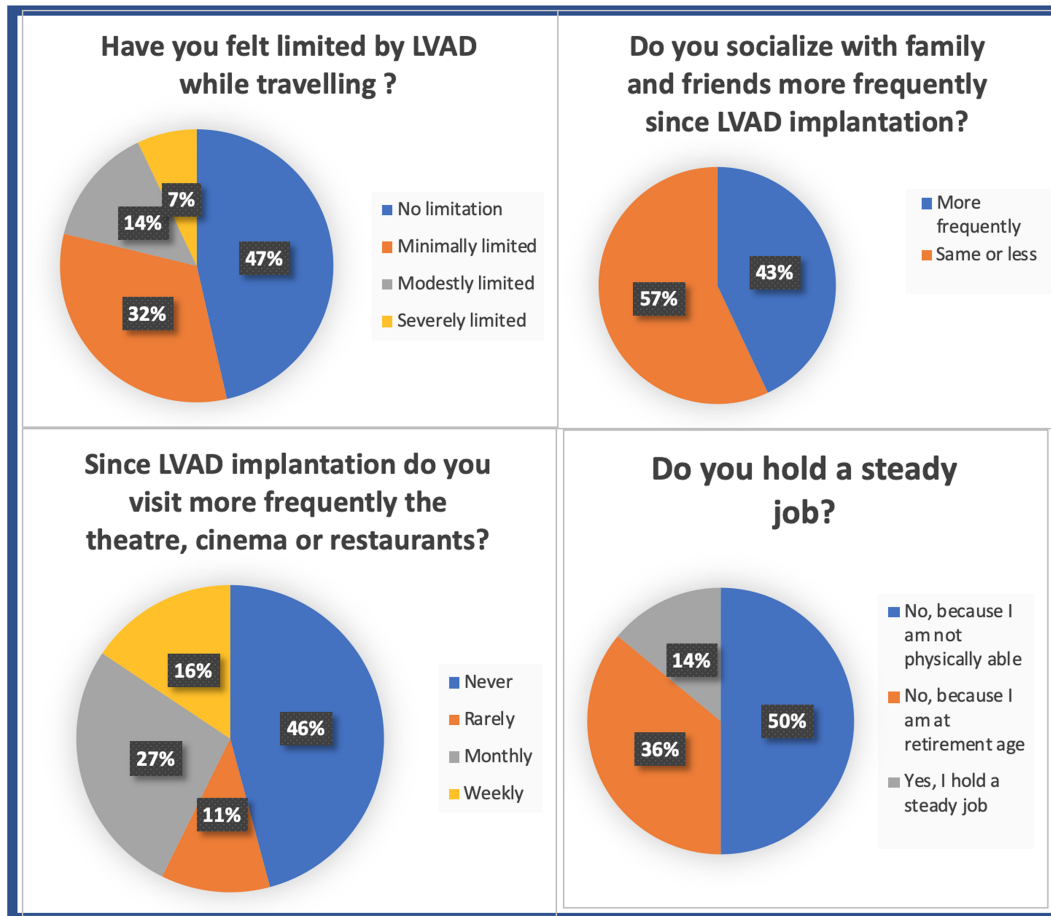
long-term follow-up. However, patients reported improvement in the frequency of HF symptoms and in their ability to execute their daily activities and social interactions.

The KCCQ is a validated questionnaire for assessing HF-specific QoL¹³ and is widely used as a patient-reported outcome instrument in HF.⁹ It has also been used in evaluating the population of newly implanted LVAD patients showing an improvement in their HR-QoL from before surgery to 6 and 12 months after surgery.^{6,19} In this study, we found low KCCQ-12 scores across a wide range of short-term and long-term LVAD-supported patients with no significant improvement in their status over long-term follow-up. The discrepancy between studies could result from different patient baseline characteristics and co-morbidities in the different cohorts or may reflect an impaired HR-QoL on longer-duration LVAD support. Nevertheless, it should be noted that despite a low median KCCQ-12 summary score we found in our cohort of LVAD-supported patients, it improved relatively to published pre-LVAD implantation HR-QoL data. Patients with HF with reduced ejection fraction in New York Heart Association Class IV were reported to have a mean KCCQ summary score of 29,¹⁵ much lower than our LVAD-supported patients. Moreover, as previously noted,^{6,9} the KCCQ does not fully evaluate all of the HR-QoL domains experienced by the LVAD patient, and a more specific tool may be needed for their evaluation. Indeed, our findings

demonstrated an association between the KCCQ-12 score and other well-being aspects of LVAD-supported patients such as driving and travelling, social interactions, and sexual function. We therefore elaborated our study to include these fields of interest.

Intimacy and sexual activity can improve QoL and make life more enjoyable for both patients and their partners.²⁰ Several studies have focused their research on this aspect demonstrating a decrease in the degree of satisfaction with sexual life following LVAD implantation.^{18,21} Moreover, sexual dysfunction was more prominent in LVAD-supported patients compared with patients after HTx.²² In an older multicentre study, the mean total CSFQ score for LVAD-supported men was 34.6 ± 10.4 , and 71% met the criteria for sexual dysfunction.¹⁸ We observed even higher rates of sexual dysfunction (81%) along with worsening sexual dysfunction during follow-up despite our cohort being more contemporary and despite the implantation of third generation LVADs in the majority of patients. Moreover, we found that refraining from sexual activities after LVAD implantation was, at least partially, in the interest of avoiding possible partner's injury or partner's distress. It is reasonable to assume that pre-LVAD implantation sexual education and consultation to both the patient and his or her partner regarding future intimate relationships could address most of these concerns and possibly improve patient's HR-QoL.

Figure 4 Social activity and interaction in left ventricular assist device (LVAD)-supported patients. Patients' questionnaire responses to the five-item social instrument.



Driving restrictions increase dependence on others and reduce HR-QoL. Because of lack of evidence-based data, current driving recommendations by the European Union suggest an individual assessment for LVAD-supported drivers with Group 1 licence.²³ Regardless of national government regulations, many physicians choose to err on the cautious side and counsel patients to refrain from driving.²⁰ Nevertheless, even if patients are given an approval to resume driving (as is the case in our centre), patients often choose to refrain from driving because of family's advice or another medical consult. This could also be ameliorated by proper education for the patient, the patient's family, and his surrounding medical community.

Social isolation and low participation rates in social activities are recognized difficulties following LVAD implantation.²⁴ We therefore aimed to characterize the social status of interactions and activities in our cohort. LVAD-supported patients tend to socialize more frequently with family and friends relatively to the pre-LVAD implantation period, and the majority of them are running active social lives. Furthermore, we also

found an increased rate of domestic travelling with LVADs, most probably a reflection of patient's independency and sense of security.

The majority of the study cohort reports not holding a steady job after LVAD implantation, a finding that may signify complicated rehabilitation after surgery and low independency status. However, when analysing these findings, one must take into consideration that work has not been part of the daily life routine for most of these patients for many years before LVAD implantation, mostly due to advanced HF-related physical limitations. Moreover, the majority of LVAD-supported patients receive governmental financial support due to either their physical disabilities or retirement status. Therefore, returning to the labour market was not expected in the majority of our LVAD-supported cohort.

Altogether, we showed that despite the low perception of health reflected by HF-QoL instruments such as the KCCQ-12, other aspects of the HR-QoL milieu experienced by the LVAD patient have improved. These findings are important in an era where an increasing number of HF patients are

designated for LVAD as destination therapy or are facing a prolonged waiting for HTx using LVAD as a bridge to transplantation. We believe that broader, integrative preparation of LVAD-designated patients and their caregivers, which will include the HR-QoL aspects investigated in this study, may pave the way for further improvement in the well-being of LVAD patients.

This study has several limitations. First, it is limited by its relatively small sample size, in particular, the study's follow-up cohort, which suffered from loss to follow-up (mostly due to HTx or death). Nevertheless, the study's follow-up cohort was used only in the evaluation of the long-term changes in patients' HR-QoL, an analysis, which was statistically based on paired analysis, thus, we believe, allowed for the elimination of known and unknown confounders in our cohort and increased the validity of our results. Nevertheless, a larger cohort would permit an analysis of the effect of other possible factors on patients' HR-QoL (such as device type and caregiver characteristics). Second, as our analysis was based on a single-centre database, our results may not allow for generalizability. Third, because of the small number of female patients in this cohort, we were not able to properly analyse sexual dysfunction on this population.

Conclusion and clinical implications

Contemporary technological advancements, which brought along a significant improvement in the longevity of LVAD-supported patients, have allowed for a shift in management focus to improve their HR-QoL, another vital component of device success. Consultation and education that capture the whole spectrum of 'living with an LVAD' including social interactions, driving, and sexual function should be integrated into the pre-LVAD implantation assessment and

preparation, thus allowing a better-informed decision of the patient and his caregiver. Further study and expert consensus recommendations should focus on the development of LVAD-specific HR-QoL instrument, which should be based on patient-reported outcomes.

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Conflict of interest

None declared.

Funding

None.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Participant flow and study design.

Data S1. Study's questionnaire.

Table S1. KCCQ-12 scores of patients supported with LVADs stratified by VAD support duration.

Table S2. CSFQ scores of patients supported with LVADs stratified by VAD support duration.

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