Quality of Life and Influential Factors in Patients Implanted With a Left Ventricular Assist Device

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Background: Improving quality of life (QOL) has become an important goal in left ventricular assist device (LVAD) therapy. We aimed (1) to assess the effect of an implantable LVAD on patients’ QOL, (2) to compare LVAD patients’ QOL to that of patients in different stages of heart failure (HF), and (3) to identify factors associated with patients’ QOL.

Methods and Results: The QOL of 33 Japanese implantable LVAD patients was assessed using the Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Short-form 8 (SF-8), before and at 3 and 6 months afterwards. After LVAD implantation, QOL significantly improved [MLHFQ, SF-8 physical component score (PCS), SF-8 mental component score (MCS), all P<0.05]. Implanted LVAD patients had a better QOL than extracorporeal LVAD patients (n=33, 32.1±21.9 vs. n=17, 47.6±18.2), and Stage D HF patients (n=32, 51.1±17.3), but the score was comparable to that of patients who had undergone a heart transplant (n=13). In multiple regression analyses, postoperative lower albumin concentration and right ventricular failure were independently associated with poorer PCS. Female sex and postoperative anxiety were 2 of the independent factors for poorer MCS (all P<0.05).

Conclusions: Having an implantable LVAD improves patients’ QOL, which is better than that of patients with an extracorporeal LVAD. Both clinical and psychological factors are influence QOL after LVAD implantation.

Key Words: Heart failure; Mechanical circulatory support; Patient-reported outcomes; Quality of life

Left ventricular assist device (LVAD) therapy is expected to be increasingly indicated as a bridge to transplant or/and destination therapy. However, studies focusing on the effect of LVAD therapy on patients’ quality of life (QOL) are limited. In Japan, the number of LVAD patients has been increasing since implantation became covered by health insurance in 2011. It is important to know the effect of LVAD therapy from the patients’ perspective.

Comparison of the QOL of patients with an implantable LVAD and those in different stages of heart failure (HF) might help healthcare professionals to understand how much improvement in QOL can be expected from implantable LVADs. Several studies have shown that implantable LVAD patients have a better QOL than heart transplantation (HTx) patients.

Meanwhile, there are no studies evaluating the difference in QOL between implantable and extracorporeal LVAD patients. The 2 types of LVADs provide similar results in terms of systemic circulation assist and cardiac unloading effect, but the effect on patients’ QOL may differ.

It is important to understand the factors associated with patients’ QOL in order to outline management strategies for LVAD patients that do not only focus on objective goals, but also on the patients’ perceptions. Prior studies have shown limited associations between psychological distress and QOL, suggesting that factors other than psychological problems may be important in determining QOL after LVAD implantation.

The purpose of the present study was (1) to evaluate the effect of an having an implantable LVAD on patients’ QOL,
(2) to compare implantable LVAD patients’ QOL to that of patients in different HF stages, and (3) to identify factors associated with patients’ QOL after LVAD implantation.

**Methods**

**Study Patients and Procedure**

We used data from a follow-up study of LVAD patients and data from a cross-sectional study of HF patients from the University of Tokyo Hospital between December 2011 and August 2014.

**Follow-up Study**  A prospective, observational, repeated-measure design was chosen to characterize changes in QOL over time among patients undergoing LVAD implantation. The study participants were consecutive patients who underwent continuous-flow implantable LVAD therapy, including DuraHeart (Terumo Heart, Ann Arbor, MI, USA), HeartMate II (Thoratec Corporation, Pleasanton, CA, USA), and EVAHEART (Sun Medical, Nagano, Japan) as a bridge to transplant. Patients were instructed to complete the questionnaire at hospital before implantation and at the home 3 and 6 months after implantation.

**Cross-Sectional Study** At 3 months after LVAD implantation we compared the patients’ QOL to that of patients in different stages of HF: (1) stage D HF patients without any LVAD, who were listed for HTx, (2) patients receiving a pulsatile-pump extracorporeal LVAD (NIPRO-VAD, National Cardiovascular Center/Toyobo ventricular system) within 2 years, and (3) patients at 3 months after HTx. They were instructed to complete the questionnaire at hospital or at home.

The study was approved by the Institutional Review Board at the University of Tokyo Hospital (No. 3265-1). All participating patients provided written informed consent.

**QOL** Disease-specific QOL was examined by the Minnesota Living with Heart Failure Questionnaire (MLHFQ). The MLHFQ has 21 items that cover HF-related physical, psychological, and social impairments, and is one of the most widely used questionnaires for evaluating HF-specific QOL in patients on implantable LVAD support. The total MLHFQ score is obtained by adding the scores for all 21 items (range 0–105), with higher scores indicating worse QOL. The psychometric properties of the MLHFQ have been confirmed.

Generic QOL was assessed using the Medical Outcomes Study 8-item Short-Form Health Survey (SF-8), which is compatible with SF-36. The physical health component summary score (PCS) and mental health component summary score (MCS) were measured using the Japanese Norm-Based Scoring method. For PCS and MCS, higher scores represent better QOL. The valid-
metric properties of the HADS have been demonstrated. A higher score indicating severe symptoms. The psycho-
anxiety subscale. The score for anxiety ranges from 0 to 21, items), and depression (7 items). In this study, we used the HADS consists of 14 items and has 2 subscales: anxiety (7

The patients’ anxiety level was also measured using the Hospital Anxiety and Depression Scale (HADS).

A univariate analysis was initially performed. Pearson’s correlation coefficient, Student’s t-test or Mann-Whitney U-test was used. After assessing multicollinearity, we performed a multiple regression analysis with backward method, in which we included variables related to the QOL score at P<0.15 in the univariate analysis. In this study, we only used a variable LVDD instead of LVDS in the multivariate model, because there were significant associations between these 2 parameters (r=0.97, P<0.01). The amount of missing data for items was estimated with the average score for the valid items in the questionnaire. When the missing data accounted for more than 30% of the questionnaire, we excluded it from the analysis. All statistical tests were two-tailed, and statistical significance was defined as P<0.05. All analyses were performed with SAS version 9.3 (SAS Institute Inc, Cary, NC, USA).

Results
We enrolled and analyzed 33 patients with implantable LVADs in our study (Table 1). The mean age of the implantable LVAD patients was 38±12 years, and 82% were male. In total, 12% had ischemic cardiomyopathy, and 76% had dilated cardiomyopathy. One-third of the patients were preoperatively treated with an extracorporeal LVAD. Of the 33 patients, 15 had the EVHEART (45%), 9 had the DuraHeart (27%), and 9 had the HeartMate II (27%). After LVAD implantation, mean serum albumin level was 3.9±0.5 g/dl, and HAD-anxiety score was 4.3±2.5 (range 0–21). During the follow-up, 6 patients were hospitalized for ventricular fibrillation and ventricular tachycardia (n=2), transient ischemic attack (n=1), thrombosis (n=1), infection (n=1), and pulmonary hypertension (n=1). Approximately 40% of the patients (n=13) had RVF postoperatively.

The QOL of the implantable LVAD patients was compared with that of 62 patients in different stages of HF, including 32

Table 2. Characteristics of Study Patients in 4 Groups

<table>
<thead>
<tr>
<th>Demographic and clinical characteristics</th>
<th>All (n=95)</th>
<th>Implantable LVAD (n=33)</th>
<th>Stage D (n=32)</th>
<th>Extracorporeal LVAD (n=17)</th>
<th>Heart transplant (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, male</td>
<td>72 (76%)</td>
<td>27 (82%)</td>
<td>23 (72%)</td>
<td>14 (82%)</td>
<td>8 (62%)</td>
</tr>
<tr>
<td>Age, years</td>
<td>39±12</td>
<td>38±12</td>
<td>42±12</td>
<td>36±11</td>
<td>41±13</td>
</tr>
<tr>
<td>Marital status, married</td>
<td>42 (44%)</td>
<td>14 (42%)</td>
<td>18 (56%)</td>
<td>6 (35%)</td>
<td>4 (31%)</td>
</tr>
<tr>
<td>Ischemic etiology</td>
<td>10 (11%)</td>
<td>4 (12%)</td>
<td>2 (6.3%)</td>
<td>3 (18%)</td>
<td>1 (7.7%)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>28.0±21.1</td>
<td>18.8±12.0</td>
<td>21.0±13.6</td>
<td>26.1±12.9</td>
<td>70.7±7.1*</td>
</tr>
<tr>
<td>BNP pg/ml</td>
<td>399±405</td>
<td>263±167</td>
<td>749±497*</td>
<td>194±212</td>
<td>153±113*</td>
</tr>
<tr>
<td>BNP pg/ml, geometric mean (95% CI)</td>
<td>259 (213–314)</td>
<td>217 (172–274)</td>
<td>593 (455–773)*</td>
<td>134 (86–209)</td>
<td>124 (83–185)*</td>
</tr>
<tr>
<td>Time on LVAD support or time elapsed since heart transplant, days, median (Q1–Q3)</td>
<td>113 (92–161)</td>
<td>115 (102–142)</td>
<td>90 (55–512)</td>
<td>136 (108–174)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are n (%) or mean±SD. *P<0.05 vs. implantable LVAD patients by Dunnett’s multiple comparison test for continuous variables with a normal distribution or Bonferroni correction for continuous variables with a non-normal distribution and categorical variables. CI, confidence interval. Other abbreviations as in Table 1.
stage D HF patients, 17 extracorporeal LVAD patients, and 13 patients who had undergone HTx (Table 2). Compared with patients on implantable LVAD support, the HTx patients had higher LVEF (19% vs. 71%) at the time of data collection, whereas stage D HF patients had higher BNP level (217 pg/ml vs. 593 pg/ml). There were no significant differences in clinical characteristics, including body surface area (1.67±0.14 vs. 1.66±0.13), between implantable and extracorporeal LVAD patients. The time on implantable LVAD support (median 115 days, Q1–Q3 102–142) when they answered the questionnaire was comparable to that of the extracorporeal LVAD patients (90 days, 55–512).

In our study, approximately half of the extracorporeal LVAD patients (n=9, 53%) had undergone LVAD therapy before implantable LVAD was covered by Japanese health insurance in 2011; 6 extracorporeal LVAD patients (35%) had been on LVAD therapy for more than 1 year at the time of data collection; 7 patients (41%) with extracorporeal LVADs eventually converted to an implantable one. Of the 32 stage D HF patients, 24 (75%) had INTERMACS profile 3, 4 patients (13%) had profile 2 and 4 patients (13%) had the profile 4. The mean INTERMACS profile was 3.0±0.5.

Changes in QOL Scores
The MLHQF score of the implanted LVAD patients decreased over time, indicating an improvement in QOL (P<0.01, Figure 1A). When compared with the MLHQF score (42.6±16.1) before implantation [median 24 days before implantation (Q1–Q3, 11–57)], patients’ QOL scores significantly improved at 3 months (32.1±21.9, P<0.01), as well as at 6 months (37.2±22.8, P=0.049). PCS and MCS also improved over time (Figure 1B, both P=0.02). Compared with the PCS and MCS scores before implantation (PCS, 36.2±8.1; MCS, 41.4±8.7), the scores were significantly higher at both 3 months (PCS, 42.8±9.3, P=0.02; MCS, 46.0±7.0, P=0.03), and 6 months (PCS, 42.1±9.9, P=0.049; MCS, 46.6±7.3, P=0.01).

Figure 1. Changes in QOL. (A) Lower scores on the MLHQF (Minnesota Living with Heart Failure Questionnaire) indicate better QOL. (B) Higher scores on the Short-form 8 (SF-8) indicate better QOL. MCS, mental component summary score; PCS, physical component summary score; QOL, quality of life. *P<0.05 compared with baseline by Dunnett’s multiple comparison method.

Figure 2. Comparisons of MLHQF (Minnesota Living with Heart Failure Questionnaire) score. Lower scores indicate better QOL. *P<0.05 vs. implanted LVAD at 3 months by Dunnett's multiple comparison test. Bars indicate 25th, 50th, and 75th percentiles, whiskers indicate 5th and 95th percentiles. LVAD, left ventricular assist device.
**Discussion**

The major findings of the study were that (1) QOL improved after LVAD implantation, and those patients’ QOL was better than that of extracorporeal LVAD patients, and (2) lower postoperative albumin levels and RVF are independent factors related to lower physical QOL at 3 months after LVAD implantation. Female sex and higher postoperative level of anxiety are 2 of the independent factors associated with lower mental QOL.

We believe this is the first study to show a significant effect of RVF on physical QOL at 3 months after LVAD implantation. RVF occurs in approximately 10–40% of patients undergoing LVAD implantation.12,15,16 Despite significant advances in device technology and pre- and postoperative care, RVF remains a major cause of death, higher rate of re-operation for bleeding and renal failure, and longer hospital stay.12,15,16 Our study expands these findings and highlights the importance of appropriate RVF management and prevention to improve patients’ QOL as well as clinical outcomes.

The preoperative albumin level is considered an important risk factor for death after LVAD implantation,17,18 but our study did not confirm this. However, we found a positive relationship between postoperative albumin levels and physical QOL.

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**Table 3. Factors Associated With QOL Among Implantable LVAD Patients at 3 Months in a Univariate Analysis**

<table>
<thead>
<tr>
<th>QOL score</th>
<th>Total MLHFQ score</th>
<th>SF-8, physical score</th>
<th>SF-8, mental score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD or r P value</td>
<td>Mean ± SD or r P value</td>
</tr>
<tr>
<td>Demographic and clinical parameters at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27</td>
<td>29.9±20.0</td>
<td>0.22</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
<td>42.1±28.8</td>
<td>-</td>
</tr>
<tr>
<td>Preoperative parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>33</td>
<td>0.254</td>
<td>0.15</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>33</td>
<td>0.272</td>
<td>0.13</td>
</tr>
<tr>
<td>HAD-anxiety score</td>
<td>24</td>
<td>0.409</td>
<td>0.047</td>
</tr>
<tr>
<td>Postoperative parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVDD, mm</td>
<td>33</td>
<td>0.038</td>
<td>0.83</td>
</tr>
<tr>
<td>LVDS, mm</td>
<td>33</td>
<td>0.057</td>
<td>0.75</td>
</tr>
<tr>
<td>Log plasma BNP, pg/ml</td>
<td>33</td>
<td>0.290</td>
<td>0.10</td>
</tr>
<tr>
<td>PCWP, mmHg</td>
<td>33</td>
<td>0.187</td>
<td>0.30</td>
</tr>
<tr>
<td>CVP, mmHg</td>
<td>33</td>
<td>0.305</td>
<td>0.08</td>
</tr>
<tr>
<td>CVP/PCWP ratio</td>
<td>33</td>
<td>0.001</td>
<td>0.99</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>33</td>
<td>0.263</td>
<td>0.14</td>
</tr>
<tr>
<td>Serum albumin, g/dl</td>
<td>33</td>
<td>-0.119</td>
<td>0.51</td>
</tr>
<tr>
<td>Serum AST, U/L</td>
<td>33</td>
<td>-0.062</td>
<td>0.73</td>
</tr>
<tr>
<td>Serum total bilirubin, mg/dl</td>
<td>33</td>
<td>-0.153</td>
<td>0.40</td>
</tr>
<tr>
<td>HAD-anxiety score</td>
<td>33</td>
<td>0.326</td>
<td>0.06</td>
</tr>
<tr>
<td>RVF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20</td>
<td>28.9±21.5</td>
<td>0.30</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>37.2±22.3</td>
<td>38.5±6.0</td>
</tr>
<tr>
<td>Hospitalization for LVAD complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27</td>
<td>29.7±22.9</td>
<td>0.07</td>
</tr>
<tr>
<td>Yes</td>
<td>6</td>
<td>43.3±12.7</td>
<td>40.9±7.0</td>
</tr>
</tbody>
</table>

Table 3 shows results of univariate analysis in which some variables were related to QOL scores at P<0.15. Other results are shown in Table S1. For the Minnesota Living with Heart Failure Questionnaire, higher scores represent more impaired QOL. For the SF-8 summary scores, higher scores represent better QOL. QOL, quality of life; RVF, right ventricular failure. Other abbreviations as in Table 1.

**QOL Comparison**

Patients with implantable LVADs (32.1±21.9) had significantly better QOL than those with stage D HF (51.1±17.3), and those with extracorporeal LVAD (47.6±18.2) (both P<0.05, Figure 2). However, the patients’ QOL at 3 months after LVAD implantation was comparable to that of patients at 3 months after HTx (38.0±19.5).

**Factors Associated With Patients’ QOL**

Table 3 and Table S1 show the results of univariate analysis to identify factors associated with QOL at 3 months after LVAD implantation. In the multiple regression analysis (Table 4), a preoperative higher level of anxiety [standard partial regression coefficients (β)=0.35, P=0.08], and history of hospitalization for LVAD complications (β=0.36, P=0.07) showed a tendency to be associated with lower QOL (higher MLHFQ). Lower levels of postoperative serum albumin (β=0.36, P=0.03), and RVF (β=−0.34, P=0.04) were independent factors related to lower PCS. Determinants of lower MCS were female sex (β=−0.50, P<0.01), higher preoperative systolic blood pressure (β=−0.37, P=0.01), higher postoperative levels of serum creatinine (β=−0.29, P=0.04), and higher postoperative levels of anxiety (β=−0.31, P=0.049).
after LVAD implantation. Postoperative normalization of albumin levels was associated with improved survival in an earlier study. Although we expected that serum albumin levels would be related to RVF, this was not observed (r = −0.12, P = 0.51). Lower albumin levels in our study might reflect a multifactorial derangement, including inflammation, malnutrition and volume status, rather than liver function. These results suggest the importance of postoperative albumin level as a factor influencing patients’ survival, as well as QOL. Hospitalization for LVAD complications was also likely to influence HF-specific QOL. Similar results have been found in a qualitative study. In the present study, 2 of 6 patients were hospitalized for ventricular fibrillation or ventricular tachycardia. Such life-threatening complications might have a more negative effect on the QOL of these patients.

Higher postoperative level of anxiety was one of the independent determinants of lower mental QOL after LVAD implantation, similar to a prior study. Patients need to learn new strategies to manage the physical and psychosocial issues associated with living with a LVAD. Some patients successfully coped with the reality of living with the LVAD, but other patients were anxious about adjusting to the device. Despite the remarkable advancements in LVAD technology, anxiety remains the most common distressing symptom contributing to poor QOL. Although all of our patients received preoperative psychological care from liaison nurses, the results emphasize the need for postoperative psychological assessment and care to support patients after LVAD implantation.

Female sex was also related to lower mental QOL. Currently, approximately 20% of patients in the United States on LVAD support as a bridge to transplantation are women. In our study, women accounted for approximately 20% and most of their caregivers were men. Caregiving is known to be experienced differently by men and women and, likewise, receiving care might also be different for the different sexes. In Japanese culture, women usually play the caregiver role in the family. Under such conditions, it is often difficult for male caregivers to cope and adapt to the new situation, which might influence the QOL of the LVAD patient.

To date there are no studies comparing the QOL of patients with implantable and extracorporeal LVADs. It is noteworthy that we demonstrated that patients undergoing LVAD implantation have a better QOL than extracorporeal LVAD patients. Considering that there were no significant differences in the 1-year survival rate between the 2 types of LVAD, our result is important with respect to the different effects of LVADs on patients’ QOL. The disadvantages of extracorporeal LVADs in Japan is that the use of this device is restricted to the hospital. The advantage of an implantable LVAD is that patients can be discharged from hospital, which might influence the QOL scores. On the other hand, one-third of patients received extracorporeal LVAD and eventually converted to an implantable LVAD. The preoperative physiological and psychological conditions of those patients might be different from patients who received an implantable LVAD directly, which might influence QOL after LVAD implantation.

Meanwhile, no significant differences in QOL scores were observed between the HTx and implantable LVAD groups, which is not in agreement with earlier results showing that HTx patients had a better QOL. This discrepancy might be influenced by the fact that their LVAD patients’ MLHFQ scores were slightly higher (ie, worse QOL) than our score (54–57 vs. 32). Further studies with larger sample sizes are necessary to confirm these observations.

Our result showing that an implantable LVAD enhances patients’ QOL is consistent with earlier studies. In the present study, patients were implanted with 3 different types of continuous-flow LVAD (DuraHeart, HeartMate II, and EVAHEART) as a bridge to transplant, and in Japan they are regularly followed up. Our MLHFQ score at 6 months (37±23) is consistent with the score reported by the HeartMate II study (eg, Slaughter et al, 37±22), which suggests that implantable LVADs could achieve equivalent effects on QOL in the Japanese setting.

### Clinical and Research Implications

The use of implantable LVADs is increasing among patients with advanced HF. Our study confirms the findings from Western countries, showing that implantable LVADs can enhance patients’ QOL in the Japanese setting. However, postoperative RVF, lower albumin levels, anxiety, and female sex are some important factors affecting patients’ QOL after LVAD implantation. Appropriate postoperative assessment of these factors and specific care/management of these patients are essential.

### Study Limitations

First, the small, single-center sample limits the generalizability of our findings. Second, because of the sample size, we could
not include numerous variables in the multivariate analysis, and it was not possible to stratify our results for the type of LVAD. Third, although there were no significant differences in time spent on LVAD support between implantable and extracorporeal LVAD patients, 6 extracorporeal patients were on LVAD support for more than 1 year, which might influence our findings. Fourth, patient selection for implantable LVAD and the circumstances around extracorporeal LVADs changed during the recruiting period of the study. For example, some patients receiving extracorporeal LVAD therapy before 2011 could have received an implanted LVAD in 2014. These changes potentially affected the results. However, in terms of the effect of the LVAD device on patient’s QOL, these changes would not have had much influence on our results. Finally, patients who could not participate in the study might have suffered from more impaired QOL. Therefore, our results could represent an overestimation of the health status experienced by patients.

**Conclusions**

In Japan, patients undergoing LVAD implantation as a bridge to transplantation have a better QOL after the implantation. Implantable LVAD patients have a better QOL than extracorporeal LVAD patients. Postoperative RVF and postoperative lower levels of albumin are independent risk factors for poor physical QOL at 3 months after LVAD implantation. Female sex and higher levels of postoperative anxiety are independently associated with lower mental QOL of LVAD patients.

**Acknowledgments**

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**Conflict of Interest**

None.

**References**


**Supplementary Files**

**Supplementary File 1**

**Table S1.** Factors associated with QOL among implantable LVAD patients at 3 months in a univariate analysis