Prophylactic Intra-Aortic Balloon Pump Before Ventricular Assist Device Implantation Reduces Perioperative Medical Expenses and Improves Postoperative Clinical Course in INTERMACS Profile 2 Patients

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**Background:** Although intra-aortic balloon pump (IABP) is sometimes used before cardiac surgery to achieve better outcome in high-risk patients, the clinical impact of prophylactic IABP support before left ventricular assist device (LVAD) implantation in patients with worsening hemodynamics was unknown.

**Methods and Results:** We enrolled 22 patients with worsening hemodynamics who had received IABP support before LVAD (IABP group), and also enrolled 22 patients receiving neither IABP nor extracorporeal membrane oxygenation before LVAD, who were selected on propensity score matching (non-IABP group). Although both groups had similar preoperative background, the IABP group had shorter postoperative intensive care unit (ICU) stay, and more improved hemodynamics (P<0.05 for all). Serum total bilirubin and creatinine decreased significantly in the IABP group compared with the non-IABP group during 1 month after LVAD implantation (P<0.05 for both). Medical expenses during perioperative ICU stay were significantly lower in the IABP group compared with the non-IABP group, even including the cost of preoperative IABP support (P<0.05).

**Conclusions:** Prophylactic IABP support in heart failure patients with worsening hemodynamics improves post-LVAD clinical course and reduces perioperative medical expenses.

**Key Words:** Cost; Heart failure; Intra-aortic balloon pump; Ventricular assist device

Treatment with the intra-aortic balloon pump (IABP) is the most common form of mechanical support for the failing heart, owing to its overall effect of significant increase in the myocardial oxygen supply/demand ratio due to diastolic augmentation and presystolic balloon deflation.\(^1\),\(^2\)

Since the first clinical use of IABP in patients with cardiogenic shock following myocardial infarction in 1968,\(^3\) the clinical indications for IABP have been expanding from explantation of cardiopulmonary bypass to prophylaxis during percutaneous coronary intervention or cardiac surgery in high-risk patients, not only for emergency but also for elective operations.\(^4\)–\(^16\)

The prognostic advantage of such prophylactic IABP support, however, including postoperative mortality and morbidity, has recently become a matter of debate again, especially with regard to the urgent setting.\(^5\)–\(^10\),\(^13\),\(^17\)

Little has been reported on prophylactic IABP support in patients with advanced heart failure (HF) on the hemodynamics decline before left ventricular assist device (LVAD) implantation.\(^18\) We herein investigated the clinical impact of prophylactic IABP insertion in patients with INTERMACS profile 2 before LVAD implantation, compared with a propensity score-matched control group without IABP.

**Methods**

**Patients**

We enrolled 22 patients who had been assigned to INTERMACS profile 2 and who received prophylactic IABP support prior to LVAD implantation at University of Tokyo Hospital between 2007 and 2014 (IABP group). All patients had received IABP <1 week before surgery. IABP support was continued for 4 ± 2 days in average and terminated at the time of LVAD implantation in all cases. Patients without IABP were managed in the general ward until just before surgery, whereas those who had received IABP support were managed in the intensive care unit (ICU). The decision to insert prophylactic IABP was made...
by the attending physicians. Profile 2 was defined according to INTERMACS criteria: hemodynamic decline despite inotrope infusion.19–21 Profile 1 was defined as critical cardiogenic shock requiring extracorporeal membrane oxygenation (ECMO) and concomitant IABP if necessary. No patients were assigned to profile 1.

Among 52 patients who had received LVAD without prior IABP or ECMO, we selected 22 patients according to propensity score matching of the preoperative variables including age, hemoglobin (Hb), platelets (Plt), serum albumin, total bilirubin (TB), and creatinine (Cre), plasma B-type natriuretic peptide (BNP), systolic blood pressure, heart rate (HR), pulmonary capillary wedge pressure (PCWP), cardiac index (CI), LV diastolic diameter, and LV ejection fraction (LVEF; non-IABP group). All participants in the IABP/non-IABP groups had deteriorating hemodynamics accompanied by worsening of end-organ function, and received semi-urgent LVAD within days.

Written informed consent was obtained from all participants before enrollment. The study protocol was approved by the Ethics Committee of Graduate School of Medicine, University of Tokyo (application number 779 [1]).

**Preoperative Variables**

Clinical parameters obtained <1 week before LVAD implantation were used as baseline variables. In the IABP group, variables obtained immediately before IABP support were used. Hemodynamic variables before/5 min after initiation of IABP were also measured. Changes in laboratory and echocardiographic data immediately before LVAD implantation during IABP support were also obtained. In contrast, data obtained 4 days before LVAD implantation, the mean duration of preoperative IABP support, were used as baseline parameters in the non-IABP group.

**Postoperative Variables**

Postoperative data including duration of respirator support, length of ICU stay, medical expenses during ICU stay, and time course of serum TB and Cre within 1 month after surgery were obtained. Hemodynamic data including central venous pressure (CVP), CI, and right ventricular stroke work index (RVSWI)

### Table 1. Baseline Variables Before LVAD

<table>
<thead>
<tr>
<th></th>
<th>Total (n=44)</th>
<th>IABP (+) (n=22)</th>
<th>IABP (−) (n=22)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>40±13</td>
<td>37±11</td>
<td>43±14</td>
<td>0.217</td>
</tr>
<tr>
<td>Male</td>
<td>37 (84)</td>
<td>20 (91)</td>
<td>17 (77)</td>
<td>0.216</td>
</tr>
<tr>
<td>BMI</td>
<td>19.4±3.4</td>
<td>19.2±3.1</td>
<td>19.5±3.4</td>
<td>0.743</td>
</tr>
<tr>
<td>Etiology of ischemia</td>
<td>4 (9)</td>
<td>3 (14)</td>
<td>1 (7)</td>
<td>0.321</td>
</tr>
<tr>
<td><strong>Devices</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extracorporeal pulsatile flow</td>
<td>18 (41)</td>
<td>11 (50)</td>
<td>7 (32)</td>
<td>0.221</td>
</tr>
<tr>
<td>Implantable continuous flow</td>
<td>26 (59)</td>
<td>11 (50)</td>
<td>15 (68)</td>
<td>–</td>
</tr>
<tr>
<td><strong>Laboratory variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>11.2±1.4</td>
<td>10.8±1.3</td>
<td>11.4±1.3</td>
<td>0.132</td>
</tr>
<tr>
<td>Platelets (10⁴/μl)</td>
<td>21±6</td>
<td>21±6</td>
<td>22±7</td>
<td>0.423</td>
</tr>
<tr>
<td>Serum albumin (mg/dl)</td>
<td>3.3±0.3</td>
<td>3.2±0.3</td>
<td>3.4±0.3</td>
<td>0.132</td>
</tr>
<tr>
<td>Serum total bilirubin (mg/dl)</td>
<td>1.9±1.1</td>
<td>2.0±1.1</td>
<td>1.9±1.0</td>
<td>0.587</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.2±0.5</td>
<td>1.1±0.4</td>
<td>1.2±0.6</td>
<td>0.198</td>
</tr>
<tr>
<td>Plasma BNP (pg/ml)</td>
<td>958±641</td>
<td>1,012±619</td>
<td>943±623</td>
<td>0.594</td>
</tr>
<tr>
<td><strong>Echocardiographic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVDd (mm)</td>
<td>75±14</td>
<td>77±12</td>
<td>72±15</td>
<td>0.291</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>20±8</td>
<td>20±8</td>
<td>19±8</td>
<td>0.428</td>
</tr>
<tr>
<td>AR (grade)</td>
<td>0.4±0.7</td>
<td>0.3±0.6</td>
<td>0.5±0.7</td>
<td>0.366</td>
</tr>
<tr>
<td>MR (grade)</td>
<td>2.7±0.9</td>
<td>2.9±1.0</td>
<td>2.5±0.8</td>
<td>0.271</td>
</tr>
<tr>
<td>TR (grade)</td>
<td>2.2±0.6</td>
<td>2.1±0.6</td>
<td>2.2±0.7</td>
<td>0.197</td>
</tr>
<tr>
<td><strong>Hemodynamic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>88±11</td>
<td>86±10</td>
<td>90±11</td>
<td>0.332</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>89±17</td>
<td>92±15</td>
<td>86±17</td>
<td>0.143</td>
</tr>
<tr>
<td>mRAP (mmHg)</td>
<td>10±6</td>
<td>11±5</td>
<td>9±6</td>
<td>0.402</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>27±7</td>
<td>28±7</td>
<td>26±6</td>
<td>0.343</td>
</tr>
<tr>
<td>Cardiac index (L·min⁻¹·m⁻²)</td>
<td>2.1±0.4</td>
<td>2.1±0.4</td>
<td>2.0±0.5</td>
<td>0.331</td>
</tr>
</tbody>
</table>

Data given as mean ± SD or n (%). AR, aortic regurgitation; BMI, body mass index; BNP, B-type natriuretic peptide; HR, heart rate; LVAD, left ventricular assist device; LVDd, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; mRAP, mean right atrial pressure; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure; TR, tricuspid regurgitation.
Prophylactic IABP Before LVAD

Categorical variables were compared using Chi-squared test or Fisher's exact test as appropriate. Propensity score matching analysis was performed to select background-matched patients to the IABP group. Each postoperative variable was compared with preoperative ones or those for postoperative day 1 on Dennett's test when repeated analysis of variance was significant. Kaplan-Meier analysis was performed to compare 1-year survival between the groups.

Statistical Analysis
We used SPSS Statistics 22 (SPSS, Chicago, IL, USA). Statistical tests were 2-tailed, and P<0.05 was assumed as significant. All data are expressed as mean±SD. Continuous variables were compared using unpaired t-test or Mann-Whitney U-test, and categorical variables were compared using Chi-squared test or Fisher’s exact test as appropriate. Propensity score matching analysis was performed to select background-matched patients to the IABP group. Each postoperative variable was compared with preoperative ones or those for postoperative day 1 on Dennett’s test when repeated analysis of variance was significant. Kaplan-Meier analysis was performed to compare 1-year survival between the groups.

Figure 1. Acute changes in (A–F) hemodynamics and in (G, H) heart rate (HR) variability parameters (n=9) after the introduction of intra-aortic balloon pump. *P<0.05 (paired t-test). CI, cardiac index; DBP, diastolic blood pressure; HF, high frequency; LF, low frequency; mRAP, mean right atrial pressure; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure.

were obtained during 3 days after LVAD implantation. All-cause mortality was also monitored during 1 year after LVAD implantation.
Table 2. Preoperative Variables Immediately Before LVAD

<table>
<thead>
<tr>
<th>Laboratory variables</th>
<th>IABP (+) (n=22)</th>
<th>P value vs. Pre-IABP</th>
<th>IABP (−) (n=22)</th>
<th>P value vs. IABP (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.2±1.3</td>
<td>0.532</td>
<td>11.6±1.4</td>
<td>0.058</td>
</tr>
<tr>
<td>Platelets (10^9/μl)</td>
<td>22±6</td>
<td>0.858</td>
<td>22±6</td>
<td>0.965</td>
</tr>
<tr>
<td>Serum albumin (mg/dl)</td>
<td>3.3±0.3</td>
<td>0.854</td>
<td>3.4±0.3</td>
<td>0.324</td>
</tr>
<tr>
<td>Serum total bilirubin (mg/dl)</td>
<td>1.5±0.9</td>
<td>0.028*</td>
<td>1.8±1.1</td>
<td>0.042†</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.9±0.3</td>
<td>0.032*</td>
<td>1.3±0.6</td>
<td>0.018†</td>
</tr>
<tr>
<td>Plasma BNP (pg/ml)</td>
<td>714±512</td>
<td>0.038*</td>
<td>904±672</td>
<td>0.128</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Echocardiographic variables</th>
<th>LVDD (mm)</th>
<th>LVEF (%)</th>
<th>AR (grade)</th>
<th>MR (grade)</th>
<th>TR (grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP (+) (n=22)</td>
<td>76±12</td>
<td>21±8</td>
<td>0.3±0.6</td>
<td>2.6±0.9</td>
<td>1.8±0.6</td>
</tr>
<tr>
<td>P value vs. Pre-IABP</td>
<td>0.876</td>
<td>0.756</td>
<td>0.875</td>
<td>0.165</td>
<td>0.213</td>
</tr>
<tr>
<td>IABP (−) (n=22)</td>
<td>72±15</td>
<td>19±8</td>
<td>0.5±0.7</td>
<td>2.5±0.8</td>
<td>2.2±0.7</td>
</tr>
<tr>
<td>P value vs. IABP (−)</td>
<td>0.312</td>
<td>0.376</td>
<td>0.876</td>
<td>0.824</td>
<td>0.211</td>
</tr>
</tbody>
</table>

Data given as mean±SD. *P<0.05 (paired t-test); †P<0.05 (unpaired t-test). Abbreviations as in Table 1.

Results

Preoperative Variables

Both the 22 patients assigned to profile 2 who had received IABP prior to LVAD implantation (IABP group) and the 22 background-matched patients without IABP (non-IABP group) were enrolled (Table 1). Eighteen patients (41%) received extracorporeal pulsatile flow LVAD, and 26 (59%) received an implantable continuous flow device. There were no statistical differences in baseline variables between the groups.

Acute Effect of IABP

In the IABP group (n=22), both HR and PCWP were decreased, and CI was increased significantly after IABP initiation (P<0.05 for all, Figures 1A–F). Among 9 patients in whom HRV analysis was performed, HF was increased and LF/HF was decreased significantly (P<0.05 for both, Figures 1G,H).

Both serum TB and Cre and plasma BNP were significantly decreased during 4±2 days of IABP support (Table 2; P<0.05 for all). Serum TB and Cre were significantly lower in the IABP group than the non-IABP group immediately before LVAD implantation (P<0.05 for both).

There were no complications during IABP support including bleeding needing transfusion, balloon rupture, leg ischemia, vascular injury, embolism, or sepsis. Hb and Plt count remained unchanged during IABP support (Hb, from 10.8±1.3 to 10.2±1.3 mg/dl; Plt, from 21±6 to 20±6×10^4/µl, P>0.05 for both).

Postoperative Effects of Preoperative IABP

In the IABP group, postoperative ICU stay was significantly shorter than in the non-IABP group (P<0.05; Figure 2B). During 3 days after LVAD implantation, CVP decreased and CI increased significantly in the IABP group as compared with the non-IABP group (P<0.05 for both, Figures 2C,D). Patients in the IABP group had relatively higher RVSWI than those in the non-IABP group (4.5 g/m vs. 3.5 g/m, P=0.062). Serum TB and Cre were lower in the IABP group after LVAD implantation, and the differences reached statistical significance from 14 days for TB and from 7 days for Cre (P<0.05 for both, Figures 2E,F). Perioperative medical expenses during ICU stay including the cost of IABP support were lower in the IABP group compared with the non-IABP group (P<0.05, Figure 2G).

There was no statistically significant difference in 1-year survival irrespective of preoperative usage of IABP (IABP group, 96%; non-IABP group, 85%; P=0.330).

Discussion

In the present study, patients with INTERMACS profile 2 who had received prophylactic IABP insertion preoperatively had a better post-LVAD clinical course, including shorter ICU stay and lower perioperative medical expenses, as well as faster improvement of hemodynamics and end-organ dysfunction compared with a propensity-matched control group.

Acute Effects of IABP

Consistent with a previous report, CI was increased and PCWP decreased significantly by approximately 20% after IABP initiation in patients with INTERMACS profile 2.24 We observed decreases in both HR and sympathetic activity during IABP support, probably due to the improvement of cardiac output.23,25,26

Recent Evidence in Prophylactic IABP Support

Although the use of prophylactic IABP support has been expanding in real-world practice,7 recent accumulating evidence is casting doubt on its advantage in various clinical settings. Recent studies including randomized controlled trials found no survival benefit nor lower in-hospital mortality and morbidity in prophylactic IABP support before emergency revascularization treatment in patients with acute coronary syndrome.4–8

Although the survival advantage of prophylactic IABP support in patients with reduced LVEF before elective cardiac surgery is also still controversial,11–17 preoperative insertion of IABP and hemodynamic stabilization were found to have an advantage in convalescence compared with perioperative or postoperative IABP support.14,15

IABP and LVAD in Advanced HF

IABP alone is rarely used in patients with chronic HF, probably because such a temporary mechanical device (in the order of weeks) is insufficient to support progressive disease such as dilated cardiomyopathy.27 In other words, IABP alone is not a suitable alternative to LVAD with regard to sufficient improvement of hemodynamics.

In contrast, LVAD has emerged recently as a powerful
Therefore, we here investigated the post-LVAD clinical impact of prophylactic IABP insertion in patients with INTERMACS profile 2.

**Efficacy of Prophylactic IABP Before LVAD**

Shorter postoperative ICU stay as well as greater improvement of hemodynamics was observed in the IABP group, long-term mechanical weapon to support failing heart.\textsuperscript{19,21} Considering the several scoring systems stratifying postoperative survival,\textsuperscript{29} preoperative stabilization of hemodynamics and end-organ dysfunction improve post-LVAD prognosis. Although we usually use ECMO in patients with cardiogenic shock before urgent LVAD implantation,\textsuperscript{29} little was known about the advantage of preoperative prophylactic IABP in less-sick patients.\textsuperscript{18} Therefore, we here investigated the post-LVAD clinical impact of prophylactic IABP insertion in patients with INTERMACS profile 2.
consistent with early studies on patients with reduced LVEF who had received prophylactic IABP before non-LVAD cardiac surgery.\textsuperscript{11,15,16} Although the precise mechanism remains unknown, preoperative repression of sympathetic activity accompanied by stabilization of hemodynamics (Figure 1) may have anti-inflammatory and cardiac protective effects, facilitating postoperative systemic recovery and reducing cardiac complications.\textsuperscript{23,26,30,31}

End-organ dysfunction was significantly recovered in the IABP group, whereas serum TB and Cre remained higher in the non-IABP group at 2 weeks after LVAD implantation. Preoperative serum TB and Cre have been widely used as markers for post-LVAD reversibility of end-organ function.\textsuperscript{32} Preoperative decrease in serum TB and Cre during IABP support due to stabilization of hemodynamics might have contributed to significant postoperative recovery.\textsuperscript{33,34} Postoperative recovery of congestion and improvement of systemic circulation in the IABP group might also have facilitated recovery of end-organ dysfunction.\textsuperscript{39}

Prophylactic IABP insertion lowered perioperative medical expenses, even including IABP cost, probably because of the better post-LVAD clinical course in the IABP group. Prophylactic IABP support had no survival advantage, probably because overall post-LVAD survival in profile 2 patients has already improved thus far.\textsuperscript{41} Keeping medical expenses as low as possible would be the next challenge, because medical costs have been increasing owing to the recent increasing number of LVAD implantations.\textsuperscript{21}

In contrast, perioperative ICU stay between the groups was similar when including preoperative prophylactic IABP support in the ICU (IABP group, 12±3 days; non-IABP group, 11±6 days, P=0.643). Longer ICU stay itself may be associated with worse hospital management and decreased quality of life irrespective of before or after the surgery. We believe, however, that improved post-LVAD clinical course along with lower perioperative medical expense overcomes the disadvantage of several days’ ICU stay for prophylactic IABP support.

**Optimal Timing of IABP**

Preoperative IABP support seems to have an advantage over peri/postoperative support in patients with reduced LVEF before elective cardiac surgery.\textsuperscript{12,14,15} In contrast, longer IABP support increases vascular or hemorrhagic complications.\textsuperscript{38} Although the absolute duration of IABP support varies strongly with institution, early insertion of IABP before end-organ dysfunction exceeds the reversible threshold, is essential. We maintained duration of IABP support at <1 week. Consistently, we encountered no IABP-related complications such as significant disruption of red blood cells or Plt for an IABP support duration <1 week. Moreover, the advantage in reducing post-LVAD medical expenses by prophylactic IABP insertion justified the IABP treatment, at least when IABP support was continued <1 week.

**Study Limitations**

First, the present study was conducted in a single center among a small number of patients in a retrospective manner. The result should be validated in a future prospective study. Second, the timing of extubation or discharge from ICU was determined by the attending physicians. Therefore, the absolute values of these variables may vary among institutes. Third, all participants received prophylactic IABP insertion, but none of them were hemodynamically dependent on mechanical support, that is, INTERMACS profile 1. Fourth, we did not insert IABP >1 week before LVAD implantation, and we do not have any evidence of such usage. And fifth, indwelling Swan-Ganz catheter was not used in the preoperative period, to avoid catheter-induced bacterial infection. Preoperative hemodynamic data immediately before LVAD implantation during IABP support, however, may provide more information about the preconditioning effect of IABP.

**Conclusions**

Preoperative prophylactic IABP support in HF patients with worsening hemodynamics leads to better post-LVAD clinical course, along with lower medical expenses.

**Acknowledgments**

None.

**Disclosures**

None.

**References**


Prophylactic IABP Before LVAD


