

Analysis of Hemodynamics and Biochemical Profile during Coronary Artery Bypass Surgery using Cardiopulmonary Bypass

Suna Aydin¹, Mehmet Kalayci², Mehmet Nesimi Eren³, Musa Yilmaz⁴ and Suleyman Aydin^{4*}

¹Clinic of Cardiovascular Surgery, Elazig Research and Education Hospital, Elazig, 23119, Turkey

²Department of Anatomy, School of Medicine, Firat University, Elazig, 23119, Turkey

³Department of Cardiovascular Surgery, School of Medicine, Dicle University, Diyarbakir, 21280, Turkey

⁴Department of Medical Biochemistry (Firat Hormones Research Group), School of Medicine, Firat University, Elazig, 23119, Turkey

Abstract

Cardiopulmonary Bypass (CPB), a non-physiological intervention that maintains the blood circulation outside the body, brings about hemodynamic and biochemical changes, but these have not been elucidated in detail. Therefore, the aim of this study was a thorough examination of the changes in hemodynamic and biochemical parameters in patients at each stage of coronary bypass graft surgery (T1; before induction of anesthesia; T2: before CBP; T3: 5 min before placement of the cross clamp; T4: 5 min after removal of the cross clamp; T5: upon admission to intensive care; T6: 24 h post-operation). Pulmonary artery pressure, Mean Pulmonary Artery Pressure (MPAP), Central Venous Pressure (CVP), and Pulmonary Capillary Wedge Pressure (PCWP) were monitored and measured using a Swan-Ganz catheter introduced via the jugular vein at five of the six periods (not the period before anesthesia was induced). Mean Arterial Pressure (MAP) was monitored and measured through an arterial line. The blood lactate level was quantified during the same time periods using a blood gas device: it fell before the placement of the cross clamp (40 mmHg), but increased after the clamp was removed and rose to 80-100 mmHg at 24 h post-operation. The heart rate decreased after anesthesia

was normal in all other periods. CVP also declined slightly after removal of the cross clamp (T4), but remained in the normal range during the remaining periods. The MPAP and PCWP values were in the normal range throughout all steps during the bypass. Among the biochemical parameters, only lactate exhibited a noteworthy change. Lactate levels increased significantly in the T1-T3 period but gradually returned to normal in T4 (5 min after removal of the cross clamp). We contend that it is essential to measure hemodynamic parameters and lactate levels in order to track the physiological changes in patients during a successful CPB operation.

Keywords: Cardiopulmonary Bypass; Graft Surgery; Cross Clamp; Artery Pressure; Venous Pressure; Lactate; Heart

***Corresponding author:** Suleyman Aydin, Department of Medical Biochemistry (Firat hormones Research group), School of Medicine, Firat University, Elazig, 23119, Turkey, E-mail: saydin1@hotmail.com

Introduction

Cardiopulmonary Bypass (CPB) is a non-physiological intervention in which the blood circulation is maintained outside the body [1]. Contacts between blood and various materials and the two rounds of clamping during the operation can cause hemodynamic changes [1-3]. In order to monitor cardiovascular physiology during CPB, hemodynamic parameters such as the heart rate, Mean Arterial Pressure (MAP), Mean Pulmonary Artery Pressure (MPAP), Central Venous Pressure (CVP), Pulmonary Capillary Wedge Pressure (PCWP), Cardiac Index (CI), Cardiac Output (CO), Pulmonary Vascular Resistance (PVR), Stroke Volume Index (SVI), Systemic Vascular Resistance (SVR), Left Ventricle Stroke Work Index (LVSWI), and Right Ventricle Stroke Work Index (RVSWI) are generally measured [4, 5]. However, there is no consensus among surgeons about some of these parameters, especially MAP [3, 6-8]. Thus, while it is widely accepted that a mean arterial pressure of 50 mmHg is safe during bypass [6], some surgeons argue that a higher intra-bypass pressure (about 70 to 80 mmHg) is safer [7]. Despite this lack of consensus [6, 7], no extensive hemodynamics studies have covered all the stages and the outcome of Coronary Artery Bypass Grafting (CABG).

CPB also alters biochemical parameters. In order to reduce morbidity and mortality during CPB, a thorough examination of cardiovascular biochemistry and physiology during the operation is needed to increase our knowledge. One of the major parameters used in monitoring CPB is lactate (2-hydroxypropanoic acid) [9-11], which is formed from pyruvate through the mediation of lactate dehydrogenase in the last step of glycolysis [12]. Lactate, discovered in sour milk in 1780, is continuously produced [13] and consumed under normal aerobic conditions [12, 13]. Since the elevation of blood lactate levels during a bypass (hyperlactatemia) is a major indicator of circulatory failure [14, 15], lactate is used in the hemodynamic monitoring of CPB [9-11]. Reportedly, some 10-20% of patients undergoing CPB have elevated lactate levels, and these are associated with high morbidity and mortality [16]. It is not clear why lactate increases during and after cardiac surgery, but most

authors argue that the increase results from the hypoxia caused by the reduced peripheral blood supply to tissues [9-11, 16]. Parameters such as glucose, potassium and lipid profiles are also utilized for physiological monitoring of CPB [17, 18].

However, the literature offers no detailed data about the effects of CPB and CABG operations on hemodynamic and biochemical parameters. The aim of the present study was to reveal how CPB affects hemodynamic parameters and whether the changes in these parameters are correlated with biochemical parameters. The variables were measured during different stages of the operation: T1: before induction of anesthesia; T2: before CPB; T3: 5 min before placement of the cross clamp; T4: 5 min after removal of the cross clamp; T5: upon admission to intensive care; T6: 24 h post-operation.

Materials and Methods

After local ethics committee approval was obtained (resolution date 29 January 2009, number 08), 15 patients undergoing CPB and CABG in the Cardiovascular Surgery Department of the University Hospital were enrolled in the study. Twelve of the patients were male and three were female, and their mean age was 68.4 ± 10.3 years. Written informed consent was obtained from all participants. The patients used no anti-hyperlipidemic drugs before or after the operation and were fed on a low-cholesterol and salt-free diet. They were on a special hospital diet for one week (percentages of carbohydrate, fat and protein 50%, 35%, 15%, respectively). The anamneses of the patients were recorded and physical examinations were performed. Exclusion criteria were: previous Chronic Obstructive Pulmonary Disease (COPD), liver disease, acute MI (Myocardial Infarction), diabetes mellitus, renal failure, history of hypo- or hyper-thyroidism, cardiac cachexia, morbid obesity, age over 80 years, active infections, history of cerebrovascular disease and severe valvular diseases [(such as mitral stenosis (MS), tricuspid regurgitation (TR)]. The Body Mass Index (BMI) of each patient was calculated by dividing the body weight in kilograms by height in meters and BMI-matched patients were included in the study.

Anesthesia and Surgical Procedure

In order to monitor the hemodynamic parameters, a central venous catheter (8F Introducer, St Jude Medical Company, USA) and a Swan-Ganz catheter (7F, Abbott Lab., USA) were inserted through the jugular vein, and an arterial catheter was placed through the femoral artery after anesthesia was induced. Anesthesia was induced and maintained using standard phentanyl (20-40 µg/kg induction, 0.3-1 µg/kg/min maintenance), Fentanyl Citrate, Abbott, midazolam (0.1 mg/kg induction, 0.8 µg/kg/min maintenance, Dormicum, Roche) and vecuronium (0.1 mg/kg induction, Norcuron, Organon).

The operation was started in all patients with a standard median sternotomy incision. Taking histological structure, the characteristics of the case, and possible technical problems into account, internal thoracic artery (gold standard) and Vena Cava Saphena Magna grafts (VSM) were prepared. Following 3 mg/kg heparinization (Nevparin, Mustafa Nevzat), an arterial cannula was inserted into the ascending aorta, a two-stage venous cannula into the right atrium, and an antegrade cardioplegia catheter into the aortic root. When the Activated Clotting Time (ACT) reached 450 s, CPB was initiated and performed using a roller pump (Stockert Instrumente, Germany) and membrane oxygenator (Dideco D 708 simplex III, Italy) under moderate hypothermia (28-32°C). In order to maintain the patient's hematocrit at 24%-26% or higher [19], the pump priming solution was a mixture of Ringer's lactate, modified gelatin solution, fresh frozen plasma, fresh whole blood and heparin. This enabled the pump to maintain the hematocrit at 25% and CPB was performed using nonpulsatile blood flow at $2.4 \text{ L min}^{-1} \text{ m}^{-2}$. The flow rate most commonly used during CPB ($2.2\text{--}2.5 \text{ L min}^{-1} \text{ m}^{-2}$) also approximates to the CI of a normothermic anesthetized patient with a normal hematocrit [20]. Care was taken to ensure that the MAP was above 60 mmHg. Following cardiac arrest, the aortic cross clamp was placed (total CPB). After the final distal anastomosis, warming was initiated. Proximal anastomoses were conducted under partial CPB using a side clamp on the aorta. At the end of the CPB, the effect of heparin was neutralized with protamine sulfate (Protamin, Roche). First the venous cannula and then the arterial cannulae were withdrawn. All other procedures are

explained in detail in our previous article [21] and in the first author's medical specialty dissertation [22].

Protection of Myocardium

Cardiac arrest was induced in all patients by blood cardioplegia, which helps to maintain myocardial tissue viability by preserving ATP stores and decreasing intramyocardial acidosis. After the cross clamp was placed on the aorta, cold (9°C) blood cardioplegia (15 mL/kg, including 30 mEq/L KCl and 24 mEq/L MgSO_4 in the first injection; and 10 mL/kg, including 15 mEq/L KCl and 12 mEq/L MgSO_4 in subsequent injections) was given anterogradely under 70-80 mmHg pressure for at least 2 min. Following the cardiac arrest, cardioplegia was maintained by repeated antegrade infusions of 500 ml every 20 min. Through the end of the bypass and before the cross clamp was removed, warm blood cardioplegia (32°C) was given anterogradely at high pressure (hot shot 400 ml).

Hemodynamic Measurements

The hemodynamic parameters measured in this study were Heart Rate (HR), Mean Arterial Pressure (MAP), Mean Pulmonary Artery Pressure (MPAP), Central Venous Pressure (CVP), Pulmonary Capillary Wedge Pressure (PCWP), Cardiac Index (CI), and Cardiac Output (CO). They were determined at six different periods: before induction of anesthesia (T1); before CPB (T2); 5 min before placement of the cross clamp (T3); 5 min after removal of the cross clamp (T4); upon admission to intensive care (T5); 24 h post-operation (T6). CO was measured through the Swan-Ganz catheter and reported using the cardiac output set (Edwards Life Sciences USA) and cardiac output device (Spectramed Hemopro, USA). Serum biochemical parameters (triglyceride, HDL cholesterol, LDL cholesterol, VLDL cholesterol, glucose) were retrieved from the hospital records.

Statistical Analyses

Statistical analyses were conducted using the software package SPSS 21.00. Study parameters were recorded as mean $\pm$ standard deviation. A Wilcoxon test was used to assess repeated measurements. Spearman test was used to examine the

correlation between hemodynamic parameters and biochemical values. The chi square (X^2) test was used to investigate whether distributions of categorical variables differ from one another. The level of statistical significance was set at $p \leq 0.05$.

Results

The demographic characteristics of the patients were as follows: mean age 68.4 ± 10.3 years, mean height 171.5 ± 30.7 cm, mean weight 74.3 ± 13.7 kg. The mean BMI was 27.5 ± 5.2 kg/m². There was no statistical difference among the patients in terms of age or BMI. The operative characteristics were: Ejection Fraction (EF) $49.3 \pm 5.3\%$, graft number 4.0 ± 0.1 , body surface

area (BSA) 1.8 ± 0.1 m², CPB duration 146 min, cross clamp time 93 ± 2.6 min, duration of stay in intensive care 2.2 days, and total duration of hospital stay 7.3 days. None of our patients had a kidney dysfunction since the creatinine levels were normal.

The MAP was 100 mmHg before anesthesia was induced but decreased slightly before CPB and dropped further to 40 mmHg 5 min before cross clamping. An attempt was made to control this decrease by increasing the pump flow. The MAP started to increase again 5 min after cross clamp removal and continued to increase when the patient was taken to intensive care. After a mild increase at 24 h post-operation it remained in the 80-100 mmHg range [Figure 1].

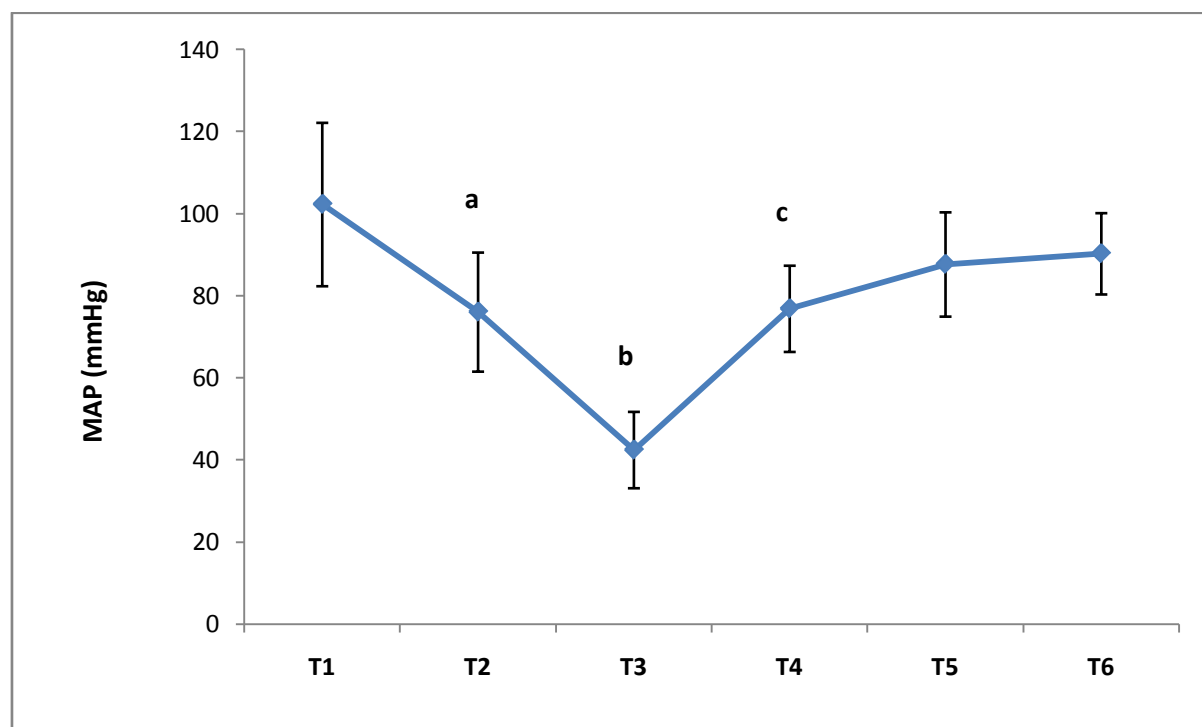


Figure 1: Changes in the mean arterial pressure of patients. a: T1 versus T2 ($p < 0.05$); b: T1 versus T3 ($p < 0.05$); c: T1 versus T4 ($p < 0.05$).

The MPAP was around 20 to 25 mmHg before anesthesia induction and declined very slightly before CPB and 5 min before cross clamping. This decrease ceased 5 min after removal of the cross clamp and the MPAP increased very

mildly when the patient was taken to intensive care. At 24 h post-operation the MPAP took a horizontal course and approached the value before anesthesia induction [Figure 2].

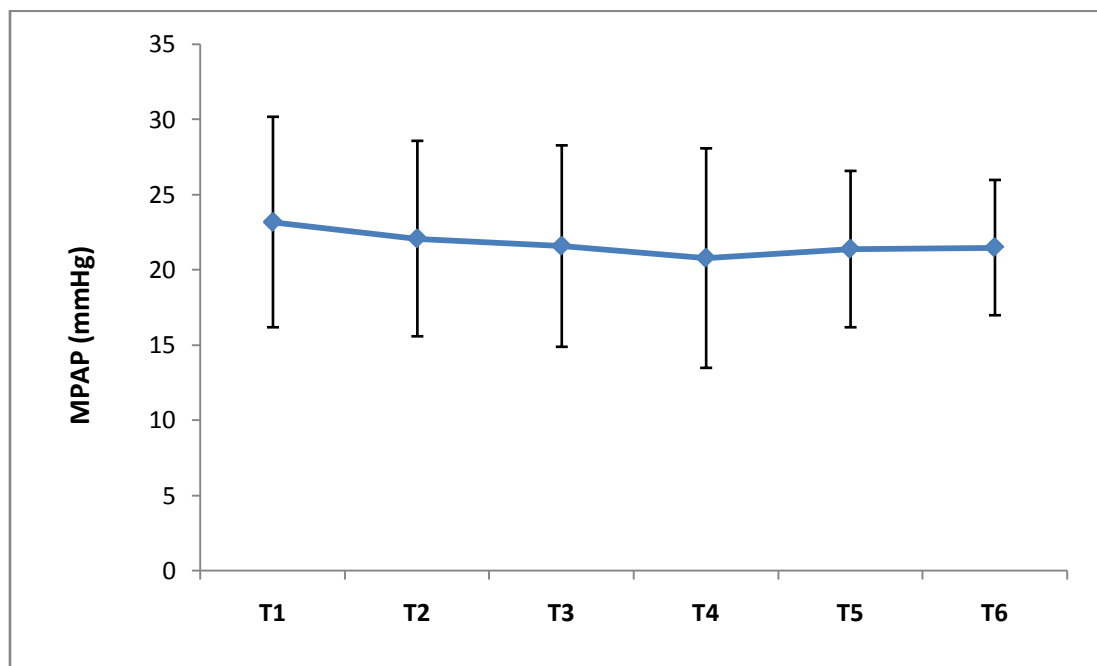


Figure 2: Changes in mean pulmonary artery pressure of patients.

The mean CVP before anesthesia induction was 8 mmHg; it decreased slightly before CPB. This decrease continued into the period starting 5 min before cross clamping (the values were not considered when the cross clamp was placed and the heart was stopped because all the values were set to zero then). The CVP

5 min after the cross clamp was removed was fixed at around 6 mmHg and increased rapidly when the patient was taken to intensive care. Following a small increase at 24 h post-operation, the CVP regained the value before anesthesia induction [Figure 3].

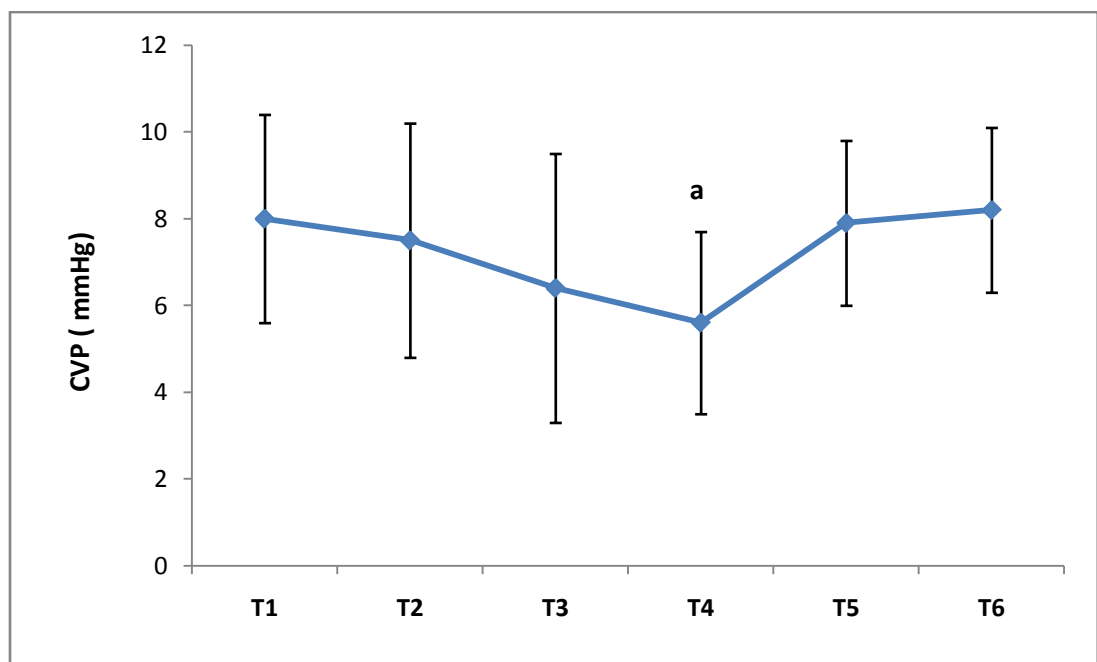


Figure 3: Changes in central venous pressure of patients. a: T1 versus T4 ($p < 0.05$).

The PCWP was around 15 mmHg before anesthesia induction and dropped before CPB. However, the mean PCWP increased 5 min before cross clamp placement, rising to the level before anesthesia induction. There was a very slight

decline 5 min after the removal of cross clamp. However, the value leveled off when the patient was taken to intensive care. The PCWP at 24 h post-operation approached a value slightly lower than that before anesthesia induction [Figure 4].

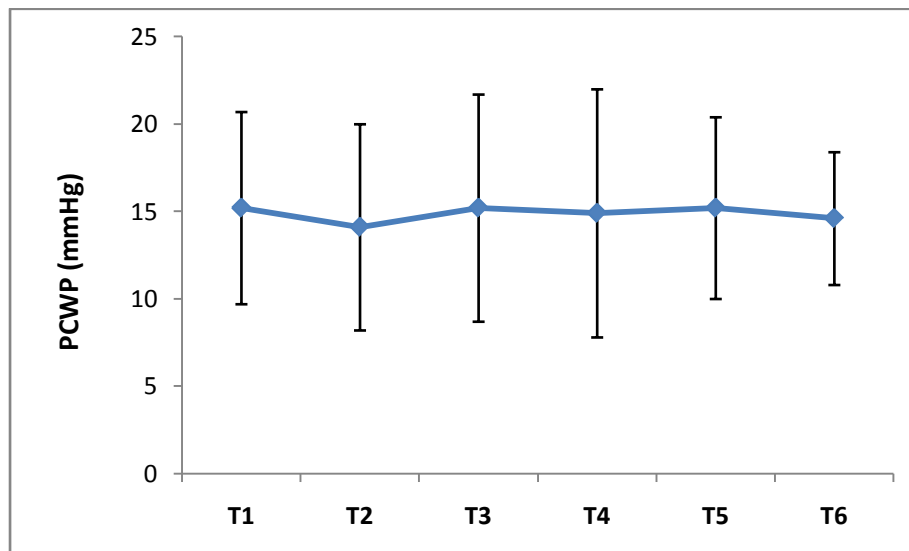


Figure 4: Changes in pulmonary capillary wedge pressure of patients.

The heart rate, which was zero at T3 during CPB surgery (when the heart is stopped and cardioplegia is delivered) was not included in the statistics or illustrated on the graph. The mean HR was 85-90 beats/min before anesthesia induction but decreased sharply to 80-85 beats/min before CPB. Five min

after removal of the cross clamp the HR increased to 90 beats/min. It followed a horizontal course when the patient was taken to intensive care and decreased slightly 24 h post-operation to the value before anesthesia induction [Figure 5].

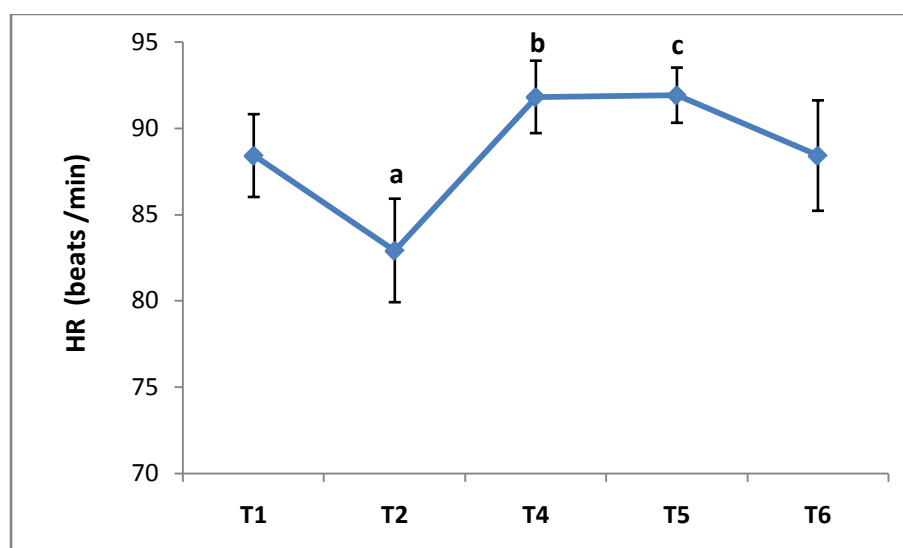


Figure 5: Changes in the heart rate of patients. a: T1 versus T2 ($p < 0.05$); b: T1 versus T4 ($p < 0.05$); c: T1 versus T5 ($p < 0.05$).

The blood lactate level was 1.0-1.5 mmol/L before anesthesia, increased slightly before CPB, and reached a peak 5 min before cross clamping. It dropped slightly 5 min after

removal of the cross clamp and declined further upon admission of the patient to intensive care. At 24 h post-operation it was at the same level as before anesthesia induction [Figure 6].

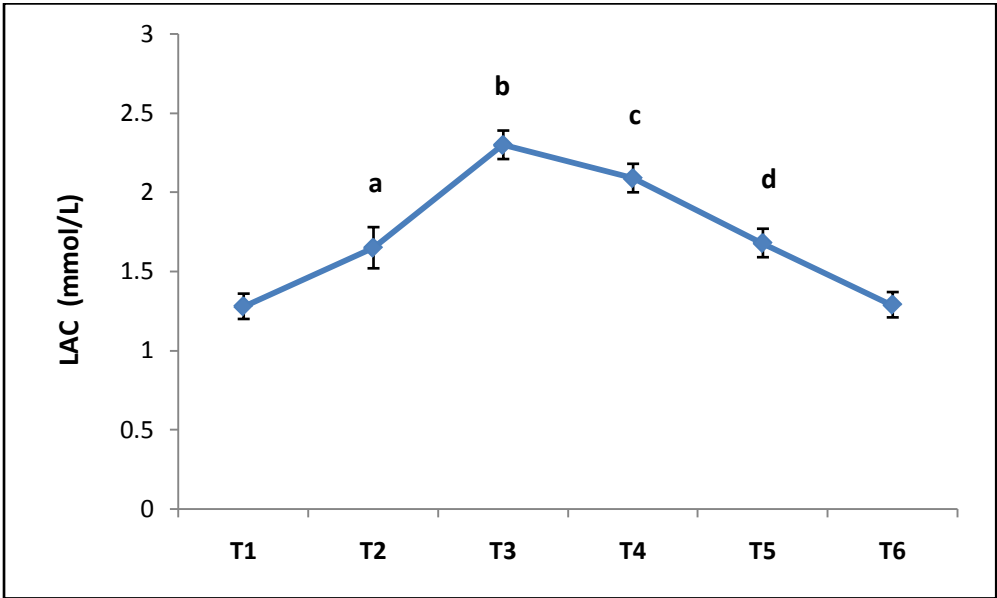


Figure 6: Changes in CPB-dependent lactate values of patients. a: T1 versus T2 ($p < 0.05$); b: T1 versus T3 ($p < 0.05$); c: T1 versus T4 ($p < 0.05$); d: T1 versus T5 ($p < 0.05$).

[Table 1] demonstrates that there were no statistical differences between the pre-operative glucose (91.4 ± 10.3 mg/dL), HDL cholesterol (47.1 ± 9.0 mg/dL), LDL cholesterol (141.6 ± 43.6 mg/dL), VLDL cholesterol (54.4 ± 38.8 mg/dL), triglyceride (249.3 ± 20.3 mg/dL), calcium (9.6 ± 0.8 mg/dL), potassium (4.3 ± 0.4 mEq/mL), or sodium (139.8 ± 2.0 mEq/mL) levels and

the post-operative glucose (89.4 ± 9.9 mg/dL), HDL cholesterol (47.9 ± 10.3 mg/dL), LDL cholesterol (120.4 ± 25.9 mg/dL), VLDL cholesterol (49.9 ± 36.7 mg/dL), triglyceride (166.2 ± 80.7 mg/dL), calcium (9.6 ± 0.3 mg/dL), potassium (4.4 ± 0.2 mEq/mL), and sodium (140.4 ± 2.6 mEq/mL) levels.

Parameter	Before operation	After operation
Glucose (mg/dL)	91.4 ± 10.3	89.4 ± 9.9
HDL-C (mg/dL)	47.1 ± 9.0	47.9 ± 10.3
LDL-C (mg/dL)	141.6 ± 43.6	120.4 ± 25.9
VLDL-C (mg/dL)	54.49 ± 38.8	49.9 ± 36.7
Triglyceride (mg/dL)	249.3 ± 20.3	166.2 ± 80.7
Calcium (mg/dL)	9.6 ± 0.8	9.6 ± 0.3
Potassium (mEq/mL)	4.3 ± 0.4	4.4 ± 0.2
Sodium (mEq/mL)	139.8 ± 2.0	140.4 ± 2.6

Table 1: Pre- and post-operation biochemical values of patients.

HDL-C: High-Density Lipoprotein-Cholesterol; LDL-C: Low-Density Lipoprotein-Cholesterol; VLDL-C: Very Low-Density Lipoprotein-Cholesterol.

There were positive correlations (r) between CVP and MAP (+0.225); CVP and PCWP (+0.269); CVP and MPAP (+0.332); HR and LAC (+0.473); MPAP and PCWP (+0.708). There were

negative correlations between CVP and LAC (-0.319); MAP and HR (-0.242); and MAP and LAC (-0.703) [Table 2].

Correlation	r value	P value
CVP – LAC	- 0.319	< 0.01
CVP – MAP	+ 0.225	< 0.05
CVP – PCWP	+ 0.269	< 0.01
CVP – MPAP	+ 0.332	< 0.001
HR – LAC	+ 0.473	< 0.001
MAP – HR	- 0.242	< 0.05
MAP – LAC	- 0.703	< 0.001
MPAP – PCWP	+ 0.708	< 0.001

Table 2: Correlations between hemodynamic and biochemical data.

CVP: Central Venous Pressure; HR: Heart Rate; LAC: Lactate; MAP: Mean Arterial Pressure; MPAP: Mean Pulmonary Artery Pressure; PCWP: Pulmonary Capillary Wedge Pressure.

Discussion

Progressive atherosclerotic narrowing of the coronary arteries disrupts the blood supply to the heart. The blood supply to the heart is restored by a CPB operation. In order to increase survival during this operation it is essential to monitor the accompanying physiological changes. For instance, the incidence of hypertension during the first 6-8 h following a coronary artery operation is reported to range between 33 and 70% [23-25]. Therefore, the MAP of the patients was monitored in this study. Although it was around 100 mmHg before anesthesia induction, it decreased slightly before CPB and dropped to 40 mmHg 5 min before the cross clamp was placed. It started to increase 5 min after removal of the cross clamp, possibly because the heart started beating again, and the increase continued after admission of the patients to intensive care possibly because the heart was regaining normal function. The values at 24 h post-operation were 80-100 mmHg.

Hypertension can develop temporarily when the anesthesia deepens during the operation and upon recovery of consciousness after anesthesia [24]. The elevation of MAP 5 min after removal of the cross clamp can be attributed to increased epinephrine and norepinephrine levels [24, 25]. Since enhanced plasma renin activity (RAA, humoral factors and autonomous reflexes, consciousness changes following anesthesia, hypothermia or painful stimuli) is involved in modulating blood pressure, we believe this could have caused the MAP and other pressure changes observed in our patients [24, 25]. However, the mean MPAP took a horizontal course through all stages of the study (from T1 to T7), with no remarkable changes before, during or after bypass surgery. These results are consistent with the unchanging MPAP in patients who underwent off-pump CABG. Like the MPAP, the PCWP exhibited no evident change. The MPCP was about 15 mmHg in our patients. It is thought that these pressure changes

could have been influenced by the inotropic support, which can modify the patient's hemodynamics during and after CPB in coronary bypass surgery [23].

This study also addressed the changes in central venous pressure [(right atrium pressure) (CVP)], another critical hemodynamic parameter: The mean CVP was 8 mmHg before anesthesia induction but fell slightly before CPB and continued to decrease 5 min before placement of the cross clamp (subsequent values were not considered since they were zero when cardioplegia was given and heart was stopped). The mean CVP stabilized close to 6 mmHg 5 min after removal of the cross clamp and increased rapidly when the patient was taken to intensive care. Following a slight increase at 24 h post-operation, the CVP regained the mean level measured before anesthesia induction. CVP values in our study were in the 6-8 mmHg range. The usual range is between 4 and 15 mmHg [26]. Therefore, the CVP remained in the normal range throughout CPB, indicating a hypovolemic state during the procedure [27]. Transfusion of large amounts of fluid into hypovolemic patients causes only minor changes in CVP, whereas increased blood volume resulting from over-transfusion elevates it significantly. Although fluid therapy to individuals with a cardiac problem can lead to remarkable increases in CVP, it is not advisable to form an opinion about blood volume on the basis of CVP values. Nevertheless, a CVP in the 4 to 15 mmHg range indicates the smooth progression of CPB surgery. Thus, CVP is a crucial hemodynamic parameter for monitoring CPB. A correlation between CVP and left heart filling pressure during blood volume changes has been reported in coronary artery disease patients (Cheung et al. 1994) where the ejection fraction was greater than 0.4 [28, 29]. The heart rate at T2 (before CPB) was lower than at T1 (before anesthesia induction). It increased between the T3 and T6 periods, becoming similar to the T1 value. The decrease can be attributed to the anesthesia, as anesthetics reduce the HR by causing vasodilatation. The increase observed after T3 could be a compensatory change to ensure the steady progression of CO. In the event of a sudden drop in CO, catecholamine secretion from the suprarenal glands increases and the HR is elevated [30]. Also, the CO decreased,

albeit statistically insignificantly, after anesthesia induction, but the HR took a normal course after the operation. These results are parallel to those obtained by Mathison et al. on CABG surgery patients [31]. The lower output could have resulted from impaired diastolic expansion of the right ventricle, left ventricle out-flow tract compression, impaired myocardial contractility, or reduced ventricular volume [32]. Although CO displays no noteworthy change during CABG, it is beneficial to measure it to monitor whether the surgery is proceeding uneventfully [31].

We studied the pre- and post-operative biochemical values of patients and found no remarkable changes. However, we contend that it is important to measure the biochemical parameters to ensure that the patient is following the normal physiological course. Hyperlactatemia is common, resulting from tissue hypoxia during coronary artery surgery, and is associated with post-operative mortality and morbidity [9-12]. Therefore, we investigated changes in blood lactate levels in our patients at all steps during the bypass. The blood lactate was 1.0-1.5 mmol/L before anesthesia induction and peaked 5 min before placement of the cross clamp. The normal lactate level is below 1.5 mmol/L [33]. We presume that the peak 5 min before cross clamping can be attributed to the degree of hemodilution, low peripheral oxygen delivery, and anaerobic cellular metabolism [34, 35]. The increased lactate in this study can be attributed to one or both of the following mechanisms: the "primary type" (type B; there is no tissue hypoxia but pyruvate is reduced to lactate) [35] and the "secondary type" (type A; there is tissue hypoxia). In the normal physiological state, lactate production is equal to lactate removal or use: 70 to 75% of the lactate is oxidized to pyruvate in the mitochondria. This is how 20% of the lactate utilized in gluconeogenesis is obtained [34].

The lactate levels in our study started to fall 5 min after removal of the cross clamp. This decrease continued after the patient was taken to intensive care. However, at 24 h post-operation, lactate was restored to the level measured before anesthesia induction. The reason for this sequence of changes, i.e. why hyperlactatemia did not develop after CPB, is that the

CPB was of short duration [34]. In procedures requiring more prolonged CPB, the oxygen supply has been reported to fall below a critical level, leading to lactic acidosis [34]. Another possible reason why the lactate levels took a normal course after surgery in our study is that no β_2 agonist was used in any patient, as a high dose of β_2 agonist for hemodynamic stabilization is also a risk factor for hyperlactatemia [36, 37].

Limitations of study

First, venous oxygen saturation (SvO_2), oxygen delivery (DO_2), and carbon dioxide production (VCO_2) were not reported although measuring these metabolic parameters during CPB is recommended by cardiac surgeons. Second, our main purpose was to investigate hemodynamics and biochemical profile alterations during coronary artery bypass surgery using CPB in patients without acute MI, diabetes mellitus, renal failure, history of hypo-or hyper-thyroidism, or cardiac cachexia, etc., as detailed in our exclusion criteria (see Materials and Methods). Therefore, our subject numbers were low (n:15) so whether the results reflected the population average can be doubted. However, it was difficult to find patients matching our criteria, and so our finding should be validated in the larger number of the prospective study.

As far as we know, this is the first study to investigate hemodynamics and biochemical profile alterations during coronary artery bypass surgery using CPB. Over the six time points, blood was taken from patients who had coronary artery occlusion but no other known diseases according to their medical records.

Conclusions

Despite these above limitations our results reveal that local myocardial ischemia resulting from clamping during coronary artery surgery leads to disruptions in hemodynamics. As known, total body oxygen consumption decreases with clamping as tissues go to anaerobic metabolism. Carbon dioxide (formed during respiration) is altered in venous and arterial blood with cross-clamp. That is why myocardial ischemia could

be occurred during clamping. Since increased cross-clamp and cardiopulmonary bypass times were associated with a significant rise in postoperative lactate levels [9]. Although all these hemodynamic changes are reported to be reversible, we believe it is essential to measure them: they are clinically important in coronary artery surgery cases as they indicate whether physiological events are proceeding normally. There was no mortality in our 15-case series of CABG. Therefore, we think that the biochemical and hemodynamic parameter values we report here could contribute to the monitoring of CPB in the future.

References

1. Aydin S, Eren MN, Sahin I, Yilmaz M, Kalayci M, et al. (2013) The cardiovascular system and the biochemistry of grafts used in heart surgery. Springerplus 2: 612.
2. Czajkowski M, Dabrowski W (2006) Changes in intra-abdominal pressure during CABG with normovolemic hemodilution. Med Sci Monit 12: 487-492
3. Ono M, Brady K, Easley RB, Brown C, Kraut M, et al. (2014) Duration and magnitude of blood pressure below cerebral autoregulation threshold during cardiopulmonarybypass is associated with major morbidity and operative mortality. J Thorac Cardiovasc Surg 147: 483-489.
4. Shinn HK, Oh YJ, Kim SH, Lee JH, Lee CS, et al. (2004) Evaluation of serial haemodynamic changes during coronary artery anastomoses in patients undergoing off-pump coronary artery bypass graft surgery: initial experiences using two deep pericardial stay sutures and octopus tissue stabilizer. Eur J Cardiothorac Surg 25: 978-984
5. Charlson ME, Peterson JC, Krieger KH, Hartman GS, Hollenberg JP, et al. (2007) Improvement of outcomes after coronary artery bypass II: a randomized trial comparing intraoperative

- high versus customized mean arterial pressure. *J Card Surg* 22: 465-472
6. Slogoff S, Reul GJ, Keats AS, Curry GR, Crum ME, et al. (1990) Role of perfusion pressure and flow in major organ dysfunction after cardiopulmonary bypass. *Ann Thorac Surg* 50: 911-918
7. Gold JP, Charlson ME, Williams-Russo P, Szatrowski TP, Peterson JC, et al. (1995) Improvement of outcomes after coronary artery bypass. A randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg* 110: 1302-1311
8. Murphy GS, Hessel EA 2nd, Groom RC (2009) Optimal perfusion during cardiopulmonary bypass: an evidence based approach. *Anesth Analg* 108: 1394-1417
9. Toraman F, Evrenkaya S, Yuce M, Aksoy N, Karabulut H, et al. (2004) Lactic acidosis after cardiac surgery is associated with adverse outcome. *Heart Surg Forum* 7: 155-159
10. Ranucci M, Isgrò G, Carlucci C, De La Torre T, Enginoli S, et al. (2010) Surgical and Clinical Outcome Research Group. Central venous oxygen saturation and blood lactate levels during cardiopulmonary bypass are associated with outcome after pediatric cardiac surgery. *Crit Care* 14: 149
11. Loor G, Li L, Sabik JF, Rajeswaran J, Blackstone EH, et al. (2012) Nadir hematocrit during cardiopulmonary bypass: end-organ dysfunction and mortality. *J Thorac Cardiovasc Surg* 144: 654-662
12. Sola-Penna M (2008) Metabolic regulation by lactate. *IUBMB Life* 60: 605-608
13. Robergs RA, Ghiasvand F, Parker D (2004) Biochemistry of exercise-induced metabolic acidosis. *Am J Physiol Regul Integr Comp Physiol* 287: 502-516
14. Weil MH, Afifi AA (1970) Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). *Circulation* 41: 989-1001
15. Rashkin MC, Bosken C, Baughman RP (1985) Oxygen delivery in critically ill patients. Relationship to blood lactate and survival. *Chest* 87: 580-584
16. Demers P, Elkouri S, Martineau R, Couturier A, Cartier R (2000) Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. *Ann Thorac Surg* 70: 2082-2086
17. Zuurbier CJ, Hoek FJ, van Dijk J, Abeling NG, Meijers JC, et al. (2008) Perioperative hyperinsulinaemic normoglycaemic clamp causes hypolipidaemia after coronary artery surgery. *Br J Anaesth* 100: 442-450
18. Veljović M, Popadić A, Vukić Z, Ilić R, Trifunović Z, et al. (2013) Myocardial protection during elective coronary artery bypasses grafting by pretreatment with omega-3 polyunsaturated fatty acids. *Vojnosanit Pregl* 70: 484-492
19. Vandewiele K, Bové T, De Somer FM, Dujardin D, Vanackere M, et al. (2013) The effect of retrograde autologous priming volume on haemodilution and transfusion requirements during cardiac surgery. *Interact Cardiovasc Thorac Surg* 16: 778-783.
20. Cook DJ, Proper JA, Orszulak TA, Daly RC, Oliver WC Jr (1997) Effect of pump flow rate on cerebral blood flow during hypothermic cardiopulmonary bypass in adults. *J Cardiothorac Vasc Anesth* 11: 415-419.
21. Aydin S, Eren MN, Aydin S, Ozercan IH, Dagli AF (2012) The bioactive peptides salusins and apelin-36 are produced in human arterial and venous tissues and the changes of their levels during cardiopulmonary bypass. *Peptides* 37: 233-239
22. Aydin S (2011) Effects of cardiopulmonary bypass on expression of apelin and salusin and investigation of whether or not they are locally synthesized in the aorta, saphenous vein and artery graft. Dicle University, Diyarbakir, Turkey [Specialization Thesis in Medicine]
23. Underwood SM, Davies SW, Feneck RO, Lunn MW, Walesby RK (1991) Comparison of isradipine

- with nitroprusside for control of blood pressure following myocardial revascularization: effects on hemodynamics, cardiac metabolism, and coronary blood flow. *J Cardiothorac Vasc Anesth* 5: 348-356
24. Lawrence CJ, Lestrade A, Chan E, De Lange S (1993) Comparative study of isradipine and sodium nitroprusside in the control of hypertension in patients following coronary artery-bypass surgery. *Acta Anaesthesiol Scand Suppl* 99: 48-52
25. Varon J, Marik PE (2008) Perioperative hypertension management. *Vasc Health Risk Manag* 4: 615-627
26. Legrand M, Dupuis C, Simon C, Gayat E, Mateo J, et al. (2013) Association between systemic hemodynamics and septic acute kidney injury in critically ill patients: a retrospective observational study. *Crit Care* 17: 278
27. Denai MA, Mahfouf M, Ross JJ (2009) A hybrid hierarchical decision support system for cardiac surgical intensive care patients. Part I: Physiological modelling and decision support system design. *Artif Intell Med* 45: 35-52
28. Chandraratna PA, Rashid A, Tolentino A, Hildner FJ, Fester A, et al. (1977) Echocardiographic assessment of left ventricular function in coronary arterial disease. *Br Heart J* 39: 139-144
29. Brown ML, Schaff HV, Suri RM, Li Z, Sundt TM, et al. (2009) Indexed left ventricular dimensions best predict survival after aortic valve replacement in patients with aortic valve regurgitation. *Ann Thorac Surg* 87: 1170-1175
30. Boldt J, Adams HA, Zickmann B, Kling D, Hempelmann G (1990) Comparative effects of enoximone and theophylline on plasma catecholamines and haemodynamics in cardiosurgical patients. *Eur J Clin Pharmacol* 38: 431-436
31. Mathison M, Edgerton JR, Horswell JL, Akin JJ, Mack MJ (2000a) Analysis of hemodynamic changes during beating heart surgical procedures. *Ann Thorac Surg* 70: 1355-1360
32. Mathison M, Buffolo E, Jatene AD, Jatene FB, Reichensperner H, et al. (2000b) Right heart circulatory support facilities coronary artery bypass without cardiopulmonary bypass. *Ann Thorac Surg* 70: 1083-1085
33. Ghaffari S, Malaki M (2013) Arterial lactate level changes in first day after cardiac operation. *J Cardiovasc Thorac Res* 5: 143-145
34. Landow L (1993) Splanchnic lactate production in cardiac surgery patients. *Crit Care Med* 21: 84-91
35. Raper RF, Cameron G, Walker D, Bowey CJ (1997) Type B lactic acidosis following cardiopulmonary bypass. *Crit Care Med* 25: 46-51
36. Brister NW, Barnette RE, Schartel SA, McClurken JB, Alpern J (1991) Isradipine for treatment of acute hypertension after myocardial revascularization. *Crit Care Med* 19: 334-338
37. Cheung AT, Savino JS, Weiss SJ, Aukburg SJ, Berlin JA (1994) Echocardiographic and hemodynamic indexes of left ventricular preload in patients with normal and abnormal ventricular function. *Anesthesiology* 81: 376-387