Laboratory Investigation

Peripheral Organ Perfusion Augmentation during Left Ventricular Failure

A Controlled Bovine Comparison between the Intraaortic Balloon Pump and the Hemopump®

Robert T. Baldwin, MD
Branislav Radovančević, MD
Jeff L. Conger, BS
Ryousuke Matsuwaka, MD, PhD
J. Michael Duncan, MD
William K. Vaughn, PhD
Richard K. Wampler, MD
O.H. Frazier, MD

Despite the use of inotropic therapy and the intraaortic balloon pump (IABP), inadequate peripheral organ perfusion and subsequent multiorgan failure from left ventricular dysfunction is a major cause of death following cardiac surgery. To compare the end-organ perfusion provided by the IABP with that of the recently developed Hemopump® Cardiac Assist System, blood flow from visceral organs was measured by ultrasonic flow probes during separate periods of support with each of these pumps.

Ten calves underwent coronary artery ligations with β-receptor blockade; hemodynamic parameters were recorded before the induction of failure, during unsupported cardiac failure, and during Hemopump and IABP support. Improvement in mean cardiac output, mixed venous oxygen saturation, and pulmonary artery wedge pressure was significantly greater ($p < 0.05$) during Hemopump support than during IABP support. Renal artery flow was significantly greater during Hemopump support (276 ± 74.2 cc/min) than during IABP support (164 ± 79.6 cc/min). Hepatic artery flow was significantly greater during Hemopump support (34.7 ± 25.7 cc/min) than during IABP support (24.4 ± 18.9 cc/min), and portal vein flow was significantly greater during Hemopump support (1588 ± 315 cc/min) than IABP support (1259 ± 310 cc/min). There were no significant differences, however, between carotid artery flow during Hemopump support (292 ± 171 cc/min) and that during IABP support (317 ± 204 cc/min).

We conclude that renal, hepatic, and mesenteric perfusion provided by the nonpulsatile Hemopump is superior to that of the IABP in this bovine model of left ventricular failure. Therefore, the Hemopump may be more effective in preventing multiorgan failure during recovery of ventricular function. ***(Texas Heart Institute Journal 1993;20:275-80)***

Key words: *Cardiogenic shock; Hemopump; intraaortic balloon pump; multiorgan failure; perfusion, renal*

From: *The Cullen Cardiovascular Research Laboratories and the Department of Cardiovascular Surgery, Texas Heart Institute, Houston, Texas; and Johnson & Johnson Interventional Systems, Inc. (Dr. Wampler), Rancho Cordova, California*

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Address for reprints: *O.H. Frazier, MD, Mail Code 3-147, Texas Heart Institute, P.O. Box 20345, Houston, TX 77225-0345*

After cardiac surgery, some patients experience low-cardiac-output syndrome, which can lead progressively to multiorgan failure and death. The conventional treatment for postcardiotomy shock consists of inotropic therapy and insertion of the intraaortic balloon pump (IABP), which will frequently maintain peripheral organ perfusion during ventricular recovery. In 30% to 50% of such patients requiring an IABP, however, conventional therapy does not provide adequate support and the patient dies as a result of either irreversible shock or multiorgan failure.[1]

Clinicians, in focusing on the treatment of these patients having the most severe low-cardiac-output syndromes, have considered several options that may be beneficial. These options consist of using a larger intraaortic balloon pump that produces a stroke volume closer to that of the native left ventricle[2] or inserting a temporary left ventricular assist device, such as the Biomedicus centrifugal pump (Biomedicus, Inc.; Eden Prairie, Minnesota, USA), that is capable of fully supporting the circulation. A 3rd support option is that of the Hemopump® Cardiac Assist System* (Johnson & Johnson Interventional Systems, Inc.; Rancho Cordova, California, USA), which requires a less invasive insertion technique than that of other left ventricular assist devices. The Hemopump is capable of augmenting cardiac output by approximately 3.5 L/min, but is not able to achieve the 6 to 7 L/min

* Hemopump is a registered trademark of Johnson & Johnson Interventional Systems Company, Rancho Cordova, California. The Hemopump is commercially available outside the United States; however, it is still an investigational device in the US. The Phase II clinical trial is in progress.

flow that may be attained with the Biomedicus pump. In order to assess how well the Hemopump supports peripheral organ perfusion in comparison with the conventional methods of inotropic support and with the intraaortic balloon pump, we undertook a controlled study using a bovine model of left ventricular failure.

Methods

Acute experiments were completed in 10 calves (some of each sex) ranging in weight from 70 to 90 kg. All animals received humane care in compliance with the "Guidelines for the Care and Use of Laboratory Animals" (NIH Publication No. 85-23, revised 1985).

Anesthesia was induced with ketamine hydrochloride (4 to 8 mg/kg, intravenous) after premedication with xylazine hydrochloride (0.03 mg, intramuscular) and atropine (0.04 mg/kg, intramuscular). A cuffed endotracheal tube was used for airway intubation, and the calves were ventilated on a volume cycled ventilator with 100% inspired oxygen. Arterial blood gas levels were measured to further assist with adjustments in inspired oxygen content and minute ventilation. Anesthesia was maintained with isoflurane (0 to 4%), and body temperature was maintained at 36 to 37 °C. A right neck incision was made under clean conditions, and a catheter was inserted into the right common carotid artery to monitor carotid blood pressure. An oximetric pulmonary artery catheter was inserted through the right internal jugular vein to obtain cardiac outputs by thermodilution. The left common femoral artery was exposed, and an arterial pressure catheter was inserted. The bladder was drained by catheter.

A midline laparotomy was performed to expose the common hepatic artery, portal vein, and left renal artery. Transonic flow probes (Transonic Systems, Inc.; Ithaca, New York, USA) of appropriate size were placed around each vessel. A contralateral neck incision was made, and a flow probe was placed around the left common carotid artery. Probes were connected to a Transonic dual-channel flowmeter (Model T/201/D). For the range of various flow probes used, the absolute accuracy was within ± 15%; relative accuracy for all probes was ± 2%. A median sternotomy was then performed and a pericardial cradle created to expose the heart.

After all monitoring devices were functioning well, baseline measurements were taken and repeated every 15 minutes until a steady hemodynamic state occurred. Left ventricular failure was initiated by pretreatment with propranolol (4 to 6 mg, intravenous), bretylium tosylate (5 mg/kg, intravenous), and continuous lidocaine infusion (40 mg/kg/min). In each calf, ligation was performed sequentially on the diagonal coronary arteries and the distal left anterior descending coronary artery as needed for the desired indices of left ventricular failure. Such failure was characterized by a 40% to 50% decrease in cardiac output and a left atrial pressure greater than 15 mmHg. Continuous esmolol infusion (400 mg loading, then 50 to 400 mg/kg/min) was used to titrate to the desired level of left ventricular failure. Measurements of hemodynamic variables were repeated until a stable state was reached.

Both the Hemopump and the IABP were assessed in each calf so that each animal served as its own control. The Hemopump was placed before IABP insertion in half of the animals and the order reversed in the other half on an alternating basis. Hemodynamic measurements were taken either after 30 minutes of support or until there was evidence of stable mixed venous oxygen saturation (SvO_2). The SvO_2 was considered stable when there was a change of less than 2% during a 10-minute period. Measurements of failure variables that were made during periods with no support were repeated between periods with support and at the completion of the experiment, to assess whether drift of the model of left ventricular failure occurred.

Moderate systemic heparin (1000 U/kg) was administered after all flow probes had been placed and ligation completed. A 12-mm Dacron graft diverticulum was sewn onto the infrarenal abdominal aorta, with fluoroscopic visualization to ensure that IABP placement would be above the renal arteries and below the arch vessels. An 8.5-F, 40-cc adult IABP (Datascope Inc.; Paramus, New Jersey, USA) was then inserted through the Dacron diverticulum. Balloon pumping was triggered by electrocardiography at a 1:1 frequency by use of a Datascope System 84 console. The Hemopump was inserted through the same Dacron diverticulum and placed at full support (setting 7). Consistent with clinical usage of the hemopump and recognizing the importance of proper afterload management,[3] efforts were made, by pharmacologic manipulation, to maintain the mean arterial pressure between 60 and 70 mmHg during Hemopump support. In the rare event that calves were hypertensive during Hemopump support, a continuous sodium nitroprusside infusion was started to maintain a mean arterial pressure of 60 to 70 mmHg. Fluoroscopy was used to ensure proper placement of the Hemopump across the aortic valve into the left ventricle.

In all 10 animals, data were collected at 6 time intervals (postinduction baseline, failure #1, 1st pump support, failure #2, 2nd pump support, and failure #3) for the 13 hemodynamic variables (renal artery flow, carotid flow, hepatic artery flow, portal vein flow, thermodilution cardiac output, pulmonary capillary wedge pressure [PCWP], central venous

pressure [CVP], heart rate, mean carotid pressure, mean femoral pressure, carotid pulse amplitude, femoral pulse amplitude, and mixed venous oxygen saturation [SvO_2]). These data were entered onto a 386 microcomputer and analyzed by using the GLM procedure available on the Statistical Analysis System (SAS). Results were compared using analysis of covariance and the Student-Newman-Keuls test. All results reported as statistically significant in this paper were significant at a level of $p < 0.05$.

Results

In our model of left ventricular failure, the mean preinduction cardiac output decreased by 49.9%, from 7.82 ± 1.6 L/min to a mean time-averaged cardiac output of 3.92 ± 0.73 L/min after the induction of failure. The PCWP increased from a mean of 6.0 ± 1.5 mmHg to a mean of 19.3 ± 1.56 mmHg after the induction of failure. Central venous pressure increased from 4.5 ± 1.4 to 8.9 ± 3.0 mmHg. Mean SvO_2 decreased from 78% ± 4.8% to 58.4% ± 5.1%, and heart rate (reflecting mostly β blockade) decreased from 100 ± 17.4 to 64.3 ± 20.3 beats/min during the same period. All of these changes in hemodynamic parameters induced by coronary ligation and β blockade were statistically significant; however, a given parameter did not vary greatly through the course of the experiments (from heart failure interval #1 to interval #2 to interval #3) (Fig. 1, Table I).

The mean cardiac output during Hemopump support (5.29 ± 0.84 L/min) was significantly greater than that during IABP support (4.27 ± 0.78 L/min). The mean PCWP was significantly less during Hemopump support (10.7 ± 2.5 mmHg) than it was during support with the IABP (15.4 ± 3.4 mmHg). Similarly, a significantly greater mean SvO_2 was seen during Hemopump support (67.3% ± 4.4%) than during IABP support (62.3% ± 4.0%). The periods of Hemopump support and IABP support showed no significant difference in mean CVP (7.3 ± 1.8 mmHg and

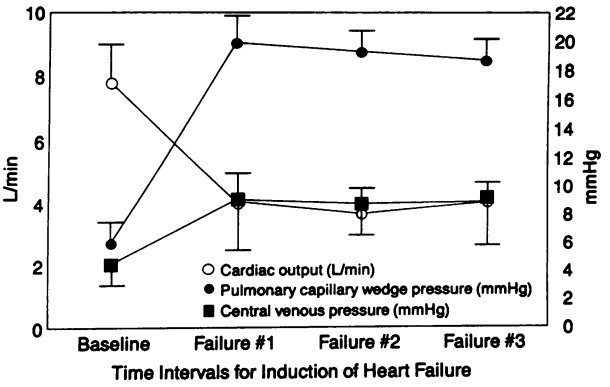

Fig. 1 *The creation of left ventricular failure was accomplished by conservative coronary artery ligation and β-adrenergic-receptor blockade. This resulted in a 40% to 50% reduction in cardiac output, an increase in pulmonary capillary wedge pressure >15 mmHg, and only a minor drift of baseline failure parameters during the course of the experiments. Error bars are depicted as ascending for cardiac output and pulmonary capillary wedge pressure, and descending for central venous pressure; they represent the ± numerical values as presented in Table I.*

Table I. Cardiac Indices

	CO (L/min)	PCWP (mmHg)	SvO_2 (%)	CVP (mmHg)	HR (beats/min)
Baseline	7.82 ± 1.58	6.0 ± 1.51	78.0 ± 4.8	4.5 ± 1.4	100.0 ± 17.4
Failure #1	4.08 ± 0.91	19.9 ± 1.91	58.0 ± 6.0	9.1 ± 3.6	62.4 ± 24.0
Hemopump support	5.29 ± 0.84	10.7 ± 2.54	67.3 ± 4.4	7.3 ± 1.8	64.7 ± 21.6
Failure #2	3.67 ± 0.70	19.3 ± 1.34	59.0 ± 3.9	8.8 ± 2.5	66.2 ± 21.5
IABP support	4.27 ± 0.78	15.4 ± 3.37	62.3 ± 4.0	8.9 ± 2.8	64.8 ± 16.8
Failure #3	4.03 ± 0.64	18.7 ± 1.25	58.2 ± 5.7	8.9 ± 3.1	64.8 ± 16.8
Time average (heart failure)	3.92	19.3	58.4	8.9	64.3

Measurements are displayed as mean ± standard deviation for parameters obtained during the creation of left ventricular failure and during periods of Hemopump intraaortic balloon pump (IABP) support.

Time average (heart failure) is the average of indices for heart failure #1, #2, and #3.

CO = cardiac output; CVP = central venous pressure; HR = heart rate; PCWP = pulmonary capillary wedge pressure; SvO_2 = mixed venous oxygen saturation

8.9 ± 2.8 mmHg, respectively) or mean heart rate (64.7 ± 21.6 beats/min and 64.8 ± 16.8 beats/min, respectively) (Table I).

The mean femoral arterial pressure was greater during Hemopump support (70.0 ± 14.7 mmHg) than during IABP support (55.3 ± 9.2 mmHg), but there was no significant difference in mean carotid arterial pressure between periods of support with the Hemopump (65.9 ± 17.1 mmHg) and periods of support with the IABP (62.7 ± 10.2 mmHg). Pulse amplitude was greater in both the femoral artery and the carotid artery with the IABP (39.0 ± 11.7 mmHg and 52.2 ± 9.9 mmHg, respectively) than with the Hemopump (17.3 ± 5.0 mmHg and 15.1 ± 7.3 mmHg, respectively); these results were consistent with the mechanism of action for each device. During IABP support, the carotid arterial pressure was greater than the femoral arterial pressure. In contrast, the femoral pressure was greater than the carotid pressure during Hemopump support (Table II).

Visceral organ perfusion was significantly better during periods of Hemopump support than it was during periods of IABP support (Fig. 2, Table III). The mean renal arterial flow during Hemopump support was 276 ± 74.2 cc/min compared with 209.6 ± 83.9 cc/min during heart failure with no mechanical support. The mean renal arterial flow, however, was only 164.2 ± 79.6 cc/min during IABP support. The difference between renal artery flow with IABP support and with no support was not statistically significant. The mean hepatic arterial flow was 34.7 ± 25.7 cc/min with the Hemopump, compared with 24.3 ± 18.9 cc/min during IABP support. The mean portal vein flow was 1588 ± 315 cc/min with Hemopump support and 1259 ± 310 cc/min with IABP support. The mean carotid artery flow, however, was greater during IABP support (317 ± 204 cc/min) than during Hemopump support (292 ± 171 cc/min), although this difference did not reach statistical significance. Carotid perfusion with the Hemopump support improved over that during periods with no support, but this difference was not statistically significant.

Table II. Peripheral Arterial Blood Pressure Indices

	Pressure (mmHg)		**Pulse Amplitude** (mmHg)	
	Femoral	**Carotid**	**Femoral**	**Carotid**
Baseline	102.5 ± 21.2	101.5 ± 19.7	29.0 ± 10.2	25.0 ± 8.2
Failure #1	52.5 ± 12.1	53.9 ± 10.8	27.0 ± 11.8	28.2 ± 10.1
Hemopump support	70.0 ± 14.7	65.9 ± 17.1	17.3 ± 5.0	15.1 ± 7.3
Failure #2	54.0 ± 13.3	58.5 ± 13.1	30.0 ± 8.5	27.5 ± 10.1
IABP support	55.3 ± 9.2	62.7 ± 10.2	39.0 ± 11.7	52.2 ± 9.9
Failure #3	56.3 ± 9.0	55.5 ± 7.98	27.5 ± 7.2	27.2 ± 4.2
Time average (heart failure)	54.3	56.0	28.2	27.6

Measurements are displayed as mean ± standard deviation for parameters obtained during the creation of left ventricular failure and during periods of Hemopump and intraaortic balloon pump (IABP) support.

Time average (heart failure) is the average of indices for heart failure #1, #2, and #3.

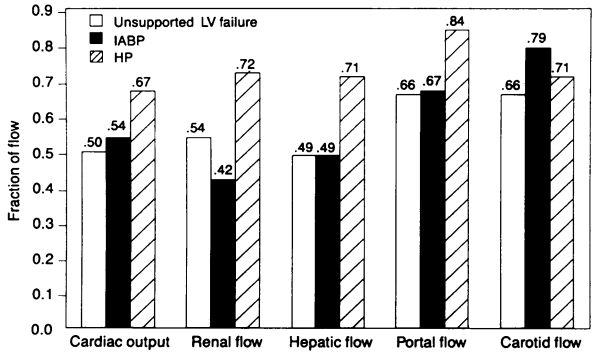

Fig. 2 *Visceral organ perfusion was significantly greater during Hemopump® support than during IABP support. Both the Hemopump and the IABP appeared to augment carotid artery flows compared with those of baseline failure; statistical significance was not attained with either device.*

Discussion

The beneficial effects of the Hemopump on cardiac performance indices in laboratory studies,[4-6] as well as its effects on clinical outcome in small series of patients,[7-11] are now being reported. Since the work

Table III. Peripheral Organ Blood Flow Indices

	Arterial Flow (cc/min)			
	Renal	**Hepatic**	**Portal**	**Carotid**
Baseline	383.9 ± 101	49.1 ± 33.6	1890 ± 668	402.7 ± 169
Failure #1	177.9 ± 63.6	24.4 ± 20.3	1208 ± 266	265.8 ± 139
Hemopump support	276 ± 74.2	34.7 ± 25.7	1588 ± 315	292 ± 171
Failure #2	224.9 ± 90.1	23.0 ± 15.4	1289 ± 362	250.9 ± 62.3
IABP support	164.2 ± 79.6	24.3 ± 18.9	1259 ± 310	317 ± 204
Failure #3	224.7 ± 94.2	26.2 ± 16.9	1263 ± 432	279.1 ± 172
Time average (heart failure)	209.6	24.5	1253	265.2

Measurements are displayed as mean ± standard deviation for parameters obtained during the creation of left ventricular failure and during periods of Hemopump and intraaortic balloon pump (IABP) support.

Time average (heart failure) is the average of indices for heart failure #1, #2, and #3.

of Clauss in 1961[12] and Moulopoulos in 1962,[13] the beneficial effects of the IABP have also been established. It is apparent, however, that 30% to 50% of patients are unable to survive with IABP support alone, and many of these patients ultimately die of multiorgan failure.[1] Many investigators have postulated a relationship between the prolonged low flow states following cardiothoracic surgery and the gastrointestinal translocation of bacteria, in the development of multiorgan failure in these patients.[14-16]

It is interesting to note, therefore, that both portal vein flow and hepatic arterial flow appear to be augmented to a greater extent during Hemopump support than during IABP support. Other investigators have reported similar favorable responses in splanchnic flow with the IABP[17,18] and with the nonpulsatile Biomedicus left ventricular assist device[19] when compared with no support during heart failure.

The observation that renal artery perfusion was augmented during Hemopump support but decreased during IABP support (in comparison with no support) correlates with a recent investigation[20] that used a canine model. In that study, blood flow was redistributed above the IABP, with a resultant compromise of blood flow below the diaphragm. Another report[2] emphasized the importance of the volume of the balloon, the percentage of aortic luminal compromise during balloon expansion, and the length (and therefore proximity to the renal artery orifices) of the IABP relative to the aorta of the experimental animal in developing a model that can be adapted for use in humans. These studies indicated that efforts to increase the hemodynamic support that a conventionally positioned IABP may offer, by increasing the balloon's volume from the standard 40 cc to a level closer to a typical cardiac stroke volume, may result in impedance of aortic blood flow to the infradiaphragmatic organ.[21]

Carotid artery flow was enhanced by both the Hemopump and the IABP in this study. Concerns about the location of blood egress being distal to the arch vessels from the femorally introduced Hemopump appear to be unwarranted, because carotid perfusion was enhanced in all animals. The mean carotid arterial pressure was slightly less than the mean femoral arterial pressure during Hemopump support; these results indicate that the percentage of aortic lumen occupied by the impeller and the distance of the exit port from the arch vessels may be important variables. We believe the calf may be a better model than the dog for this type of study, because the aortas of calves are closer in size to the aortas of humans.

This study suggests that renal, hepatic, and portal perfusion during states of cardiogenic shock may be augmented to a greater extent by use of the Hemopump than by use of the more widely accepted intraaortic balloon pump. Such advantages in visceral perfusion might decrease the incidence of multiorgan failure in patients with low-cardiac-output syndrome if cardiac function were regained.

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