
Evaluation of the Bio Pump for Long-Term Cardiac Support Without Heparinization

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Abstract

A three-part study was designed to evaluate whether the Bio Pump^a and a heparinless regimen could prevent the complications of hemorrhage and inflow destruction in patients needing long-term cardiac support following cardiopulmonary bypass surgery. Five dogs underwent venoarterial membrane support for 24 hours using the Bio Pump with heparinization to maintain ACT's in the range of 150–175 sec. All dogs survived with no sequelae. Five dogs received left ventricular support without oxygenation using the Bio Pump and no heparinization. These also survived 24 hours of support with no sequelae. Minimal bleeding, no inflow obstruction, slight increases in serum hemoglobin were common in both groups. Group 2 suffered less platelet depletion and aberration of clotting parameters than did Group 1. A sheep undergoing left ventricular support for 14 days showed few effects until a thrombus, apparently thrown from the bearing housing of the Bio Pump, lodged in the right kidney causing a large infarct. Left ventricular assist using the Bio Pump and no anticoagulation has been used on six patients with survival in 50% of the cases.

Introduction

Since 1976 we have had occasion to use long-term

extracorporeal circulatory assist on 25 patients. These cases included veno-arterial membrane oxygenation, left ventricular bypass, right ventricular bypass, and combined right and left ventricular bypass.

Support was required in every case but one because of profound ventricular failure after cardiac surgery. There have been two recurrent major complications: 1) obstruction of inflow cannula (that is, venous return to pump), and 2) hemorrhage. Both of these problems have been present intermittently since our initial attempts at long-term support. The inflow cannula obstruction was felt to be caused, in part, by the negative pressure created at the orifice of the inflow cannula due to the occlusive, or nearly occlusive, nature inherent in roller pump design. Hemorrhage became a problem in patients who required support for more than 24–36 hours, despite titration of heparin dose to activated clotting time (ACT). During this frustrating period it came to our attention that the Bio Pump^a, because of its centrifugal pumping action, is non-occlusive and flow responsive. These characteristics seemed to make the Bio Pump ideal for long-term support. The purpose of this study was to evaluate the Bio Pump for use as a long-term assist pump, and to re-evaluate our heparinization routine.

Materials and Methods

Ten conditioned, male, mongrel dogs weighing 28–33 kg. were used in this study. Each animal was anesthetized with IV Pentothal, 20 mg/kg, intubated, and endotracheal anesthesia maintained with halothane, N₂O, and oxygen except during membrane ox-

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Presented at AmSECT's 19th International Conference in San Francisco, CA, March 1981.

^a Bio Medicus, Inc., Minneapolis, MN

xygenation when morphine and curare were used. The femoral artery and vein were cannulated for arterial pressure (AP) and central venous pressure (CVP) respectively. All of the tubing used for the extracorporeal system in this study was made of polyvinyl chloride (Tygon^b) and the connectors were polycarbonate (Cobe^c). The prime was Plasmalyte^d with a pH of 7.4. The animals' arterial blood gases were measured and maintained at normal levels by either manipulation of oxygenator gas flows or ventilator adjustments. Volume and hematocrit were maintained by the infusion of cross-matched whole blood drawn in CPD solution. Data obtained included hemoglobin, hematocrit, platelets, serum hemoglobin, and electrolytes. Sampling times were: baseline (T = 0), 2, 4, 8, 12, 16, 20, and 24 hours. After the initial surgery all the wounds were closed and the animal sedated for the duration of the experiment. When the experimental period was over, the animals were reopened and, under sterile conditions, the cannulae removed. The animals were closed, allowed to recover from anesthesia, and then transferred to their cages.

Method #1: Veno-arterial Membrane Assist with Heparin

Under sterile conditions the left femoral artery and vein were isolated for the perfusion cannula. The Kolobow^e membrane was used for oxygenation and the Bio Pump was used to pump blood. The system consisted of a 28 Fr. cannula inserted into the femoral vein for venous return which drained blood directly into the Bio Pump. The blood was then directed through a flow probe into the Kolobow and returned to the dog via an 18 Fr. femoral artery cannula. The blood inlet and outlet pressures of the membrane were monitored. Anticoagulation was maintained with a continuous heparin infusion adjusted to maintain the ACT (via the Hemochron)^f at 150-175 seconds.

Results of Group I

All five animals survived the 24-hour procedure and recovered with no sequelae. There were minimal

^b Norton Co., Akron OH 44309

^c Cobe Laboratories, Inc., Lakewood, CO 80215

^d Travenol Laboratories, Inc., Deerfield, IL 60015

^e Sci-Med Life Systems, Inc., Minneapolis, MN 55441

^f International Technidyne Corp., Edison, NJ 08820

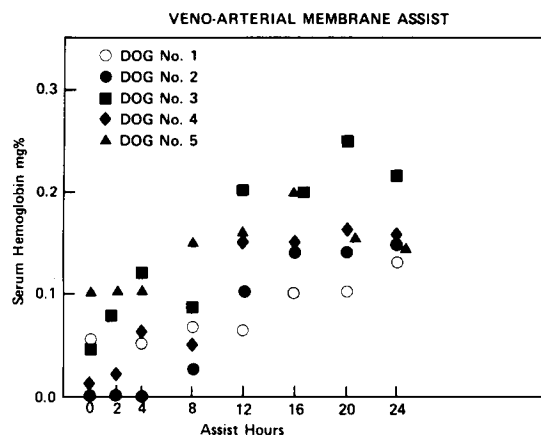


FIGURE 1. Serum hemoglobin levels during veno-arterial membrane assist.

problems with bleeding. The Bio Pump functioned well. There were no instances of inflow obstruction or cavitation during any of the perfusion runs. The flow rates ranged from 1-2.5 liters/min. and were related to the size of the dog and the CVP. The fibrin split products (FSP) were negative at all times. Serum hemoglobin levels rose gradually during the experiment (Figure 1). The platelet counts (Figure 2) were extremely variable with most animals showing thrombocytopenia after 24 hours. The fibrinogen levels (Figure 3) dropped slightly. Prothrombin time (PT) (Figure 4) and partial thromboplastin time (PTT) (Figure 5) were elevated, reflecting the heparin therapy.

Method #2: Left Ventricular Bypass without Heparinization

Under sterile conditions the left femoral artery was

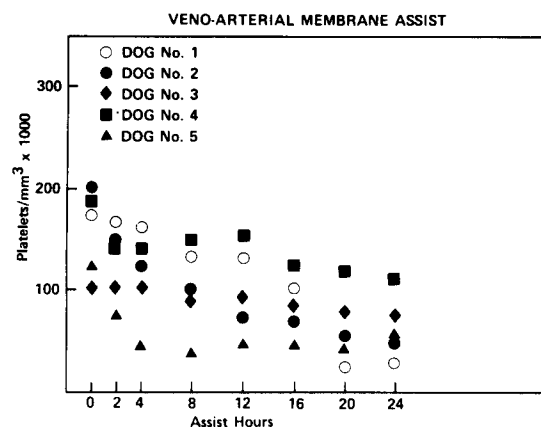


FIGURE 2. Platelet counts (phase microscopy) during veno-arterial membrane assist.

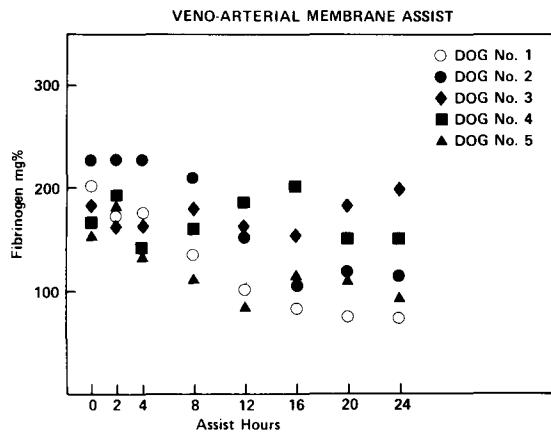


FIGURE 3. Fibrinogen levels decreased slightly during veno-arterial membrane assist.

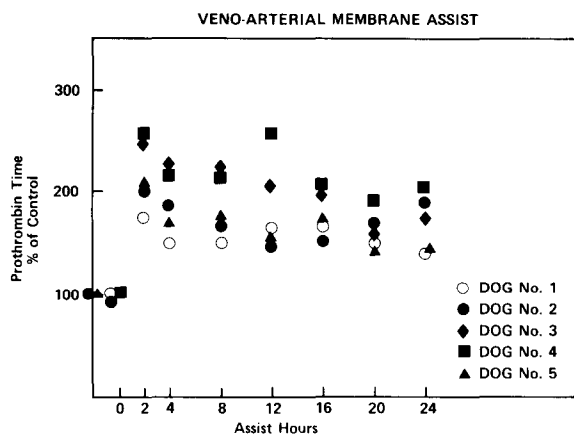


FIGURE 4. The prothrombin time is elevated during veno-arterial membrane assist reflecting the anticoagulation therapy.

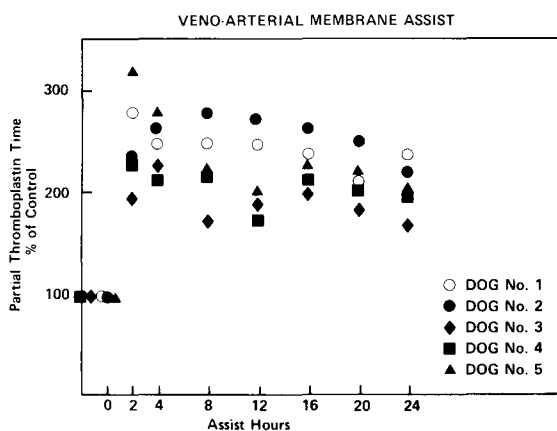


FIGURE 5. The partial thromboplastin time is elevated during the assist period.

exposed for arterial perfusion, and a left thoracotomy performed in the fourth intercostal space. The pericardium was opened parallel to the phrenic nerve over the left atrial appendage. A 28 Fr. Bahnsen caval cannula was inserted through a 2-O silk purse string suture in the left atrial appendage and advanced through the mitral valve into the left ventricle. Blood was drained directly from the left ventricle into the Bio Pump, then through the flow probe and returned to the dog via the left femoral artery. No venous reservoir was used. No anticoagulation was used, i.e. no heparin for cannulation, no antithrombogenic coatings on the cannula, tubing, or Bio Pump, and no platelet anti-clumping agents were used.

Results of Group 2

All five of the animals survived the 24-hour procedure and recovered with no sequelae. There was no bleeding from any wound site. Chest drainage was minimal. The Bio Pump functioned well. There were no instances of inflow obstruction or cavitation during any of the perfusion runs. The flow rates ranged from 1.8–3.2 liters/min. The FSP were negative at all times. The ACT's were normal at all times.

The serum hemoglobin (Figure 6) levels rose slightly during the course of the run. However, contrary to expectations, the platelet count (Figure 7) did not drop, and in some animals even rose, during the perfusion run. Fibrinogen levels (Figure 8) remained constant through the entire experiment as did the PT (Figure 9) and PTT (Figure 10).

Encouraged by these results, but aware that the dog's

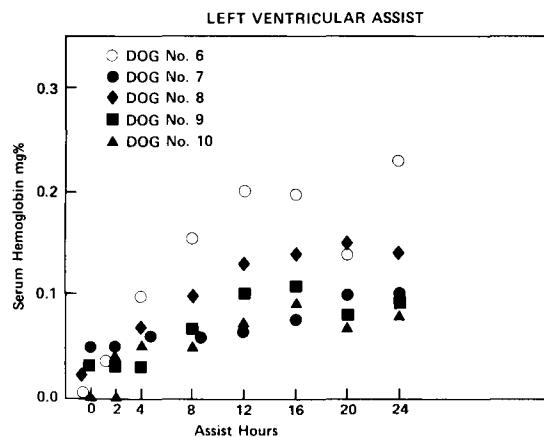


FIGURE 6. The serum hemoglobin levels on left ventricular assist increased during the assist period and were essentially the same as the veno-arterial membrane assist animals (Fig. 1).

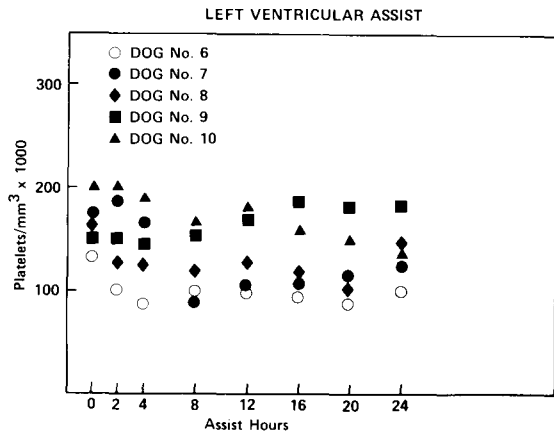


FIGURE 7. Contrary to expectations the platelet count did not fall during the left ventricular assist period despite lack of anti-coagulation.

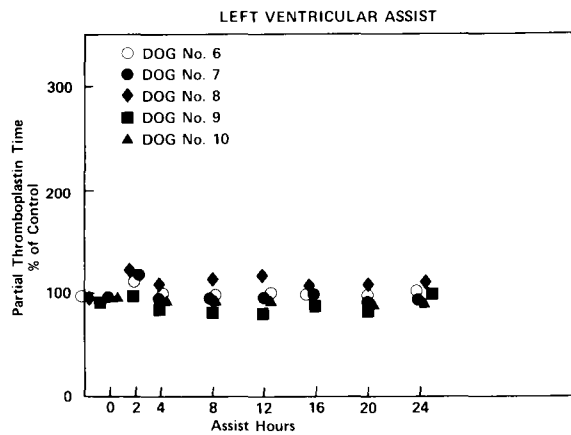


FIGURE 10. Partial thromboplastin time did not fluctuate during the run.

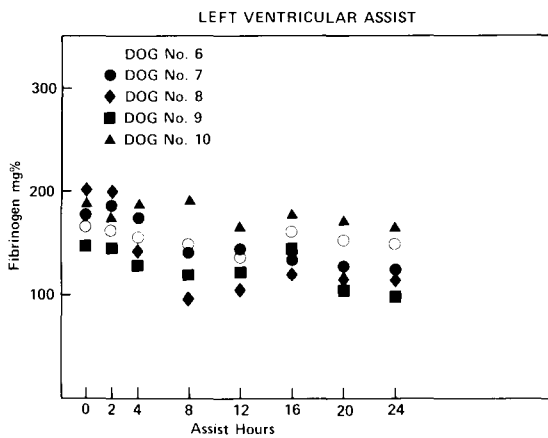


FIGURE 8. Fibrinogen levels remained constant during the assist.

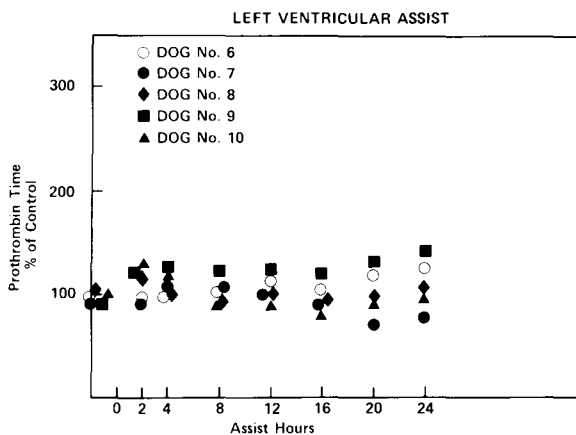


FIGURE 9. The prothrombin time did not deviate from control levels at any time during the 24 hours of assist.

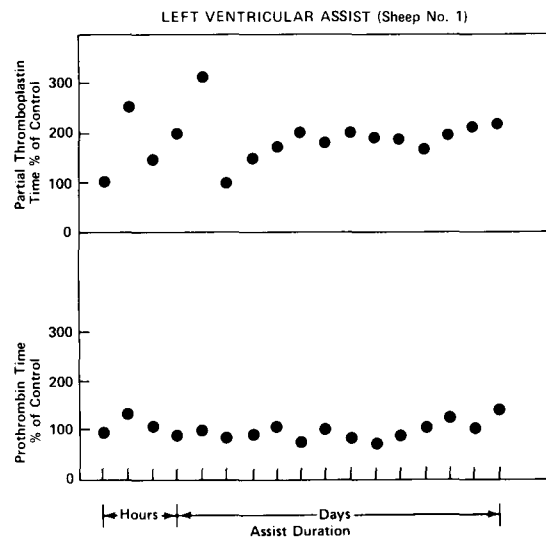


FIGURE 11. The partial thromboplastin time of the sheep fluctuated widely for the first 3 days then stabilized at 2X control level, while the prothrombin time remained at control levels for the entire assist period.

coagulation system may not be the best model for evaluation, we placed a 65 kg male sheep on long-term ventricular assist without anticoagulation as described above, except that arterial return was accomplished through a graft sutured to the descending thoracic aorta. The animal was assisted for 14 days and then sacrificed. At no time did the inflow cannula show obstruction or cavitation even though the animal was very active within the limits of its stall. The FSP never were positive. The Bio Pump flow rate was 4.0–4.4 liters/minute. The sheep's cardiac output (thermodilution) was 5.3–5.8 liters/minute. The PT (Figure 11)

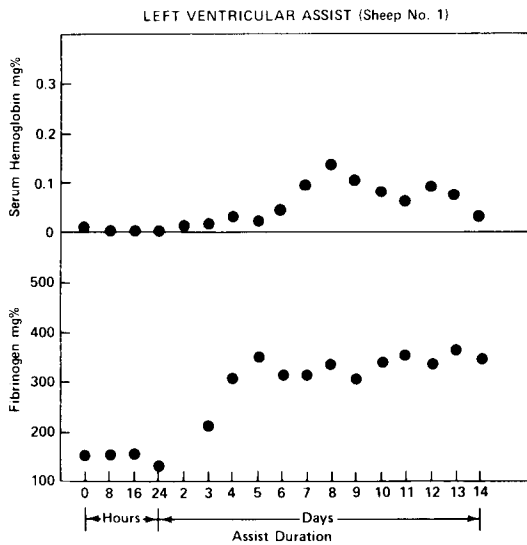


FIGURE 12. The serum hemoglobin of the sheep rose for about the first week, then decreased, while the fibrinogen level rose quickly and then leveled off at day 3.

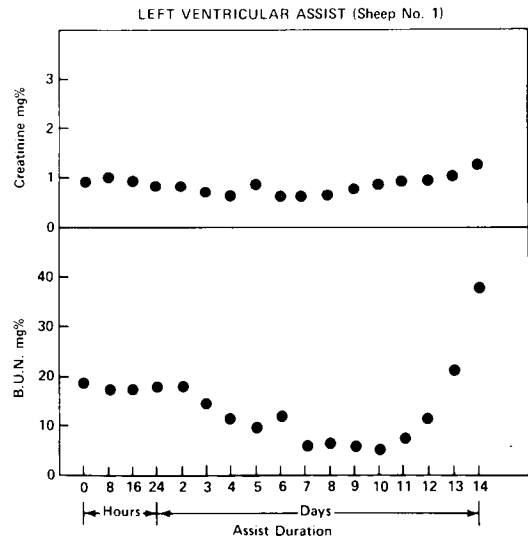


FIGURE 14. The creatinine remained normal throughout the entire run. However, the B.U.N. rose dramatically on day 12 due to an infarction of the right kidney.

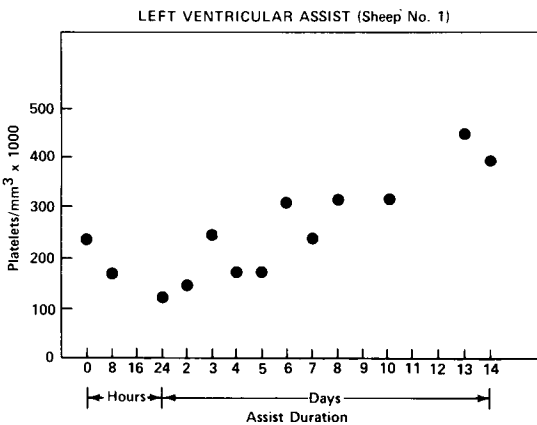


FIGURE 13. The platelet count dropped on the first days then began to rise steadily over the remainder of the experimental period.

was normal during the entire perfusion period, and although the PTT (Figure 11) fluctuated early in the experiment, it stabilized within normal limits after five days. The serum hemoglobin levels (Figure 12) rose gradually after the first day until day 7 when it began to decrease while the fibrinogen level (Figure 12) rose quickly and then leveled off at day 3.

The platelet count (Figure 13) dropped during the first two days, but then continued to rise over the remainder of the experimental period. Although the creatinine (Figure 14) remained normal, the BUN

(Figure 14) rose dramatically at the twelfth day. The reason for this became obvious after the animal was sacrificed.

At autopsy all organs except the right kidney were normal. The right kidney showed evidence of a large infarct due to a thromboembolic event. There were no other clots found.

The perfusion circuit was carefully and gently rinsed with normal saline. Examination revealed that a large thrombus formation had built up around the bearing housing of the Bio Pump. This is an area of low flow and low shear rates, and was probably the source of the thromboembolism that caused the infarction of the right kidney.

Discussion

There are several interesting findings in this study. First, the fact that there were no instances of inflow cannula obstruction in any experiment is significant. Previous long-term assist in our institution, both in the clinic and in the lab, with the standard roller pump almost invariably led to inflow cannula obstruction and cavitation with the resultant air emboli. The fact that this did not occur with the Bio Pump is a result of the nonocclusive nature of the centrifugal pump. Second, the low serum hemoglobin levels in the dogs supported on left ventricular assist for 24 hours and the sheep supported for 14 days reinforces previous data^{1,2} that

TABLE 1
Long Term Support With Left Ventricular Bypass

Patient	Age/Sex	Procedure	Duration	Results	Comments
A.R.	59/M	SVG, AVR	44 hrs.	CTB***	Heparin/Hemorrhage
B.W.	52/F	DSVG*	48 hrs.	Survival	No Heparin
R.W.	56/M	DSVG	44 hrs.	Survival	No Heparin
A.K.	61/M	TSVG**	21 hrs.	Survival	No Heparin
E.H.	56/M	DSVG	24 hrs.	CTB	No Heparin
H.P.	64/F	DSVG	36 hrs.	CTB	No Heparin
M.D.	53/F	DSVG	39 hrs.	CTB	No Heparin

* DSVG—double saphenous vein graft

** TSVG—triple saphenous vein graft

*** cease to breathe

the Bio Pump handles the blood in an atraumatic manner. Third, anticoagulation may not be necessary in instances of left heart assist using the Bio Pump. The second group of dogs and the sheep were supported without any form of anticoagulation. Several factors may be at work here. These animals may have been in a state of “controlled” fibrinolysis. That is, the activation stimulus to the clotting system was small enough that it could be effectively counter-balanced by the animal’s own fibrinolytic system. The magnitude of this “controlled” fibrinolysis had to be very small because the FSP by latex screen were negative at all times. Also, the controlled fibrinolysis theory could explain the fact that there were no thrombi in any part of the perfusion system, with the exception of the Bio Pump used to assist the sheep. Also at work could be the effects of shear forces in the Bio Pump. Schultz, et al³ have shown, in vitro, that shear alone is a very important factor in thrombus formation. They were able to show reduction in thrombus formation in their chamber at 800 rpm. The Bio Pump in our experiment was run at 2000–3000 rpm. It is likely that platelet stimulation and other coagulation factors are activated in passing through the Bio Pump³, but that as a result of fibri-

nolysis and the effects of shear, accumulation of coagulation particles does not occur.

As a result of this study, and considering the obvious alternative when a patient cannot be weaned from cardiopulmonary bypass after cardiac surgery, we have used the Bio Pump without anticoagulation for left ventricular assist on six patients (Table 1). Three patients have been successfully weaned from assist after 40, 44, and 21 hours of support. One died five months after being discharged from sudden cardiac arrest; one died three days after being weaned from the assist from sudden cardiac arrest; and one is still surviving at four months after being weaned from the assist.

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