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Effect of Pulsatile Cardiopulmonary Bypass in Adult Heart Surgery

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ABSTRACT

Background: This study aimed to examine the effect of pulsatile flow pattern on tissue perfusion, particularly cerebral tissue perfusion, at pre-determined intervals during CPB, as well as its effects on postoperative morbidity and mortality.

Methods: This retrospective study included 134 adult patients, who underwent cardiac surgery with cardiopulmonary bypass (CPB). Patients were grouped based on the flow pattern used during CPB: non-pulsatile CPB group (N = 82) and pulsatile CPB group (N = 52). Cerebral oxygen saturation, arterial pH and arterial lactate levels were measured at four time points, during the operation and the 2 groups were compared with regard to changes over time as well as differences in postoperative outcomes.

Results: The 2 groups were similar, in terms of mean values and intraoperative changes in cerebral oxygen saturation and arterial pH. Non-pulsatile CABG group had significantly higher arterial lactate levels over the measurement period, which was not affected by the timing of the measurements. Postoperative drainage, duration of ventilation and duration of hospital stay significantly were higher and postoperative blood urea nitrogen significantly was lower in the non-pulsatile CPB group. Other postoperative outcomes were similar across the groups.

Conclusion: Findings of this study do not support the superiority of pulsatile flow pattern during CPB, in terms of cerebral oxygen saturation or postoperative mortality/morbidity. Further and larger comparative studies are warranted before pulsatile blood flow pattern can be established as a routine clinical method.

INTRODUCTION

A variety of techniques have been introduced to reduce the significant negative impact of cardiopulmonary bypass (CPB) on vital organ perfusion and oxygenation, during cardiac surgery [Butler 1993; Schell 1993]. One such technique involves the use of pulsatile versus non-pulsatile blood flow pattern during CPB.

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At the microcirculatory level, several studies have reported an augmentation of the circulation in vital organs when pulsatile flow pattern is used [Alkan 2007; Ji 2007; Undar 2001]. This phenomenon is known to be a consequence of the surplus hemodynamic energy produced during the pulsatile flow [Alghamdi 2006] that causes a physiological flow-pattern effect leading to an increase in the circulation, particularly in the brain and kidneys. Furthermore, more rapid recovery of vital organ functions has been reported following CPB with pulsatile flow [Kim 2005; Undar 2002], leading to reduced systemic inflammation and edema.

Near-infrared spectroscopy (NIRS) is a non-invasive technique that measures the oxygen supply to organs, hence providing information on tissue perfusion [Skowno 2008]. Although NIRS allows the clinicians to collect information on hepatic, muscular, or renal blood flow, it mostly is used for measuring the oxygenation of the brain [Hoffman 2005]. Pulsatile flow significantly reduces the cranial vascular resistance during warming period and at the termination of CPB, and it improves the cranial circulation [Undar 2001].

Despite the weight of evidence suggesting numerous positive effects of pulsatile flow pattern, this approach has not routinely been used in cardiac surgery, mainly due to the challenges associated with the use of this technique together with a specific perfusion technique.

In this study, our objective was to examine the effect of pulsatile flow pattern on tissue perfusion, particularly cerebral tissue perfusion, at pre-determined intervals during CPB, as well as its effects on postoperative morbidity and mortality.

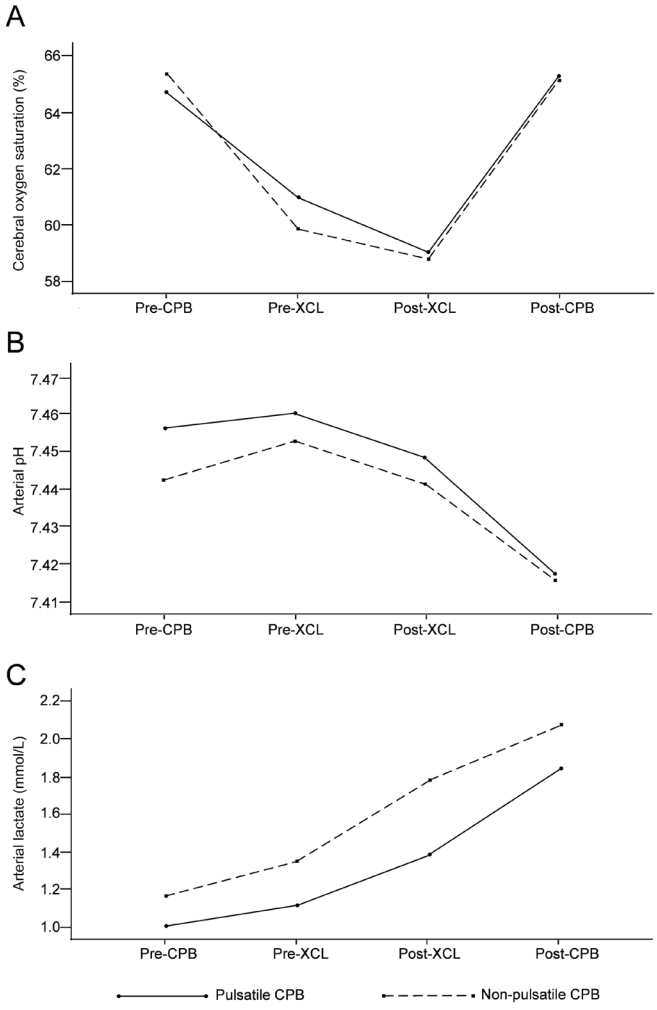
MATERIALS AND METHODS

In this study, 134 adult patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) between January and September 2018 retrospectively were evaluated. Patients were grouped based on the flow pattern used during CPB: non-pulsatile CPB group (N = 82) and pulsatile CPB group (N = 52). All operations were performed by the same surgical team. Patient demographics and clinical data were retrieved. Patients who underwent emergency operation, adult congenital cardiac surgery, redo surgery, and cases with a significant carotid artery stenosis (at least unilateral 60% stenosis) were excluded from the study. Study protocol was approved by the Institutional Ethics Committee and conducted in accordance with the principles of the Declaration of Helsinki.

Table 1. Demographical and baseline characteristics

	Pulsatile CPB (N = 52)	Non-pulsatile CPB (N = 82)	*P*
Age, y	60.1 ± 11.0	55.8 ± 14.0	.076
Male gender, n (%)	44 (84.6%)	54 (65.9%)	.017
Body surface area, m^2	1.9 ± 0.1	1.9 ± 0.2	.434
EuroSCORE	1.4 ± 0.7	2.6 ± 4.8	.860
Co-morbidities			
Hypertension, n (%)	10 (19.2%)	19 (23.2%)	.722
COPD, n (%)	19 (36.5%)	33 (40.2%)	.668
Diabetes, n (%)	17 (32.2%)	6 (19.5%)	.084
Preoperative laboratory findings			
Platelets, $x10^9/L$	239.0 ± 67.0	243.0 ± 87.0	.775
BUN, mg/dL	17.4 ± 5.9	18.5 ± 12.0	.242
Creatinine, mg/dL	1.0 ± 0.3	1.0 ± 0.7	.115
AST, U/L	23.3 ± 17.4	22.3 ± 16.8	.585
ALT, U/L	25.0 ± 19.4	21.9 ± 20.7	.067
Ejection fraction, %	56.6 ± 9.0	56.7 ± 7.6	.693

Unless otherwise stated, data presented in mean ± standard deviation.
COPD, chronic obstructive pulmonary disease; BUN, blood urinary nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase



Intraoperative changes in cerebral oxygen saturation, arterial pH and arterial lactate levels.

Intraoperative anesthesia management: Intravenous midazolam (0.1–0.2 mg/kg), fentanyl (1.0–1.5 µg/kg), propofol (2 mg/kg), and rocuronium (0.6 mg/kg) were used for anesthesia induction. Continuous infusion of fentanyl 0.3 µg/kg/h and sevoflurane inhalation were used for anesthesia maintenance. Ventilator settings were adapted to maintain normocapnia. Dexamethasone at a dose of 1 mg/kg was used to all patients. Subsequent to anesthesia induction and intubation, internal jugular vein catheter was inserted in all patients. Body temperature was monitored via thermal sensors placed in the nasopharynx.

Pulsatile and non-pulsatile CPB technics: The same cardiopulmonary bypass circuit (Stöckert S5; Sorin Biomedica, Mirandola, Italy) was used in all patients. Following systemic heparinization, arterial and venous cannulas were placed and subsequently CPB was led traditionally with pump flow rate of 2.4 L/min/m^2 of body surface area (BSA). Mostzeller formula ([(height × weight)/3600]1/2 was used to calculate BSA. In all patients, central arterial cannulation was done (to the ascending aorta with a right-angled tip cannula). Venous cannulation was accomplished by the cannulation of right atrial appendage, using two-stage cannula or by selective cannulation of inferior or superior vena cava.

Following cross-clamping of the ascending aorta, cardiac arrest was achieved by antegrade isothermic blood cardioplegia. Heart topically was cooled in all patients. In the non-pulsatile group, continuous flow was administered throughout the CPB procedure. In the pulsatile group, a pulsatile flow was administered with following parameters: heart rate, 70-75 beats/min; base flow 30-50%; pulse width, 50-70%. In this group, a minimum pulse pressure of 25 mm Hg was targeted for the duration of CPB.

In both groups, mean arterial pressure of 60 mm Hg was maintained throughout the course of CPB. Phenylephrine was used for hemodynamic regulation. The body temperature was reduced during CPB and rewarmed prior to termination. None of the patients underwent hypothermic circulatory arrest. Intermittent blood cardioplegia was performed in 15- to 20-minute intervals, during cross-clamping for myocardial protection. After the completion of surgical repair, CPB was terminated upon confirmation of normal body temperature and hemodynamic stability.

Hemodynamic measurements and NIRS monitoring: Cerebral oxygen saturation, arterial pH and arterial lactate levels were measured at four time points during the operation: T1, just before the initiation of CPB (pre-CPB); T2, at the end of cooling period just before the placement of aortic cross-clamp (pre-XCL); T3, at the end of warming period

Table 2. Comparison of the groups with regard to intraoperative features and early postoperative outcomes

	Pulsatile CPB (N = 52)	Non-pulsatile CPB (N = 82)	*P*
Intraoperative			
CABG, n (%)	43 (82.7%)	44 (53.7%)	.001
Valvular surgery, n (%)	14 (26.9%)	42 (51.2%)	.005
Heparin administered, x10^3 U	38.8 ± 11.0	36.5 ± 8.8	.117
Protamine administered, x10^3 U	36.1 ± 7.9	39.2 ± 9.2	.036
Maximum ACT, sec	691.8 ± 154.5	701.1 ± 146.5	.708
CPB time, min	82.8 ± 33.2	88.2 ± 35.0	.376
Cross clamp time, min	47.2 ± 23.6	53.6 ± 29.3	.309
Postoperative			
APACHE score	5.8 ± 2.2	7.1 ± 3.9	.078
Drainage, mL	517.3 ± 307.9	386.6 ± 254.7	.004
Tamponade, n (%)	3 (5.8%)	3 (3.7%)	.565
Need for revision, n (%)	10 (19.2%)	7 (8.5%)	.070
Need for inotropic agent, n (%)	13 (25.0%)	22 (26.8%)	.814
Duration of ventilation, h	10.5 ± 7.7	14.0 ± 16.4	.013
Duration of ICU stay, h	31.4 ± 20.9	35.6 ± 26.2	.235
Duration of hospital stay, d	6.7 ± 1.7	7.4 ± 2.4	.032
Platelets, x109/L	181.0 ± 59.1	191.8 ± 76.4	.387
Arterial PH*	7.4 ± 0.1	7.4 ± 0.1	.286
Arterial lactate*, mmol/L	2.1 ± 2.5	2.7 ± 2.5	.008
ALT, U/L	29.2 ± 58.6	24.4 ± 33.3	.422
AST, U/L	46.4 ± 92.7	49.3 ± 50.4	.050
BUN, mg/dL	19.0 ± 7.0	17.2 ± 9.2	.041
Creatinine, mg/dL	1.04 ± 0.36	0.96 ± 0.44	.050
Atrial fibrillation	3 (5.8%)	5 (6.1%)	.624
Pleural effusion, n (%)	1 (1.9%)	5 (6.1%)	.246
Pneumonia	0	0	
Acute renal failure, n (%)†	1 (1.9%)	4 (4.9%)	.354
Neurological complication	0	0	
Early mortality, n (%)	2 (3.8%)	4 (4.9%)	.570

*At ICU. †requiring dialysis. Unless otherwise stated, data presented in mean ± standard deviation. CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ACT, activated clotting time; ICU, intensive care unit; BUN, blood urinary nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase

following the removal of aortic cross-clamp (post-XCL); and T4, several minutes after the termination of CPB (post-CPB).

A four-channel trend monitor (Somanetics 5100B, Troy, MI) was used for cerebral oxygen saturation monitoring. The NIRS sensor was placed on mid-forehead, following the endotracheal intubation. Siemens Rapidlab ®1265 (Siemens Healthcare Diagnostics Inc.) device was used for arterial blood gas analysis. In addition, clinical and laboratory parameters were recorded in intensive care unit and during the first 12 postoperative hours.

Statistical analysis: IBM SPSS Statistics version 20.0 software (SPSS Inc., Chicago, IL) was used for data analysis. Descriptive data are presented in number (percentage), mean ± standard deviation, where appropriate. Kolmogorov Smirnov test and graphical methods were used to test the normality of the distribution. Continuous variables were compared using student t test or Mann Whitney U test, depending on data distribution. Categorical variables were compared with Pearson's chi-square test or Fisher's Exact test. Intraoperative changes in cerebral oxygen saturation, arterial pH and arterial lactate levels (within-subject variables) across two groups (pulsatile vs. non-pulsatile CPB, between-subject variable) were examined using two-way ANOVA for repeated measurements. Post hoc comparisons of within subject variables at different time points were done by t-test for paired samples with Bonferroni correction. Comparisons of the 2 groups at each time point were done by t-test for independent samples. Logistic regression was used to identify the independent predictors of a maximum decrease in cerebral oxygen saturation during measurements. A *P* value <.05 was considered the indication for statistical significance.

RESULTS

Table 1 shows demographical and baseline characteristics. Male gender (84.6% versus 65.9%) was more common among patients that operated with pulsatile CPB (Table 1). The 2 groups were similar with regard to other baseline and demographical characteristics. Regarding intraoperative characteristics, the 2 groups also were similar except for a higher amount of protamine administered in the non-pulsatile CPB group (39.2 versus 36.1 x103 U) (Table 2).

Intraoperative changes in cerebral oxygen saturation, pH and lactate levels shows intraoperative changes in cerebral oxygen saturation, arterial pH and arterial lactate levels (Figure). In both the non-pulsatile and pulsatile CPB groups, a sharp and significant decrease was observed in cerebral oxygen saturation after initiation of CPB ($P < .001$), forming a plateau during cross-clamp before a sharp increase after removal of cross-clamp ($P < .001$) (Figure A). However, overall the 2 groups did not differ with regard to the changes in cerebral oxygen saturation over time ($P = .901$), without any interaction between the timing of the measurements and the type of CPB ($P = .584$).

In both groups, a significant decrease in arterial pH was evident only after the removal of CPB ($P < .001$) (Figure B). Overall, the 2 groups did not differ with regard to the changes over time ($P = .685$), without any interaction between the timing of the measurements and the type of CPB ($P = .313$).

In both groups, a steady increase in arterial lactate levels was observed over time (Figure C). Overall, the non-pulsatile CABG group had significantly higher arterial lactate levels over the measurement period ($P = .017$), which was not

affected by the timing of the measurements (P = .350).

In addition, the changes in venous pH and venous lactate were similar across the non-pulsatile and pulsatile group before and after CPB: pH, -0.04 ± 0.05 versus -0.04 ± 0.07, P = 0.989; lactate, 0.97 ± 0.85 versus 0.86 ± 1.36, P = .165.

An additional analysis of potential predictors for a high maximum decrease in cerebral oxygen saturation (based on the difference between the baseline value and the lowest value measured) identified preoperative platelet level as a significant independent predictor of a maximum decrease. For a platelet count < 150 x10^9/L, OR for a maximum decrease greater than median (>11% decrease) was 8.6 (95% CI, 1.9-40.7, P = .006). Corresponding figure for a platelet count smaller than median (<238 x10^9/L) was 2.4 (95% CI, 1.2-4.9, P = .015).

Postoperative outcomes: Postoperative drainage, duration of ventilation and duration of hospital stay significantly were higher in the non-pulsatile CPB group. On the other hand, postoperative blood urea nitrogen (BUN) significantly was higher in the pulsatile CPB group. The 2 groups did not differ with regard to other postoperative outcomes, including complications and early mortality. None of the patients developed mediastinitis or cerebrovascular accident postoperatively.

DISCUSSION

Our study comparing the use of pulsatile versus non-pulsatile flow patterns during CPB did not detect any positive effect of the former approach on cranial NIRS measurements performed at different stages of the CPB. Again, there were no significant differences in postoperative morbidity and mortality rates when the 2 methods were compared.

Despite numerous drawbacks associated with its use, CPB remains an indispensable component of cardiac surgical procedures [McKhann 2006]. In this regard, the ideal flow pattern to minimize the disadvantages of CPB remains a matter of controversy. While a non-pulsatile flow pattern is associated with vasoconstriction and capillary collapse in the arterial and venous systems [Watanabe 1990], a pulsatile flow pattern augments microcirculation via an associated surplus hemodynamic energy, reduces the release of vasoconstrictive agents, and increases tissue perfusion [Undar 2004], as evidenced by a number of previous studies [Alkan 2007; Undar 2000; Undar 2002; Undar 2001].

Furthermore, some authors have claimed that pulsatile blood flow may increase tissue oxygenation through augmentation of the cranial blood flow and microcirculation [Tranmer 1986; Watanabe 1990], in addition to observations suggesting better cranial protection, particularly during the warming period [Mutch 2000]. It may be assumed that NIRS may fail to provide accurate results, since it measures the oxygenation in both arterial and venous components, during the cooling stage in CPB [Grubhofer 2000]. However, it still is considered to be one of the most valuable follow-up tools for cranial oxygenation, since it is not an invasive method [Haydin 2013]. In one study utilizing NIRS for measuring cerebral tissue oxygenation, pulsatile flow pattern was associated with a lower degree of reduction in NIRS as well as with a reduced rate of neurological complications [Su 2011]. In contrast with these observations, the 2 groups in our study were not significantly different, in terms of NIRS change at different measurement time-points, i.e. pre-CPB, after initiation of CPB, post-cross-clamp, and at the termination of CPB, suggesting no additional advantages for pulsatile flow with regard to NIRS change.

Better postoperative hemodynamic indices after termination of CPB has been reported with the use of pulsatile flow [Murkin 1995]. Increased lactate levels represents one of the best indicators of tissue perfusion and may be associated with increased morbidity and mortality [Ranucci 2006]. In a comparative study of pulsatile vs. non-pulsatile flow, significantly lower lactate levels at different phases of CPB have been reported with pulsatile flow [O'Neil 2012], which was explained on the basis of better microcirculation at tissue level akin to normal perfusion. In line with these observations, we also found lower lactate levels with pulsatile flow than with non-pulsatile flow at every test point. However, despite significantly higher lactate in the non-pulsatile group, no mortality differences could be found between the 2 groups. Again, higher drainage levels in the pulsatile flow group and longer ventilation and hospitalization times in the non-pulsatile flow group may be considered to represent their respective advantages and disadvantages.

In spite of studies suggesting a positive effect of the pulsatile flow on renal perfusion, the exact nature of the impact of the flow pattern on kidneys is not completely understood [Alghamdi 2006; Alkan 2007]. In a recent meta-analysis categorizing postoperative renal complications into 2 groups as acute renal injury and acute renal failure [Nam 2015], pulsatile flow was found to be associated with a significant reduction in the parameters indicative of the acute renal injury, while no significant differences between non-pulsatile and pulsatile flow was observed with respect to acute renal failure rates [Nam 2015]. In the current study, a marker of renal injury, i.e. BUN, was significantly higher with the pulsatile flow, contradicting the abovementioned observations. However, similar to the study above, the 2 groups in our study exhibited no significant differences, in terms of the percentage of patients with acute renal failure.

Some authors reported a positive effect of the pulsatile flow on pulmonary function via a reduction in the pulmonary vascular resistance [Chiu 1984], while others found no positive effect on the lung function in a group of elderly subjects [Engels 2014]. When complications associated with increased pulmonary morbidity is considered, we found shorter duration of ventilation in the pulsatile group; however, groups did not differ with regard to the frequency of pulmonary effusion or pneumonia.

Despite the weight of evidence suggesting various positive effects of pulsatile flow pattern, this approach routinely has not been used in cardiac surgery, mainly due to the challenges associated with the use of this technique together with a specific perfusion technique. Furthermore, hemolysis in case of high flow and inadequate tissue perfusion in case of low flow may lead to increased morbidity. Therefore, a common

pulsatile flow scheme should be developed by clinics contemplating to use pulsatile flow pattern. Also, other circuitry elements (pump head, temperature of the perfusate, connection lines, cannula etc.) may lead to postoperative neurological problems arising from low perfusion, due to possible turbulent flow as well as from gas embolism. Again, a good quality arterial filter always should be utilized within the pumping equipment [Milano 2013]. Furthermore, the choice of the arterial cannula is important, and each component of the system should be able to convey the extra energy produced by the pulsatile flow to tissues [Undar 1998]. This study has several limitations, such as its retrospective nature and small sample size. The effect of the pumping flow pattern on cranial oxygenation has been measured with NIRS as well as with postoperative neurological evaluation. However, the impact of the pulsatile flow pattern on the brain was not investigated with an imaging study. Again, despite the presence of several other biomarkers of acute renal injury, only BUN and creatinine were utilized.

CONCLUSION

A multitude of evidence has suggested a positive effect of pulsatile flow pattern on tissue perfusion in general and on renal and cranial perfusion in particular, when it is utilized during cardiopulmonary bypass. As a result of such observations, it has been advocated as having various advantages. However, our study could not detect a hemodynamic or neurological superiority of the pulsatile flow pattern versus the non-pulsatile pattern. Despite significantly lower ventilation and hospitalization times with the use of the pulsatile flow pattern, the 2 groups did not differ significantly, in terms of postoperative morbidity and mortality. We believe that further and larger comparative studies are warranted before pulsatile blood flow pattern can be established as a routine clinical method.

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