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ORIGINAL ARTICLE
Heart Failure

Impact of Different Therapeutic Strategies With Left Ventricular Assist Devices on Health-Related Quality of Life During Prolonged Device-Based Support

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Background: Left ventricular assist device (LVAD) implantation improves survival and health-related quality of life (HRQoL) of patients with heart failure. However, the impact of LVADs or different LVAD-based therapeutic strategies on long-term HRQoL has not been investigated. We evaluated the long-term HRQoL of Japanese patients who were treated with different LVAD-based therapeutic strategies.

Methods and Results: Patients whose data were recorded in the Japanese Registry for Mechanical Assisted Circulatory Support between January 2010 and December 2018 were divided into 3 groups: primary implantable LVAD (G-iLVAD; n=483), primary paracorporeal LVAD (n=33), and bridge-to-bridge from paracorporeal to implantable LVAD (n=65). HRQoL was evaluated using the EuroQoL 5-dimension 3-level (EQ-5D-3L) before and 3 and 12 months after LVAD implantation; the mean EQ-5D-3L visual analog scale (VAS) score in the G-iLVAD group at these time points was 47.4, 71.1, and 72.9, respectively (where scores of 0 and 100 indicate worst and best imaginable health state, respectively). Changes in the least squares means of the VAS scores at 3 and 12 months after implantation differed significantly among the 3 groups. Social function, disability, and physical and mental problems were significantly lower in the G-iLVAD than other groups.

Conclusions: HRQoL improved significantly at 3 and 12 months after LVAD implantation in all groups. Physical function showed a stronger improvement than did social function, disability, and mental function.

Key Words: Health-related quality of life; Heart failure; Japan; Left ventricular assist device

Therapeutic strategies using left ventricular assist devices (LVADs) have improved the prognosis of patients with severe heart failure.[1–3] Among developed countries, Japan has a severe shortage of donor hearts; more than 90% of patients in Japan require LVAD implantation as a bridge to transplantation (BTT) while awaiting heart transplantation (HTx).[4] Since the beginning of the HTx program in Japan (1999), extracorporeal pulsatile LVADs (pLVADs) have been commonly used for BTT.[5] However, since 2011, insurance has started covering implantable continuous-flow LVADs (iLVADs) for BTT for patients with poor prognoses but without any systemic diseases and for patients expected to return to society while awaiting HTx and receiving caregiver assistance from those who understand the characteristics of long-term home care. Because patients with severe heart failure and cardiogenic shock are not immediately eligible for HTx and iLVAD, many still require pLVAD implantation as a bridge to decision.[6] pLVAD also plays important roles in cases of bridge to recovery and bridge to candidacy (BTC), as well as in patients indicated for biventricular assist devices.[7] Bridging from a pLVAD to an iLVAD is called a "bridge-to-bridge" (BTB) strategy; this is gaining popularity in Japan.[8]

Although the prognosis of patients with iLVADs is good, the chronic donor shortage remains. Therefore, patients with implanted ventricular assist devices (VADs) live longer with every passing year. In 2020, the mean waiting period for HTx for Status 1 patients (medically urgent candidates with the highest priority for HTx) was 1,516 days.[4] iLVADs improve survival rate and functional capacity; they enable patients to live at home with their families and

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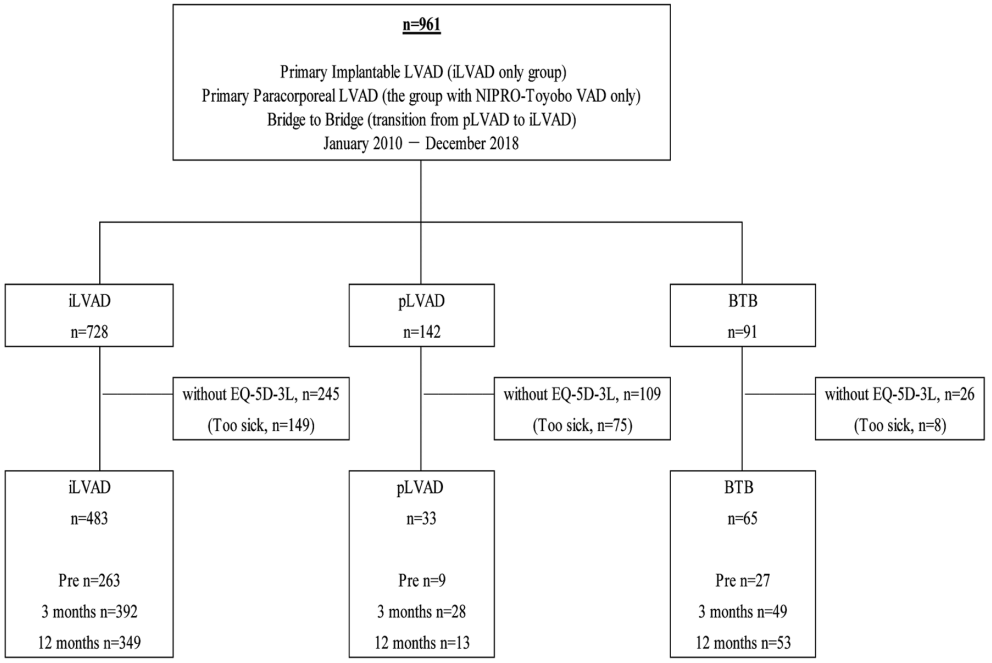

Figure 1. Participant flowchart. 3 months, 3 months after implantation; 12 months, 12 months after implantation; BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; EQ-5D-3L, EuroQoL 5-dimension 3-level version; iLVAD, primary implantable left ventricular assist device; pLVAD, primary paracorporeal left ventricular assist device; pre, preimplantation.

to reintegrate into society with quantifiable improvements in health-related quality of life (HRQoL).[1,9–15] Conversely, patients with pLVADs have more difficulty than those with iLVADs in maintaining their HRQoL because of the particular device management required for pLVADs (which limits the range of activities and prevents patients from living at home).[9,14,16] In Japan, the use of iLVAD for destination therapy (DT) has been covered by insurance since May 2021.[17] Therefore, it will become increasingly important in the future to help patients with LVADs live for extended periods with a high HRQoL.[18] However, only short-term and single-center studies have been performed investigating the HRQoL of patients with LVADs in Japan.[14,19] To the best of our knowledge, no studies have examined the long-term HRQoL of patients with LVADs or of those managed with different LVAD-based therapeutic strategies (e.g., pLVADs, iLVADs, and BTB). Thus, in the present study, we compared the long-term changes in HRQoL among patients managed with various LVAD-based therapeutic strategies in Japan.

Methods

Participants

The Japanese Registry for Mechanical Assisted Circulatory Support (J-MACS)[20] is a prospective registry of patients who undergo durable LVAD implantation with either a primary device or the BTB strategy (i.e., a secondary device). J-MACS contains clinical data on the enrolled patients before implantation, 1 week and 3 and 6 months after implantation, and every 6 months thereafter. Data recorded in the J-MACS database between 2010 and 2018 were analyzed in the present study; these data comprised clinical and demographic characteristics (age, sex, marital status, highest educational level, working status, type of heart disease, treatment history, New York Heart Association [NYHA] functional classification for heart failure, Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS] profile, incidence of 4 major complications [device failure, major infection, stroke, and major bleeding])[20] and HRQoL. All participants provided informed consent at their respective institutions before LVAD implantation, and institutional review board approval was obtained from each participating institution. Patients were required to provide written consent before enrollment in J-MACS.

Patients were divided into 3 treatment strategy groups in this study: the primary implantable LVAD group (G-iLVAD; patients with only iLVADs); the primary paracorporeal LVAD group (G-pLVAD; patients with only Nipro-Toyobo VADs [Nipro VAD; Nipro, Osaka, Japan]); and the BTB from paracorporeal to implantable LVAD group (G-BTB; patients transitioning from pLVADs to iLVADs). Accordingly, we initially screened 961 patients from the 1,165 patients registered at 40 Japanese institutions between January 1, 2010 and December 31, 2018.

HRQoL Assessment

The primary outcome of this study was obtained using the EuroQoL 5-dimension 3-level version (EQ-5D-3L), which comprises a visual analog scale (VAS) and scores for 5 dimensions. The VAS enables self-rating on a 20-cm vertical scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).[21] The 5 dimensions comprise the following domains: social function (usual activities), mental function (anxiety/depression), physical function (mobility and self-care), and disability (pain/discomfort).[22]

Table. Preimplantation Characteristics of Patients According to Therapeutic Strategy

	iLVAD (n=483)	pLVAD (n=33)	BTB (n=65)	P value
Age (years)	44.7±12	35.4±11.7	40.1±11.6	<0.001
Male sex (%)	77.0	51.5	76.9	<0.05
Marital status, married (%)	63.3	39.4	56.9	<0.05
Final education, >high school (%)	52.8	51.5	55.4	0.91
Working for income, yes (%)	32.1	24.2	20.0	0.10
Primary cardiac diagnosis (%)				0.10
Dilated cardiomyopathy	67.9	72.7	70.8	
Coronary artery disease	7.7	3.0	16.9	
Hypertrophic cardiomyopathy	11.8	12.1	7.7	
Other	12.6	12.1	4.6	
INTERMACS profile (%)				<0.001
Level 1	2.3	51.5	12.3	
Level 2	40.0	45.5	13.9	
Level 3	50.7	3.0	70.8	
Levels 4–7	7.0	0.0	3.1	
NYHA class (%)				<0.001
I	0.0	0.0	15.4	
II	1.9	0.0	32.3	
III	18.2	3.0	30.8	
IV	79.9	97.0	21.5	
Laboratory data				
Hemoglobin (g/dL)	11.9±1.8	10.7±1.9	10.2±1.5	<0.001
Albumin (g/dL)	3.7±0.5	3.2±0.6	3.6±0.5	<0.001
Total bilirubin (mg/dL)	1.3±1.3	2.6±2.6	1.0±0.5	<0.001
Urea nitrogen (mg/dL)	20.9±12.8	24.4±14.5	12.6±8.4	<0.001
Serum creatinine (mg/dL)	1.1±0.4	1.1±0.6	0.8±0.3	<0.001
BNP (pg/mL)	723 [668–780]	1,175 [959–1,391]	367 [208–526]	<0.001

Unless indicated otherwise, data are given as the mean±SD or median [interquartile range]. BNP, B-type natriuretic peptide; BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; iLVAD, primary implantable left ventricular assist device; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; NYHA, New York Heart Association; pLVAD, primary paracorporeal left ventricular assist device.

Each dimension has 3 levels, namely "no problem," "some or moderate problems," and "extreme problems". Patient-reported results for each dimension were measured in terms of the percentage of respondents indicating moderate or extreme problems.[22]

Statistical Analysis

Preimplantation patient characteristics, with and without EQ-5D-3L, are summarized as the mean±SD for continuous variables or as numbers and percentages for categorical variables. The significance of intergroup differences in these variables were evaluated using analysis of variance (ANOVA) and the Chi-squared test, respectively. ANOVA (followed by the Tukey-Kramer test where applicable) was used to evaluate the significance of differences in mean VAS scores among the 3 groups before implantation and at 3 and 12 months after implantation. These data were also compared using analysis of covariance to adjust for age, sex, and NYHA class. To examine whether quality of life (QoL) improved after implantation in each group, we compared VAS scores before implantation with those at 3 and 12 months after implantation using mixed-effects models for repeated measures. A change of ≥10 points in the VAS score over time was considered clinically important.[12] The proportions of patients with problems across the 5 dimensions before implantation and at 3 and 12 months after implantation were compared among the groups using Chi-squared and Fisher's exact tests. Furthermore, we performed a similar analysis in patients with NYHA Class IV. Finally, the proportions of patients in each group with problems in each dimension before implantation and at 3 and 12 months after implantation were compared using mixed-effects logistic regression models for repeated measures. All significance levels were set at $P<0.05$. Data analyses were performed using JMP Pro® 14 and SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Among the 961 patients who met the criteria for iLVAD, pLVAD, and BTB treatments, 380 were excluded because of a lack of VAS score or data on the 5 dimensions at any time point (before and 3 and 12 months after implantation). Thus, 581 patients were included in the final analysis (**Figure 1**). The most common reason for not obtaining EQ-5D-3L was being "too sick" (n=232). The least amount of complete data was available for the G-pLVAD group (n=109). The respective number of participants before implantation and 3 and 12 months after implantation was 263, 392, and 349 in the G-iLVAD group; 9, 28, and 13 in

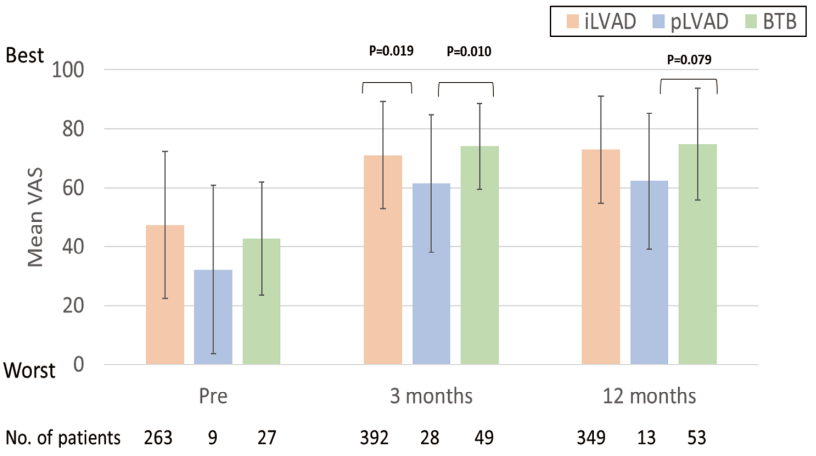

Figure 2. Mean (±SD) EuroQoL 5-dimension 3-level (EQ-5D-3L) visual analog scale (VAS) scores according to different therapeutic strategies. 3 months, 3 months after implantation; 12 months, 12 months after implantation; BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; iLVAD, primary implantable left ventricular assist device; pLVAD, primary paracorporeal left ventricular assist device; pre, preimplantation.

the G-pLVAD group; and 27, 49, and 53 in the G-BTB group. Of the 581 participants in this study, 18.3% and 45.3% experienced major complications 3 and 12 months after implantation, respectively. The incidence of major complications in the G-iLVAD, G-pLVAD, and G-BTB groups at 12 months was 43.3%, 94.1%, and 43.4%, respectively (P<0.001). Furthermore, 49 (10.1%), 4 (12.1%), and 4 (6.2%) patients in the G-iLVAD, G-pLVAD, and G-BTB groups, respectively, died during follow-up through June 31, 2019. Conversely, 123 (25.5%), 13 (39.4%), and 20 (30.8%) patients in the G-iLVAD, G-pLVAD, and G-BTB groups, respectively, underwent HTx.

The demographic characteristics of patients in each of the 3 groups with available HRQoL data are summarized in the **Table**. The mean age at LVAD implantation in the G-iLVAD, G-pLVAD, and G-BTB groups was 44.7±12.0, 35.4±11.7, and 40.1±11.6 years, respectively. Moreover, in the G-iLVAD, G-pLVAD, and G-BTB groups, 77.0%, 51.5%, and 76.9% of patients, respectively, were men, and 63.3%, 39.4%, and 56.9%, respectively, were married. Patients in the G-pLVAD group were significantly younger and more likely to be women and unmarried. Age, sex distribution, and marital status differed significantly among the 3 groups (P<0.001, P=0.004, and P=0.018, respectively; **Table**).

Dilated cardiomyopathy was the most common primary underlying cardiac diagnosis in all 3 groups (67.9%, 72.7%, and 70.8% in the G-iLVAD, G-pLVAD, and G-BTB groups, respectively; **Table**). The INTERMACS profile differed significantly among the 3 groups (P<0.001). The percentage of patients with INTERMACS profile Level 1 at target LVAD implantation was higher in the G-pLVAD than G-iLVAD and G-BTB groups (51.5% vs. 2.3% and 12.3%, respectively; **Table**). Conversely, the percentage of patients with a Level 2 profile was similar in the G-pLVAD and G-iLVAD groups (45.5% and 40.0%, respectively; **Table**). The percentage of patients with a Level 3 profile was highest in G-BTB group (70.8%), followed by the G-iLVAD (50.7%) and G-pLVAD (3.0%) groups (**Table**). The NYHA class at target LVAD implantation also differed significantly among the groups (P<0.001). The percentage of patients with NYHA Class IV was higher in the G-iLVAD and G-pLVAD groups than in the G-BTB group (79.9% and 97.0% vs. 21.0%, respectively; **Table**). The percentage of patients with NYHA Class III was higher in the G-BTB than G-iLVAD and G-pLVAD groups (30.8% vs. 18.2% and 3.0%, respectively; **Table**). All LVAD preimplantation laboratory data also differed significantly among the 3 groups (P<0.001; **Table**).

The preimplantation characteristics differed among the 581 patients with EQ-5D-3L, and were compared with the corresponding characteristics of the 380 excluded patients without EQ-5D-3L (**Supplementary Table**). Furthermore, the proportion of patients with INTERMACS profiles Levels 1/2, NYHA Class IV, coronary artery disease, a low level of education, and inconsistent income before implantation was higher among patients without than with EQ-5D-3L.

EQ-5D-3L VAS Scores

The mean preimplantation VAS scores in the G-iLVAD, G-pLVAD, and G-BTB groups were 47.4, 32.2, and 42.7, respectively. Three months after implantation, the mean VAS scores in the G-iLVAD, G-pLVAD, and G-BTB groups were 71.1, 61.4, and 74.0, respectively, with the scores being significantly lower in the G-pLVAD group than in the G-iLVAD (P=0.019) and G-BTB (P=0.010) groups (**Figure 2**). The VAS score at 3 months was significantly lower in the G-pLVAD than G-iLVAD group, even after adjusting for age, sex, NYHA Class IV, primary cardiac diagnosis, and laboratory data. Twelve months after implantation, the mean VAS scores in the G-iLVAD, G-pLVAD, and G-BTB groups were 72.9, 62.3, and 74.7, respectively. The scores at 12 months after implantation differed significantly between the G-pLVAD and G-BTB groups (P=0.079; **Figure 2**). Similar results were obtained at 12 months after adjusting for age, sex, NYHA Class IV, primary cardiac diagnosis, and laboratory data. A primary cardiac diagnosis of dilated cardiomyopathy, B-type natriuretic peptide level, and therapeutic strategy were significantly associated with the VAS score at 3 months. However, only therapeutic strategy was significantly associated with the VAS score at 12 months (data not shown).

Changes in the least squares mean VAS scores at 3 and 12 months after implantation differed significantly among the 3 groups. The respective changes in the least squares mean VAS scores at 3 and 12 months after implantation were 23.3 (95% confidence interval [CI] 20.6–25.9; P<0.001)

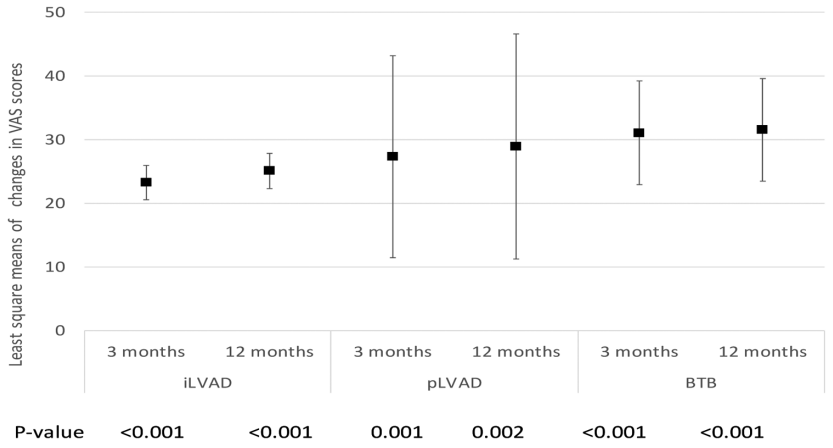

Figure 3. Least squares means (±95% confidence intervals) of changes in EuroQoL 5-dimension 3-level (EQ-5D-3L) visual analog scale (VAS) scores from preimplantation to 3 and 12 months after implantation. BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; iLVAD, primary implantable left ventricular assist device; pLVAD, primary paracorporeal left ventricular assist device.

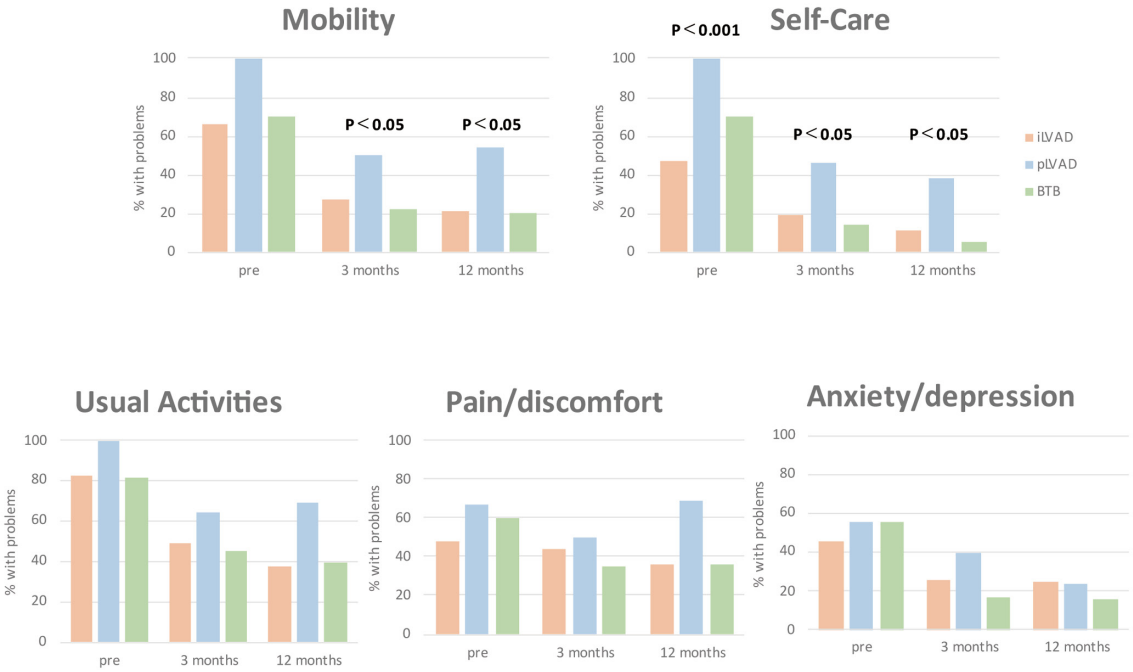

Figure 4. Percentage of patients reporting problems in each of the 5 dimensions of the EuroQoL 5-dimension 3-level (EQ-5D-3L) before (pre) implantation and 3 and 12 months after implantation according to therapeutic strategy. BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; iLVAD, primary implantable left ventricular assist device; pLVAD, primary paracorporeal left ventricular assist device.

and 25.1 (95% CI 22.3–27.8; P<0.001) in the G-iLVAD group; 27.3 (95% CI 11.5–43.2; P=0.001) and 28.9 (95% CI 11.3–46.6; P=0.002) in the G-pLVAD group; and 31.1 (95% CI 22.9–39.2; P<0.001) and 31.5 (95% CI 23.5–39.6; P<0.001) in the G-BTB group (**Figure 3**). Furthermore, changes in the least squares mean VAS scores at 3 and 12 months after implantation in the complete dataset also differed significantly in each of the 3 groups.

Changes in EQ-5D-3L Dimensions

In all groups, the percentage of patients with problems in the EQ-5D-3L dimensions decreased from before implantation to 3 months after implantation. Similarly, the percentage of patients with problems in the EQ-5D-3L dimensions decreased from before implantation to 12 months in all 3 groups, with the exception of pain/discomfort in the G-pVLAD group. In this group, pain/discomfort decreased from 66.7% before implantation to 50% at 3 months, before increasing to 69.2% at 12 months (**Figures 4**,**5**). Before implantation, there was a tendency for a difference among the 3 groups in the percentage of patients experiencing mobility issues (P=0.098) and a significant difference in the

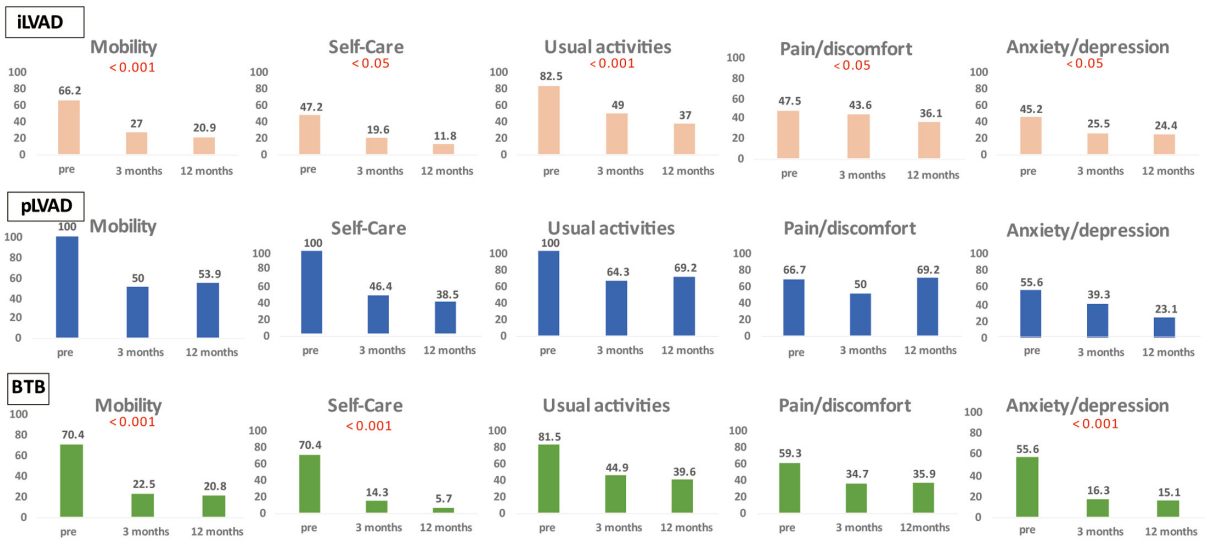

Figure 5. Temporal changes in the percentage of patients reporting problems in each of the 5 dimensions of the EuroQoL 5-dimension 3-level (EQ-5D-3L) before (pre) implantation and 3 and 12 months after implantation according to therapeutic strategy. BTB, bridge-to-bridge from paracorporeal to implantable left ventricular assist device; iLVAD, primary implantable left ventricular assist device; pLVAD, primary paracorporeal left ventricular assist device.

percentage of patients experiencing self-care problems (P<0.001). At 3 and 12 months, the percentage of patients experiencing mobility and self-care problems was significantly higher in the G-pLVAD group (mobility: 50.0% and 53.9%, respectively; self-care: 46.4% and 38.5%, respectively) than in the G-iLVAD (mobility: 27.0% and 20.9%, respectively [P=0.002]; self-care: 19.6% and 11.8%, respectively [P=0.002]) and G-BTB (mobility: 22.5% and 20.8%, respectively [P=0.018]; self-care: 14.3% and 5.7%, respectively [P=0.005]) groups (**Figure 4**). A comparison of patients with NYHA Class IV there were similar percentages of patients with NYHA Class IV across the 3 groups at each time point (data not shown). In particular, all patients in the G-pLVAD group had problems with mobility, self-care, and usual activities before implantation. However, the percentage of patients experiencing mobility and self-care problems in the G-pLVAD group decreased from 100% to 50% after implantation. Similarly, the percentage of patients in the G-iLVAD and G-BTB groups experiencing mobility and self-care problems also decreased significantly after LVAD implantation (P<0.001 and P<0.006, respectively, in the G-iLVAD group; P<0.001 and P<0.001, respectively, in the G-BTB group; **Figure 5**).

Conversely, more than 80% of patients in all groups had problems with usual activities before implantation, with the highest percentage in the G-pLVAD group (100%). Although the proportion of patients with problems with usual activities decreased 3 and 12 months after implantation, some patients continued to experience problems with usual activities at these time points (G-pLVAD: 64.3% and 69.2%, respectively; G-iLVAD: 49.0% and 37.0%, respectively; G-BTB: 44.9% and 39.6%, respectively).

The trends in pain/discomfort and anxiety/depression differed from those in the other 3 dimensions. The percentage of patients experiencing pain/discomfort decreased by 10–25% from before to 3 and 12 months after implantation in the G-iLVAD and G-BTB groups. However, in the G-pLVAD group, the percentage of patients experiencing pain/discomfort increased from 66.7% before implantation to 69.2% 12 months after implantation. In all 3 groups, the decreases in the percentage of patients with pain/discomfort after VAD implantation were lower than the decreases in the percentage of patients with problems regarding mobility, self-care, and usual activities. There was no significant difference among the G-iLVAD, G-pLVAD, and G-BTB groups in the percentage of patients with anxiety/depression before implantation (45.2%, 55.6%, and 55.6%, respectively). However, the trends in anxiety/depression differed from those in pain/discomfort. First, the percentage of patients with anxiety/depression decreased significantly from before implantation (55.6%) to 3 and 12 months after implantation (16.3% and 15.1%, respectively; P<0.001) in the G-BTB group. Second, the incidence of anxiety/depression decreased over time among patients in the G-pLVAD group. The anxiety/depression reported by patients in the G-iLVAD and G-pLVAD groups decreased by approximately 20% at 3 and 12 months after implantation.

Discussion

To the best of our knowledge, this is the first study in Japan to comparatively investigate long-term HRQoL according to different VAD-based therapeutic strategies. With the G-pLVAD, G-iLVAD, and G-BTB strategies, HRQoL improved 3 months after implantation (BTB was extracorporeal at this point) and this improvement was maintained at 12 months. Significant changes in the EQ-5D-3L VAS scores (i.e., by ≥10 points) were noted for all treatment groups. Although HRQoL was lower in the G-pLVAD than G-iLVAD group before and 3 and 12 months after implantation, it improved with conversion from G-pLVAD

to G-iLVAD (BTB group). Patients with pLVADs were more severely ill than those with iLVADs. Major complications were reported at the 12-month follow-up after pLVAD implantation in >90% of patients and after iLVAD implantation in >45% of patients. A higher proportion of patients in the G-pLVAD group had missing EQ-5D-3L (52.8%); accordingly, compared with the group with fewer complications (G-iLVAD), the group with more major complications (G-pLVAD) also had a higher proportion of patients with missing EQ-5D-3L. Thus, even if the data were available, the difference in the EQ-5D-3L between the G-pLVAD and G-iLVAD groups would have been greater. Therefore, HRQoL may have been underestimated in the G-pLVAD group.

The improvement in HRQoL from before to after VAD implantation was in line with previously reported findings.[10–15] However, in the previous studies, several participants were managed with DT strategies.[10–13,15] HRQoL has been compared among the BTT, DT, and BTC strategies.[10] Sato et al reported an improved QoL at the 60-month follow-up in patients who underwent VAD implantation for BTT, even in the presence of serious adverse events.[23] However, there are no reports on extracorporeal VADs and no detailed findings on HRQoL.[23] Therefore, the present study is the first Japanese study to reveal improvements in HRQoL (with detailed findings) after implementation of the pLVAD and BTB therapeutic strategies. Studies have compared pLVADs and iLVADs at an early time point (3 months) after implantation.[14] However, the present study also included data for evaluations at 12 months, which showed that the VAS scores were higher for the G-iLVAD than G-pLVAD group before and 12 months after implantation. This was supported by the findings that the VAS scores in the G-BTB group improved from before implantation (with pLVADs) to 3 and 12 months after implantation (with iLVADs). Furthermore, the VAS scores at 3 and 12 months after VAD implantation improved by a greater extent in the G-BTB than G-pLVAD and G-iLVAD groups. Therefore, although the survival rate is slightly lower for BTB than for iLVADs,[7,24] BTB was significantly better than pLVAD alone in terms of patient survival and HRQoL in the present study.

In the present study, the therapeutic strategy was the only factor affecting the QoL at 12 months. Although not all factors could be considered, our findings suggest that the influence of the device itself (i.e., the therapeutic strategy) on the HRQoL may be greater than that of the clinical factors. Therefore, advances in VAD technology may enable QoL enhancement. Regarding VAD development in terms of extracorporeal systems, the use of "BIOFLOAT NCVC" (Nipro Corporation, Osaka, Japan), an extracorporeal continuous-flow VAD system, has increased in recent years.[25,26] However, in light of the increasing use of the EXCOR Pediatric VAD (Berlin Heart, Berlin, Germany) with a pulsatile flow pump[27] and the fact that J-MACS data on extracorporeal VAD-only enrollment ended on December 31, 2018, the present study provides the only valuable data on long-term QoL with pulsatile flow extracorporeal VAD implantation. Therefore, our findings may be useful for managing patients with EXCOR and for comparison with findings on the use of newly approved extracorporeal centrifugal VADs (BIOFLOAT NCVC).

The percentage of patients with problems in the social function (usual activities), mental function (anxiety/depression), physical function (mobility and self-care), and disability (pain/discomfort) domains decreased in all groups from before to after VAD implantation. This trend was similar to that reported previously.[11,12] Before VAD implantation, 100% of patients in the G-pLVAD group had problems with mobility, usual activities, and self-care. However, after implantation, problems with mobility and self-care improved in all groups, with significant improvements in the G-iLVAD and G-BTB groups.

The percentage of patients with self-care problems differed significantly among the 3 groups at all time points (i.e., before and 3 and 12 months after implantation). Self-care reportedly affects patients with VADs both physically and psychologically,[28] and is an important assessment item of the HRQoL in these patients. Although the percentage of patients with self-care problems decreased with each therapeutic strategy, these problems were still more common in the G-pLVAD group (which required treatment in the hospital) than in the G-iLVAD and G-BTB groups (which allowed treatment at home). Self-care for patients with VADs extends beyond the questionnaire items (i.e., washing and dressing), and 24-h VAD management is essential. Yamanaka et al[29] reported on the suffering of patients with VADs (either iLVADs or pLVADs) who "cannot live without the help of others". However, the EQ-5D-3L does not provide detailed data. Kato et al,[30,31] referring to Riegel et al,[32] classified the self-care of patients with LVADs in terms of "maintenance", "monitoring", and "management"; from these, specific subscales (e.g., LVAD system operation) were further developed. These measures should be used in conjunction with disease- and treatment-specific scales to identify and evaluate specific patient problems.

Usual activities are an item of social functioning and refer to the patient's social relationships and roles. In all 3 groups, many patients continued to experience problems with usual activities from before to after implantation. Yamanaka et al[19] reported that patients with iLVADs faced difficulties reintegrating into society (including difficulties with appointing caregivers). Limited social functioning is a common problem in patients with VADs.[11,12,33] The International Society for Heart and Lung Transplantation guidelines recommend a social psychological assessment before VAD placement,[34,35] and are beginning to use the Stanford Integrated Psychosocial Assessment for Transplantation.[36,37] In Japan, there is an urgent need to apply these indicators.

The percentage of patients with disability (pain/discomfort) and mental function (anxiety/depression) problems did not differ among the 3 groups. Pain/discomfort underwent a small improvement after VAD implantation, suggesting that it may not be directly alleviated by VAD implantation. However, in the G-BTB group, the incidence of anxiety/depression was reduced and a large improvement in these problems was noted after bridging from extracorporeal to implantable VADs. This may be explained by the patients' perceptions of the advantages iLVADs offer over pLVADs. This is an important finding for the BTB strategy.

This study has 3 major limitations. First, 24% of all patients were too ill to participate, and HRQoL data were not available in many cases. Therefore, the number of patients with serious conditions may have been underestimated. It is necessary to consider methods that ensure that HRQoL data can be obtained, followed, and evaluated over time, even in patients with severe diseases and other populations. For instance, a proxy assessment is available

for children, namely the EuroQoL Five-Dimensional Questionnaire, Youth Version (EQ-5D-Y).[38] Second, because iLVAD with BTT is currently the mainstream therapeutic strategy in Japan, the number of patients analyzed differed among the 3 groups. The number of patients in the G-pLVAD group was particularly small; this may have affected the group comparisons. Finally, because the EQ-5D-3L is a comprehensive HRQoL scale, disease-specific problems may not be fully understood. However, by combining the 5 dimensions and the VAS, the overall health of patients with VADs could be evaluated according to the therapeutic strategy.

Conclusions

This study showed that the HRQoL of patients receiving iLVAD, pLVAD, and BTB improved at 3 and 12 months after VAD implantation. The VAS scores and scores for the 5 dimensions on the EQ-5D-3L were lower for the G-pLVAD than G-iLVAD (which reported more problems) group; however, these parameters improved after converting G-pLVAD to G-iLVAD (BTB). Greater improvements were reported in physical function after LVAD treatment than in social function, disability, and mental function, regardless of the therapeutic strategy. Therefore, more detailed and unified indicators, specific to patients with VADs, must be constructed and evaluated with the inclusion of these items. A long-term study should be conducted on patients receiving both BTT and DT. Furthermore, as LVAD treatments undergo technological advances, data must be validated by comparison with data from existing HRQoL instruments.

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Disclosures

The authors declare that there are no conflicts of interest.

IRB Information

This study was approved by the National Cerebral and Cardiovascular Center Ethics Review Committee (R19074; November 7, 2019) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (R2278-1; February 17, 2020).

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
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