How Can We Predict Reversibility of Organ Dysfunction After Implantation of Left Ventricular Assist Device?

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Circulatory support with a left ventricular assist device (LVAD) has greatly improved the survival and quality of life for patients with advanced stage heart failure. Restoring circulation in severe heart failure patients can dramatically improve their overall condition and functional status. Most patients undergoing LVAD support for bridge-to-transplant (BTT) or destination therapy (DT; ie, long-term LVAD for patients who have a contraindication to transplantation) have been effectively supported for long durations, while end-organ function normalizes or is maintained within normal limits.1–3

Optimizing cardiac output and perfusion pressure from the outset of LVAD support has a major role in avoiding or reversing end-organ dysfunction. Since mechanical circulatory support systems were first devised over 50 years ago, clinicians and researchers have attempted to define the optimal blood flow pattern for both long- and short-term support, and many types of LVAD had been invented. Recently, several investigators reported that continuous flow (CF) LVAD support for extended durations will be as safe and effective in patients with pre-implant multiorgan failure (MOF) as pulsatile flow LVAD.4,5 Yoshioka et al reported that the cumulative survival curve after LVAD implantation mainly depends on the existence of renal dysfunction rather than on extracorporeal membrane oxygenation (ECMO) support.6 Therefore, LVAD implantation should be considered without delay if further deterioration of end-organ dysfunction is noted even with ECMO support.

However, the ravages of long-standing severe heart failure can cause irreversible multiorgan system failure, which continues to be a common cause of death during LVAD support for the most severely ill patients. Although the use of 2 CF-LVADs has been covered by Japanese governmental health insurance for heart transplant candidates since April 2011, the use of these LVADs for DT is not yet approved. Therefore, in Japan many patients with organ failure had undergone implantation of extracorporeal pulsatile LVAD for decision-making purposes. Therefore, it would very useful to predict the reversibility of end-organ function, especially in these cases, as Imanura et al describe in this issue of the Journal.7 Several published analyses of death and morbidity related to LVAD support have reported institutional experiences with single or multiple LVADs, multi-institutional experiences with a single LVAD, or data from voluntary multi-institutional registries. From these reports, renal dysfunction,4 hepatic dysfunction, infection, cardiogenic shock, advanced age and right ventricular failure8 are considered to be risks for LVAD implantation. The first multi-institutional study done prospectively reviewed 420 patients from 75 institutions and concluded that cardiogenic shock, advanced age and severe right heart failure manifesting as ascites or increased bilirubin are risk factors for death after LVAD therapy8 (Table).

However, those reports mainly analyzed implantable LVADs. Fujita et al reported that preoperative renal function predicts post-implantation renal function and length of intensive care unit (ICU) stay and that particularly when implanted in heavier patients, the Toyobo LVAD tended to provide poorer renal perfusion, probably because it gives less circulatory support than an implantable LVAD.9 Fujita et al suggested that it was essential to maintain the cardiac index at the highest levels possible to avoid postoperative hyperbilirubinemia in LVAD patients.10 Taken together, these results suggest that extracorporeal LVAD can not provide sufficient blood flow for severely ill patients, especially with MOF. Therefore, in the Japanese clinical setting, predictive factors for reversibility of end-organ function should be estimated in patients with extracorporeal LVAD, as well as implantable LVAD, as was done in the present study7 (implantable CF-LAD 18 and extracorporeal LVAD 51).

Masai et al reported that patients with hyperbilirubinemia and inflammatory reactions before LVAD support showed increased hyperbilirubinemia and inflammatory cytokine and

### Table. INTERMACS Summary (June 2006 to December 2007)

<table>
<thead>
<tr>
<th>Risk factors for death*</th>
<th>Relative risk</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERMACS Level 1</td>
<td>1.59</td>
<td>0.02</td>
</tr>
<tr>
<td>Age (older)**</td>
<td>1.41</td>
<td>0.01</td>
</tr>
<tr>
<td>Ascites</td>
<td>2.04</td>
<td>0.003</td>
</tr>
<tr>
<td>Bilirubin (higher)†</td>
<td>1.49</td>
<td>0.05</td>
</tr>
<tr>
<td>BiVAD implant</td>
<td>2.12</td>
<td>0.002</td>
</tr>
<tr>
<td>Total artificial heart</td>
<td>2.41</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* Determined using multivariate analysis; ** compares increased risk from age 50 to 60 years; † compares increased risk from bilirubin 1–6 mg/dl.
hyaluronan levels, despite adequate hemodynamics achieved under LVAD support. Shiga et al suggested that age and preoperative total bilirubin (TB) level can stratify prognosis after extracorporeal LVAD implantation. Ma et al reported that preoperative serum creatinine (Cre) correlated with prolonged high postoperative Cre levels and that a preoperative Cre level >1.95 mg/dl predicted an ICU stay >30 days. The Pearson’s correlation of patients’ body weights and their final Cre levels when transferred from the ICU was 0.758 (P=0.011).

On this basis, the new scoring system used by Imamura et al is interesting. In the present study, the TB or Cre score was calculated: 0.15×age + 1.1×(preoperative TB) or 0.2×age + 3.6×(preoperative Cre), in which coefficients were determined on the basis of odds ratios for persistent hepatic or renal dysfunction, respectively. Receiver-operating characteristic analyses showed good predictabilities for persistent end-organ dysfunction (area under curve: 0.794 for TB score and 0.839 for Cre score). High-risk strata of TB score (>11.0 points) or Cre score (>14.1 points) were associated with persistently increased high postoperative Cre levels when transferred from the ICU was 0.758 (P=0.011).

References