Original Article

The Effect of Pulsatile Blood Flow during Proximal Graft, on Liver Function in Coronary Artery Bypass Graft Surgery

Seyed Mohammadreza Amouzegar Zavareh[1], Marzieh Lak[1]*

1. Department of Anesthesiology, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Abstract

Background: Liver dysfunction is a rare complication with high mortality and morbidity rate in coronary artery bypass grafting (CABG) surgery. Pulsatile blood flow probably maintains liver function during cardiopulmonary bypass (CPB).

Methods: In this randomized clinical trial study, 68 patients who underwent CABG surgery were divided into two groups: pulsatile and non-pulsatile groups. We transferred continuous blood flow to pulsatile blood flow during proximal graft by using cardiac contraction.

Results: There was no significant difference in Alanine transaminase (ALT) and alkaline phosphatase (ALP) values at variable times between the groups. In addition, the procedure of ALT and ALP in the case and control groups was not significantly different in three days. There was no significant difference between AST values at variable times in two groups. However, the trend of AST in the case group was significantly increased while it was not significantly different in the control group during the next three postoperative days.

Conclusion: It seems that hemodynamic stability is more important than type of blood flow in maintaining liver function.

Keywords: pulsatile perfusion, cardio pulmonary bypass, liver function

Please cite this article as: Amouzegar Zavareh SMR, Lak M. The Effect of Pulsatile Blood Flow during Proximal Graft, on Liver Function in Coronary Artery Bypass Graft Surgery. J Cell Mol Anesth. 2018;3(3):108-13.

Corresponding Author: Marzieh Lak, MD, Baqiyatallah University of Medical Sciences Tehran, Iran.
Email: marziehlak@yahoo.com

Introduction

Liver dysfunction is a rare complication with high mortality and morbidity in coronary artery bypass grafting (CABG) surgery (1). Maintenance of pulsatile circulation during cardiopulmonary bypass (CPB) is simple and is closer to natural physiology (2). According to Pappas and his colleagues who evaluated glutamic oxaloacetic transaminase as a marker of liver function found that pulsatile blood flow preserves liver function. Mathie *et al.* found similar results in canine models and furthers clinical studies showed that pulsatile blood flow improves tissue perfusion and microcirculation with maintenance of liver function and lower blood levels of AST than non-pulsatile circulation (3).

Pulsatile blood flow probably maintains microcirculation in selective arterioles, which are collapsed during non-pulsatile flow. It reduces the increased blood levels of AST, ALT and liver cellular damage (4).

Koning *et al*. stated that pulsatile circulation lead to rapid recovery of microcirculatory perfusion at the end of CPB in CABG surgery. This is the first study with the use of side stream dark field imaging of the sublingual micro circulation which showed maintenance of microcirculatory perfusion during pulsatile blood flow (5).

Methods

This prospective, randomized study was composed of 70 consecutive patients who underwent a CABG surgery. Ethics committee approval was received along with the informed consent of each patient. The same surgical team operated on all of the patients who were randomly divided into two groups. Randomization was stratified using a random table number. Non-pulsatile CPB was performed on 35 patients, and pulsatile flow CPB was carried out on 35 others. We assessed the preoperative liver function of each patient by examining the serum AST, ALT and alkaline phosphatase (ALP).

Patients with a history of renal disease, a history of liver disease and impaired liver function tests, insulin dependent diabetes mellitus (DM), morbid obesity (BMI≥40), redo surgery, needing intra-aortic balloon pump, and valvular heart disease were excluded from the study. All of the participants underwent elective surgeries; emergent cases were not included.

For patients who took anticoagulant medication, the drug was stopped 7 days before surgery. Patients received intramuscular Morphine (5 mg) and oral Lorazepam (1 mg) 1 hour before surgery.

The patients were taken to the operating room under standard monitoring. In addition, vital signs and invasive blood pressure monitoring via left radial artery were recorded. Induction of anesthesia was carried out by Fentanyl (7 µg/kg), Diazepam (0.15 mg/kg), and Atracurium (0.5 mg/kg), if needed to the loss of eyelash reflex by continuous Propofol infusion.

After orotracheal intubation, maintenance of anesthesia consisted of Fentanyl (0.07 µg/kg/min), Midazolam (0.5 µg/kg/min), Atracurium (0.8 µg/kg/min) and, if necessary, Propofol (20–200 mg/h). All patients underwent Mechanical ventilation while ETCO2 was maintained between 35 and 40 mmHg. Central venous catheter (CVC) was inserted in right internal jugular vein. Patient's vital signs, including blood pressure (BP) by the invasive method, prothrombin ratio (PR), core temperature via nasal probe, SPO2 and ET CO2 and CVP were recorded every five minutes. Arterial blood gas analysis (ABG) was performed after installing the arterial line, induction of anesthesia and immediately after the starting and stopping the CPB. Systolic blood pressure was kept between 100 to 110 mm Hg by using beneficial effects of nitroglycerin (TNG) and inotrope agents . After sternotomy and releasing of internal thoracic artery and saphenous vein, Heparin was injected.

Activated coagulation time (ACT) was controlled 3 to 5 minutes after injection of Heparin. In case of ACT≥480s patient were connected to CPB pumps (pump type was Stockert S3 which is a roller Pump, and fluid Prime includes Ringer, Voluven, heparin, sodium bicarbonate, mannitol, Tranexamic acid). Patients were cooled to 32°C to 34°C. During cardiopulmonary bypass mean arterial pressure was maintained between 60 to 80 mm Hg by using noradrenaline or TNG. After completion of the flow (Full Flow) mechanical ventilation was stopped. Transformation of total cross clump to partial clump was started after completing–the distal grafts. In pulsatile group, ventilation resumed with 1/3 of tidal volume and heart was filled by partial clumping of venous cannula accompanied with reduction of 20-30% in venous return.

In this way, the non-pulsatile blood flow was transformed to pulsatile blood flow by using patient’s own cardiac contraction. In non-pulsatile group continuous blood flow was kept on. In both groups, temperature was increased to 36-37°C and ventilation was completed after the completion of proximal grafts. After confirming acceptable situation such as Hct≥22, normal electrolytes and acid base status, patients were separated from CPB. Protamine sulfate was administered to reverse the heparin. After completion of surgery, patients transferred to ICU-OH.

Weaning and extubation were performed according to standards of ICU-OH such as full consciousness, hemodynamic stability, control of drainage, and chest X-ray acceptable. Patients' laboratory tests such as serum AST and ALT were measured at the arrival to the ICU-OH and 24 and 48 hours after admission.

Descriptive statistics such as mean, SD and percentage were calculated for the presented data. The Kolmogorov–Smirnov test was used for normality of the data. Chi-square test, repeated measure, ANOVA and t-test were used for determining the association between variables. SPSS® software version 18 (SPSS Inc., Chicago, Ill., USA) was used for data analysis. The significance level for all the tests was considered less than 0.05.

Results

Seventy patients were evaluated in this study. Two patients in control group were excluded due to lack of blood samples to check for liver tests. Total of 33 patients in the control group and 35 patients in the case group were examined. There was no significant difference between the two groups regarding gender, age, BMI, DM, and hypertension (Table 1). In addition, there was no significant difference between the two groups regarding CPB time, cross clamp time, and the number of grafts, systolic and diastolic blood pressure preoperative (Table 2). Table 3 depicts AST mean of the study sample. The average AST of the participants preoperatively, day 1, day 2 and day 3 post-operative was not a significant difference between the two groups (P=0.067, P=0.194, P=0.480 and P=0.726, respectively). But the procedure of AST in the case group were significantly different in three days (P=0.004) but in the control group were not significant (P=0.051) (Table 3, Figure 1)

Average ALT of the participants preoperatively and in the post-operative period was not significantly different between the two groups (P=0.575, P=0.261,

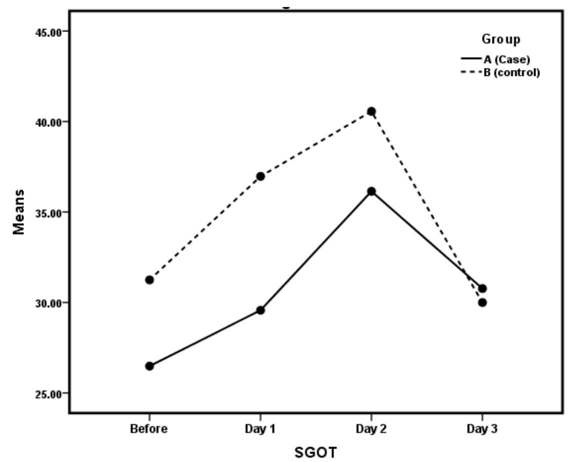

Figure 1. Comparison between mean AST values at Variable Times in Two Groups.

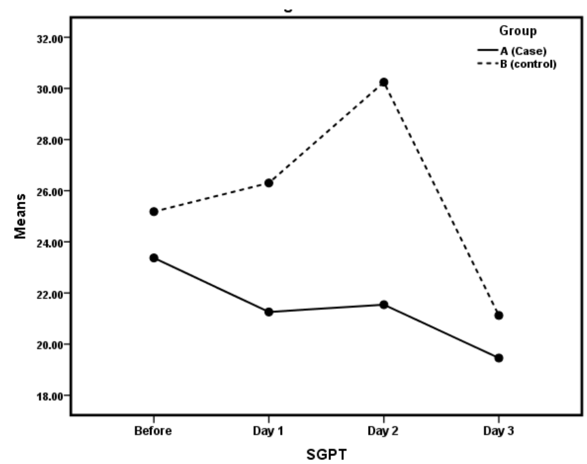

Figure 2. Comparison between mean ALP values at different times in the two study groups.

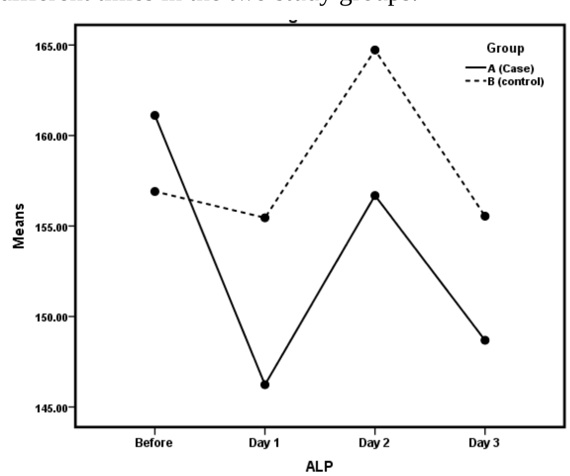

Figure 3. Comparison Between mean ALP values at different times in the two study groups

Table 1: Demographic values and history of comorbidities in the two study groups

		Case n = 35	**Control** n = 33	**P value**
Age Mean (±SD)		61.89(±8.98)	62.06(±7.64)	0.931
BMI Mean (±SD)		30.59(±2.97)	30.88(±3.33)	0.773
Gender Frequency (%)	Male	25(71.4%)	27(81.8%)	0.313
	Female	10(28.6%)	6(18.2%)	
Diabetes Mellitus Frequency (%)	Negative	25(71.4%)	17(51.5%)	0.091
	Positive	10(28.6%)	16(48.5%)	
Hypertension Frequency (%)	Negative	13(38.2%)	9(27.3%)	0.339
	Positive	21(61.8%)	24(72.7%)	

Table 2: Comparison between two groups regarding mean CPB (cardiopulmonary bypass) and cross clump times, systolic and diastolic blood pressure and number of grafts

	Case n = 35	**Control** n = 33	**P**
CPB Time (hour: minute) Mean (±SD)	1:03(±0:22)	0:58(±0:19)	0.357
Cross Clamp (hour: minute) Mean (±SD)	0:31(±0:14)	0:33(±0:15)	0.620
Systolic (before) mean(±SD)	120.61(±21.48)	112.18(±21.76)	0.110
Diastolic (before) Mean (±SD)	64.29(±15.39)	57.02(±14.18)	0.073
Graft Mean (±SD)	3.45(±0.72)	3.42(±0.61)	0.871

Table 3: Comparison between mean AST values at different times in the two study groups

	SGOT Before	**SGOT Day1**	**SGOT Day2**	**SGOT Day3**	**P**
Case (n = 35)	26.49(±10.44)	29.57(±10.25)	36.14(±19.11)	30.77(±10.69)	0.004
Control (n = 33)	31.25(±16.44)	36.97(±28.05)	40.56(±26.32)	30.00(±14.44)	0.051
P value	0.167	0.194	0.480	0.726	-

P=0.107 and P=0.583, respectively). In addition, the ALT values in the case and control groups were not significantly different in three days (P=0.104 and P=0.218, respectively) (Table 4, Figure2).

The average ALP of the participants preoperatively in days 1-3 post-operative was not a significant difference between the two groups (P=0.755, P=0.442, P=0.493 and P=0.499, respectively). Procedure of ALP in the case and control groups were not significantly different in three days (P=0.166 and P=0.390, respectively) (Table 5, Figure 3).

Discussion

In this study, we examined 33 patients in control group and 35 patients in case group. There was no significant difference between two groups regarding age, sex, BMI, history of DM or HTN, CPB time, cross clump time and number of grafts. Pre-operative systolic and diastolic blood pressure was not significantly different between two groups. We tried to maintain intra operative and cross clump blood pressure by proper application of several drugs. There was no significant difference in ALT and ALP values at variable times in two groups. In addition, the procedures of ALT and ALP in the case and control groups were not significantly different in three days.

There was no–significant difference in AST values at variable times in two groups. However, the trend of AST was significantly increased in the case group; while this trend was not significantly different in the control group during the next three days. However, due to the P=0.051 in control group, this significant increase could be anticipated. Perhaps increasing the number of samples can resolve this ambiguity.

Given that even a very short time pulsatile flow can be effective on hemodynamics and vital organ function, in this study, we transferred continuous blood flow to pulsatile blood flow during proximal graft by using cardiac contraction. In this way after completion of distal graft, the surgeon turned cross clump to partial clump and after starting of heartbeat, we decreased the venous return 20-30% by partial clumping in venous cannula. This effect on liver function was benchmarked.

In a study by Mori *et al*. on 56 dogs, they did cardiopulmonary bypass with hypothermia in 20 C and total circulatory arrest for 40 minutes. They found that liver blood flow gradually decreased in both groups due to cooling while this effect was more in non-pulsatile than pulsatile group and this difference was significant between two groups before total circulatory arrest but it wasn't significant during rewarming (6).

In an another study by Poswal *et al*. on 100 patients undergone coronary artery bypass grafting (CABG) on CPB with normal left ventricular function, the effect of pulsatile blood flow on the platelet number and function, coagulation state, renal and liver function was studied. They found that the platelet number was decreased in both groups but they were not significant. The hemoglobin concentration was decreased in both groups. The liver enzymes were increased in two groups similarly which was not significant. The increase in AST and ALT levels postoperatively at 24 and 48 hours in non-pulsatile group were higher than pulsatile group (4).

Sabzi *et al*. evaluated the liver function tests on 200 patients undergoing CPB. They saw the significant elevation in Bilirubin and aspartate aminotransferase (AST) and ALP levels on the 3rd day postoperatively. They found a clear relation between hypotension and change in ALP and AST (7).

Bingyangji and Akifundar by studying of 194 article (74 study on animals and 85 clinical trials) in 1952-2006 explained that pulsatile blood flow increases the blood flow of the brain, heart, liver and pancreas significantly and it decreases the inflammatory responses and the mortality and morbidity rate after surgery with CPB. They didn't report any side effects of pulsatile flow (8).

Conclusion

The results of this study suggests that if hemodynamic stability is restored (using vasoactive agents), liver damage and increasing liver enzymes could be prevented in both study groups (*i.e.* surgical operation under CPB with pulsatile and non-pulsatile blood flow). However, pulsatile blood flow has no negligible effect on the liver enzymes changes. Judgment about the effects of this technique on liver function is dependent on the results of further studies.

Acknowledgment

The authors would like to acknowledge the kind help of their colleagues in the operating room and Anesthesiology Department.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

1. Shahbazi S, Panah A, Sahmeddini MA. Evaluation of factors influencing liver function test in on-pump coronary artery bypass graft surgery. Iran J Med Sci. 2013;38(4):308-13.
2. Hökenek F, Gürsoy M, Bakuy V, Kavala AA, Demir T, Gülcan, F, et al. An evaluation of renal functions in pulsatile and non-pulsatile cardiopulmonary bypass in the elderly. Turk J Thorac Cardiovasc Surg. 2013; 21(3): 610-5.
3. Gravlee GP. Epidural analgesia and coronary artery bypass grafting: the controversy continues. J Cardiothorac Vasc Anesth. 2003;17(2):151-3.
4. Poswal P, Mehta Y, Juneja R, Khanna S, Meharwal ZS, Trehan N. Comparative study of pulsatile and nonpulsatile flow during cardio-pulmonary bypass. Ann Card Anaesth. 2004;7(1):44-50..
5. Koning NJ, Vonk AB, van Barneveld LJ, Beishuizen A, Atasever B, van den Brom CE, Boer C. Pulsatile flow during cardiopulmonary bypass preserves postoperative microcirculatory perfusion irrespective of systemic hemodynamics. J Appl Physiol (1985). 2012;112(10):1727-34. .
6. Mori A, Watanabe K, Onoe M, Watarida S, Nakamura Y, Magara T, Tabata R, Okada Y. Regional blood flow in the liver, pancreas and kidney during pulsatile and nonpulsatile perfusion under profound hypothermia. Jpn Circ J. 1988;52(3):219-27.
7. Sabzi F, Faraji R. Liver Function Tests Following Open Cardiac Surgery. J Cardiovasc Thorac Res. 2015;7(2):49-54.
8. Ji B, Undar A. An evaluation of the benefits of pulsatile versus nonpulsatile perfusion during cardiopulmonary bypass procedures in pediatric and adult cardiac patients. ASAIO J. 2006;52(4):357-61.

Table 4: Comparison between mean ALP values at different times in the two study groups

	ALT Before	ALT Day1	ALT Day2	ALT Day3	P
Case (n = 35)	23.37(±12.79)	21.26(±10.42)	21.54(±10.35)	19.46(±10.29)	0.104
Control (n = 33)	25.19(±13.68)	26.30(±23.35)	30.24(±28.57)	21.12(±14.38)	0.218
P	0.575	0.261	0.107	0.583	-

Table 5: Comparison between mean ALP values at different times in the two study groups

	ALP Before	ALP Day1	ALP Day2	ALP Day3	P
Case (n = 35)	161.11(±57.72)	146.23(±49.61)	158.69(±48.89)	148.69(±40.06)	0.166
Control (n = 33)	156.91(±52.64)	155.45(±48.64)	164.73(±47.21)	155.55(±41.94)	0.390
P	0.755	0.442	0.493	0.499	-