Original Article

Comparative Study of Pulsatile and Nonpulsatile Flow During Cardio-Pulmonary Bypass

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The use of nonpulsatile flow during extracorporeal circulation remains popular despite theoretical advantages of pulsatile cardiopulmonary bypass (CPB). Pulsatile CPB is considered to be more physiological than nonpulsatile flow as the pulsatile energy ensures the patency of the vascular bed and mechanical motion of tissue fluid around the cell membrane, improves microcirculation and enhances diffusion. The purpose of this study was to compare the effect of pulsatile and nonpulsatile flow on the coagulation profile, liver and kidney function and also on the haemodynamics in patients undergoing coronary artery bypass grafting on CPB.

One hundred patients between 35 and 65 years of age with normal left ventricular function were randomly divided into two equal groups: Pulsatile (P) and nonpulsatile (NP). Haematological parameters, clotting profile, renal parameters, hepatic function tests and haemodynamic variables were measured preoperatively and postoperatively at specific intervals. Surgical, anaesthetic and CPB regimen was standard in all cases.

There was a decrease in platelet count during and after CPB in both groups. Coagulation profile and renal function parameters remained similar in both groups except that creatinine clearance was better in group P on the first postoperative day. Urine output was also better in group P. There was no change in liver function tests in both groups. The haemodynamic variables were comparable in both groups. The systemic vascular resistance was higher in group NP postoperatively and oxygen consumption was higher in group P post CPB.

In conclusion we did not find any significant difference between pulsatile and nonpulsatile flow during CPB except the creatinine clearance and urine output were better in pulsatile group. **(Annals of Cardiac Anaesthesia 2004; 7: 44–50)**

Key words: – Cardiopulmonary bypass, Pulsatile flow, Nonpulsatile flow

Pulsatile cardiopulmonary bypass (CBP) is considered to be more physiological than nonpulsatile flow as the pulsatile energy ensures the patency of the vascular bed[1–3] and mechanical motion of tissue fluid around the cell membrane, improves microcirculation and enhances diffusion.[4] It also provides a lower systemic vascular resistance and higher oxygen consumption.[4–7] Despite theoretical advantages, pulsatile CPB has not been widely accepted due to lack of clear objective data on organ metabolism and fear of increased haemolysis[8,9] because of platelet destruction.

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CPB itself has profound effects on the number and function of platelets.[10] Atleast 10-20% of patients undergoing cardiac surgery exhibit inadequate haemostasis.[11] The major known causes of bleeding after cardiac operations are usually inadequate surgical haemostasis (surgical bleeding)[12] a decrease in plasma coagulation factors,[13,14] thrombocytopenia and platelet dysfunction.[15,16] Contact between blood and gaseous or synthetic solid surfaces during CPB causes a decrease in circulating platelet count,[17] formation of circulating platelet aggregates,[18] loss of platelet sensitivity to activating agents,[19] release of platelet granules and disruption of subcellular architecture.[10,19–21]

The purpose of this study was to compare the effects of pulsatile and nonpulsatile flow on platelet count, bleeding and coagulation profile, liver and kidney function and haemodynamics in patients undergoing coronary artery bypass grafting (CABG) on CPB.

Methods

One hundred patients between 35 and 65 years of age with normal left ventricular ejection fraction (LVEF) scheduled for elective CABG were randomly divided into two equal groups. Non-pulsatile flow was used in group NP and pulsatile flow in group P. Patients in whom reoperation and emergency procedures were performed and those receiving anticoagulants and antiplatelet medications during the two weeks preceding their admission for surgery were excluded from the study. Informed consent was obtained from each patient after approval of the study by the institutional review board.

Pre and postoperative haematological parameters studied in both the groups, were haemoglobin, coagulation profile (bleeding time, clotting time, prothrombin time, partial thromboplastin time) and platelet count. Postoperative drainage, blood and blood component requirement were also noted. Renal function parameters (urine output, blood urea nitrogen, serum creatinine and creatinine clearance) and hepatic function parameters consisting of serum bilirubin, alkaline phosphatase, serum glutamate oxalate transferase (SGOT) and serum glutamate phospho transferase (SGPT) were also measured pre and postoperatively in both groups. Haemodynamic variables which included mean arterial pressure, cardiac output, systemic vascular resistance and oxygen consumption were also recorded in both groups. Age, sex, body weight and body surface area were noted.

Surgical, anaesthetic regimens, and CPB were standard in all the cases. Anaesthesia was induced with fentanyl, midazolam, thiopentone sodium and tracheal intubation was facilitated by pancuronium bromide. Patients received heparin sulphate at an initial dose of 4 mg/kg followed by additional doses as necessary to maintian the activated clotting time (ACT) greater than 400 seconds. The extracorporeal system consisted of polyvinyl chloride tubing, Capiox SX-18 membrane oxygenator (Terumo, Terumo Corporation, Shibuya-KU, Tokyo, Japan), Sarns 9000 roller pump (Sarns, 3M Health Care, Ann Arbor, USA) and Affinity arterial line filter (AVE Ireland Ltd, Parkmore Business Park West, Gallway, Ireland). The circuit was primed with 1500 mL of Ringers solution and 200 mL of 20% mannitol. A perfusion flow of 2.2 - 2.42 L/min/m^2 body surface area was maintained during CPB in both groups and pulse flow width 60%, base 25% with rate of 60 beats per minute was used in the pulsatile group. Sarns 9000 roller pump has an in-built system to provide pulsatile flow. Normothermic CPB with temperature drift was used. The heart was arrested using potassium chloride in blood cardioplegia solution. Rectal and blood temperatures were monitored throughout the surgery.

The patient was rewarmed up to 36.6° C rectal temperature before discontinuation of CPB. After weaning from CPB, the residual blood in the circuit was transfused through the aortic cannula and 14 G intravenous peripheral line until the end of surgery. Protamine sulphate was given in the same dose as the initial heparin dose and adequate reversal was assessed by confirming that the ACT has returned to the preoperative value. The patients remained on mechanical ventilation after the operation till they met the extubation criteria.

Blood samples were collected at following intervals: Preoperative in ward (preop), Preoperative in OT (Pre CPB), 5 minutes after heparin administration but before the start of CPB (5 hep), 40 minute after start of CPB (CPB 40), just after CPB off (post CPB), 2 hours after completion of CPB (Post 2), 12 hours after completion of CPB (Post 12), 24 hours after completion of CPB (Post 24), 48 hours after completion of CPB (Post 48) and at the time of discharge of the patient (discharge).

All blood samples were drawn through the arterial or central venous line. All data are expressed as mean ± standard deviation (SD). Statistical significance of the differences were evaluated by student's 't' test and a, $p < 0.05$ was considered as significant.

Results

Mean age, body weight, body surface area, bypass time, aortic cross clamp time, pump flow and mean arterial blood pressure were comparable in both groups (table 1).

Preoperative platelet counts were normal in all patients and ranged between 1,50,000 to 3,25,000/ mm^3 in both groups.

The platelet counts gradually decreased during and after CPB in both groups (table 2). Platelet counts were lower in group NP as compared to group P but there was no statistical difference at any time point between groups.

The coagulation profile, postoperative bleeding and blood component requirement remained similar in both groups.

There was a decrease in the haemoglobin concentration, 24 hours post surgery in both groups (table 3) without statistical difference between the two groups. Mean postoperative chest tube drainage was less in group P (374±134 mL) than in group NP (419±263 mL) but was not statistically significant.

Blood and blood component requirement was also similar in both groups.

Renal function: The increase in blood urea nitrogen and serum creatinine levels post operatively at 24 and 48 hours were similiar in both groups (table 4). Creatinine clearance was significantly higher in the group P on the 2nd post-operative day (48 hours). Urine output was also better in the group P as compared to the group NP.

Liver function tests were comparable in both groups at all time periods (table 5) and the increase in their values in the postoperative period was also similiar. The increase in SGOT and SGPT was higher in the group NP as compared to the group P at 24 hours and 48 hours postoperatively.

Table 1. Clinical data Mean ± S.D

	Group NP (n=50)	Group P (n=50)
No of patients	50	50
Age (years)	56.4±7.7	54.5±8.6
Body wt. (Kg)	66±11	68±11
Body surface area (m^2)	1.72±0.19	1.7±0.14
CPB time (min)	95.46±20.9	90.08±20.9
Aortic crossclamp time (min)	52.77±14.5	49.48±13.8
Pump flow (L/min/m^2)	3.5 – 3.9	3.2-4.2
Mean arterial BP (mm Hg)	63.08±6.5	60.5±8.0

CPB: cardiopulmonary bypass; BP: blood pressure

Table 2. Platelet counts (lakh/mm^3)

	Group NP	Group P	p value
Preop	2.9±0.96	3.2±0.99	NS
Preop CPB	2.0±0.6	2.1±0.59	NS
5-Hep	1.84±0.58	2.02±0.62	NS
CPB –40	1.43±0.91	1.73±1.84	NS
Post CPB	1.36±0.52	1.46±0.62	NS
Post 2	1.49±0.57	1.73±0.69	NS
Post 12	1.49±0.55	1.71±0.63	NS
Post 24	1.36±0.48	1.52±0.52	NS
Post 48	1.42±0.5	2.4±0.9	NS
Discharge	2.0±0.69	3.1±0.98	NS

NS - not significant

Table 3. Haemoglobin (gm%)

	Group NP	Group P	p value
Preop	13.02±1.5	13.39±1.16	0.17
Post 24	9.84±0.96	10.1±1.12	0.10
Post 48	9.6±1.15	9.5±0.8	0.5
Discharge	10.4±0.9	10.5±1.12	0.8

Table 4. Renal function

	Group NP	Group P	p value
Blood urea nitrogen (mg/dL)			
Pre op	27.3±9.3	28.54±7.6	0.4
Post 24	32.23±10.42	31.49±8.9	0.7
Post 48	34.33±7.2	36.24±13.7	0.3
At discharge	33.17±8.37	35.01±10.24	0.3
Serum creatinine (mg/dL)			
Pre op	1.05±0.21	1.11±0.18	0.18
Post 24	1.10±0.25	1.19±0.31	0.10
Post 48	1.06±0.27	1.11±0.32	0.37
At discharge	1.28±1.70	1.51±2.3	0.5
Creatinine clearance (mL/min)			
Pre op	55.47±7.6	56.85±16.6	0.10
Post 24	52.05±16.91	60.03±9.8	0.70
Post 48	58.15±14.13	65.01±11.8	0.05
At discharge	62.44±7.3	69.08±8.9	0.15
Urine output (mL)			
Pre op	235.24±205	260±169.6	0.5
Post 24	452.65±247	484±255	0.09*
Post 48	537.46±242	669±310.6	0.5

The preoperative mean arterial pressure (table 6) was comparable in both groups. A decrease was observed post induction which continued till CPB was instituted. On CPB also the perfusion pressure was similar except at 60 and 80 minutes when it was significantly higher in group NP ($p<0.05$). Post CPB the mean arterial pressure was similiar in both groups. The systemic vascular resistance (table 7) was significantly higher in group NP in the post CPB period and at 24 and 48 hours post-operatively. There was no significant difference in the pulmonary vascular resistance and cardiac indices. Oxygen consumption (table 8) improved after CPB in both groups. The increase was comparable in both groups at all time intervals but was significantly higher ($p = 0.002$) at 48 hours post CPB in group P.

Table 5. Liver function

	Group NP	Group P	p value
Serum bilirubin (total) mg%			
Pre op	0.52±0.2	0.6±0.8	0.4
Post 24	0.7±0.3	0.79±0.4	0.7
Post 48	0.8±0.3	1.04±0.8	0.14
At discharge	0.8±0.2	0.8±0.5	0.9
Alkaline phosphatase (KIU)			
Pre op	223±66.3	204.5±63	0.15
Post 24	159.8±55.8	147.5±43.3	0.2
Post 48	167.8±50.1	154.6±44.9	0.17
At discharge	190.3±73.07	203.3±101.3	0.46
SGOT (IU/L)			
Pre op	27.5±13.2	25.7±9.8	0.43
Post 24	48.7±17.4	38.8±13.01	0.02
Post 48	43.9±21.3	36.8±16.7	0.06*
At discharge	41.9±21.8	35.5±12.8	0.07
SGPT (IU/L)			
Pre op	32.7±18.4	30.8±17.3	0.6
Post 24	29.7±12.6	25.9±10.4	0.11
Post 48	27.9±13.6	21.6±7.9	0.006
At discharge	32.1±18.9	37.0±15.3	0.5

SGOT: serum glutamic oxaloacetic transaminase, SGPT: serum glutamic pyruvic transaminase

Table 6. Average haemodynamic data

Mean arterial pressure mm Hg

	Group NP	Group P	p value
Preop	94.7±12.14	95.1±15.2	0.9
Pre CPB	85.07±18.14	88.3±13.5	0.36
5-Heparin	79.16±13.5	76.54±11.06	0.35
CPB			
0	53.6±8.9	53.6±11.07	0.9
20	59.7±10.5	594±84.4	0.9
40	61.5±11.4	60.56±8.04	0.6
60	65.4±10.1	61.6±11.2	0.07
80	67.3±15.4	61.6±9.2	0.07
100	63.6±6.5	62.2±8.4	0.06
Post CPB	75.7±9.8	76.9±9.99	0.5
Post CPB –2	90.34±11.04	91.89±14.6	0.5
Post CPB –12	81.33±9.51	85.7±9.04	0.03
Post CPB – 24	79.65±7.22	84.05±8.8	0.01
Post CPB – 48	92.44±10.2	84.9±9.9	0.01
Discharge	69.75±10.28	95.02±13.13	0.42

Table 7. Derived haemodynamic parameters

	Group NP	Group P	p value
SVR (dynes sec. cm^{-5})			
Preop	1687.8±436	1654.2±512	0.7
Pre CPB	1545.08±418	1315.4±495	0.01
Post CPB	1468.8±335	1325.6±336	0.04
Post CPB –2	1567.8±308	1392.4±338	0.01
Post CPB –12	1491.2±262	1231.9±266	0.01
Post CPB – 24	1485.36±263	1226.1±232	0.01
Post CPB - 48	1421.1±179	1222.2±226	0.01
PVR (dynes sec. cm^{-5})			
Preop	168.4±1203	149.5±96.2	0.3
Pre CPB	160.7±83.3	145.08±80.6	0.3
Post CPB	142.5±88	139.8±65.9	0.5
Post CPB –2	164.8±74.4	149.2±69.3	0.2
Post CPB –12	140.9±73.9	160.3±22.6	0.5
Post CPB – 24	140.1±67.6	121.0±54.5	0.1
Post CPB - 48	145.2±61.4	137.7±63.04	0.5
CI			
Preop	3.17±4.1	2.2±0.4	0.11
Pre CPB	2.78±2.9	2.39±0.57	0.35
Post CPB	2.94±0.58	2.81±0.5	0.24
Post CPB –2	2.37±0.39	2.45±0.47	0.37
Post CPB –12	2.48±0.4	2.52±0.32	0.75
Post CPB – 24	2.65±0.3	2.6±0.46	0.69
Post CPB – 48	2.86±0.47	2.9±0.5	0.58

SVR: Systemic vascular resistance; PVR: pulmonary vascular resistance, CI: cardiac index

Discussion

Pulsatile CPB is considered to be more physiological than nonpulsatile because pulsatile energy ensures the patency of the vascular bed and mechanical motion of tissue fluid around the cell membrane, improves microcirculation and enhances cell diffusion.[4]

During CPB, contact between blood and nonphysiological surfaces affects both cellular and non cellular constituents.[11] Activation of platelets by CPB leads to decreased adhesiveness, reduced

Table 8. Oxygen consumption mL/min.

	Group NP	Group P	p value
Pre CPB	182.6±79.8	177.88±104.68	0.79
Post CPB	167.04±65.06	171.46±67.47	0.73
Post CPB –2	213.4±69.6	218.42±64.63	0.71
Post CPB –12	199.8±59.8	212.43±97.6	0.44
Post CPB – 24	214.9±69.3	220±97.24	0.78
Post CPB - 48	197.08±74.7	253.13±101.11	0.002

membrane binding to fibrinogen, alpha granule release and a reduced in-vitro response to adenosine diphosphate and collagen.[11]

In our study, 50 patients in each group underwent CABG on pulsatile and nonpulsatile CPB. The platelet counts decreased in CPB in both groups although not significantly. The decrease in platelet count persisted till 48 hours postoperatively. Laufer et al observed a decrease in platelet count following CPB which returned to normal levels only after 6 to 7 days.[22] These changes in platelet counts have been attributed in part to the formation of platelet aggregates on the oxygenator and in part to a temporary sequestration in the liver. They also demonstrated a reduction in the mean platelet volume on CPB which could be attributed to the loss of larger, younger platelets from the circulation.[12,23,24] This leaves the older, smaller and less active platelets in circulation and could explain the decreased platelet adhesiveness and haemostatic response in the post CPB period. Pulsatile flow itself causes mechanical disruption of the blood components including platelets and is also responsible for a decrease in platelet count. Platelet count by the Coulter counter measures the cellular debris and may be responsible for the similar decrease in the platelet count in both groups of our study. Measurement of the mean platelet volume in the pulsatile group would have helped us to get a true picture of the platelet destruction.

The decrease in haemoglobin was also comparable in both groups. There was a slight increase in bleeding time, clotting time, prothrombin time and partial thromboplastin time in both groups, although it was not statistically significant.

The postoperative bleeding and blood requirement was also similiar in both groups. Taylor et al compared pulsatile perfusion with a modified roller pump to the conventional non-pulsatile ECC and found no increase in haemolysis or depletion of red blood cells, white blood cells or platelets at the same flow rate and mean arterial pressure.[8]

Pulsatile CPB is also associated with improvement in renal and hepatic function as compared to non pulsatile CPB. Many studies[25–27] have shown that pulsatile flow decreases peripheral vascular resistance and offers better tissue perfusion. Nonpulsatile flow is associated with a depression in kidney function not found during pulsatile perfusion.[3] It has been demonstrated that moderate to severe hydropic degeneration of kidney tubules occurs only after nonpulsatile perfusion.[5,28,29] Many et al[30,31] found that sodium excretion and urine volume decreased during nonpulsatile perfusion. Hooker[32] demonstrated increased urine flow and decreased proteinuria with pulsatile perfusion. We also observed an improvement in creatinine clearance and urine output in the pulsatile group. Mukherjie et al[33] found improved renal blood flow and tissue oxygenation during pulsatile perfusion. In patients with pre existing renal disease some investigators have reported improved renal function and outcome with pulsatile flow. Olinger et al[34] reported that pulstile flow helped to preserve renal function in patients with serum creatinine over 1.7 mg/dL. Matsudar et al[25] reported similar beneficial effects in patients with decreased creatinine clearance preoperatively. Metabolic studies have demonstrated lower renal vein lactate levels, greater renal oxygen consumption and better tissue oxygen levels with pulsatile CPB. A theoretical advantage of pulsatile over nonpulsatile flow that has been proposed by Shepard et al [3,4,27,35] is that it is the energy gradient and not pressure gradient which produces blood flow. It has been hypothesised that the increased "energy equivalent pressure" of pulsatile flow may enhance interstitial diffusion by oscillating cell fluid boundary layers and ensure the patency of end arterioles which otherwise collapse during non pulsatile flow.[35,36] The lower percentage of SGOT and SGPT increase in the pulsatile group in our study might indicate

a lesser degree of hepatocellular damage in this group.

In this study patients in the pulsatile group had a lower arterial pressure on CPB and lower systemic vascular resistance in the post CPB period. The mechanisms for elevation of systemic vascular resistance in nonpulstile CPB include poor compliance of the blood vessel and increased levels of renin angiotensin, catecholamines and vasopressin.

Oxygen consumption was also higher in group P compared to group NP. Many variables are known to influence oxygen consumption during anaesthesia and CPB. These include temperature, a calorigenic effect of catecholamine release induced by anaesthesia or hypoxia, muscle activity and influence of muscle relaxants, the pre-existing basal metabolic rate, pH, arterial blood oxygen content and perfusion rate.[3,37-43] Reasons for difference in oxygen consumption between the two groups are also speculative and are as follows: 1) Jiggling of the tissues during pulstile fow, which may act to change the boundary layer of interstitial fluid flow around cell membranes and thus enhance diffusion, 2) lymph and interstitial fluid flow during CPB may be enhanced when blood flow is pulsatile.[3,44] 3) Pulsatile energy may be required to ensure that a normal percentage of the total number of arterioles in a vascular bed are open at any one time.[3,45]

In conclusion we did not find any significant difference between pulsatile and nonpulsatile flow during CPB except that creatinine clearance and urine output were better in the pulsatile group, which may be beneficial in patients with pre-existing renal dysfunction. This needs to be shown in a larger study.

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