Acute Experimental Study of Abiomed BVS5000 as a V-A Bypass to Cardiogenic Shock Models

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Purpose: Abiomed BVS5000 is generally used as a ventricular assist device, and there have been no reports of its application to a veno-arterial bypass (V-A bypass). In the present study, we developed a new V-A bypass system using this pump and examined its usefulness experimentally.

Materials and Methods: Pigs ($n=21$; $37.4\pm2.2$ kg) with cardiogenic shock were divided into the following three groups: (1) Abiomed group (Abiomed BVS5000); (2) nonpulsatile pump (NP) + intra-aortic balloon pump (IABP) group (centrifugal pump and IABP); and (3) NP group. In all three groups, assisted circulation using the pumps was performed for 3 h after the shock. Hemodynamic data and blood specimens were measured before and immediately after the shock, and again at 1, 2, and 3 h after. The individual variations were reduced by evaluation of the measured value/preshock value ratio, not by evaluation of the absolute values.

Results: The coronary arterial blood flows at 3 h after the shock were significantly larger in the Abiomed and NP+IABP groups than in the NP group ($1.32\pm0.34$ and $1.24\pm0.05$ vs. $1.05\pm0.11$, $P<0.05$), and the renal arterial and renal cortical tissue blood flows were significantly larger in the Abiomed group than in the NP+IABP and NP groups (renal artery: $1.30\pm0.17$ vs. $0.89\pm0.20$ and $0.68\pm0.10$, $P<0.05$; renal cortical tissue: $0.74\pm0.25$ vs. $0.62\pm0.05$ and $0.43\pm0.18$, $P<0.05$). The lactate/pyruvate ratios were significantly lower in the Abiomed groups than in the NP group ($25.2\pm1.6$ vs. $36.0\pm3.1$, $P<0.05$).

Conclusion: The results suggest that a V-A bypass using an Abiomed BVS5000 is a useful treatment for organ blood flow redistribution after shock. (Ann Thorac Cardiovasc Surg 2007; 13: 308–315)

Key words: Abiomed BVS5000, cardiogenic shock, pulsatile flow, veno-arterial bypass

Introduction

With the development of assisted circulation, the survival rate following cardiogenic shock has been improved. The use of a ventricular assist device (VAD), percutaneous cardiopulmonary support (PCPS), and veno-arterial bypass (V-A bypass) has been confirmed to assist the recovery of cardiac function in cardiogenic shock or post-operative low output syndrome. In our institution, 43 patients have received PCPS over the past 10 years. Although their weaning rate was 60.5% (26 patients), their survival rate was just 39.5% (17 patients). It is well established that even though cardiac function can be restored by mechanical assistance, multiple organ failure has already developed because of microcirculatory failure in the vital organs. Therefore to further improve the survival rate, a clarification of the problems associated with assisted circulation is urgently required. We previously demonstrated experimentally that pulsatile flow is a more useful treatment for organ blood flow redistribution after shock than steady nonpulsatile flow. The clinical usefulness of a pulsatile-type assist pump, the Abiomed
BVS5000 (Abiomed Inc., Danvers, MA), has been reported. In Japan, the use of this device has been covered by insurance since September 2001, and clinical application was initiated. This type of pump is generally used as a VAD, and there have been no reports of its application to a V-A bypass. In the present study, we developed a new V-A bypass system using an Abiomed BVS5000 and examined its usefulness experimentally.

**Materials and Methods**

**Animals and shock model**

For the experimental model, pigs ($n=21$; body weight, $37.4\pm2.2$ kg) were used. Anesthesia was induced by intramuscular administration of pentobarbital (20 mg/kg) and ketamine hydrochloride (10 mg/kg). For the maintenance of anesthesia, vecuronium bromide (0.1 mg/kg) was administered intravenously for muscular relaxation, followed by an administration of ketamine hydrochloride (20 mg/kg). After intratracheal intubation, a respirator (Servo 900E; Siemens-Elema AB, Solna, Sweden) was set to the following conditions to maintain the percutaneous (Servo 900E; Siemens-Elema AB, Solna, Sweden) was set to the following conditions to maintain the percutaneous arterial oxygen saturation ($SpO_2$) at 97%–100%: inspired by insurance since September 2001, and clinical application was initiated. This type of pump is generally used as a VAD, and there have been no reports of its application to a V-A bypass. In the present study, we developed a new V-A bypass system using an Abiomed BVS5000 and examined its usefulness experimentally.

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The shock model was prepared by ligation of the first diagonal branch of the anterior descending branch of the left coronary artery, and the animal was regarded as a model of cardiogenic shock when the systolic blood pressure decreased to 60% of the original value. If ligation of the first diagonal branch alone did not induce shock, the second diagonal branch was also ligated. Assisted circulation was initiated immediately after the occurrence of cardiogenic shock. The circulation was assisted for 3 h after the shock using the following pumps for V-A bypass: (1) pulsatile pump (Abiomed group); (2) centrifugal pump + IABP (NP+IABP group); and (3) centrifugal pump (NP group). IABP was synchronized with the R wave of the electrocardiogram (ECG) and assisted at 1:1. In the Abiomed group, the chamber was placed to allow good pump flow. No catecholamines were administered during the assisted circulation in any of the groups. Measurements of the hemodynamics, membrane oxygenator-associated pressure loss, and tissue blood flows, as well as blood samples, were taken before shock, at shock, and...
then 1, 2, and 3 h after the initiation of assisted circulation. Blood was sampled before and immediately after the shock and again at 1, 2, and 3 h after the shock to measure the lactate/pyruvate ratios and creatinine (Cr) levels.

Hemodynamic data and a blood specimen were measured before and immediately after the shock, and again at 1, 2, and 3 h after the shock. The individual variations were reduced by evaluation of the measured value/preshock value ratio, not by evaluation of the absolute values.

Statistical analysis
The results were presented as means ± SD. Differences among values for the three groups were analyzed by Scheffe’s test, and values of P<0.05 were considered to indicate statistical significance.

Results

Hemodynamic data
The mean aortic blood pressure (mAoP) decreased to about 60 mm Hg after cardiogenic shock in all three groups and did not differ significantly among the three groups during the assisted period (Fig. 2). The NP+IABP and NP groups were maintained at 100–110 mm Hg by adjusting the number of revolutions of the centrifugal pump to about 2,000 bpm.

Regarding the volume load, assisted circulation was performed with no associated problems in the blood supply or withdrawal. The pump flows at 3 h after the initiation of assistance were 2.32±0.15, 2.40±0.10, and 2.44±0.12 L/min in the Abiomed, NP+IABP, and NP groups, respectively. No significant difference was noted among the three groups.

The pulse pressures at 3 h were 38.3±1.96, 29.0±0.74, and 16.4±2.09 mm Hg in the Abiomed, NP+IABP, and NP groups, respectively, showing that the pulse pressure was maintained at significantly higher levels in the Abiomed and NP+IABP groups than in the NP group (P<0.05; Fig. 3). The pulse pressure was higher in the Abiomed group than in the NP+IABP group at 3 h, but the difference did not reach statistical significance.

The pressure losses associated with the membrane oxygenator at 3 h were 24.2±2.12, 27.0±2.45, and 26.3±2.54 mm Hg in the Abiomed, NP+IABP, and NP groups, respectively (Fig. 4). No significant differences were noted at 3 h among the three groups.

The coronary arterial blood flow at shock decreased to 77.1% of the original value in all three groups (Fig. 5A). The values at 3 h were 1.32±0.34, 1.24±0.05, and 1.05±0.11 in the Abiomed, NP+IABP, and NP groups, respectively, indicating that significantly higher coronary arterial blood flows were obtained in the Abiomed and NP+IABP groups than in the NP group (P<0.05). No significant difference was noted between the values at 3 h for the Abiomed and NP+IABP groups.

The myocardial tissue blood flow at shock decreased to 74.2% of the original value in all three groups (Fig. 5B). In the Abiomed and NP+IABP groups, no significant differences were found between the two groups at 3 h. The myocardial tissue blood flows at 3 h were significantly higher in the Abiomed and NP+IABP groups than in the NP group (P<0.05).

The renal arterial blood flow at shock decreased to 65.4% of the original value in all three groups (Fig. 6). The renal arterial blood flows at 3 h were significantly higher in the Abiomed and NP+IABP groups than in the NP group (1.30±0.17 and 0.89±0.20 vs. 0.68±0.10, P<0.05) and the difference between the Abiomed and NP+IABP groups was also significant (P<0.05).

The renal cortical tissue blood flow at shock decreased to 60.5% of the original value in all three groups (Fig. 7A). In the NP group, the blood flow continued to decrease during the 3 h assisted period. In the Abiomed and NP+IABP groups, the blood flows continued to increase throughout the assisted period, and the values did not return to their preshock levels at 3 h. The renal cortical tissue blood flows at 3 h were significantly higher in the Abiomed and NP+IABP groups than in the NP group (0.74±0.25 and 0.62±0.05 vs. 0.43±0.05, P<0.05).

The renal medullary tissue blood flow at shock de-
Mean aortic pressure (mAoP) and pump flow (PF) (L/min) at the point of preshock, shock, and 1, 2, and 3 h after the shock in the Abiomed group, the centrifugal pump [nonpulsatile pump (NP)] + intra-aortic balloon pump (IABP) group, and the centrifugal pump group (NP group).

Fig. 2.

Pulse pressure (mm Hg) (*P<0.05).
NP, nonpulsatile pump; IABP, intra-aortic balloon pump.

Fig. 3.

Pressure losses (mm Hg) caused by the membrane oxygenator.
NP, nonpulsatile pump; IABP, intra-aortic balloon pump.

Fig. 4.

Coronary arterial blood flow (A), myocardial tissue blood flow (B) (ratio: 1, 2, and 3 h after the shock value/preshock value; *P<0.05).
NP, nonpulsatile pump; IABP, intra-aortic balloon pump.

creased to 63.9% of the original value in all three groups (Fig. 7B). The tissue blood flows continued to increase, but there were no significant differences among the Abiomed, NP+IABP, and NP groups at 3 h (0.96±0.06, 0.96±0.04, and 0.91±0.09, respectively).

The lactate/pyruvate ratios at 3 h differed significantly between the Abiomed and NP groups (36.0±3.1 vs. 25.2±1.6, P<0.05; Fig. 8A) and tended to increase throughout the 3 h period in all three groups. The Cr level at 3 h showed no significant differences among the Abiomed, NP+IABP, and NP groups (0.98±0.09, 0.98±0.09, and 1.00±0.06, respectively; Fig. 8B).
The Abiomed BVS5000 is an external air-driven temporary assistive artificial heart. Blood is withdrawn because of head drop, and the blood flow is calculated from the air pressure by a built-in compressor. The heart rate for a stroke volume of about 82 mL is determined, and pulsatile blood flow is supplied without synchronization with the ECG (full-to-empty mode). The pump is clinically applied mainly in Europe and America. In Japan, the pump was approved for medical insurance coverage in September 2001 and has been increasingly used in clinical cases. Minami et al. reported that the duration of assistance was 2–7 days, the wean rate was 62%, and the discharge rate was 50%, including patients who subsequently received a heart transplant.1) Jett reported that the mean duration of assistance was 6.2 days,2) the wean rate was 60%, and the discharge rate was 27%.

Various discussions have been presented regarding the usefulness of circulation assistance via pulsatile and nonpulsatile blood flows, and pulsatile blood flow was reported to be useful for difficulties associated with weaning from extracorporeal circulation and cardiogenic shock induced by various causes.3–6) Centrifugal pumps are widely used clinically because of their simplicity and low cost.7,8) However, Sezai et al. investigated skin and renal microcirculation, gastric mucosal and liver tissue blood flows, and gastric mucosal pH and found that pulsatile blood flow was superior.9) Minami et al. reported a clinical study in which Abiomed BVS5000-induced pulsatile blood flow allowed a reduction in the use of catecholamines in extracorporeal circulation and drip infusion and positively affected the duration of the postoperative recovery and time of weaning from a respirator.3,10)

In general, the Abiomed BVS5000 is used as a VAD, and its use as a V-A bypass has not been reported. Thus we investigated a V-A bypass system using an Abiomed BVS5000 experimentally.
Regarding the driving conditions of the pump, we successfully maintained a constant mAoP. As shown in Fig. 2, the mAoP significantly decreased to about 60 mm Hg in all three groups at cardiogenic shock. There were no significant differences in the mAoP during the assisted period among the three groups. The pump was set manually at a height of about 20–30 cm from the heart, and a pump flow of 2.32±0.15 L/min was obtained without any problems in the Abiomed group. The centrifugal pump was controlled at about 2,000 bpm, and pump flows of 2.40±0.10 and 2.44±0.12 L/min were obtained in the NP+IABP and NP groups, respectively, revealing no significant differences among the three groups. As a result, there were no significant differences in the total flows and assist rates among the three groups (Table 1), and we were able to compare the three groups under constant conditions.

The pulse pressures at 3 h were maintained at significantly higher levels in the Abiomed and IABP groups than in the NP group (Fig. 3). In the Abiomed group, the mAoP did not exhibit a constant waveform (Fig. 9A) because the pump flow output was in either the systolic or diastolic phase (Fig. 9B). When the diastolic phases of the autologous heart and pump overlapped, the blood pres-
sure decreased and the pulse pressure increased. In the NP+IABP group, the pulse pressure increased because of a counter-pulsation effect. In the NP group, the pulse pressure was derived from pulsation of the autologous heart and was small. To secure an appropriate pulse pressure, the pressure loss in a membrane oxygenator should be taken into account. However, the pressure losses resulting from the presence of a membrane oxygenator were low among the three groups throughout the 3 h period (Fig. 4).

Regarding the coronary circulation, the coronary blood flows at 3 h were maintained at significantly higher levels in the Abiomed and NP+IABP groups than in the NP group (Fig. 5A). The pump systolic phase in the Abiomed group, which was not synchronized with the autologous heart, was long, and the coronary blood flow increased when the output occurred in the diastolic phase of the autologous heart (Fig. 9C). Even when the pump output was in the systolic phase of the autologous heart, the pump was able to provide a high pressure during the diastolic phase of the autologous heart because of the duration of the pump systolic phase, and this may be the reason for its usefulness for coronary arterial blood flow. The animals supported by IABP showed increased aortic and coronary diastolic blood pressures associated with a diastolic augmentation effect that increased the coronary arterial and myocardial tissue blood flows. As mentioned above, the pulse pressure in the NP group was derived from the pulsation of the autologous heart and was small. It is suggested that there may have been insufficient pulse pressure for animals in which cardiogenic shock-associated nonhomogeneous blood flow distribution occurred.

Regarding the renal circulation, the renal arterial blood flow decreased to 65.4% of the preshock level when cardiogenic shock was induced in all three groups (Fig. 6). The decreased coronary arterial blood flow remained at 77.1%, revealing nonhomogeneous blood flow distribution around the body. With assistance for 3 h, the renal arterial blood flows were maintained at significantly higher levels in the Abiomed and IABP groups than in the NP group. In the present study, assistance for 3 h induced a higher distribution of blood flow in the renal medullary tissue than in the renal cortical tissue, showing nonhomogeneous distribution of the renal blood flow (Fig. 7). However, the renal cortical blood flow tended to increase during the assistance period in the Abiomed and NP+IABP groups, indicating the usefulness of the assistance. In contrast, the cortical blood flow tended to decrease with increased nonhomogeneous distribution in the NP group, suggesting that pulsatile blood flow acted more effectively on the cardiogenic shock-induced decrease in renal blood flow than nonpulsatile blood flow did. The renal arterial blood flow directly reflected the aortic pressure, and the waveforms were similar (Fig. 9D). In a comparison of the renal blood flows under a specific mAoP, the blood flows were significantly higher in the Abiomed and NP+IABP groups than in the NP group, suggesting that the pulse pressure has a marked influence on the peripheral circulation.

Cr is not absorbed by renal tubules following its excretion by the glomeruli. Therefore its level tends to increase under renal dysfunction, and the condition of the patient can deteriorate markedly as a result of poor renal blood flow and glomerulus filtration rate. Among the three groups, the renal arterial blood flow at shock decreased to about 65.4% of the original level, but subsequently increased after assistance for 1 h. The Abiomed group maintained the renal arterial and tissue blood flows at significantly higher levels than the NP+IABP and NP groups at 3 h, though there were no differences among the serum Cr levels in the acute experimental study at 3 h (Fig. 8B). A higher distribution of renal blood flow remained in each of the groups after assistance for 3 h, and damage to the glomeruli will increase in the future if these aspects are not improved. Furthermore, it is thought that the serum Cr value increases.

### Table 1. Hemodynamic data (preshock, shock, and at 3 h in three groups)

<table>
<thead>
<tr>
<th></th>
<th>Preshock</th>
<th>Shock</th>
<th>Abiomed group</th>
<th>NP+IABP group</th>
<th>NP group</th>
</tr>
</thead>
<tbody>
<tr>
<td>mAoP (mm Hg)</td>
<td>97.7±4.1</td>
<td>66.2±10.6</td>
<td>91.4±4.4</td>
<td>103.0±12.3</td>
<td>104.5±13.0</td>
</tr>
<tr>
<td>PF (L/min)</td>
<td>—</td>
<td>—</td>
<td>2.32±0.15</td>
<td>2.40±0.10</td>
<td>2.44±0.12</td>
</tr>
<tr>
<td>TF (L/min)</td>
<td>3.93±0.31</td>
<td>2.43±0.25</td>
<td>5.27±0.20</td>
<td>5.32±0.12</td>
<td>5.48±0.10</td>
</tr>
<tr>
<td>AR (%)</td>
<td>—</td>
<td>—</td>
<td>44.0±3.6</td>
<td>44.4±2.9</td>
<td>45.1±2.4</td>
</tr>
<tr>
<td>PP (mm Hg)</td>
<td>22.1±2.7</td>
<td>22.8±4.8</td>
<td>38.3±1.9</td>
<td>29.0±0.74</td>
<td>16.4±2.0</td>
</tr>
</tbody>
</table>

mAoP, mean aortic blood pressure; PF, pump flow; TF, total flow; AR, assist rate; PP, pulse pressure; NP, nonpulsatile pump; IABP, intra-aortic balloon pump.
Lactate is produced as the final product of the glycolytic metabolic pathway via anaerobic glycogen metabolism from pyruvate. The serum lactate level reflects the metabolic states of organs such as the liver, kidneys, and skeletal muscle, as well as increased states of imperfect circulation organization, such as myocardial infarction, shock, and left ventricular dysfunction. When it is necessary to judge metabolic changes, it is useful to know the relative lactate/pyruvate ratios. The lactate/pyruvate ratio tended to increase after shock in all three groups and expresses invasion of the living body in shock (Fig. 8A). There was a significant difference between the Abiomed and NP groups at 3 h in the present study. The Abiomed group was able to obtain much higher coronary and renal blood flows than the NP group, and the lactate/pyruvate ratio was lower in the Abiomed group than in the NP group. It is suggested that the pulsatile flow produced by this system contributes to the recovery from cardiogenic shock by supplying enough pulse pressure, as well as sufficient coronary arterial, renal arterial, and tissue blood flows. Therefore we propose that pulsatile flow is useful for preventing multiple organ failure.

Conclusion

The pulsatile flow created by using an Abiomed BVS5000 achieved sufficient levels of coronary and renal arterial blood flows. It is suggested that the introduction of an Abiomed BVS5000 is effective for preventing organ failure.

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References