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Abstract

The present study was undertaken to determine whether a biventricular bypass system operated in an independent variable rate (VR) mode can maintain the entire circulation. Two pusher-plate pumps which incorporated the Hall effect position sensors were used to bypass the right and left ventricles in 10 sheep under fibrillation. The flow distributions of the pump output to the carotid and renal arteries were investigated every 6 h using ultrasonic blood flow meters for 24 h in 5 animals, and the controllability of the VR mode was evaluated in 5 long-term experiments. The carotid artery flow ratio to the pump output decreased significantly from 4.7 +/- 0.8% before the bypass to 2.7 +/- 0.9% after 24 h. However, the renal artery flow ratio did not change throughout the experiments. In the long-term experiments, the animals were kept alive from 3 to 48 days (mean 15.6 days). The mean pump output had been maintained at more than 90 ml/min/kg for the first 7 days. After the surgery, the pump driving conditions were not readjusted in any experiment. The results indicate that the biventricular bypass system operated in the independent VR mode automatically maintains the entire circulation at a satisfactory level.

KEYWORDS: biventricular bypass, pusher-plate pump, variable rate mode, flow distribution

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The present study was undertaken to determine whether a biventricular bypass system operated in an independent variable rate (VR) mode can maintain the entire circulation. Two pusher-plate pumps which incorporated the Hall effect position sensors were used to bypass the right and left ventricles in 10 sheep under fibrillation. The flow distibutions of the pump output to the carotid and renal arteries were investigated every 6h using ultrasonic blood flow meters for 24h in 5 animals, and the controllability of the VR mode was evaluated in 5 long-term experiments. The carotid artery flow ratio to the pump output decreased significantly from 4.7 ± 0.8% before the bypass to 2.7 ± 0.9% after 24h. However, the renal artery flow ratio did not change throughout the experiments. In the long-term experiments, the animals were kept alive from 3 to 48 days (mean 15.6 days). The mean pump output had been maintained at more than 90 ml/min/kg for the first 7 days. After the surgery, the pump driving conditions were not readjusted in any experiment. The results indicate that the biventricular bypass system operated in the independent VR mode automatically maintains the entire circulation at a satisfactory level.

Key words : **biventricular bypass, pusher-plate pump, variable rate mode, flow distribution.**

Since the successful use of a left heart bypass by Spencer (1) in 1964 and a ventricular assist device (VAD) by DeBakey (2) in 1966, extensive efforts have been made to develop prosthetic ventricles for the treatment of refractory heart failure. Recent interest in this field centers on use of a VAD as a bridge to cardiac transplantation and a variety of devices have been employed for this, including a centrifugal pump, a sac-type or diaphragm-type pneumatic pump, and a pusher-plate electrical pump. The risk of irreversible myocardial failure or high incidence of ventricular fibrillation in transplant candidates (3) makes the ability to maintain total circulation desirable in these devices.

Since 1988, we have been developing a biventricular bypass system which consists of air-driven, pusher-plate (PP) type blood pumps for use in the future as a bridge to cardiac transplantation. This study was undertaken to determine whether a biventricular bypass system operated in a left and right independent variable rate (VR) mode can maintain the entire circulation. Special emphases were placed on investigating flow distribution and hemodynamic controllability of the independent VR mode.

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Materials and Methods

The biventricular bypass system consisted of two PP type pumps (The National Cardiovascular Center, Osaka, Japan) with a stroke volume of 60 ml for the left side and 40 ml for the right side. Each pump consisted of three parts; inner (blood side) and outer (air side) pump housings, and a flexible diaphragm attached to the PP on the air side. The blood contacting surface of the pump was coated with a seamless segmented polyurethane. Björk-Shily valves of 25 mm and 21 mm were used in the inflow and outflow ports, respectively. The pumps incorporated the Hall effect position sensors which were used to precisely regulate the PP movement and compute the pumping rate, beat-to-beat stroke volume and minute pump output. The pumps were driven pneumatically by a control-drive unit (Model 113, Yasuhisa Biomechanics Co., Tokyo, Japan) which can operate two pumps in three different modes: the VR, the fixed rate and the synchronized mode. In the VR mode, the Hall effect signal was utilized to regulate the pump stroke at a constant level, while its rate was allowed to change depending on its preload and afterload.

Five sheep, weighing 45 to 67 kg, were used for the short-term experiments and 5 sheep, weighing 50 to 60 kg, were selected for the long-term experiments. Anesthesia was induced and maintained during surgery using 1.0 to 1.5 % fluothane and 50 % nitrous oxide mixed with oxygen. Respiration was controlled by a volume-cycle respirator with a tidal volume of 15 ml/kg. The chest was opened through the fifth intercostal space. Following administration of heparin sodium (1 mg/kg), the drainage cannulae of the left and right bypass pumps were inserted into the left and right atria, while the return cannulae of both pumps were anastomosed to the descending aorta and pulmonary artery, respectively (Fig. 1). The left and right pumps, primed with a saline solution, were connected to the cannulae and then driven independently in the VR mode. The conditions of the control-drive unit to actuate the pumps were as follows. The positive air pressure to eject blood from the pump ranged from 200 to 240 mmHg for the left side and 80 to 100 mmHg for the right side, while the negative air pressure to withdraw blood to the pump was adjusted between − 20 and − 30 mmHg for both sides. After the control data acquisition, the native heart was fibrillated by an electrical shock, and thereafter the two pumps maintained the circulation.

In the short-term experiments, a Fr. 7 balloon-tipped thermodilution catheter was inserted into the pulmonary artery via the left jugular vein for the measurement of cardiac output, pulmonary artery and right atrial pressure. Another Fr. 7 polyethylene fluid-filled catheter was advanced into the ascending aorta via the left internal thoracic artery to measure arterial blood pressure. Before the thoracotomy, the cardiac output as a control value of the total flow was measured by a thermodilution computer (American Edwards Laboratories, CA, USA). After fibrillation of the native heart, the right pump output was employed for the total flow, which was computed by multiplying the beat rate obtained from the Hall signal by the stroke volume of 40 ml. Systemic vascular resistance (SVR) was calculated by dividing the difference between the mean arterial pressure and the right atrial pressure by the total flow. For the study of the flow distribution, the left carotid and left renal arteries were exposed and those flows measured using an ultrasonic blood flow meters (T201, Transonic Systems Inc., NY, USA). To describe the changes in the carotid and renal artery flows, the ratio of each flow to the total flow was compared with the control value.

In the long-term experiments, 16 gauge fluid-filled catheters were advanced into the ascending aorta and the right atrium via the left internal thoracic artery and vein, respectively. The right pump output was employed for the total flow.

All experiments were performed without any blood transfusion, and anticoagulants were not used after the sugery. Once complete filling and ejection of both pumps

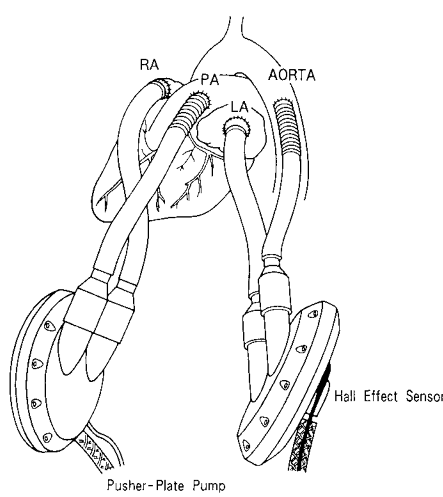

Fig. 1 Experimental set-up of the pusher-plate type biventricular bypass system.

were established, the pump driving conditions were not changed thereafter.

Significance of the difference between values was examined by the unpaired Student's t test and a difference of $p < 0.05$ was regarded as significant. Values are expressed as the mean ± SD.

Results

In the short-term experiments, 5 animals were killed after 24 h. The parameters obtained at 6 h intervals are listed in Table 1. The total bypass flow, expressed in ml/min/kg, and the venous lactate levels were at the same level as the control subjects. The SVR was kept within the normal range. The carotid artery flow decreased significantly, and its ratio also declined to 2.7 ± 0.9 % after 24 h. The renal artery flow ratio was around 7 % throughout the experiment. There were no significant changes in hematocrit, serum free hemoglobin, arteriovenous oxygen differences, and oxygen consumption.

In the long-term experiments, the bypass time ranged from 3 to 48 days (meam 15.6 days). The first subject experienced accidental bleeding from the arterial line on the eighth day and died on the twelfth day. The second subject died suddenly on

Table 1 Hemodynamic and metabolic changes in the short-term experiments

		Control	Postoperative hours			
			6 h	12 h	18 h	24 h
Total flow	(ml/min/kg)	75.0 ± 13.4	75.6 ± 8.8	76.1 ± 9.3	77.3 ± 10.7	77.1 ± 9.9
SVR	(dyn·sec·cm^{-5})	1704 ± 272	1635 ± 268	1597 ± 384	1669 ± 372	1659 ± 310
Carotid flow	(ml/min)	175 ± 16	115 ± 35*	116 ± 34*	120 ± 36*	105 ± 32*
Renal flow	(ml/min)	271 ± 68	294 ± 47	280 ± 61	280 ± 94	302 ± 76
Carotid flow ratio	(%)	4.7 ± 0.8	2.9 ± 0.9	3.0 ± 1.0	3.0 ± 1.1	2.7 ± 0.9*
Renal flow ratio	(%)	7.3 ± 2.5	7.5 ± 2.0	7.1 ± 2.1	6.9 ± 2.5	7.6 ± 2.5
Hematocrit	(%)	26.8 ± 2.0	29.2 ± 4.8	29.4 ± 4.2	30.0 ± 5.2	31.2 ± 4.4
Serum f-Hgb	(mg/dl)	0.94 ± 0.65	1.52 ± 1.50	2.69 ± 1.92	2.46 ± 1.30	2.92 ± 1.52
Venous lactate	(mg/dl)	18.4 ± 8.3	18.5 ± 6.6	18.9 ± 5.1	14.2 ± 5.3	18.9 ± 9.0
A-V DO_2	(vol%)	37.2 ± 7.6	41.4 ± 18.9	19.7 ± 2.5	27.4 ± 10.5	39.0 ± 13.3
O_2 consump.	(ml/min/kg)	2.93 ± 0.53	2.90 ± 1.02	1.46 ± 0.22	1.99 ± 0.70	2.82 ± 0.72

Values are mean ± SD. SVR: systemic vascular resistance. Serum f-Hgb: serum free hemoglobin. A-V DO_2: arteriovenous oxygen differences. O_2 consump.: oxygen consumption. *: Significant compared with control value ($p < 0.05$).

Table 2 Hemodynamic and metabolic changes in the long-term experiments for postoperative 7 days.

		Postoperative days				
		1 (n = 5)	2 (n = 5)	3 (n = 4)	5 (n = 4)	7 (n = 3)
Total flow	(ml/min/kg)	90.2 ± 11.6	91.0 ± 12.7	93.8 ± 8.5	95.8 ± 8.8	98.7 ± 6.4
SVR	(dyn·sec·cm^{-5})	1313 ± 241	1349 ± 248	1369 ± 227	1283 ± 229	1093 ± 168
Hematocrit	(%)	27.3 ± 3.2	29.7 ± 3.3	27.9 ± 0.9	24.5 ± 1.9	23.3 ± 2.6
Hemoglobin	(mg/dl)	9.3 ± 1.1	10.1 ± 1.1	9.5 ± 0.3	8.3 ± 0.7	7.9 ± 0.9
Serum f-Hgb	(mg/dl)	4.06 ± 2.52	5.27 ± 4.36	7.04 ± 6.61	5.77 ± 5.39	5.67 ± 5.33
Venous lactate	(mg/dl)	9.7 ± 2.1	7.9 ± 1.9	5.4 ± 2.1	10.8 ± 3.2	10.1 ± 3.9
A-V DO_2	(vol%)	27.5 ± 9.0	27.6 ± 10.5	27.5 ± 9.6	30.9 ± 10.9	24.3 ± 3.1
O_2 consump.	(ml/min/kg)	2.39 ± 0.54	2.43 ± 0.79	2.55 ± 0.84	2.98 ± 1.08	2.39 ± 0.16

Values are mean ± SD. SVR: systemic vascular resistance. Serum f-Hgb: serum free hemoglobin. A-V DO_2: arteriovenous oxygen differences. O_2 consump.: oxygen consumption.

the third day because the control-drive unit was incorrectly set. The third died of respiratory failure on the sixth day. The fourth survived for 48 days, and died of bacteremia. In the case of the fifth subject, both pumpings were stopped suddenly by the obstruction of a compressor line on the ninth day. The parameters acquired for the first 7 days are listed in Table 2. The total flow was kept between 90 and 100 ml/min/kg with venous lactate levels of about 10 mg/dl. The SVR was maintained about 1,300 dyn·sec·cm^{-5}. The values for hematocrit and hemoglobin tended to decrease for the first 7 days. Serum free hemoglobin levels were lower than 3 mg/dl in 2 subjects, and higher than 6 mg/dl in 3 subjects. Arteriovenous oxygen differences and oxygen consumption were not changed.

Discussion

The goal of our study was to establish a biventricular bypass system which could maintain the entire circulation precisely, safely, and automatically. The method of control is an important factor in achieving optimum pump performance in the development of such a circulatory support system. The left and right independent VR mode was developed for a fully implantable total artificial heart (TAH) at the Cleveland Clinic Foundation and its hemodynamic controllability was confirmed by Takatani *et al.* (4). When the VR mode controls the bypass system, however, a question arises concerning the pump flow sensitivity to the preload. The pump diaphragm of the TAH reacts directly to its filling pressure, but the pump in the bypass system senses preload through the inflow cannula. In our study, good pump filling was achieved by adding the vacuum pressure of between −20 and −30 mmHg.

Emphasis was placed on the study of the flow distribution in the short-term experiments. We selected the carotid and renal artery flows because the fractional distribution of flows to the brain and kidney change conversely in a state of shock: the cerebral blood flow increase at the expense of the splanchnic bed and kidney flow (5, 6, 7). Although the renal flow and its ratio were maintained at normal rates, the carotid flow decreased throughout the bypass and its ratio declined after 24 h pumping. According to the report of Lassen (8), following factors are thought to be a cause of the decrease in the corotid flow; high oxygen or low carbon dioxide tension, and anesthetics. As far as anesthetics are concerned, there is a possibility that fluothane increased carotid flow because anesthesia was maintained using nitrous oxide mixed with oxygen after the surgery. Conversely, high oxygen and low carbon dioxide due to hyperventilation during the 24 h postoperative period may have caused the decrease in the carotid flow. From our experimental model, it is difficult to determine the cause of decrease in the carotid flow. Our results, however, indicate that none of the animals fell into a state of shock.

The total flow in the long-term group was relatively higher with lower SVR than the short-term experimental group. The surgery or anesthetics may have influenced on the animal's hemodynamics during postoperative 24 h. Murakami *et al.* reported that, in TAH animals, the immediate postoperative elevation of arterial pressure and SVR returned to normal levels after one week and the circulating blood volume decreased to normal level within one month (9). Although only one animal survived for longer than one month in our series, its hemodynamic state was stabilized in 2 weeks (10). Therefore, further study for longer than 2 weeks is necessary in order to overcome the effect of surgical intervention on animal's hemodynamics.

In the long-term experiments, two PP pumps functioned like the native heart according to the change in its preload. For example, from sitting to standing position, the pump output increased automatically resulting from an increase in the pumping rate. Based on a total of 78 days of pumping, the following advantages of the independent VR mode were found: manual readjustments and invasive monitorings were no longer required once the pump operating conditions were established.

In conclusion, the biventricular bypass system utilizing two PP type pumps was developed and its hemodynamic performance was evaluated in sheep with a fibrillating heart. The biventricular bypass operated in the left and right independent VR mode maintained the renal artery flow in normal, and kept the animals as long as 48 days without changing the pump driving conditions.

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