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Original Article

Effects of pulsatile perfusion during cardiopulmonary bypass on biochemical markers and kidney function in patients undergoing cardiac surgeries

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Abstract: For several years there is no conclusive guideline on the effectiveness of pulsatile or non-pulsatile perfusion during cardiopulmonary bypass (CPB) in patients undergoing cardiac surgeries. In this study, we evaluated the effect of pulsatile versus continuous perfusion on the myocardial release of the cardiac biochemical markers including, creatine phosphokinase (CPK), cardiac creatine kinase (CK-MB), and lactate dehydrogenase (LDH), and also kidney function tests including: blood urea nitrogen test (BUN) and creatinine test (Cr) in patients that underwent both pulsatile and non-pulsatile methods before and after heart surgeries. A total of 80 patients were enrolled in this study, 40 patients in each pulsatile and non-pulsatile group. Venous blood samples were drown from each patient in two groups before operation and after operation at, 24, 48, and 72 h and analyzed separately for CPK, its cardiac isoenzyme (CK-MB), LDH, BUN and Cr. There were no significant differences between the two groups with regard to preoperative parameters such as sex, age, and body surface area. Our study shows that the effect of pulsatile perfusion on cardiac and kidney function is better than the non-pulsatile method.

Keywords: Cardiopulmonary bypass, pulsatile, non-pulsatile, biochemical markers, kidney function

Introduction

Cardiopulmonary Bypass (CPB), during open-heart surgeries facilitates cardiac manipulation and helps maintenance of hemodynamic stability [1]. CPB causes increased vascular permeability, release of oxygen free radicals and lysosomal enzymes from white blood cells, and endothelial damage. Even though non-pulsatile or continuous cardiopulmonary bypass (CPB) is used more widely than pulsatile CPB, it enhances transient dysfunction of the pulmonary system [2]. Pulsatile CPB is considered to be more natural and beneficial than continuous perfusion, because pulsatile flow provides motion of the tissue fluid around cell membrane, improves microcirculation and increases diffusion. It also facilitates decreased systemic vascular resistance and enhanced oxygen consumption [3].

Despite accepted theoretical concepts, pulsatile CPB has not been widely used; the reason is lacking objective data on the effectiveness of this method. This study aims to explore advantages or beneficial effects of pulsatile versus continuous perfusion during CPB in patients undergoing cardiac surgeries. In this study, in order to evaluate the effect of pulsatile versus continuous perfusion, the myocardial release of the important cardiac biochemical markers were examined, these factors are common markers of the myocardial stable state [4, 5]. These biochemical markers include, creatine phosphokinase (CPK), cardiac creatine kinase (CK-MB), and lactate dehydrogenase (LDH), and also kidney functional tests including: blood urea nitrogen test (BUN) and creatinine test (Cr) in patients that underwent both pulsatile and non-pulsatile methods before and after heart surgeries were examined.

Patients and methods

This randomized controlled trial was carried out at Imam Khomeini Hospital, Ardabil, Iran. An

Table 1. Demographics and characteristics

	Pulsatile	Non-pulsatile
Gender (male/female)	20/20	21/19
Age (years old)	61.4 ± 12.3	60.1 ± 8.7
Height (cm)	167.1 ± 9.7	165.3 ± 8.7
Weight (kg)	75.2 ± 11.9	73.8 ± 15.6
Body Surface (m^2)	1.884 ± 0.255	1.826 ± 0.209

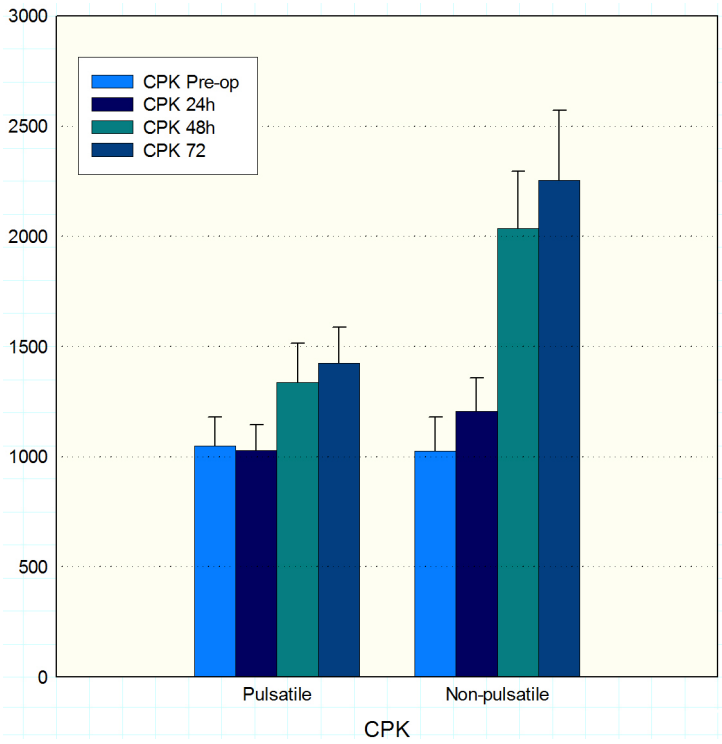

Figure 1. Creatine phosphokinase (CPK) concentration in pulsatile and non-pulsatile groups, 24 h, 48 h, and 72 h after operation.

ethics committee of Human Research of Ardabil University of Medical Sciences approved the study. Measurement of biochemical markers and kidney function after cardiovascular surgeries is routine and all patients gave an informed consent before enrolment.

Anesthesia

Anesthetic technique was standardized and performed according to a standard protocol [6].

All patients underwent central venous pressure (CVP) through the right internal jugular vein for continuous hemodynamic monitoring before anesthetic induction.

Postoperative chest roentgenogram approved its exact positioning. Anesthetic technique was the same for all patients: induction of anesthesia consisted of intravenous propofol infusion at 3 mg/kg combined with fentanyl administration at 0.1 mg/kg. Neuromuscular blockade was achieved by 4 mg/hour pancuronium bromide, and lungs were ventilated to normocapnia with air and oxygen (45% to 50%). A positive end-expiratory pressure (PEEP) was set at 5 mm Hg.

Application of cardiopulmonary bypass perfusion was performed using Stöckert S5 roller pump.

Blood sampling and biochemical markers

Venous blood samples were drown from each patient in two groups before operation and postoperatively at, 24, 48, and 72 h and analyzed separately for CPK, its cardiac isoenzyme (CK-MB), LDH, BUN and Cr.

All samples were immediately centrifuged for 10 min at 3000 g (rcf), and serum enzyme activities were measured at 37°C. Serum BUN, Cr, CPK, CK-MB, and LDH determinations were done by means of test kits (Pars Azmoon, Iran) using an auto-analyzer system (BT 3000, Italy).

Statistical analysis

Statistical analysis was performed using a graph and data analysis software package (SigmaPlot 12.0, Systat Software, Inc.). Data are presented as mean ± SD, except in figures where error bars represent SEM. ANOVA tests followed by the pairwise Student-Newman-Keuls test for multiple comparisons were performed to check for differences. *P* value less than 0.05 was considered significant.

Results

There was no recorded case of mortality or morbidity in the two groups of patients. There were no significant differences between the two groups with regard to preoperative param-

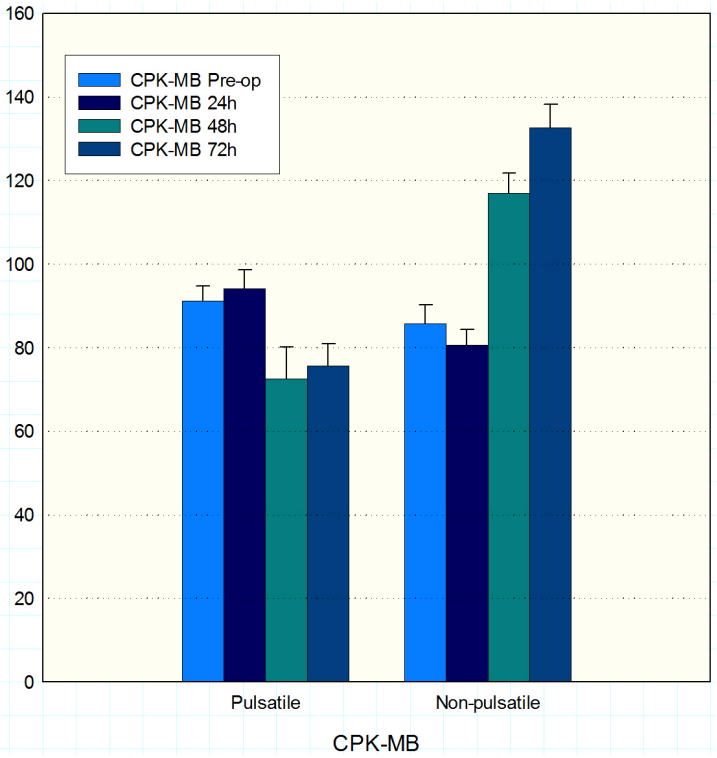

Figure 2. Cardiac creatine kinase (CK-MB) concentration in pulsatile and non-pulsatile groups, 24 h, 48 h, and 72 h after operation.

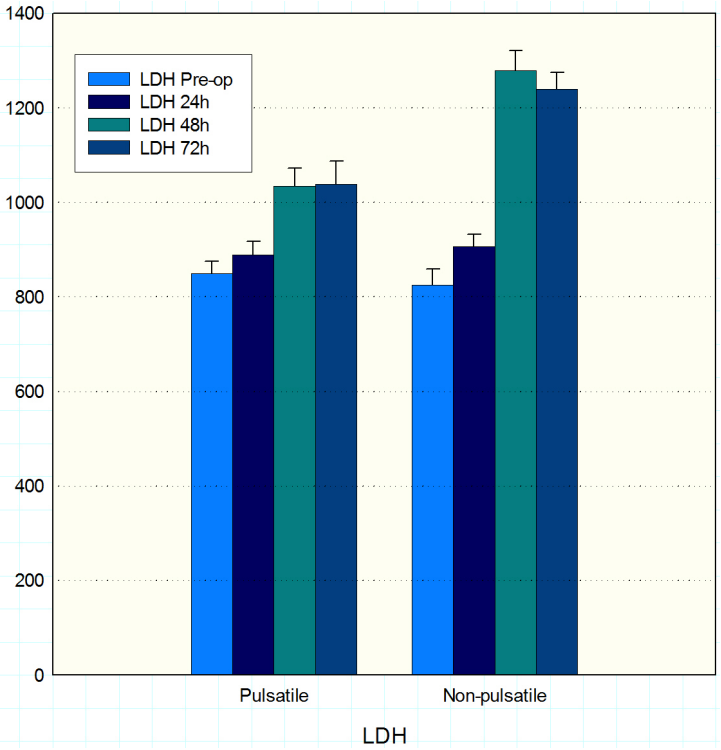

Figure 3. Lactate dehydrogenase (LDH) concentration in pulsatile and non-pulsatile groups, 24 h, 48 h, and 72 h after operation.

eters such as sex, age, and body surface area. Cumulative cardiac biochemical markers and kidney function release were calculated as the mean net release before operation and at all 3 measuring time points after operation.

Baseline characteristics of the two groups are summarized in **Table 1**. Both kidney function tests showed that the BUN and Cr were dysregulated more in non-pulsatile group in comparison to the pulsatile group.

Serum concentrations of CPK decreased at 24 h ($p = 0.03$). but increased afterward and reached a peak level at 72 h after operation in both groups; but these increase were much higher in the non-pulsatile group (**Figure 1**, $p \leq 0.001$).

Levels of CK-MB postoperatively were markedly greater in the non-pulsatile at 48 h and 72 h, in contrast, its levels were decreased in the same time points in pulsatile group (**Figure 2**, $P \leq 0.001$).

Serum levels of LDH were increased in both groups postoperatively, but its levels were increased significantly in non-pulsatile patients (**Figure 3**, $p \leq 0.001$).

In addition, same with myocardial injury markers, kidney function markers, were also dys-regulated much more in non-pulsatile group than the pulsatile group. Blood Cr was increased at 48 and 72 hours more considerably in non-pulsatile than in pulsatile group (**Figure 4**). Additionally, blood BUN values were decreased in pulsatile patients at 24 h ($p \leq 0.001$), also at 48 h and 72 h ($p = 0.01$), (**Figure 5**). However, in non- pulsatile patients, BUN was diminished at 24 h ($p = 0.01$), but it were increased at 48 h and 72 h ($p \leq 0.001$).

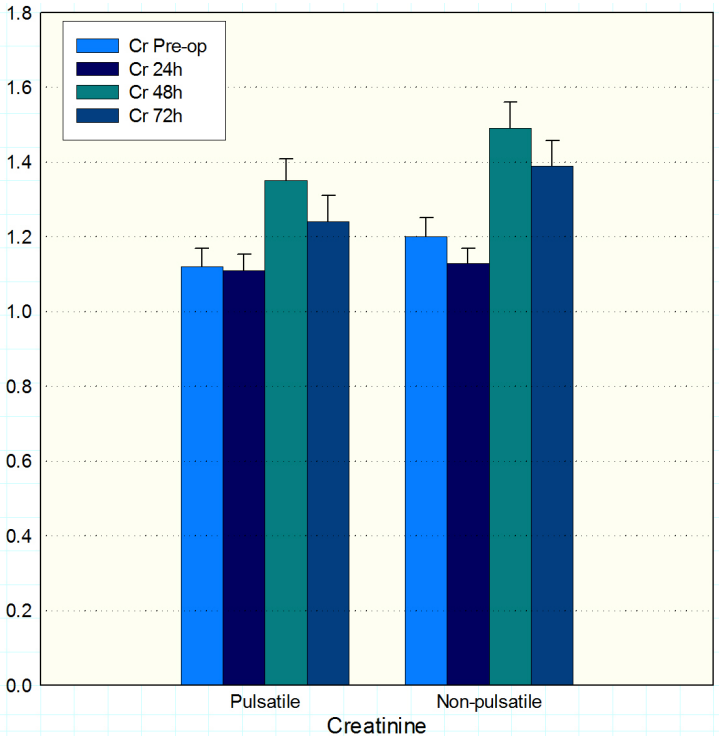

Figure 4. Creatinine (Cr) concentration in pulsatile and non-pulsatile groups, 24 h, 48 h, and 72 h after operation.

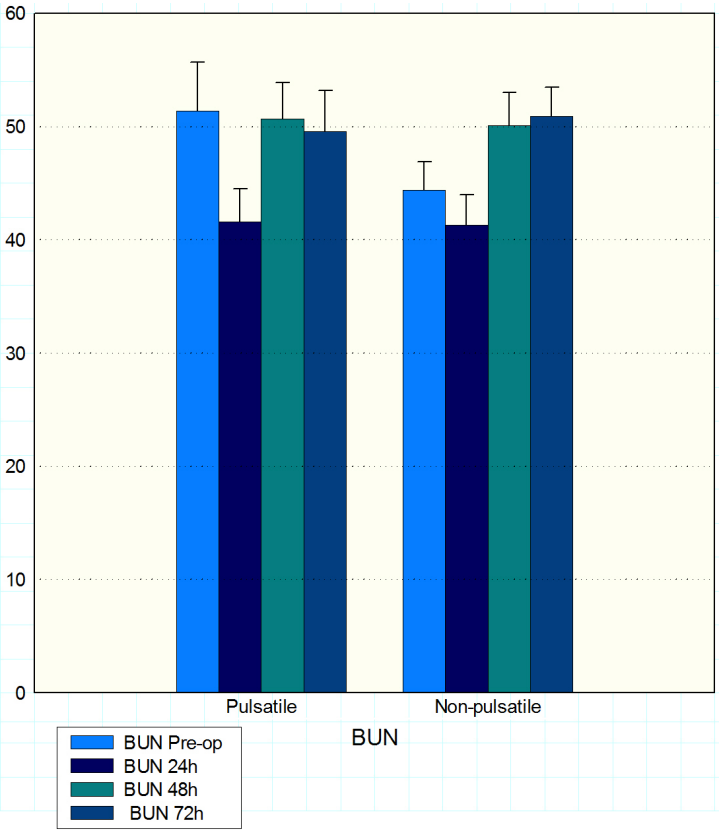

Figure 5. Blood urea nitrogen test (BUN) concentration in pulsatile and non-pulsatile groups, 24 h, 48 h, and 72 h after operation.

Discussion

The literature suggests that pulsatile flow should be routinely used during CPB in moderate- to high-risk open heart surgery. In recent years, increasing evidence supports a shift toward pulsatility in open heart cardiac surgeries over non-pulsatility [7]. Clinical evidences show better cardiac, renal, and pulmonary outcomes in patients receiving pulsatile perfusion [8-10]. The beneficial impact of pulsatile flow include reducing the systemic inflammatory response syndrome associated with bypass, decreased need for inotropic support, shortened hospital stay, and superior organ preservation [9, 11, 12]. Additionally, it has been found that the use of pulsatile flow during and after pediatric open heart surgery resulted in improved patient outcomes in terms of preserving better cardiac, renal, and pulmonary functions in the early post-CPB period [13].

There is a continuing debate about the physiologic impact of non-pulsatile perfusion. Possible reasons for inconsistency and ongoing controversy could be the difference in the hemodynamic energy levels produced by specific pulsatile and nonpulsatile pumps, using improper patient-selection criteria, inappropriate manipulation of pulsatile flow during CPB, and choosing unsuitable extracorporeal-circuit components [14].

However, our results are consistent with other findings that demonstrate the effectiveness of the pulsatile perfusion. Myocardial injury markers showed that changes in non-pulsatile method were more significant. Surprisingly, CPK-MB levels were decreased in pulsatile group at 48 h and 72 h after operation, on the contrary, its levels in non-pulsatile group were drastically increased at the

same time points (**Figure 2**). Furthermore, results for CPK and LDH have the same meaning. CPK and LDH values were markedly increased in non-pulsatile group than the pulsatile group (**Figures 1** and **3**).

On the other side, kidney function markers showed consistent results with cardiac biochemical markers. Cr levels were increased more significantly in non-pulsatile group at 48 h and 72 h postoperatively than the pulsatile group (**Figure 4**) In addition, BUN levels were decreased in pulsatile patients at three time points especially after 24 h; but in non-pulsatile patients its levels decreased at 24 h and increased 48 h and 72 h after operation (**Figure 5**).

All in all, our study shows that the effect of pulsatile perfusion on cardiac and kidney function is better than the non-pulsatile method. It would be beneficial if other studies evaluate other of circuit components and patient outcomes. Nonetheless, it has to be mention that other large-scale clinical trials would be much more confirmative.

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Disclosure of conflict of interest

None.

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