EXPERIMENTAL APPROACHES

Comparison of Nonpulsatile and Pulsatile Extracorporeal Circulation on Renal Tissue Perfusion*

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This study was designed to compare the physiologic effects of nonpulsatile (NP) and pulsatile (P) perfusion on the kidney. Serial specimens for blood gases and serum lactic acid (L) were taken from the renal artery and vein in three groups of dogs; one group served as control. The aortic arch was crossclamped and NP and P left atrial to left subclavian artery bypass was performed for two hours on two groups of dogs. Renal blood flow (RBF) and arterial (AP) and the venous pressures (VP) were continuously monitored. Vascular resistance (VR) was calculated by the formula $VR = (AP-VP)/RBF$. In order to maintain nearly equal arterial pressures above and below the crossclamped aorta, a higher flow rate was required with NP (80 ml/kg/min) than with P (60 ml/kg/min). Marked reduction in pH (7.255) along with elevated L (50 mg/100 ml) were consistent with NP. There was less reduction in pH (7.37) and less elevation of L (35 mg/100 ml) with P, whereas control pH was 7.37 and L was 17 mg/ml.

Pulsatile pumping provides better tissue perfusion during extracorporeal bypass.

Total body extracorporeal circulation employing nonpulsatile pumping has become a routine procedure for open heart surgery during the last decade. However, it has been noted that if perfusions are prolonged beyond five hours, the mortality rate is greatly increased. This rise in mortality may be due to the inability to correct the underlying lesion, problems with prolonged oxygenation, effects of nonpulsatile pumping, or a combination of these three. There is increasing evidence, however, that prolonged nonpulsatile pumping itself leads to deleterious physiologic alterations.

In our attempts to develop mechanical methods to support the failing circulation, we have found that periods of many hours or even days of pump support may be necessary. We have found that few dogs survive more than 12 hours of nonpulsatile bypass, whereas we have consistently had survivors at 30 hours of bypass when we employed pulsatile pumping. Paquet, Trinkle and associates, and Jacobs and co-workers have recently shown that pulsatile extracorporeal circulation results in a more normal vascular resistance and venous return than does nonpulsatile pumping. They have also demonstrated that pulsatile pumping maintains more normal tissue perfusion as evidenced by lower serum lactates, a higher systemic pH, and a higher venous oxygen saturation. Shepard and Kirklin have reported less obvious differences between pulsatile and nonpulsatile flow. However, there is a question as to whether the pulsatile pump they used produced the high amplitude pulsation which we feel is a prerequisite of a true pulsatile pump. We selected the kidney for comparison of tissue perfusion as it seemed important to assess the effects of two types of pumping on a specific organ system.
Central venous pressure catheter
Proximal aorta pressure catheter
Clamp
Arterial return line
Aorta
Pump
S.V.C.
Venous line
L.A.
R.A.

**LEFT HEART BYPASS SCHEME**

Figure 1. Left atrial to left subclavian artery extracorporeal circuit and systemic pressure monitoring catheters in place. The aortic arch is crossclamped proximal to the left subclavian artery.

**METHODS**

Eighteen experiments were done on three groups of mongrel dogs, each dog weighing between 14.5 and 35 Kg. Group 1 (seven dogs) underwent two hours of nonpulsatile left heart bypass with a DeBakey roller pump. Group 2 (six dogs) underwent two hours of left heart bypass with a Wakayayashi-Connolly pressure-activated pulsatile pump. Group 3 (five dogs) served as a control and underwent the same surgical procedure including left atrial and left subclavian artery cannulation but without crossclamping of the aorta or bypass. This control group was fully monitored for two hours.

In groups 1 and 2 (Fig 1) the aortic arch was crossclamped proximal to the subclavian artery at the start of bypass. The bypass system diverted blood from the left atrium to the pump and from the pump to the left subclavian artery via a large cannula. Because of its larger diameter the subclavian artery was used in place of the femoral artery to return blood from the pump. Flow rates were regulated so that the mean pressure gradient between the proximal and distal aorta was maintained under 40 mm Hg during bypass. Proximal and distal aortic pressures, central venous pressure, electrocardiogram, and renal blood flow (electromagnetic flow probes) were recorded on a Beckman Dynograph R* (Fig 1 and 2). Serial arterial and renal vein specimens were collected for blood gases and serum lactate levels before bypass and every 30 minutes during the bypass period. Blood gases were determined with a Radiometer Astrup machine.† Serum lactic acid levels were determined spectrophotometrically using a Sigma kit.‡

Esophageal temperature, urine output, and nonblood pump priming values were constant for each group. A heparin dose

*Beckman Instruments, Fullerton, California.
†Radiometer, Copenhagen, Denmark.
‡Sigma Chemical Company, St. Louis.

**DIAGRAM of the RENAL VASCULAR SHUNT SYSTEM**

Figure 2. Renal blood flow probe and systemic pressure monitoring catheters in place. The plastic tubular shunt totally diverted the left renal vein blood to the right femoral vein. The rubber diaphragm covered side arm allowed withdrawal of serial blood specimens.

**NON PULSATILE TRACING - 21.5 kg DOG**

| MEAN DISTAL AORTIC PRESSURE - 100 mm Hg |
| PROXIMAL AORTIC PRESSURE - 175/125 mm Hg |
| MEAN - 140 mm Hg |

**RENAI BLOOD FLOW - \( \text{about} 170 \text{cc/min} \)**

*Figures 3 and 4 show the low amplitude flow pattern in the distal aorta and a flat renal blood flow of 8 ml/Kg/min.*
of 3 mg/Kg was administered to all animals prior to renal vein cannulation.

Statistical significance was calculated by means of a Student's T test with a confidence level of 5 percent or P = 0.05.

**RESULTS**

Representative tracings in Figures 3, 4, and 5 demonstrate the different pulse patterns, renal blood flow pattern, and renal blood flow rate for each experimental group.

Average values for group 1 showed that nonpulsatile flow rates of 80 ml/Kg/min were required to equilibrate distal and proximal aortic pressures.

Group 2 pulsatile flow rates, in contrast, averaged only 60 ml/Kg/min and allowed easy equilibration of distal and proximal pressures. Renal blood flow rates varied with pump flow rates and distal aortic pressures and averaged 8 ml/Kg/min during nonpulsatile and 4 ml/Kg/min during pulsatile bypass. Control values for renal blood flow averaged 6 ml/Kg/min (Fig 6).

Vascular resistance was derived from the formula VR = (mean AP—VP) / RBF (VR = vascular resistance).
Renal vein lactic acid values remained stable at 35.00 ± 1.51 (mg/100 ml) during the two hours of pulsatile bypass. They rose rapidly and remained high at 50.85 ± 4.04 (mg/100 ml) during nonpulsatile extracorporeal bypass. Control lactic acid values remained low and stable at 17.00 ± 2.19 (mg/100 ml) (Fig 9).

**DISCUSSION**

We believe that a high amplitude pulsatile form of pumping is required to truly assess the physiologic effects of pulsatile versus nonpulsatile pumping. The high amplitude pulse pattern produced by the Wakabayashi-Connolly pump employed in our experiments closely resembles the normal pulsatile pattern (Fig 4).

Some investigators have related specific organ responses to pump flow rates, venous return, and changes in peripheral resistance to the type of pumping employed for bypass. Most authors have observed that systemic peripheral resistance increases during total body bypass and that the increase is more pronounced with nonpulsatile flow than with high amplitude pulsatile flow. Nonoyama showed that in both types of bypass, systemic peripheral resistance rose to above normal immediately after the onset of extracorporeal perfusion but then began to progressively decrease 15 minutes after the start of nonpulsatile pumping and subsequently fell to below normal levels. Peripheral resistance returned to a relatively normal value after 15 minutes and remained normal for the remaining 45 minutes of pulsatile bypass.

In our studies renal vascular resistance appeared to increase with nonpulsatile flow above control values, but the change was not striking. More investigation is necessary to clarify changes in specific organ vascular resistance during extracorporeal circulation.

Nonpulsatile bypass required higher pump flow rates to equilibrate arterial pressures above and below the crossclamped aorta than did pulsatile pumping. This higher flow rate produced an appreciably higher renal blood flow than did pulsatile pumping. The higher nonpulsatile renal blood flow rate of 8 ml/Kg/min was not as effective in the maintenance of renal tissue perfusion as the lower pulsatile renal blood flow rate of 4 ml/Kg/min (Fig 6). This was documented by changes in the biochemical values of pH and lactic acid which we used to reflect the status of tissue perfusion. Arteriovenous PO2 differences observed by us during both forms of bypass did not differ significantly from the control group values (Fig 7). These data are compatible with the observations of Shepard and

**FIGURE 8.** Changes in pH during two types of bypass. Note that pH fell steadily with nonpulsatile flow. Pulsatile and control pH values paralleled each other.

**FIGURE 9.** Lactic acid production during two types of pumping. Note that lactic acid quickly increased and remained high during bypass with nonpulsatile flow. Baseline and zero values appear to vary widely but did not differ significantly while average experimental values changed significantly with respect to each other a few minutes after the start of bypass.
Kirklin that oxygen extraction may not accurately reflect the status of tissue perfusion as well as pH and serum lactate levels.

Paquet recently compared prolonged nonpulsatile and pulsatile flow in isolated pig kidney perfusion experiments. He demonstrated that nonpulsatile pumping results in less oxygen consumption with progressive acidosis. Our data indicate that the metabolic acidosis of prolonged nonpulsatile bypass may be due to increased lactic acid values, suggesting poor tissue perfusion.

Pulsatile pumping appears to maintain a more normal vascular resistance, higher venous return, and sustained function of the microcirculation than does nonpulsatile pumping. Ogata and colleagues in their classic experiments on the microcirculation, found that after 20 minutes of nonpulsatile bypass blood flow in the omental capillary bed first slowed and then ceased. A high velocity flow rate was noted in dilated arterioles which they called preferential channels or precapillary arteriovenous shunts. In their experiments pulsatile pumping was observed to adequately distribute red blood cells between arteriolar and capillary systems, demonstrating a more normal flow. Precapillary shunting was suggested by Ogata as a possible mechanism for the microcirculation stagnation and resultant tissue hypoxia seen with nonpulsatile pumping.

Our studies appear to support the observations of others that renal tissue hypoxia and metabolic acidosis proceed more rapidly during nonpulsatile extracorporeal bypass despite adequate pump flow rates, adequate renal blood flow rates, and adequate oxygen tissue extraction.

We have demonstrated that more normal physiologic maintenance of the biochemical values of pH and lactic acid occurred during pulsatile pumping than with nonpulsatile pumping, indicating that tissue perfusion is well maintained during pulsatile pumping.

The specific organ (kidney) response to extracorporeal circulation that we found in our experiments corresponds with the systemic effects of bypass reported by others, indicating that pulsatile flow is more effective than nonpulsatile flow in maintaining tissue perfusion. We concluded that arterial pressures, flow rates, and vascular resistance are not as important as direct biochemical determinations of pH and lactic acid in evaluating the effects of extracorporeal circulation on tissue perfusion. Our experiments indicate that pulsatile pumping, because it produces better tissue perfusion, is superior to nonpulsatile pumping.

References

Ingenious Pharmacologic Nomenclature

Opium is one of the oldest drugs used by man. The Papyrus Ebers mentions the power of opium to obtund pain. Galen employed opium to relieve pain and in his writings magnified its virtues. Paracelsus carried a piece of opium in the pomell of his sword. He named the extractive preparation, tincture of opium, laudanum from the Latin laudō, I praise. Friedrich W A Sertürner, an apothecary of Einbeck in Hanover, isolated morphine from opium in 1807. It was the first of all vegetable alkaloids to be isolated. It was shown that most of the narcotic activity of opium was dependent upon the crystalline base morphine which Sertürner had separated from crude opium. The alkaloid was fittingly named "morphine" from the Greek god "Morpheus", the god of dreams.

Krantz, J C Jr, Carr, C J, La Du, B N, Jr: The Pharmacologic Principles of Medical Practice, Baltimore, Williams & Wilkins, 1969