Risk Factor Analysis of Long-Term Support With Left Ventricular Assist System

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Background: This study was designed to elucidate the key factors for successful long-term support with a left ventricular assist system (LVAS) in the situation where heart transplantation is rarely available.

Methods and Results: From 1992 to 2008, 106 patients underwent 121 LVAS implantations at Osaka University Hospital (Toyobo: 77; Novacor: 18; HeartMate: 14; Jarvik2000: 8; EvaHeart: 2; DuraHeart: 2). Risk factors for infection were early on the former implanted period (odds ratio (OR) 3.30), Toyobo (OR 2.25), mechanical right heart support (OR 2.30) and cardiopulmonary bypass time (OR 1.01). Left atrium as the inflow site was the risk factor for cerebrovascular events (OR 2.84). Older age (OR 1.04) and mechanical right heart support (OR 4.70) were risk factors for mortality. Risk factors for requiring mechanical right heart support were preoperative extracorporeal membranous oxygenation support (OR 5.641), serum total bilirubin (OR 1.11) and serum creatinine (OR 2.46). On the basis of the risk analysis for mortality, patients were divided into 2 subgroups (low and high risk) and the respective cumulative survival at 1 year after LVAS implantation was 75.2% and 25.0%.

Conclusions: Appropriate selection of device, patient and the timing of implantation and less invasive operation are important for successful long-term LVAS support. (Circ J 2010; 74: 715–722)

Key Words: Bridge to transplantation; Destination therapy; Left ventricular assist system; Long-term support; Risk analysis

The left ventricular assist system (LVAS) has been successfully used as treatment of end-stage heart failure, mainly as a bridge to transplantation. From successful experiences with using LVAS in heart transplantation candidates, permanent use of LVAS has recently also become realistic in the United States and Europe. Several sophisticated devices have been developed over the years and are suitable for different patients with different therapeutic objectives. After many years of experiences with these life-saving devices, researchers have suggested that appropriate patient selection and device selection are essential for effective use of LVAS. In Japan, however, the special situation of heart transplantation and very limited device availability have made the indication and timing of LVAS implantation somewhat different from other countries. Because of the extremely severe shortage of donor hearts, heart failure patients in Japan have to wait for heart transplantation for approximately 2 years on average with LVAS support. To make the situation worse, the only commercially available device in this country has been the Toyobo LVAS, which is a paracorporeal pneumatic-type LVAS that was initially designed for short-term support. The available support flow is smaller than with other types of implantable devices, and the patient cannot leave the hospital because the driving unit is designed for the inpatient setting. Most of the heart transplantation candidates have to wait for donor hearts for a long time on this device, dealing with repeat complications such as infection and thromboembolism.

Despite this special situation, risk analysis of LVAS treatment in this country has been rarely conducted, so the purpose of this study was to elucidate the predictors of major adverse events and mortality with LVAS treatment in Japan.

Methods

From April 1992 to November 2008, 106 patients underwent a total of 121 LVAS implantations at Osaka University Hospital. The indication for LVAS implantation was irreversible end-stage heart failure with New York Heart Association (NYHA) class IV symptoms and imminent or already present end-organ dysfunction despite optimal medical therapy including inotropic agents. The patients’ demographics are summarized in Table 1. The number of LVAS implantations...
has increased since 1999 (Figure 1), when the first heart transplantation from a brain-dead donor was performed in Japan. The most commonly used device was the Toyobo paracorporeal pneumatic LVAS. Since the left ventricular apical drainage system became available in 1999, we began using that as the primary choice. Since 1994, implantable LVAS, such as the HeartMate (Thoratec Corp, Pleasanton, CA, USA) and Novacor (WorldHeart Corp, Oakland, CA, USA), also became available to us, but these devices were used in a limited number of patients, mainly patients who had been registered as heart transplantation candidates with sufficient body size (body surface area >1.50 m²). More recently, non-pulsatile LVAS such as the Jarvik 2000 (Jarvik Heart, Inc, New York, NY, USA), EvaHeart (SunMedical Technology Research, Nagano, Japan) and DuraHeart (Terumo Heart, Inc, Ann Arbor, MI, USA) were also used as part of a clinical trial, but the indication of the new devices was limited to patients without significant complications. As a result, the Toyobo LVAS was selected for patients with a smaller body size or for those with significant preexisting complications who could not be registered as transplantation candidates or with acute deterioration of heart failure.

Implantation procedures were performed either through a median sternotomy or left thoracotomy as previously described.12-14 We prefer performing all procedures without cardioplegic cardiac arrest unless the left ventricle is seriously damaged by acute myocardial infarction or a left ventricular thrombus is identified. To facilitate future LVAS explantation, we aggressively perform concomitant procedures such as left ventricular restoration, mitral valve repair, and cardiac

<table>
<thead>
<tr>
<th>Table 1. Clinical Characteristics of the Patients Requiring LVAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
</tr>
<tr>
<td>Mean body surface area (m²)</td>
</tr>
<tr>
<td>Etiology of heart failure, n (%)</td>
</tr>
<tr>
<td>Idiopathic cardiomyopathy</td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
</tr>
<tr>
<td>Myocarditis</td>
</tr>
<tr>
<td>Secondary cardiomyopathy</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Preoperative status n (%)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
</tr>
<tr>
<td>ECMO</td>
</tr>
<tr>
<td>Renal dysfunction</td>
</tr>
<tr>
<td>Serum creatinine &gt;2.0 mg/dl</td>
</tr>
<tr>
<td>Hemodialysis</td>
</tr>
<tr>
<td>Liver dysfunction</td>
</tr>
<tr>
<td>Serum total bilirubin &gt;3.0 mg/dl</td>
</tr>
<tr>
<td>Blood chemistry</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
</tr>
<tr>
<td>AST (IU/L)</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
</tr>
<tr>
<td>Total protein (mg/dl)</td>
</tr>
<tr>
<td>Albumin (mg/dl)</td>
</tr>
<tr>
<td>White blood cell (×10³/µl)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
</tr>
<tr>
<td>Brain natriuretic peptide (pg/ml)</td>
</tr>
<tr>
<td>Echocardiography data</td>
</tr>
<tr>
<td>LVDd (mm)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
</tr>
<tr>
<td>Mitral regurgitation ≥III</td>
</tr>
<tr>
<td>Right heart catheterization</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
</tr>
<tr>
<td>Central venous pressure (mmHg)</td>
</tr>
<tr>
<td>Systolic pulmonary artery pressure (mmHg)</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mmHg)</td>
</tr>
<tr>
<td>Cardiac index (L·min⁻¹·m⁻²)</td>
</tr>
</tbody>
</table>

LVAS, left ventricular assist system; ECMO, extracorporeal membranous oxygenation; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein; LVDd, left ventricular diastolic dimension.
Risk Factor Analysis of Long-Term LVAS

Resynchronization therapy, if indicated. Concomitant procedures during LVAS implantation included mitral valve annuloplasty in 29 patients, tricuspid annuloplasty in 29, biventricular lead implantation in 10, left ventricular restoration in 5, aortic valve replacement in 3, and coronary artery bypass grafting in 2. If LVAS filling was poor when weaning from cardiopulmonary bypass with adequate right atrial pressure and support for right ventricle using nitric oxide inhalation and catecholamine, right ventricular assist using an extracorporeal membranous oxygenation (ECMO-RVAS) was established with right atrial appendage and pulmonary artery cannulation. If right heart failure was so severe that the surgeon considered weaning from the ECMO-RVAS impossible within 1 week, a RVAS using a Toyobo pump was needed.

Table 2. Clinical Outcomes of the Patients Requiring LVAS

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplanted</td>
<td>17 (16.0%)</td>
</tr>
<tr>
<td>Abroad</td>
<td>4</td>
</tr>
<tr>
<td>At Osaka University Hospital</td>
<td>13</td>
</tr>
<tr>
<td>Novacor</td>
<td>6</td>
</tr>
<tr>
<td>Toyobo</td>
<td>5</td>
</tr>
<tr>
<td>HeartMate</td>
<td>3</td>
</tr>
<tr>
<td>Jarvik 2000</td>
<td>3</td>
</tr>
<tr>
<td>Removal of LVAS</td>
<td>18 (17.0%)</td>
</tr>
<tr>
<td>Emergency removal</td>
<td>6</td>
</tr>
<tr>
<td>Died after removal</td>
<td>3</td>
</tr>
<tr>
<td>Died after re-LVAS</td>
<td>3</td>
</tr>
<tr>
<td>Scheduled removal</td>
<td>12</td>
</tr>
<tr>
<td>re-LVAS</td>
<td>3</td>
</tr>
<tr>
<td>Ongoing</td>
<td>17</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>11</td>
</tr>
<tr>
<td>At home</td>
<td>6</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>17</td>
</tr>
<tr>
<td>Multiple organ failure</td>
<td>16</td>
</tr>
<tr>
<td>Cerebral bleeding</td>
<td>13</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>12</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviation see in Table 1.

Table 3. Device-Related Complications in the Patients Requiring LVAS

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
</tr>
<tr>
<td>Positive blood culture</td>
<td>46 (43.4%)</td>
</tr>
<tr>
<td>Driveline exit site infection</td>
<td>36 (34.0%)</td>
</tr>
<tr>
<td>Mediastinitis/pump pocket infection</td>
<td>15 (15.1%)</td>
</tr>
<tr>
<td>Cerebrovascular events</td>
<td></td>
</tr>
<tr>
<td>Cerebral bleeding</td>
<td>29 (27.4%)</td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>28 (26.4%)</td>
</tr>
<tr>
<td>Reoperation for bleeding/cardiac tamponade</td>
<td>28 (26.4%)</td>
</tr>
<tr>
<td>Respiratory failure (tracheostomy)</td>
<td>30 (28.3%)</td>
</tr>
<tr>
<td>Renal failure (temporary hemodialysis)</td>
<td>30 (28.3%)</td>
</tr>
</tbody>
</table>

Abbreviation see in Table 1.
established instead of ECMO.

In the first 24h postoperatively the patients received no anticoagulation therapy. Thereafter, if there was no significant drainage from the chest tube, continuous heparin infusion was started and the activated partial thromboplastin time was maintained at 1.5- to 2-fold the normal value. Long-term anticoagulation consisted of coumadin (dosage according to international normalized ratio 2.5–3.5), and aspirin 100–200 mg/day. Since 2002 ticlopidine 200 mg/day has been added as antiplatelet therapy. Patients with the HeartMate LVAS received only aspirin.

The hospital records of the 106 patients were retrospectively reviewed. Preoperative status, operative strategies, and clinical outcomes were evaluated. This study was approved by the ethics committees of the Osaka University Graduate School of Medicine. All patients gave written informed consent.

Statistical Analysis
Kaplan-Meier analysis was used to estimate the event-free provability over time. The comparison of the survival rate of the 2 groups was done by log-rank (Mantel-Cox) analysis with P values less than 0.05 considered to be significant. From the patients’ preoperative parameters and operative procedures, predictors of device-related infection, cerebrovascular events after LVAS implantation and mortality were evaluated using a Cox hazard model. Predictors of requiring mechanical right heart support during operation in order to wean off the cardiopulmonary bypass were evaluated using a logistic regression model.

Results
A total of 29 patients required mechanical right heart support during the operation. ECMO-RVAS was implanted in 22 of them and the Toyobo RVAS in the others. Of the 22 patients who underwent ECMO-RVAS support, right heart function recovered and RVAS was removed in 10 patients, ECMO-RVAS was switched to the Toyobo RVAS in 4 and the other 8 died with ECMO-RVAS support. Two patients underwent Toyobo RVAS implantation after LVAS implantation because of persistent right heart failure. None of the patients with the Toyobo RVAS survived to transplantation or recovery. The median duration of biventricular support with Toyobo pumps was 129 days (range 19–353 days).

Clinical outcomes are summarized in Table 2. Only 17 patients were successfully bridged to heart transplantation. The median duration of LVAS support of those who were bridged to transplantation was 591 days (range 21–1,233 days). LVAS was removed in 18 patients: 6 underwent emergency LVAS removal because of serious complications such as cerebral bleeding or infections and 3 of them died after LVAS removal; the other 3 died after LVAS reimplantation.
LVAS was removed in 12 patients because their own heart function recovered and all of them are alive. There was recurrence of heart failure in 3 patients, requiring reimplantation of LVAS. Two of them underwent heart transplantation and the other is ongoing.

Device-related complications are summarized in Table 3. Nearly half of the patients (43.4%) had a positive blood culture at least once. Driveline exit site infection was observed in 34.0% of patients and mediastinitis or pump pocket infection in 15.1%. Figure 2A shows freedom from device-related infections. Although the infectious events occurred most frequently in the first 6 months after LVAS implantation, they continued to occur thereafter. Predictors of device-related infections were evaluated using a Cox hazard model (Table 4).

Multivariate analysis revealed that early implanted period, Toyoobo, requiring mechanical right heart support to wean off cardiopulmonary bypass, and longer cardiopulmonary bypass time were the independent risk factors for device-related infections.

Cerebral bleeding and cerebral infarction were observed in 27.4% and 26.4% of patients, respectively, including overlap (Table 3). Figure 2B shows freedom from cerebrovascular events. As with infection, cerebrovascular events occurred most frequently in the first 6 months after LVAS implantation, but continued to occur thereafter, although the frequency seemed to decrease after 1 year. Multivariate analysis using Cox hazard model revealed that the inflow site (ie, left atrium) was the independent risk factor (Table 5).

### Table 4. Risk Factors for Device-Related Infection (Cox Hazard Model)

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Implanted period (~2002)</td>
<td>0.0008</td>
<td>0.0004</td>
<td>3.299 (1.694–6.425)</td>
</tr>
<tr>
<td>White blood cells</td>
<td>0.0061</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Device (Toyoobo)</td>
<td>0.0008</td>
<td>0.0469</td>
<td>2.251 (1.011–5.009)</td>
</tr>
<tr>
<td>Inflow site (left atrium)</td>
<td>0.0145</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Right heart support*</td>
<td>0.0004</td>
<td>0.0291</td>
<td>2.297 (1.089–4.847)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time</td>
<td>0.0009</td>
<td>0.0064</td>
<td>1.009 (1.002–1.013)</td>
</tr>
</tbody>
</table>

Entry probability set at 0.10.

* Requiring right heart support to wean off cardiopulmonary bypass during the operation.

OR, odds ratio; CI, confidence interval.

### Table 5. Risk Factors for Cerebrovascular Events (Cox Hazard Model)

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>White blood cells</td>
<td>0.0505</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Preoperative ECMO support</td>
<td>0.0369</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Concomitant mitral valve surgery</td>
<td>0.0783</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Device (Toyoobo)</td>
<td>0.0125</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Inflow site (left atrium)</td>
<td>0.0039</td>
<td>0.0263</td>
<td>2.838 (1.131–7.123)</td>
</tr>
</tbody>
</table>

Entry probability set at 0.10.

Abbreviations see in Tables 1, 4.

### Table 6. Risk Factors for Mortality (Cox Hazard Model)

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P value</td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Implanted period (~2002)</td>
<td>0.0261</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Age at implantation</td>
<td>0.0142</td>
<td>0.0083</td>
<td>1.039 (1.010–1.069)</td>
</tr>
<tr>
<td>Etiology (idiopathic)</td>
<td>0.0613</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>White blood cells</td>
<td>0.0507</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.0192</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.0376</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.0057</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Preoperative ECMO support</td>
<td>0.0079</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Preoperative hemodialysis</td>
<td>&lt;0.0001</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Device (Toyoobo)</td>
<td>0.0003</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Inflow site (left atrium)</td>
<td>0.0011</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Right heart support*</td>
<td>&lt;0.0001</td>
<td>0.0034</td>
<td>4.698 (1.668–13.230)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time</td>
<td>&lt;0.0001</td>
<td>NS</td>
<td>–</td>
</tr>
</tbody>
</table>

Entry probability set at 0.10.

* Requiring right heart support to wean off cardiopulmonary bypass during the operation.

Abbreviations see in Tables 1, 4.
The most common causes of death were multiple organ failure and sepsis, which were already present preoperatively in the majority of cases (Table 2). Cerebral infarction and bleeding were the other leading causes of death. Predictors of mortality were evaluated using a Cox hazard model (Table 6). By multivariate analysis, older age at implantation and mechanical right heart support requirement were the independent risk factors for death. As the requirement of mechanical right heart support was revealed to be the strongest risk factor for death (odds ratio (OR) 4.698) and also the independent risk factor for device-related infections, predictors for requiring mechanical right heart support to wean off the cardiopulmonary bypass during LVAS implantation were evaluated using a logistic regression model (Table 7). Multivariate analysis revealed preoperative serum total bilirubin and creatinine levels, and preoperative ECMO support were the independent risk factors.

On the basis of the risk analysis for death, patients were divided into 2 subgroups: high and low risk. The high-risk group included patients with at least 1 of age at implantation (≥60 years) and/or mechanical right heart support. The low-risk group included patients with neither of these risk factors. There was a remarkable difference between the groups in the survival rate after LVAS implantation (Figure 2C). Cumulative survival in the low-risk group was 75.0% at 1 year after LVAS implantation and 56.1% at 2 years.

**Discussion**

In a study of the Novacor European Registry, Deng et al reported that respiratory failure with septicemia, preexisting right heart failure, age at implantation, acute postcardiomyotomy and acute infarction were predictors of mortality after LVAS implantation by multivariate analysis. Cumulative survival was significantly higher in the group of patients without any of these risk factors (low-risk group) than in the group of patients with at least 1 risk factor (high-risk group). Two of the risk factors (right heart failure and age at implantation) are the same as those detected as predictors of mortality in our study. The influence of these factors on the patient survival after LVAS implantation was also similar: cumulative survival of the low-risk group and high risk group at 1 year was 60.3% and 24.1%, respectively, in Deng’s report, and 75.0% and 25.2%, respectively, in our study. The different points of the 2 studies are the number of patients that underwent heart transplantation and the duration of LVAS support until heart transplantation. In Deng’s report, 155 of 366 patients (42.3%) underwent heart transplantation and the median time on LVAS until heart transplantation was 139 days in the low-risk group and 88 days in the high-risk group, whereas in our study only 17 of 106 patients (16.0%) underwent heart transplantation and the median time on LVAS until heart transplantation was 591 days.

In addition to the severe shortage of donor hearts, limited device selection is a significant disadvantage of LVAS treatment in Japan. Although it is important to select devices according to the predicted duration of support, the Toyobo LVAS is the only commercially available LVAS today and we have no choice but to use this paracorporeal pneumatic device in most patients, no matter how long the duration of the support is expected to be. In this study, the Toyobo LVAS was detected as an independent risk factor for device-related infection. Implantable LVAS is considered to reduce the risk of device-related infection compared with paracorporeal LVAS, and it was reported more recently that device-related infection is reduced significantly by smaller continuous flow devices.

Patients with the Toyobo LVAS cannot leave hospital because this device is designed for the inpatient setting. In addition to the frequent infectious events with the paracorporeal device in the acute phase, nosocomial infection may have played a significant role in infections in the late phase (infectious events after 6 months: Figure 2A). The incidence of infections in the late phase might be reduced if patients could go home with an implantable LVAS. The other predictors of device-related infection in previous reports include renal dysfunction, hypo-albuminemia, and diabetes mellitus.

The other important complication of LVAS treatment is cerebrovascular events, and it is known that the risk increases with a longer LVAS support period. This complication seems to be device- and anti-coagulation therapy-related, and none of the patients’ preoperative factors was detected as a predictor of post-LVAS cerebrovascular events in this study. The only predictor of cerebrovascular events was left atrial drainage. When left heart bypass is established between the left atrium and ascending aorta in a heart with poor contraction, stagnation of the blood stream and thrombus formation tends to occur in the left ventricle, resulting in cerebral thromboembolism. In this study, the left atrium was selected as the inflow site in patients before the left ventricular apical drainage system was introduced in 1999, and thereafter we used the left ventricular apex as the inflow site, unless there was a special reason not to, such as not being suitable because of previous left ventricular plasty or fragility resulting from acute myocardial infarction.

Right heart failure is also known to be a significant risk
factor for unsuccessful LVAS treatment, and several studies have revealed the preoperative risk factors for developing right heart failure after LVAS implantation. Researchers in the Cleveland Clinic concluded that preoperative circulatory support, female sex and non-ischemic etiology were independent risk factors for right heart failure by multivariate analysis. Researchers in Colombia University reported that a higher preoperative total bilirubin concentration was a risk factor for right heart failure. These findings were compatible with those in our study.

Figure 3 is a summary of this study. As preoperative patient factors, pre-LVAS requirement for mechanical circulation with ECMO, as well as liver and renal dysfunction were independent risk factors for requiring mechanical right heart support during operation to wean off cardiopulmonary bypass. As operative factors, Toyobo device, extended cardiopulmonary bypass time and requirement for mechanical right heart support were independent risk factors for device-related infections, and left atrial drainage was an independent risk factor for post-LVAS cerebrovascular events. Additionally, higher patient age and requirement for mechanical right heart support were independent risk factors for mortality. The preoperative risk factors suggest that appropriate timing of LVAS implantation is essential for successful LVAS treatment. Establishing age-specific strategies, such as bridge to recovery in young patients and destination therapy in old patients, is also important. From the operative risk factors, the development and approval for clinical use of new, small implantable devices are eagerly awaited. As for the operative procedure, it is important to select an appropriate method for less invasive surgery, and to avoid using the left atrium as the inflow site. Meticulous management of right heart failure with appropriate volume control, inotropic support and nitric oxide inhalation is also required.

**Study Limitations**

A retrospective study and the urgent situation at the time of LVAS implantation are limitations; for example, hemodynamic variables such as right ventricular stroke work (RVSW) and the RVSW index, which have been reported as significant risk factors for right heart failure in a previous study, could not be obtained in more than 25% of the present patients. Another limitation was the small numbers of each device other than the Toyobo LVAS, which limited the power to detect superiority of 1 device over another. The other limitation was that factors of postoperative management, which changed from time to time according to the accumulation of experience, were not included in the risk analysis; however, the “implanted period” may partially reflect those postoperative factors.

In conclusion, from our long-term experience with LVAS treatment at Osaka University Hospital, there is still significant mortality and morbidity after LVAS implantation. Infection and cerebrovascular events are the major limitations of long-term support. Right heart failure confers significant mortality and morbidity after LVAS implantation. As preoperative factors such as pre-LVAS mechanical circulatory support, liver and renal function are predictors for right

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**Figure 3.** Summary of the study findings showing the preoperative and operative independent risk factors for major adverse events and mortality. The strategies for improving LVAS treatment are derived from these findings. ECMO, extracorporeal membranous oxygenation; LA, left atrium; LV, left ventricle; LVAS, left ventricular assist system.
heart failure, appropriate selection of patients and timing of LVAS implantation are important to reduce the risk of right heart failure. Appropriate device selection, and a simple and less invasive operation may also improve the outcomes of LVAS treatment. Although risk analyses of LVAS treatment have been reported from many institutions, this study is unique because it was conducted in the situation of heart transplantation being rarely available, and the duration of LVAS support was as long as that of destination therapy.

References