Patient-Reported Health-Related Quality of Life Is a Predictor of Outcomes in Ambulatory Heart Failure Patients Treated With Left Ventricular Assist Device Compared With Medical Management

Results From the ROADMAP Study (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management)

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**Background**—The prospective observational ROADMAP study (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management) demonstrated that ambulatory advanced heart failure patients selected for left ventricular assist device (LVAD) were more likely to be alive at 1 year on original therapy with ≥75-m improvement in 6-minute walk distance compared with patients assigned to optimal medical management. Whether baseline health-related quality of life (hrQoL) resulted in a heterogeneity of this treatment benefit is unknown.

**Methods and Results**—Patient-reported hrQoL was assessed with EuroQol questionnaire and visual analogue scale (VAS).

We aimed to identify predictors of event-free survival and survival with acceptable hrQoL (VAS≥60). LVAD patients had significant improvement in 3 of 5 EuroQol dimensions ($P<0.05$), but no significant changes were observed with optimal medical management. Among patients with baseline VAS<55, survival on original treatment was lower for optimal medical management patients compared with those assigned to LVAD (58±7% versus 82±5%; $P=0.004$). No such difference was seen if baseline VAS was ≥55 (70±7% versus 75±9%; $P=0.79$). Survival on original therapy with acceptable quality of life was also more likely with LVAD versus optimal medical management if baseline VAS was <55, whereas outcomes in patients with higher baseline VAS scores were similar regardless of treatment assignment ($P=0.046$ for treatment arm and baseline VAS interaction).

**Conclusions**—LVAD therapy resulted in improvement of patient health status in heart failure patients with low self-reported hrQoL, but not in patients with acceptable quality of life at the time of LVAD implantation. Patient-reported hrQoL should be integrated into decision making concerning the use and timing of LVAD therapy in heart failure patients who are symptom limited but remain ambulatory.

**Clinical Trial Registration**—URL: http://www.ClinicalTrials.gov. Unique identifier: NCT01452802.

(Circ Heart Fail. 2017;10:e003910. DOI: 10.1161/CIRCHEARTFAILURE.116.003910.)

**Key Words:** heart-assist devices ■ heart failure ■ health status ■ quality of life ■ risk assessment

Left ventricular assist devices (LVADs) are approved for use in patients in stage D heart failure (HF), either as bridge to transplantation or as permanent (destination) therapy. The optimal timing of LVAD implantation along the continuum of chronic HF is under active investigation. Most patients currently being implanted with LVADs have significant hemodynamic compromise, usually necessitating inotropic support or temporary mechanical support. However, severe hemodynamic derangement at the time of LVAD implantation has been associated with increased risk of mortality and morbidity compared with less-sick patients. Whether LVAD implantation at an earlier stage of chronic HF would lead to favorable outcomes as compared with continued optimal medical management (OMM) of HF was tested in the ROADMAP study (Risk Assessment and Comparative Effectiveness of LVAD and Medical Management). This was a prospective, observational study compared with optimal medical management patients compared with those assigned to LVAD (58±7% versus 82±5%; $P=0.004$). No such difference was seen if baseline VAS was ≥55 (70±7% versus 75±9%; $P=0.79$). Survival on original therapy with acceptable quality of life was also more likely with LVAD versus optimal medical management if baseline VAS was <55, whereas outcomes in patients with higher baseline VAS scores were similar regardless of treatment assignment ($P=0.046$ for treatment arm and baseline VAS interaction).

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observational study of 200 symptom limited, non–inotrope-dependent patients with advanced HF who met the US Food and Drug Administration–approved indications for destination therapy with the HeartMate II LVAD. After being evaluated for LVAD eligibility, 97 patients opted to proceed with LVAD implantation (LVAD group), whereas 103 decided to continue with OMM group. The primary end point of the study was a composite of survival on original therapy and improvement in 6-minute walk distance (6MWD) by ≥75 m. More patients who received LVAD support achieved the primary composite end point than those who were managed with OMM alone (39% versus 21% at 12 months and 30% versus 12% at 24 months, respectively), although overall survival, allowing LVAD use in OMM patients at a later time, was similar (81% versus 82% at 12 months and 70% versus 63% at 24 months, respectively). Importantly, the average improvement from baseline to 12 months in visual analogue scale (VAS) score was significantly higher in the LV AD group compared with the OMM group (29±25 versus 10±22 points; P<0.001), suggesting that earlier LVAD use, on average, led to more substantial improvements in patients’ health-related quality of life (hrQoL).

Given the comparable survival between the non–inotrope-dependent HF patients treated with LVAD compared with those who continued with OMM, and the possibility of LVAD use at a later point in time for clinical need, and large changes in hrQoL with initial LVAD treatment, we hypothesized that there may be heterogeneity in hrQoL benefit from early LVAD insertion based on patients’ baseline hrQoL. Such information could be useful in identifying which advanced HF patients benefit most from early referral to LVAD treatment. Thus, the aim of this analysis was to examine the trajectory of hrQoL over time and to identify predictors of survival with ≥75-m improvement in 6MWD, event-free survival, and survival with acceptable hrQoL.

Methods

Details of the ROADMAP study design, including study inclusion and exclusion criteria, have been previously reported. In brief, non–inotrope-dependent subjects with stage D HF, at least 1 HF hospitalization or 2 unscheduled emergency department visits in the previous year and a 6MWD <300 m were eligible for study participation. The study subjects were enrolled between October 2011 and July 2013 at 41 US medical centers. Subjects in the LVAD group received the HeartMate II device. The study was sponsored by Thoratec Corporation, Pleasanton, CA (now Abbott). The investigators and authors had independent access to study data. The study protocol was approved by the institutional review boards at each participating institution, and patients signed informed consent to participate.

QoL Assessment

HrQoL was collected at baseline, 6, and 12 months with the EuroQol 5D instrument (EQ-5D-5L). The EQ-5D defines health in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. In the 5-level version, subjects rate their health in each of the 5 dimensions from no problems, slight problems, moderate problems, severe problems, and unable to/extreme problems. The respondents also rate their overall health on a 0 to 100 VAS score, where 0 corresponds to the worst and 100 to the best possible health. The EQ-5D has been demonstrated to have face and construct validity and a good distribution across the health continuum. The EQ-5D was shown to be comparable to the 12-item Short Form Health Survey (SF-12) and to be more sensitive than the SF-6 in estimating the health burden of chronic conditions. The EQ-5D has become accepted as a standard instrument for describing hrQoL in LVAD studies, including the Interagency Registry for Mechanically Assisted Circulatory Support.

Statistical Analysis

Continuous variables are reported as mean±SD, or median and quartiles, and categorical data are reported as percentages. Differences between groups were analyzed by Fisher exact test. Differences between groups of independent, normally distributed, continuous variables were evaluated using Student’s 2-sample t test. Variables that were not normally distributed were compared with the Wilcoxon rank-sum test. Paired changes in categorical data from baseline to 12 months were analyzed with the McNemar test. A 2-sided P value <0.05 was considered statistically significant.

Event-free survival was defined by the ROADMAP study as being alive on original therapy at 1 year after study entry. As such, the events in the OMM arm would include both death and LVAD implantation within 1 year. The results for this specific outcome need to be examined in this context, that is, as answering a question of how likely is it for a patient to be alive, without a need for an LVAD, in the 12 months after the assessment. This outcome is not intended to designate whether LVAD implantation is good or bad but rather assist with decisions on timing of a possible LVAD implantation.

To examine the effect of treatment selection and baseline hrQoL on event-free survival, VAS and an interaction term between treatment...
arm and VAS and arm and VAS into a multivariate Cox proportional hazards model for event-free survival. Clinically relevant risk correlates from the HeartMate II risk score that were significant in univariable analyses were also entered into multivariable Cox proportional hazards model (age, albumin). Hazard ratios for treatment arm are presented as OMM versus LVAD (ratio >1 indicates better results with LVAD therapy compared with OMM). Data were censored at 1 year, elective transplant, or time of withdrawal.

Event-free survival was also explored with the Kaplan–Meier method in patient groups stratified by the baseline VAS score at which there was indication of a differential effect of the 2 therapies, as identified in the Cox proportional hazards model above. In a similar way, we explored intent-to-treat survival, that is, survival according to the original treatment assignment, where OMM group subjects who received delayed LVADs are analyzed as OMM subjects. Differences in event-free survival and intent-to-treat survival between LVAD and OMM groups were determined with the log-rank test.

A logistic regression model was created to examine the effect of baseline hrQoL and treatment selection on the primary end point in event-free survival and intent-to-treat survival. Odds ratios for achieving a favorable outcome for treatment arm are presented as LVAD versus OMM (ratio >1 indicates better results with LVAD therapy compared with OMM). Of the patients with a baseline VAS, those receiving an elective heart transplant, withdrawn, or missing the 6MWD at 1 year were not included in the logistic model (Figure 1). For the purpose of this analysis, an acceptable quality of life (QoL) with either treatment was defined as a VAS ≥60. Although this threshold is somewhat arbitrary, it is supported by the fact that >90% of ambulatory HF outpatients assessed to be in New York Heart Association class II score in the range of 60 to 85 on the VAS. In the ROADMAP cohort, patients with VAS ≥60 represented the top quartile of baseline VAS scores in the LVAD arm and top tertile of the OMM patients. A favorable outcome for either therapy was then defined as the binary composite of being alive on original therapy at 1 year with a VAS ≥60. A multivariable logistic regression model was created to examine the effect of baseline VAS and treatment arm on achieving a favorable outcome. Odds ratios for achieving a favorable outcome for treatment arm are presented as LVAD versus OMM (ratio >1 indicates better results with LVAD therapy compared with OMM). Of the patients with a baseline VAS, those receiving an elective heart transplant, withdrawn, or missing the VAS at 1 year were not included in the logistic model (Figure 1).

Results

Baseline Clinical Characteristics

The ROADMAP study enrolled 200 non-inotrope-dependent subjects with stage D HF. Table 1 shows baseline characteristics of the overall study group and characteristics in the LVAD and OMM groups. Differences in event-free survival and intent-to-treat survival between LVAD and OMM groups were determined with the log-rank test.

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All (n=200)</th>
<th>OMM (n=103)</th>
<th>LVAD (n=97)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment age, y</td>
<td>63±13</td>
<td>63±14</td>
<td>62±12</td>
<td>0.27</td>
</tr>
<tr>
<td>Men, %</td>
<td>146 (73)</td>
<td>71 (69)</td>
<td>75 (77)</td>
<td>0.20</td>
</tr>
<tr>
<td>Ischemic pathogenesis, %</td>
<td>109 (56)</td>
<td>51 (50)</td>
<td>58 (60)</td>
<td>0.16</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30±8</td>
<td>30±9</td>
<td>30±6</td>
<td>0.66</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.4±0.5</td>
<td>1.4±0.5 (n=103)</td>
<td>1.4±0.5 (n=97)</td>
<td>0.51</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>31±16</td>
<td>33±17 (n=103)</td>
<td>29±16 (n=97)</td>
<td>0.12</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.8±0.5</td>
<td>3.9±0.5 (n=99)</td>
<td>3.8±0.5 (n=94)</td>
<td>0.045</td>
</tr>
<tr>
<td>CI, L·min⁻¹·m⁻²</td>
<td>2.0±0.6</td>
<td>2.0±0.6 (n=50)</td>
<td>2.0±0.6 (n=65)</td>
<td>0.92</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>193±79</td>
<td>204±76 (n=103)</td>
<td>182±82 (n=97)</td>
<td>0.06</td>
</tr>
<tr>
<td>VO₂max, mL·kg⁻¹·min⁻¹</td>
<td>10.2±2.8</td>
<td>10.3±2.9 (n=61)</td>
<td>10.2±2.6 (n=72)</td>
<td>0.98</td>
</tr>
<tr>
<td>VO₂max RER ≥1.1, mL·kg⁻¹·min⁻¹</td>
<td>10.6±2.4</td>
<td>11.0±2.3 (n=23)</td>
<td>10.2±2.5 (n=27)</td>
<td>0.13</td>
</tr>
<tr>
<td>VE/VO₂</td>
<td>41.5±10.8</td>
<td>39.4±12.3 (n=51)</td>
<td>43.5±9.0 (n=58)</td>
<td>0.09</td>
</tr>
<tr>
<td>EQ-5D VAS</td>
<td>52±21</td>
<td>58±20 (n=99)</td>
<td>45±20 (n=93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SHFM score</td>
<td>1.61±0.93</td>
<td>1.45±0.87 (n=103)</td>
<td>1.78±0.97 (n=97)</td>
<td>0.013</td>
</tr>
<tr>
<td>NYHA class, %</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>124 (62)</td>
<td>77 (75)</td>
<td>47 (48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Class IV</td>
<td>76 (38)</td>
<td>26 (25)</td>
<td>50 (52)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INTERMACS profile, %</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Profile 4</td>
<td>98 (50)</td>
<td>35 (34)</td>
<td>63 (65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Profile 5</td>
<td>50 (26)</td>
<td>29 (28)</td>
<td>21 (22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Profile 6</td>
<td>45 (23)</td>
<td>35 (34)</td>
<td>10 (10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Profile 7</td>
<td>2 (1)</td>
<td>2 (2)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*P value relates to comparison of OMM vs LVAD. For the ROADMAP population, all continuous variables except for EQ-5D VAS and SHFM score were not normally distributed. 6MWD indicates 6-min walk distance; BMI, body mass index; BUN, serum blood urea nitrogen; CI, cardiac index; EQ-5D, EuroQol 5D instrument; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; NYHA, New York Heart Association; OMM, optimal medical management; RER, respiratory ratio; ROADMAP, Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management; SHFM, Seattle Heart Failure Model; VAS, visual analogue scale; VE/VO₂, ventilatory efficiency (slope of minute ventilation and carbon dioxide production ratio); and VO₂max, maximal oxygen uptake.*
OMM arms of the study. The average age of the study population was 63±13 years, and 73% were men. The mean 6MWD was 193±79 m and mean maximal oxygen uptake was 10.2±2.8 mL·kg⁻¹·min⁻¹. Subjects in the 2 groups were of similar age and had similar sex distribution. All patients were classified as New York Heart Association stage IIIB or IV, with a higher proportion of patients in the LVAD group (52%) classified as New York Heart Association class IV, as compared with the OMM group (25%). The resting invasive hemodynamics of the OMM and LVAD groups were similar. The average maximal baseline oxygen uptake (10.3 versus 10.2 mg·kg⁻¹·min⁻¹, respectively) and average maximal oxygen uptake in patients who reached anaerobic threshold (11 versus 10.2 mg·kg⁻¹·min⁻¹, respectively) were also similar and indicated a marked limitation in exertion capacity. There was a trend for a longer baseline 6MWD in the OMM group (204 versus 182 m; \(P=0.06\)). More LV AD patients (65%) were in Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) compared with OMM patients (34%), and more OMM patients were in profiles 5 to 7 compared with LVAD patients.

### Baseline QoL Measures

The average VAS of the overall study group at baseline was 52±21 but was lower in the LV AD group than the OMM group (mean VAS, 45±20 in the LVAD group versus 58±20 in the OMM group; \(P<0.001\)). There was, however, substantial overlap in the individual scores of the subjects in the 2 treatment groups—LVAD: median VAS=50 (Q1–Q3, 30–60) versus OMM: median VAS=55 (Q1–Q3, 45–75), and similar findings were observed for the individual dimensions of the EQ-5D (Figure 1 in the Data Supplement).

### QoL Changes at 12 Months

In patients treated with LVAD, VAS improved from a baseline mean of 42±19 to 71±21 (\(P<0.001\)). A small improvement in VAS was also seen in patients treated with OMM (60±20 to 70±19; \(P<0.05\)). The paired changes in the five EQ-5D dimensions with each treatment approach are shown in Figure 2 (scores for subjects with no or slight limitations) and in Figure 2 in the Data Supplement (scores for all levels of limitations). Subjects

**Table 2. Cox Proportional Hazards Model of Event-Free As-Treated Survival Through 1 Year, Multivariable Logistic Regression Model of Survival on Original Therapy With 6MWD Improvement \(\geq 75\) m at 1 Year and Multivariable Logistic Regression Model of Survival on Original Therapy With Acceptable QoL (VAS \(\geq 60\)) at 1 Year**

<table>
<thead>
<tr>
<th>Model Variables</th>
<th>Event-Free Survival at 1 y</th>
<th>Survival on Original Therapy With 6MWD Improvement (\geq 75) m at 1 y</th>
<th>Survival on Original Therapy With Acceptable QoL (VAS (\geq 60)) at 1 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(P)</td>
<td>HR (95% CI)</td>
<td>(P)</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.20</td>
<td>1.02 (0.99–1.04)</td>
<td>0.06</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>0.07</td>
<td>0.60 (0.34–1.05)</td>
<td>…</td>
</tr>
<tr>
<td>Treatment arm (LVAD vs OMM)</td>
<td>(&lt;0.001)</td>
<td>HR as a function of baseline VAS depicted in Figure 5B</td>
<td>0.006</td>
</tr>
<tr>
<td>VAS</td>
<td>0.033</td>
<td>OMM: 0.99 (0.97–1.00); LVAD: 1.03 (1–1.05)</td>
<td>0.07</td>
</tr>
<tr>
<td>Treatment arm* VAS interaction</td>
<td>0.005</td>
<td>0.046</td>
<td>0.046</td>
</tr>
</tbody>
</table>

6MWD indicates 6-min walk distance; CI, confidence interval; HR, hazard ratio; LVAD, left ventricular assist device; OMM, optimal medical management; OR, odds ratio; QoL, quality of life; and VAS, visual analogue scale.

\*Indicates interaction term.

Figure 2. Scores for EuroQol 5D at baseline and at 12 months in left ventricular assist device (LVAD) and optimal medical management (OMM) groups. Data shown for subjects with paired data. \(P<0.05\) compared with baseline.
in the LVAD group experienced improvement in mobility, usual activities, and anxiety/depression at 12 months but not in pain or self-care. In contrast, OMM subjects experienced no significant change in any of the dimensions at 12 months.

**Baseline HrQoL as Predictor of Outcome**

**Event-Free Survival (as Treated on Original Therapy)**

A multivariate Cox proportional hazards model demonstrated that baseline VAS was independently associated with event-free survival at 1 year (Table 2), with a statistically significant interaction between treatment arm and baseline VAS \((P=0.005)\). The hazard ratios associated with OMM versus LVAD treatment at different levels of baseline VAS are shown in Figure 3A. In patients with lower baseline QoL (VAS<55), event-free survival was significantly better in LVAD patients compared with OMM patients, whereas there was no significant difference between treatments for patients with baseline VAS ≥55. Of patients with baseline VAS <55 who received LVAD therapy, event-free survival was 82±5%, compared to 58±7% of OMM patients \((P=0.004; \text{Figure } 4)\).

Of note, intent-to-treat survival in the overall ROADMAP cohort was similar in patients assigned to LVAD or OMM.4 Intent-to-treat survival was also similar between the treatment groups after we stratified the study cohort by baseline VAS of <55 or VAS ≥55 (Figure 5). These analyses indicated that patients with lower baseline VAS in the OMM group were less likely to achieve event-free survival compared with patients with lower baseline VAS in the LVAD group and that the higher event rate was primarily because of a need for a delayed LVAD implantation in the OMM group with lower baseline VAS.

**Survival on Original Therapy With ≥75-m Improvement in 6MWD**

Survival on original therapy with ≥75-m improvement in 6MWD was the primary end point of the main ROADMAP study. Multivariable logistic regression modeling of this outcome (Table 2) demonstrated a significant interaction between baseline VAS and treatment arm \((P=0.046)\). The odds ratios associated with LVAD versus OMM treatment at different levels of baseline VAS are shown in Figure 3B. In patients with lower baseline QoL (VAS<62), survival with ≥75-m improvement in 6MWD was significantly better in LVAD patients compared with OMM patients, whereas there was no significant difference between treatments for patients with baseline VAS ≥62.

**Survival on Original Therapy With Acceptable QoL**

The multivariable logistic regression model of the composite favorable outcome of 1-year survival on original therapy with acceptable QoL (Table 2) also identified a statistically significant interaction between treatment arm and VAS \((P=0.046)\). Figure 3C shows the odds ratios for achieving favorable outcomes with LVAD versus OMM treatment at different baseline VAS values with patients with lower baseline VAS (<55) being more likely to achieve a favorable outcome with LVAD, as compared with ongoing OMM, but no difference was observed in those with higher baseline VAS (≥55). Indeed, a higher proportion of patients with baseline VAS <55 who received LVAD therapy achieved survival with acceptable QoL at 1 year compared with OMM therapy (60% versus 36%; \(P=0.017; \text{Figure } 6)\). Similarly, at 1 year, a higher proportion of LVAD subjects with baseline VAS <55 were alive on original therapy with no or only slight problems in all EQ-5D dimensions compared with OMM (Figure 7).

Importantly, for any of the outcomes examined, there was no significant difference between treatment arms when baseline VAS was ≥55.

**Discussion**

The ROADMAP study showed an overall benefit from early LVAD use. The goal of our work was to identify potential heterogeneity of treatment benefit with LVAD compared with OMM based on patients’ baseline hrQoL. We found a significant
interacton between treatment assignment and baseline health status on 12-month outcomes in patients assigned to OMM versus LVAD, with patients having low self-reported baseline QoL (VAS<55) being more likely to benefit from LVAD therapy as compared with those having higher hrQoL. Conversely, those with better hrQoL before treatment did not benefit more from LVAD therapy than OMM. Although it is clinically logical that those with worse hrQoL would benefit more from LVAD implantation, such quantification of the effect of LVAD therapy on QoL in a well-phenotyped non–inotrope-dependent ambulatory population, studied against a well-defined control group, has not been previously demonstrated.

The ROADMAP study provides a unique opportunity to examine QoL in a contemporary cohort of patients who received treatment with either LVAD or OMM. Assessment of QoL has been standard in clinical trials of LVAD therapy. However, the REMATCH study (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure), which enrolled patients in the late 1990s, has to date been the only destination LVAD therapy trial with an OMM arm. Although the ROADMAP study was not randomized, it is unique in that it enrolled a contemporary population of advanced HF patients eligible for destination LVAD therapy, of which approximately half received the LVAD, and half continued with OMM. The non–inotrope-dependent ambulatory advanced HF subjects enrolled in ROADMAP represent a population of great interest because the health status outcomes of this type of patients are less well described. Indeed, even the recent Food and Drug Administration post-approval studies of HeartMate II destination LVAD therapy enrolled patients with more advanced disease.

Our study provides a detailed overview of baseline QoL measures in the ROADMAP population and contrasts score
changes in the different EQ-5D QoL domains in LVAD- and OMM-treated patients. Most subjects in this non–
inotrope-dependent ambulatory HF cohort could complete self-care tasks without major difficulty (Figure 2), and, therefore, significant improvement in this domain should not be expected from LVAD. Indeed, self-care scores were not significantly different between the LVAD and OMM groups at 12 months after study entry (Figure 2). This contrasts with the marked baseline limitations of study subjects to carry out usual activities (Figure 2)—an important aspect of patient health status, which requires higher level of physical and mental stamina than self-care. LVAD-treated patients did achieve higher scores for usual activities at 12 months after study entry, as they did for mobility and anxiety/depression.

Although baseline hrQoL was worse in the LVAD group compared with the OMM group, the large overlap in QoL scores allowed us to examine for a heterogeneity of treatment benefit based on baseline health status. The fact that the all-cause mortality was similar in the LVAD and OMM groups further underscores that the expected QoL is of paramount importance when making treatment decisions in this patient population.  

In contemporary HF patients, with the exception of the most critically ill INTERMACS–profile 1 individuals, LVAD implantation results in similar survival regardless of patient acuity. This underscores the importance of careful assessment of hrQoL at the time of patient evaluation for a possible LVAD implantation and good knowledge of the expected trajectory of hrQoL after LVAD placement. Our study provides granular data on the degree of patient-reported limitation of hrQoL that is likely to respond favorably to LVAD therapy. Similarly, it provides thresholds for QoL indices where LVAD therapy is unlikely to exceed the benefits of OMM because they relate to hrQoL, which in turn helps to identify patients in whom the initial choice to stay on medical therapy is likely to provide results similar to the expected QoL achievable with an LVAD.

We believe the results of our study bring decision making on the more elective initiation of advanced HF therapies closer to the patient. Health status tools, such as EuroQol, can accurately measure the impact a disease has on patient QoL. The capture of patient-reported information is important because there is often a large discrepancy between physician and patient rating of hrQoL. Much research has been devoted to identifying risk factors for mortality in patients with HF; yet the strong influence that expected QoL has on patients’ preference for treatment approaches, even at the expense of longevity, may have been underappreciated. Our findings also highlight the importance of capturing patient-reported outcomes (PROs) in routine clinical care because this may help identify patients with advanced HF who might consider LVAD therapy. Alternatively, for ambulatory HF patients who perceive their QoL as acceptable, our data would provide reassurance that continuing on OMM will not lead to an excess risk of adverse outcomes. Assessment of PROs has become a standard in clinical trials and registries. As such, PROs have been typically scored at a later point and analyzed and

![Figure 6](http://example.com/f6.png)

Figure 6. Proportion of patients with favorable outcomes (alive on original therapy with visual analogue scale [VAS] ≥60) at 12 mo after enrollment. LVAD indicates left ventricular assist device; OMM, optimal medical management; and OR, odds ratio.

![Figure 7](http://example.com/f7.png)

Figure 7. Proportion of patients alive on original therapy with no or slight problems for EuroQol 5D at 12 mo in left ventricular assist device (LVAD) and optimal medical management (OMM) groups stratified by visual analogue scale (VAS) <55 vs VAS ≥55. *Statistically significant difference at P<0.05.
interpreted as a metric in larger patient cohorts. This has provided an opportunity to integrate hrQoL into prediction of response to treatment and define outcomes that include hrQoL.23–25—an approach that we used in our study. But PRO results have not typically been available to physicians and patients in real time. Advances in psychometric science and innovations in technology now allow for PROs to be integrated efficiently into clinical care. Responses to PRO tools can be captured on mobile platforms within minutes, immediately scored, and made available to clinicians through electronic health record.26 Our study results indicate that use of the EQ-5D instrument may help providers and potential LVAD candidates engage in more meaningful, patient-centric discussions on choices of treatments for advanced HF and the timing of their implementation. Along the same lines, our results could be used to help current investigative efforts aimed at exploring VAD placement earlier in the trajectory of HF.27 These investigations may be aided by including PRO results formally into subject screening, and possibly integrating this information into study eligibility criteria, rather than using the relatively crude New York Heart Association classification to assess patient eligibility. Including the potential study subject in this discussion by explaining the results of their health status assessment and sharing the anticipated results as they relate to hrQoL may enhance our ability to achieve a truly informed consent and streamline recruitment in these complex studies.28

Our study should be interpreted in the context of the following potential limitations. Although this was a prospective study in patients eligible for LVAD implantation based on disease severity criteria, treatment assignment was not randomized. This resulted in some baseline differences between the 2 groups, understandably indicating less severity of illness in patients remaining on OMM therapy compared with those opting for LVAD therapy. Although we controlled for some baseline differences in the multivariable analysis, residual confounding factors may have been unaccounted for. However, it should be emphasized that although patients chose their therapy arm, which poses challenges in the sense of standard outcome comparison, this can also be viewed as a strength because the findings of this study are closer to real-world conditions where patients participate in decisions. Indeed, a recent study that intended to randomize patients to continued OMM versus LVAD had to be stopped because this approach was not embraced by patients and ultimately by the investigators.26 Sixteen patients with a baseline VAS who were assigned to the OMM group received delayed LVADs in the first year after study entry. These patients were counted as failures in the event-free survival analyses. Some patients did not complete the EuroQol tool at the predetermined time intervals (Figure 1). For our 12-month analyses of changes in QoL over time, we only used data in patients who had paired EuroQol results available while remaining on original therapy, thus, not accounting for patients who died or received LVADs at a later time. However, the composite end point of alive with acceptable QoL accounts for both components and is more useful as a measure of success. Finally, a disease-specific measure of health status, which may have been more sensitive to clinical changes, was not used in the ROADMAP trial and should be tested in future studies.29

In summary, we found a significant interaction between baseline health status and the benefits of treatment assignment in non–inotrope-dependent patients with advanced stage D HF. LVAD therapy resulted in improvement of patient health status in HF patients with low self-reported hrQoL at baseline but not in patients with acceptable QoL at the time of LVAD implantation. We think that patient-reported hrQoL could be integrated into prognostication and decision making concerning the use and timing of LVAD therapy in advanced HF patients who are symptom limited but remain ambulatory and non–inotrope dependent.

Sources of Funding

The ROADMAP trial was sponsored and conducted by Thoratec Corporation, now a part of Abbott. Support for Drs Stehlik and Selzman was provided by the American Heart Association through Strategically Focused Heart Failure Research Networks Award.

Disclosures

Drs Stehlik, Estep, Selzman, Rogers, Shah, and Starling have received grant/research support from Abbott. Dr Estep has served as a consultant for Abbott and Maquet. Dr Starling has served as a member of the steering committee at Abbott. Drs Farrar and Chuang are employees at Abbott. Dr Spertus reports that he has served as a consultant for Novartis, Bayer, Cytokinetik and United Healthcare. He also owns the copyright to the Kansas City Cardiomyopathy Questionnaire.

References

CLINICAL PERSPECTIVE

Left ventricular assist devices (LVADs) are being used with increasing frequency as treatment for patients with heart failure, but better understanding of the optimal timing of LVAD implantation is needed. This analysis of the ROADMAP study (Risk Assessment and Comparative Effectiveness of LVAD and Medical Management)—a cohort of lower acuity heart failure patients referred for LVAD implantation, of whom some received LVAD and some continued on medical therapy—identified where functional disability in ambulatory patients.

In summary, although 1-year survival was similar in patients who received LVAD or continued with medical therapy, baseline QoL scores in these patients were independently associated with survival with 275-m improvement in 6-minute walk test, survival without need for urgent LVAD implantation, and survival with acceptable QoL, at 1 year after study entry. Patients with lower (worse) baseline QoL reached better results on these outcomes when treated with LVAD, whereas in patients with higher (better) QoL scores at baseline, there was no significant difference between treatments (LVAD versus continued medical therapy). These data suggest that formal assessment of QoL in heart failure patients could assist providers and patients in shared decision making on the type and the timing of treatments in advanced heart failure.
Patient-Reported Health-Related Quality of Life Is a Predictor of Outcomes in Ambulatory Heart Failure Patients Treated With Left Ventricular Assist Device Compared With Medical Management: Results From the ROADMAP Study (Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management)


on behalf of the ROADMAP Study Investigators

_Circ Heart Fail. 2017;10:

doi: 10.1161/CIRCHEARTFAILURE.116.003910

Circulation: Heart Failure is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3289. Online ISSN: 1941-3297

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circheartfailure.ahajournals.org/content/10/6/e003910

Data Supplement (unedited) at:

http://circheartfailure.ahajournals.org/content/suppl/2017/06/13/CIRCHEARTFAILURE.116.003910.DC1

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SUPPLEMENTAL MATERIAL
Supplemental Figure 1. Baseline scores for all levels of limitations for the EuroQol EQ-5D dimensions of Mobility, Usual Activities, Self Care, Pain/Discomfort and Anxiety/Depression. LVAD – left ventricular assist device; OMM – optimal medical management

Supplemental Figure 2. Scores for all levels of limitations in EuroQol EQ-5D dimensions at baseline and at 12 months in LVAD and OMM groups. Data shown for subjects with paired data. LVAD – left ventricular assist device; OMM – optimal medical management
Supplemental Figure 1.
Supplemental Figure 2.

The figure shows the percentage of patients with different levels of problems over time for various activities.

- **Mobility**
  - Slight problems: 50%
  - No problems: 25%
  - Moderate problems: 25%
  - N=68

- **Usual Activities**
  - Slight problems: 50%
  - No problems: 30%
  - Moderate problems: 20%
  - N=68

- **Self-Care**
  - Slight problems: 50%
  - No problems: 30%
  - Moderate problems: 20%
  - N=68

- **Pain**
  - Slight problems: 50%
  - No problems: 40%
  - Moderate problems: 10%
  - N=67

- **Anxiety/Depression**
  - Slight problems: 60%
  - No problems: 30%
  - Moderate problems: 10%
  - N=68

The data is measured over 0 and 12 months.