Circulation Control of Experimental and Clinical Profound Left Ventricular Failures by Automatic Left Ventricular Assist System

Hisateru Takano, M.D., Yoshiyuki Taenaka, M.D., Takeshi Nakatani, M.D.
Tetsuzo Akutsu, M.D., Tsuyoshi Fujita, M.D.
and Hisao Manabe, M.D.

It is desirable that circulation control of the patient using a left ventricular assist device (LVAD) should be achieved appropriately and safely. We have developed an automatic LVAD system, which can maintain the normal circulation irrespective of the severity of heart failure and can restore the failing heart by decreasing the bypass flow (BF) through the LVAD as the heart recovers. The main part of the control-drive unit is an automatic level control (ALC) system for left atrial pressure (LAP) and total flow (TF). Profound left ventricular failure (LVF) was made by complete interception of blood supply to the extent of 50% (5 goats) and 70% (5 goats) of the LV free wall. The air-driven diaphragm-type LVAD was implanted between LA and aorta. At the beginning of LVAD pumping, BF tended to be very high to keep LAP at the preset level (0–5 mmHg) and to maintain TF at somewhat higher level (120–140 ml/kg/min). The recovering heart was able to decrease LAP gradually. Since the LAP was set at a certain level, the ALC of LAP decreased BF to maintain LAP at the preset level. During the recovering stage from LVF, preset level of LAP was gradually raised while checking the pulmonary function. When natural heart output exceeded 100 ml/kg/min, LVAD was removed. The 50% LVF group recovered between 17 hours and 3 days, and 70% LVF group between 6th and 16th postoperative day. This LVAD system was then applied to the postoperative profound LVF in a MVR patient whose entire circulation was maintained normal during 14 day pumping. The failed heart gradually recovered and the pump was successfully removed.

We consider that the decompression of LV will prevent overextension of impaired myocardium and simultaneously accelerate the solid scar formation. And gradual increase of LV work will promote the compensation ability of the residual myocardium. Continuous LVAD assistance can therefore earn time for the impaired myocardium to recover while maintaining normal circulation.

Key Words:
Assisted circulation
Left ventricular failure
Left heart bypass
Left ventricular assist device (LVAD)
Circulation control

Recently, the use of intra-aortic balloon pumping (IABP) has yielded good results for the treatment of severe heart failure. However, at the same time limitation of the IABP in cardiac assistance has also been recognized.1,2 The left ventricular assist device (LVAD) used to replace cardiac pump function is an effective means for treatment of profound left ventricular

National Cardiovascular Center, Research Institute and Hospital
Mailing address: Hisateru Takano, M.D., National Cardiovascular Center Research Institute 5-125, Fujishiro-dai, Suita, Osaka 565, Japan

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During LVF and to see actual recovering process of the heart from induced profound LVF. We have extensively studied the circulation control for LVF using our LVAD system and then applied it to a patient with postoperative severe LVF.

MATERIALS AND METHODS

Description of LVAD System

1. Left Ventricular Assist Device (LVAD)

Our LVAD is an air-driven diaphragm-type pump having an effective capacity of 78 ml as shown in Fig. 1.\(^7,8\) Since our LVAD is developed for the purpose of temporary use, the pump is placed extracorporeally on the chest wall. The inlet and outlet conduits are connected to the left atrium and the aorta through the chest wall, respectively. The blood contacting surface is a newly developed Japanese make medical grade segmented polyether polyurethane (Toyobo's TM-series)\(^9\) Nos. 23 and 21 Björk-Shiley valves are used in the inlet and outlet ports, respectively. The pump housing is reinforced with epoxy resin to prevent overstretch as well as collapse. Since the pump housing including back-plate (air chamber) is transparent, movement of the diaphragm can be easily observed. The diameter of both inlet and outlet conduits, which are made of the same material as that of the pump, is 14 mm.

2. Automatic Control-Drive Unit (CDU)

Our CDU consists of 1) automatic ECG synchronization system, 2) pumping duration and frequency set-up system, 3) automatic level control (ALC) system for left atrial pressure (LAP) and total flow (TF: cardiac output + BF, or pulmonary arterial flow), 4) air compressor and vacuum generators with regulators, 5) alarm unit and 6) back-up system. The picture of the CDU is shown in Fig. 2.

For synchronizing pump systole with the diastolic phase of the natural heart, T-wave trigger mode is adopted because the end of T-wave corresponds to the beginning of the natural heart's diastole. If T-wave detection fails, traditional R-wave trigger mode with automatic delay according to R-R interval takes over automatically. If the ECG signal can not be obtained, the trigger mode is switched over to internal source trigger, where the built-in pacemaker generates a drive pulses according to the preset rate and %-systole. When ECG signal

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Failure (LVF) beyond the limit of IABP's capability:3-6 Objectives for temporary use of LVAD are to maintain the normal circulation irrespective of the severity of heart failure and to restore the failing heart by gradually decreasing the bypass flow (BF) as the heart recovers. We have developed a new LVAD system consisting of an air-driven diaphragm-type pump and an automatic control-drive unit (CDU). The system has been evaluated in chronic animal experiments to study the effects of LVAD on hemodynamics.
recovers, the trigger mode is returned to synchronization mode. The block diagram of trigger mode, delay mode and pumping mode of this circuit is shown in Fig. 3.

It is desirable to have BF through LVAD change closely following changes in cardiac function. Since function of the failing heart is reflected in LAP levels, we adopted the automatic level control of LAP as the primary control method for BF. Since output of our pump varies proportionally to the %-systole (pumping duration/one pump cycle time × 100) till reaching the allowable maximum output, pump output or BF can be regulated by changing the %-systole. Based on this method, with changes in cardiac function, LAP fluctuates, thus activating the ALC system for LAP and consequently changing BF to maintain LAP at the preset level. ALC system for TF has also been incorporated as the secondary control of BF. When LAP is within preset range, the ALC of TF takes an effect to keep TF within the preset range by changing %-systole (Fig. 4 right). Although both upper and lower limits of LAP and TF are preset, TF may exceed the upper limit of its own preset range to keep LAP under its upper limit, and on the contrary LAP may be forced to become below its lower limit to maintain TF larger than.

**Fig. 3.** The block diagram of trigger mode, delay mode and pumping mode of the automatic ECG synchronization system.

**Fig. 4.** Function curves of the pump (left) and the concept of automatic level control of LAP and TF (right).
TABLE I OVER-ALL RESULTS OF CHRONIC LVAD EXPERIMENT IN INDUCED PROFOUND LVF

<table>
<thead>
<tr>
<th>No.</th>
<th>NCA</th>
<th>VF</th>
<th>Duration</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>2 days</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>+</td>
<td>18 hrs.</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>3</td>
<td>50%</td>
<td></td>
<td>3 days</td>
<td>Recovered but died (bleeding)</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>+</td>
<td>6 hrs.</td>
<td>Defibrillation failed</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>17 hrs.</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>6 days</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>+</td>
<td>14 days</td>
<td>Recovered but died (sepsis)</td>
</tr>
<tr>
<td>8</td>
<td>70%</td>
<td></td>
<td>6 days</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>+</td>
<td>7 days</td>
<td>Recovered &amp; pump removed</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>+</td>
<td>16 days</td>
<td>Recovered &amp; pump removed</td>
</tr>
</tbody>
</table>

NCA = Non-contractile area of LV free wall; VF = Ventricular fibrillation at NCA formation.

its lower limit.

3. Pump Performance Test

Pump performance was evaluated in a mock circulatory system. The effective pump stroke volume is 70 ml and the maximum output is 7.0 l/min at 100 beats/min of pump rate. Output of the pump can change proportionally with the %-systole till reaching maximum output which depends on the driving air pressure (Fig. 4 left).

Experimental Study of LVAD

Ten adult goats weighing between 32 and 46 kg were used. After ketamine hydrochloride (10 mg/kg) and atropine sulfate (0.05 mg/kg) were administered intramuscularly, goats were intubated. Anesthesia was maintained with 1.5-2.0% halothane and 50% nitrous oxide mixed with oxygen.

Sterile technique was enforced throughout the surgery. Thoracotomy was performed through the left fifth costal bed. ECG, right atrial pressure (RAP), pulmonary arterial pressure (PAP), LAP, left ventricular pressure (LVP), aortic pressure (AoP), aortic root flow (ARF) or TF in the pulmonary artery and BF through LVAD were continuously monitored. The pump was installed between LA and Ao, and then placed extracorporeally on the chest wall. Profound LVF was made by 50% (five goats) or 70% (five goats) interception of blood supply (myocardial infarction: MI) to the LV free wall. After confirming that the cardiac output decreased to less than 50% of the control level or that the heart fibrillated, synchronous or asynchronous left heart bypass (LHB) by our LVAD system with ALC of LAP and TF was started. After the chest was closed, the goat was placed in the cage and awoke followed extubation. No anticoagulant was used during entire course of the experiment after implantation of the pump.

Clinical Case

A 36 year-old cardiac cachexic woman had a long-term history of rheumatic heart disease with atrial fibrillation. Her presenting symptoms were those of congestive heart failure with orthopnea and progressive exercise intolerance (NYHA: IV). Cardiac minute examinations revealed severe mitral regurgitation (4/4), tricuspid regurgitation (2/4), giant left atrium (cardio-thoracic ratio: 80%), pulmonary hypertension (mean PAP: 49 mmHg), pulmonary capillary wedge pressure: 23 mmHg, LVEDP: 15 mmHg, an ejection fraction of LV: 0.44, and cardiac index: 1.8 L/min/m². She had undergone mitral valve replacement with No. 27 Ionescu-Shiley porcine xenograft, tricuspid annuloplasty and left atrial plication. She was not readily separated from cardiopulmonary bypass (CPB) with pharmacologic therapy. Institution of IABP, therefore, was made to wean her from CPB.

On the first postoperative day (POD) cardiac index was around 2.0 L/min/m² by the thermodilution technique and LAP was between 15 and 18 mmHg in spite of vigorous pharmacologic
therapy and IABP assistance. However, suddenly she had ventricular tachyarrhythmia and then ventricular fibrillation. She recovered cardiac rhythm by direct-current countershock, but failed into profound heart failure.

She was returned to the operating room and our LVAD was then instituted under CPB. The left atrium was used for inflow cannulation and the outlet conduit was anastomosed to the ascending aorta. BF by electromagnetic flowmeter at the outlet conduit, TF by thermodilution method, RAP, LAP, AoP and ECG were monitored.

RESULTS
Results of Experimental Study
Ventricular fibrillation occurred in six of ten goats just after induction of myocardial infarction or when the goat was placed in the cage. However, defibrillation was successfully performed under LHB except Case No. 3.
Adjustment of circulating blood volume and electrolytes level, and administration of antiarrhythmic agents were performed in the same manner as clinical situation.

At the beginning of LHB, BF was very high to keep LAP at the preset level (0–5 mmHg) and to maintain TF at somewhat higher level (120–140 ml/kg/min). If TF could not be maintained at preset level, volume loading was carried out. The recovering heart was able to decrease LAP gradually. Since the LAP was set at a certain level, the ALC of LAP decreased BF to maintain LAP at the preset level. During the recovering stage from LVF, preset level of LAP was gradually raised while checking the pulmonary function. When cardiac output exceeded 100 ml/kg/min at rest, pump was removed.
Four goats of 50% MI group recovered from LVF between 17 hours and three days after the onset of LVAD pumping and pumps were removed except one that died of bleeding on the third day. One (Case No. 3) died of ventricular fibrillation when myocardial infarction was made, but circulation was maintained for about 8

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Fig. 6. Hemodynamic changes during recovery process from induced profound LVF (Case No. 6; 70% MI group) by LVAD.

hours by LHB alone. Five goats of 70% infarction group recovered from profound LVF between 6th and 16th postoperative day.

Summary of over-all results is shown in Table I. Two representative cases, one from each group will be described below.

(Case No. 2; 50% MI group) (Fig. 5)
When 50% MI was made in a goat weighing 30 kg, ventricular fibrillation occurred. Since several trials of defibrillation failed, LVAD was installed while performing cardiac massage. Under LHB defibrillation succeeded, and TF and AoP were maintained within normal range. When pumping was stopped for a few seconds, cardiac output went down almost to zero and drastic drop in blood pressure occurred. The cardiac function did not recover even five hours after the pumping started. Then 0.1 gamma/kg/min of epinephrine was administered, followed by gradual recovery of cardiac function with increase in ARF and spontaneous decrease in BF. Therefore, preset LAP level of ALC was readjusted from 7 to 12 mmHg, and thus weaning was started. After 18 hours of pumping ARF became stable at the control level, and the pump was removed.

(Case No. 6; 70% MI group) (Fig. 6)
When 70% MI was made in a goat weighing 34 kg, ventricular extrasystoles often occurred, but normal circulation was maintained by LHB without falling into ventricular fibrillation. ALC for LAP and TF were set at between 0—5 mmHg and 3.0—3.5 L/min, respectively. The TF, however, was low. Accordingly volume loading was done on the first day. Thereafter TF markedly increased being influenced also by eating and drinking. LAP was continuously maintained at preset level. At this point, when LHB was temporarily stopped, LAP and PAP increased over 25 mmHg and the goat became uneasy. Until the third postoperative day (POD) LAP was kept intentionally low and subsequently left ventricular work was somewhat reduced. From the fourth POD preset level of LAP was raised to increase left ventricular work. On the sixth day the heart recovered up to the same grade as in the mild LVF as long as LAP was kept at somewhat higher than normal. Therefore the
pump was removed. On the 14th POD the heart recovered further from LVF.

After the removal of the pump, cardiac function was stable and improved slightly in most cases, that was, cardiac output increased and LAP decreased gradually. However, the mild heart failure still remained depending upon the severity of the infarction. One goat (Case No. 10) taking 16 day pumping for recovery revealed gradual decrease of cardiac output and elevation of LAP, and died during LV-graphy.

Autopsy was performed in seven goats between eight and fifteen days after the pump removed and in three goats just after death. Fig. 7 shows the ring slice of the heart. Macro-

Fig. 7. Ring slice of the heart recovered from profound LVF (Case No. 5, 70% MI group) by LVAD.

Fig. 8. Hemodynamic changes of the patient supported with the LVAD.
HR: heart rate, mAoP: mean aortic pressure, mPAP: mean pulmonary pressure, mLAP: mean left atrial pressure, mRAP: mean right atrial pressure, MVR: mitral valve replacement, TAP: tricuspid annuloplasty, LAP: left atrial plication.
On the 14th POD when LV function seemed enough recovered, removal of fibrinous membrane adhered on the leaflets and commissures of the valve was performed under CPB. At this time the patient was readily weaned from CPB with LVAD being temporarily stopped. Cardiac index was 2.3 L/min/m² with LAP of 14 mmHg. Therefore pump and conduits were subsequently removed. Although the patient was returned to intensive care unit, unfortunately she dropped into multiple organ failure due to sepsis and died on 15th POD. Hemodynamic changes during 14 day pumping are shown in Fig. 8. During the entire course of LVAD pumping LAP was maintained at preset level by ALC system and the hemodynamic state was quite stable.

Autopsy revealed that the remaining surviving myocardium scatteredly existed, and was surrounded by granulation and fibrinous tissue which replaced the necrotic degenerated myocardium. No thrombus was found inside the pump.

**DISCUSSION**

The objectives of using LVAD for LVF are to maintain normal circulation and to help the failing heart recover. It is desirable that circulation control should be achieved appropriately, safely and automatically for these purposes. In order to achieve this goal, we have developed automatic ECG synchronization system and ALC system for LAP and TF.

1. **Automatic ECG Synchronization**

   Though LHB can maintain the normal circulation regardless of synchronization, pumping during diastolic phase of the natural heart has an advantage of positive coronary augmentation as well as decrease in afterload. For the purpose of synchronization we paid attention to T-wave of ECG instead of R-wave. Since the end of T-wave corresponds to the beginning of diastole, T-wave trigger pumping will take place exactly during diastole even in rapid changes of pulse rate or during various arrhythmias. If T-wave can not be recognized by some cause, traditional R-wave trigger mode with an appropriate delay will begin working automatically (Fig. 3). Synchronized LHB can certainly decrease LV work while maintaining the normal circulation. In the experimental and clinical studies our system showed an excellent synchronization capability with ECG signal.

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2. Control of Bypass Flow
   In our system BF is controlled by regulating the stroke volume which changes linearly with \%-systole. \%-systole is determined automatically by the level of LAP and TF (Fig. 4).
   In profound LVF it is particularly important to keep LAP low, since elevated LAP will cause pulmonary congestion resulting in deterioration of gas exchange, which in turn will deteriorate general condition. Low LAP will also help reduce left ventricular work. We usually keep LAP at around 5 mmHg in the initial stage (Fig. 9). Even when LAP is maintained at the preset level, TF may be less than preset level in some cases. Then ALC of TF takes an effect to increase BF, although LAP may become less than the preset level. As it is considered that hypovolemia may exist in such an occasion, volume loading is mandatory and actually is very effective. On the contrary, hypervolemia causes a high TF to maintain LAP at the preset level. Though the influence of too high output is not clear, readjustment of TF by volume unloading will probably be better. In the initial stage we usually keep TF between 120 and 140 ml/kg/min in a goat (Fig. 9), and between 2.5 and 3.0 L/min/m² in a patient.
   Since excessive assist may delay the recovery of the failing heart while insufficient assist certainly deteriorates the general condition including the myocardium itself, BF should be changed according to the change of cardiac function. In LA-Ao bypass there is always a competition between the natural heart and LVAD at the atrial level. Therefore BF was very high in the beginning of LVAD, followed by its gradual decrease as the heart recovered. The heart in recovering process continuously increased its stroke volume, hence lowering LAP. However, since LAP was preset at a certain level, the ALC of LAP started functioning to decrease BF and to maintain LAP at the preset level. For the actual weaning procedure during the recovering stage from LVF, LAP was gradually raised while checking the pulmonary function together with the cardiac function (Fig. 9). In profound LVF LHB was discontinued when cardiac output exceeded the control level or 100 ml/kg/min in goats and 2.0 L/min/m² in patients even though LAP was higher than control level but less than 20 mmHg (Fig. 9).

3. Joint Use of Drugs
   When myocardial contraction did not recover readily, which was encountered often, inotropic agent was successfully administered to get out of such LVAD dependent situation. Peripheral vascular collapse was also noted once in a while when profound LVF advanced. In these cases vasopressor worked to maintain an adequate perfusion pressure for vital organs. However, some cases fell into irreversible shock despite vigorous LVAD pumping together with vasopressor administration.

4. Co-existence of Right Ventricular Failure
   When right ventricular failure exists concomitantly with LVF, pulmonary venous return decreases and LAP drops. In such a case LHB alone can maintain normal circulation by means of keeping RAP higher level. In our study, even during cardiac arrest, LHB alone could keep TF within normal range if right atrial pressure was kept around 15 mmHg. However, biventricular assist may be necessary when pulmonary vascular resistance is high. In our clinical case, which was biventricular failure with pulmonary hypertension to be considered as the indication of biventricular assist, administration of isoproterenol took effect and right VAD was not necessary.

5. Recovery From Profound LVF
   The severely impaired heart can not maintain the normal circulation without LVAD assistance. However, the recovered heart from LVF by LVAD can maintain almost near the normal circulation. Pathological findings of the heart show that the necrotic myocardium was replaced with fibrous tissue and became solid scar. On the other hand residual myocardium became hypertrophic (Fig. 7). Removal of overload and decompression of LV will prevent overextension of impaired myocardium and accelerate the solid scar formation which will move dysskinetic no more, and gradual increase of LV work will promote the compensation ability of the residual myocardium.

   Continuous LVAD assist can earn time for the impaired heart to recover while maintaining normal circulation. Required time for the recovery seems to depend on the severity of myocardial damage.

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