Original Article

Clinical Comparison of Pulsatile and Nonpulsatile Perfusion During Cardiopulmonary Bypass

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ABSTRACT

Controversy exists concerning the utilization of pulsatile flow during cardiopulmonary bypass (CPB) with regard to improved patient outcomes. The purpose of the present study was to evaluate pulsatile perfusion in patients undergoing CPB in a clinical setting. Seventy patients undergoing open heart surgery for repair of valvular or congenital heart disease were prospectively entered into the study and were randomly assigned to either pulsatile perfusion (PP, n=35) or nonpulsatile perfusion (NP, n=35) groups. All patients received identical surgical, perfusion, and postoperative care. Study parameters included: rate of spontaneous cardiac conversion, inotropic drug use, urine output, skin temperature, platelet count, fibrinogen concentration, and plasma free hemoglobin level.

There were no statistically significant differences seen in either preoperative or operative parameters between groups. The PP group had a significantly higher rate of spontaneous cardiac conversion, less inotropic drug use, earlier recovery of skin temperature, and higher urine output during CPB (908.8 ± 87.2 ml/hr vs. 606.1 ± 57.5 ml/hr, $p < .01$). There were no significant differences in either platelet count or fibrinogen concentration between groups. There was a steady increase in plasma free hemoglobin during PP, which was not seen in the NP group ($p < .01$).

We conclude that the use of pulsatile flow resulted in improved patient outcomes in maintaining better renal function and preserving cardiac function in the early post-bypass period.

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INTRODUCTION

Pulsatile perfusion was used to support isolated organs early in the 20th century (1). Despite the use of pulsatile flow in the early development stages of cardiopulmonary bypass (CPB), nonpulsatile perfusion was accepted as an alternate flow technique. Nevertheless, from about the mid 1950s, it was widely believed that pulsatile flow was better than nonpulsatile perfusion during open heart surgery (2). Interest in pulsatile flow application continued as a result of feelings shared by many investigators that beneficial effects should accrue. In 1978, Taylor and colleagues described the benefits of a pulsatile pump during open heart surgery (3). In 1986, Taylor discovered a significant reduction in the number of operative and low-output-related deaths within the first 24 hours, when pulsatile flow was used (4). However, controversy continues concerning the utilization of pulsatile flow during CPB in regards to improving patient outcomes.

Several authors have shown that pulsatile flow during CPB can reduce sympathetic nerve activity and peripheral vascular resistance and thus may improve both microcirculation and organ function (5-7). Pulsatile flow has been shown to attenuate the catecholamine stress response to CPB, reduce fluid overloading of patients, and improve the postoperative recovery period as evaluated by tracheal intubation time (8). In pediatric patients, pulsatile perfusion has been shown to reduce tissue edema and preserve renal function (9). Pulsatile perfusion has shown benefits in cerebral blood flow even during profound hypothermia and is theorized to protect the brain from ischemic and hypoxic damage induced by hypothermia and total circulatory arrest (10).

All experimental and clinical investigation should begin with the definition of new terms and the development of a suitable theoretic framework (2). Further elaboration of the framework of pulsatile perfusion is required. Given the weight of evidence available, it appears that pulsatile flow during CPB provides a more physiologic milieu and probably better tissue perfusion, presumably leading to better organ function, or at least, less dysfunction (11). The intent of this study was to compare pulsatile perfusion with nonpulsatile perfusion during CPB with specific emphasis on hematology, renal function and cardiac mechanical activity.

Table 1: Patient demographic data

Items	Pulsatile	Nonpulsatile	P-value
Number of patients (n)	35	35	
Age (years)	32.6 ± 16.1	30.1 ± 15.9	NS
Gender (male/female)	14/21	16/19	NS
Weight (kg)	53.8 ± 21.7	57.9 ± 24.1	NS
Cardiac disease status:			
MVR	12	13	NS
AVR + MVR	5	6	NS
TOF	5	4	NS
ASD	5	6	NS
VSD	6	4	NS
DORV	2	2	NS
CPB time (min)	117.3 ± 40.2	112.9 ± 36.0	NS
Cross clamp time (min)	81.6 ± 31.2	78.1 ± 26.6	NS

Data are mean ± SD. CPB = cardiopulmonary bypass. MVR = mitral valve replacement. AVR = aortic valve replacement. TOF = Tetralogy of Fallot. ASD = atrial septal defect. VSD = ventricular septal defect. DORV = double outlet of right ventricle. NS = not significant.

MATERIALS AND METHODS

Seventy patients undergoing open heart surgery for repair of valvular or congenital heart diseases were prospectively entered into the study at Shandong Qianfoshan Hospital. Patients were randomly assigned to either a pulsatile perfusion (PP, n=35) or nonpulsatile perfusion (NP, n=35) group (Table 1).

Anesthesia: Anesthesia management was standard for all patients. For premedication, 10 mg of diazepam was given orally the night prior to operation. One hour prior to surgery 10 mg of diazepam and 0.2 mg/kg of morphine were administered intramuscularly. Induction of anesthesia was accomplished with 0.1 mg/kg of pancuronium bromide, 10μg/kg of fentanyl, and 0.3 mg/kg of etomidate. Anesthesia was maintained by fentanyl infusion and halothane inhalation.

Cardiopulmonary bypass: A standard technique of CPB was used for all patients. The extracorporeal circuit was primed with Ringer's lactate solution, 20% mannitol 150-250 ml, 10% KCl 10-40 ml, 5% $NaHCO_3$ 100-250 ml, Dex 5-10 mg, 25% $MgSO_4$ 5-10 ml. Heparin was administered at an initial concentration of 3 mg/kg into the right atrial appendage and 10-25 mg in the prime. Activated clotting time was maintained at greater than 450 seconds throughout CPB. Oxygenation was achieved with a bubble oxygenator[a]. The arterial return blood was passed through a 40 μ screen filter[a], and was returned to the ascending aorta through a 6 to 8 mm aortic arch cannula[b].

A Sarns 7400[b] pump was used in the PP group to produce pulsatile blood flow from placement of the aortic cross clamp until commencement of ventricular ejection after rewarming. The internal rate was set at 70/min (adults) or 80/min (pediatric). The pulsatile perfusion was 65% of the total cardiac cycle, with a target pulse pressure of 35 mmHg set as the goal. The pulse amplitude generation was measured from the arterial pressure line placed in the arterial filter purge port. The patients were weaned from CPB when the rectal temperature was 34°C to 35°C. After discontinuation of CPB, heparin was neu-

a Xijing Health Care, Inc., Xian, China
b 3M Health Care, Ann Arbor, MI

tralized with 1 mg protamine sulfate for each 100 IU heparin given. Blood products were used after weaning of CPB. Isoproterenol was used when heart rate was lower than 60 BPM in adults or 80 BPM in pediatrics. Dobutamine was used with mean arterial pressures below 75 mmHg in adult or 55 mmHg in pediatric patients. Autotransfusion was not used in all the patients.

Sampling: For determination of hemoglobin, hematocrit, red blood cell, white blood cell, fibrinogen and plasma free hemoglobin, samples were drawn from the arterial line of the circuit during CPB. Pre-CPB and post-CPB samples were drawn from the arterial monitoring line. All samples were sent to the laboratory immediately after they were drawn. Other patient parameters consisted of urine output during CPB, rate of spontaneous cardiac conversion, application of dobutamine and isoproterenol, and rewarming time to a skin temperature measured at the left ankle of 33°C.

Table 2: Perioperative laboratory parameters

Parameter	Pre-CPB	CPB 30 min	CPB 60 min	CPB 90 min	Post-CPB	t-Test
Hematocrit (%)						
PP	40.8 ± 3.8	21.2 ± 3.1	23.4 ± 3.3	24.9 ± 4.2	38.3 ± 2.5	
NP	39.1 ± 4.0	22.6 ± 3.5	23.8 ± 3.0	40.8 ± 3.8	38.1 ± 2.6	NS
Platelet Counts (10^3/mm^3)						
PP	169.0 ± 41.4	82.9 ± 37.1	76.0 ± 31.9	87.7 ± 36.2	90.8 ± 39.6	
NP	173.6 ± 47.8	83.3 ± 32.4	78.7 ± 33.1	90.2 ± 36.7	93.4 ± 41.2	NS
White Blood Cells (10^3/mm^3)						
PP	7.9 ± 4.1	4.1 ± 2.8	3.4 ± 1.9	6.3 ± 3.4	12.7 ± 4.7	
NP	8.1 ± 3.9	4.1 ± 2.1	3.6 ± 1.7	6.7 ± 3.6	12.9 ± 4.8	NS
Red Blood Cells (10^6/mm^3)						
PP	4.3 ± 0.1	2.3 ± 0.1	2.5 ± 0.1	3.0 ± 0.1	3.7 ± 0.1	
NP	4.6 ± 0.1	2.4 ± 0.1	2.6 ± 0.1	2.9 ± 0.1	3.9 ± 0.1	NS
Hemoglobin (mg/dL)						
PP	12.9 ± 1.6	6.9 ± 6.9	7.3 ± 1.3	7.6 ± 1.7	11.2 ± 2.1	
NP	12.6 ± 1.6	6.8 ± 1.0	7.2 ± 0.8	7.7 ± 1.3	10.9 ± 1.9	NS
Fibrinogen (mg/dL)						
PP	279.2 ± 41.8	231.1 ± 31.7	201.3 ± 28.6	178.9 ± 30.9	166.4 ± 21.7	
NP	273.6 ± 41.3	218.9 ± 31.2	196.6 ± 21.9	162.1 ± 29.1	158.7 ± 20.9	NS

Data are mean ± SD. PP = pulsatile perfusion. NP = nonpulsatile perfusion. CPB = cardiopulmonary bypass. NS = not significant.

Statistics: The results are expressed as the mean ± the standard deviation of the mean, and n refers to the number of patients from whom blood samples were obtained. The Student's t test and Chi-square test were used for statistical comparison, and $p < 0.05$ was considered significant.

RESULTS

There were no significant differences between the PP and NP groups with respect to age, gender, weight, bypass time, aortic cross time, and cardiac diseases (Table 1). The lowest body temperature (rectal) on bypass was 30.9 ± 1.8°C in the PP group, and 30.7 ± 1.8°C in the NP group. The average arterial blood pressures in the PP group during CPB were as follows: systolic pressure (89.2 ± 19.9 mmHg), diastolic pressure (55.4 ± 11.2 mmHg), pulse pressure (36.5 ± 9.5 mmHg), and mean arterial pressure (67.1 ± 14.7 mmHg). The mean arterial pressure in the NP group was 69.3 ± 11.8 mmHg.

Laboratory parameters: As shown in Table 2, there were no significant differences between the pulsatile and nonpulsatile groups with respect to hemoglobin, hematocrit, red blood cell, white blood cell, and fibrinogen at all preoperative samples. However, there was a steady increase in plasma free hemoglobin during pulsatile perfusion ($p < .05$), which was not observed in the NP patients (Figure 1).

Clinical parameters: A significant difference in cardiovascular outcomes was observed that favored pulsatile perfusion. The PP group had a significantly higher rate of spontaneous cardiac conversion ($p < .05$). There were statistically fewer patients treated with both dobutamine and isoproterenol in the PP group, and earlier recovery of skin temperature ($p < .001$) than the NP group (Table 3) No intraaortic balloon support was used in either group.

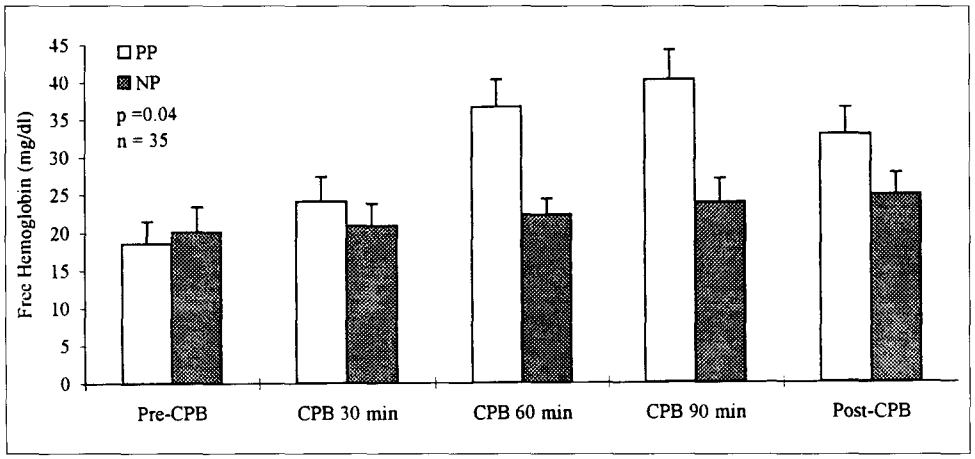
The urine of patients in both groups was clear. The urine output (ml/hr) in the PP group during CPB was significantly higher than that of the NP group (908.8 ± 87.2 vs. 606.1 ± 57.5, $p < .01$).

There was one patient in the PP group who died from left ventricular rupture 11 hours after combined aortic and mitral valve replacement. One patient in the NP group died from low cardiac output 43 hours after repair of double outlet right ventricle. All other patients in both groups recovered well after the operation, and no surgical deaths or neurological complications occurred.

DISCUSSION

The significance and contribution of pulsatile perfusion during CPB has generated debate and remained controversial since

Figure 1: Plasma free hemoglobin levels in both groups



Data are mean ± SD. NS = not significant. CPB = cardiopulmonary bypass. PP = pulsatile perfusion. NP = nonpulsatile perfusion.

Table 3: Clinical parameters

Parameters	Pulsatile	Nonpulsatile	P-value
Urine output (ml/hr)	908.8 ± 87.2	606.1 ± 57.6	< 0.001
Times of skin temperature conversion	4.9 ± 1.6	8.2 ± 2.5	< 0.001
Use of dobutamine (n)	10	19	< 0.05
Use of isoproterenol (n)	6	17	< 0.01
Use of dobutamine (hr)	4.8 ± 2.3	5.1 ± 2.6	NS
Use of isoproterenol (hr)	3.0 ± 1.9	3.7 ± 2.3	NS
Rate of spontaneous cardiac conversion	33	27	< 0.05

Data are mean ± SD. hr = hour. NS = not significant.

the beginning of open heart surgery. It has been reported that pulsatile perfusion during CPB affords benefits in maintaining aerobic metabolism and oxygen consumption (12), low vascular resistance through reduced afterload, both of which positively affect postoperative heart function (4). The presence of pulsatile perfusion has also positively maintained thyroid hormone metabolism (13), as well as yielding other benefits such as preserving renal function (9) and protecting the brain from damage during CPB (10). It has also been reported, however, that pulsatile perfusion does not appear to confer any special benefits when compared to nonpulsatile perfusion in terms of cerebral blood flow and oxygen metabolism (14), urine β-2 microglobulin levels (15), acid-base equilibrium and protection of the function of kidneys and pancreas (16).

The overall results of the current study demonstrate that pulsatile perfusion has distinct advantages over nonpulsatile perfusion in maintaining renal function and postoperative heart function, as well as peripheral perfusion. The reduced requirement for circulatory support with inotropic drugs and higher rate of spontaneous cardiac conversion supports the overall hemodynamic superiority in the immediate postoperative phase following pulsatile perfusion. Similar findings have been reported by other authors (17, 18). Taylor pointed out that the overall hemodynamic effect of pulsatile perfusion may be seen as both primary and secondary effects compared to that produced by nonpulsatile perfusion (19). The primary effect is the reduction in peripheral vascular resistance (PVR), which promoted better tissue perfusion. The secondary effect is the improvement in left ventricular performance achieved by the reduction in afterload, improving overall myocardial function.

Numerous investigations have been carried out with the object of achieving the best possible protection for myocardial energetics and function following CPB. The elevated PVR is widely recognized as being an essentially hazardous situation in the early postbypass period since left ventricular work is unnecessarily increased and subendocardial perfusion is significantly decreased (18). The use of pulsatile perfusion during CPB offers the possibility of minimizing the potentially harmful elevation in PVR during the perfusion period. The earlier recovery of skin temperature in the PP group found in the current study is the result of both the primary and secondary effects. Williams, et al., has suggested that pulsatile perfusion can provide more uniform cooling and rewarming (20). Wright reported that the presence of microcirculatory collapse during the period of NP was not easily reversed, and took approximately 20 minutes to return to normal (2).

The significantly higher urine output in the PP group shown in the study may indicate that pulsatile perfusion maintained better renal blood flow and function than nonpulsatile perfusion during CPB. This is more than likely a result of pulsatile perfusion preventing increases in plasma catecholamine levels (8), vasopressin levels (21), and endotoxin levels (22). Pulsatile perfusion has less stimulation of the renin-angiotensin system (23), less depression of the usual stress response to operation as the result of anterior pituitary secretion of adrenocorticotropic hormone and cortisol release (24), and less pituitary hypofunction , than nonpulsatile perfusion (25). The reduction of PVR improved microcirculation, organ blood flow, and organ function (25, 26).

Renal sympathetic nerve activity has been shown to be af-

fected by many factors during CPB (5). These factors include the hemodilution, the change of temperature, and activation of sinoaortic baroreceptors and cardiopulmonary receptors which are major components of the baroreflex mechanism. Baroreflex is a system that monitors change and minimizes fluctuations in blood pressure (27). It includes the arterial baroreflex, which functions according to the arterial blood pressure, and the cardiopulmonary baroreflex, which functions according to the atrial pressure, pulmonary pressure, and ventricular diastolic pressure. Pulsatile perfusion reduces the stimulation to the baroreceptors and inhibits the sympathetic nerve activity by imitating the physiological pulse blood pressure, which totally disappears in nonpulsatile perfusion.

No significant differences were observed in the study with respect to the depletion of RBC, WBC, platelet count, and fibrinogen. The plasma free hemoglobin increase in the PP group may be related to the higher shear stress created during pulsatile perfusion. However, the increase was still within the normal range, and no patient had a plasma free hemoglobin level that exceeded 70 mg/dl. Blood trauma during CPB is primarily due to the air to blood interface occurring through cardiotomy suction, not to blood pumping (28). The more frequently suction was used, the more blood trauma occurred. No direct effect of the types of operative procedures on blood trauma was observed. Blood trauma is not primarily determined by the type of flow but rather by the mechanical forces applied to the blood by the pumping mechanisms (2). Routine pulsatile perfusion with a roller pump is not associated with any increased requirements for homologous blood transfusion or excessive levels of blood cell or platelet depletion (19).

We conclude that pulsatile perfusion, compared to nonpulsatile systemic perfusion during CPB, improves patient outcomes with respect to maintaining better renal function during CPB, preserving cardiac function in the early postbypass period, but does promote a steady increase in plasma free hemoglobin within normal range.

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