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Investigation of the Effect of Cross-Clamp Time and Cross-Clamp Time on Troponin I Levels in Patients Undergoing Elective Coronary Artery Bypass Surgery

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Abstract

Background: In this present study, we studied the correlation between aortic cross clamp time and Troponin I levels for elective coronary artery bypass graft operations in 91 patients.

Methods: 51 of the patients included in the study were male and 40 of them were female. Troponin I measurements were recorded 3 times for each patient. Blood samples were taken before cross clamping, after cross-clamping (during the operation), and on postoperative 1st day for Troponin I levels. While the comparison of troponin I blood samples taken in 3 periods, the effect of prolonged cross clamp times on troponin I levels was investigated.

Results: Mean age was 54.7 ± 6.7 years. Euro score value was 3.3 ± 1.7. Mean values were 195.7 ± 61.6 mins for operation time, 55.1 ± 23.6 mins for cross clamp time, 124.9 ± 18.9 mins for cardiopulmonary bypass time and 551.9 ± 44.8 mins for intubation time. Internal mammarian artery and saphenous vein grafts were used for coronary anastomosis in all patients. Overall intensive care unit stays were 3.6 ± 1.7 days and hospitalizations were 8.6 ± 5.1 days. Troponin I measurements were significantly higher with longer cross clamping time.

Conclusion: Among patients undergoing elective coronary artery bypass graft operations, there is a direct and linear correlation between aortic cross clamp time and postoperative Troponin I levels. We strongly advocate this 50 mins' threshold as a safety limit for aortic cross clamp time in elective coronary artery bypass surgery.

Keywords: Coronary artery bypass graft; Cross clamp time; Troponin I levels

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Introduction

Cardiac surgery such as Coronary Arterial Bypass Grafting (CABG) and valve operations and other procedures including Cardiopulmonary Bypass (CPB) procedure are with myocardial damage in various levels. Cross Clamp (CC) manipulation as a part of surgery, despite the developments in cardiac perfusion, hypothermia and cardioplegic solutions, still remains as a main reason for intraoperative myocardial damage. Duration of CC presents a direct relation through the amount of affected myocardial tissue volume and the severity of ischemia. These two factors play a main role on early postoperative success and survival of the patients.

In this present study, we studied the correlation between aortic Cross Clamp Time (CCT) and Troponin I levels for elective coronary artery bypass graft operations in 91 patients.

Material and Method

Total number of the patients was 91. Male to female ratio was 51:40. Patients were not divided into groups neither to reach a statistically significance nor to gain a comparison. The aim of the study is to evaluate significant changes for Troponin I levels during surgery to determine the correlation between CCT. Troponin I measurements were recorded 3 times for each patient; before the application of Cross Clamp (CC), after cross-clamping (during operation) and in first consecutive postoperative days in our cardiovascular surgery intensive care-unit. The troponin I values of all three periods were measured. Then, changes in troponin I levels were recorded depending on the cross clamp time. Biochemical analysis was performed for Troponin I measurements. The Troponin I ELISA kits (Boehringer Mannheim) was used in the ES 300 immunoassay. Normal values for troponin I were evaluated in the range 0 ng/mL to 0.06 ng/mL. Values above 0.2 ng/mL, which

Table 1: Preoperative and operative variables.

Parameters	Mean	Number	%
Age (years)	54.7 ± 6.7		
Male/Female		51/40	56/44
Hypertension		81	89
Hyperlipidemia		77	84.6
Diabetes Mellitus		65	71.4
LVEF 35-40 40-50 >50		 11 35 45	 12.1 38.4 49.5
Smoking history		82	90
Euroscore	3.3 ± 1.7		
Coronary artery bypass counts Less than 3 vessels 3-vessels 4-vessels More than 4 vessels		 18 45 16 12	 19.8 49.5 17.6 13.1
LIMA usage		89	97.8
Saphenous vein usage		100	100
Endarterectomy		71	78
Aortic CC time (min)	55.1 ± 23.6		
CPB time (min)	124.9 ± 18.9		
Operation time (min)	195.7 ± 61.6		
Intubation time (min)	551.9 ± 44.8		
ICU stay (day)	3.6 ± 1.7		
Hospitalization (day)	8.6 ± 5.1		
Reoperation for bleeding	4		4.4

LVEF: Left Ventricle Ejection Fraction; CABG: Coronary Artery Bypass Graft; CC: Cross Clamp; CPB: Cardiopulmonary Bypass; ICU: Intensive Care Unit; LIMA: Left Internal Mammarian Artery

are indicative of cardiac injury, were considered significant. Surgery was performed by the same resident's team consisted of 2 cardiac surgeons.

Other perioperative supplementary data such as; age, sex, Euroscore, co-morbidities (diabetes, hypertension), smoking history, lung disease, echocardiographic results, coronary artery bypass graft number and type, operation time and postoperative situations (intravenous inotropic necessity, onsets of atrial-ventricular fibrillation, defibrillation and re-intubation parameters) were also recorded to clarify the conditions which might directly affect the Troponin I level measurements postoperatively. Furthermore, parameters of intensive care unit were also recorded as intubation time, daily bleeding volumes and blood and blood product usage. As a final data, patients' intensive care unit and total hospitalizations were also presented in this prospective study.

Surgical practice

Surgical premedication was propofol 2 mg/kg to 3 mg/kg, fentanyl citrate 10 to 15 microgram/kg and pancuronium bromide 0.1 mg/kg. After endotracheal intubation, anaesthesia maintenance dose included propofol 2 mg/kg/h to 5 mg/kg/h and fentanyl citrate 5 mg/kg/h to 10 mg/kg/h. Inhaled anesthesia achieved by sevoflurane. Lung ventilation performed *via* 0.4 FiO_2. Surgery was similar for each case. Initially patients received a median sternotomy. Left internal mammarian artery and great saphenous vein harvesting were performed for graft preparation. We used heparin injection with 350 units/per kg. Thus, the activated clotted time reached at least to a level of 400 seconds. After pericardiectomy, aorta-caval cannulation performed. Within 32 centigrade degrees of body core temperature, CPB was accomplished with centrifugal pump and membrane oxygenator. We applied the cross clamp to aorta alone. For myocardial protection we used three steps of cardioplegia: 500 ml of normothermic blood cardioplegia, cold cardioplegia in 10 ml/per kg in 40 mmHg pressure and 500 ml of hot shot before removal of the cross clamp. Additive cardioplegia doses applied in every 20 mins. All of our coronary anastomoses were performed *via* total cardiac arrest. Following the removal of CC and protamine sulphate administration, proximal anastomoses were performed with a side-biting clamp to the aorta. Epicardial pace and/or defibrillation for ventricular fibrillation were not a routine, these were applied only *via* necessity. Following the hemostasis maneuvers, surgical drains replaced and sternum closed conventionally. Afterwards, patients were transferred to our intensive care unit for follow-up and extubations.

Table 2: Postoperative complications and data.

Parameters	Number	%
Inotropic support (single)	16	17.6
Inotropic support (double)	12	13.2
Atrial fibrillation	11	12.1
Pulmonary dysfunction failure without intubation	7	7.7
Defibrillation for ventricular fibrillation	2	2.2
Postoperative IABP application	4	4.4
Re-intubation	2	2.2
Diuretic need	21	23.1
Neurologic dysfunction	4	4.4
Death	2	2.2
Infections associated with sternotomy and mediastinal region	9	9.8
GI dysfunction	3	3.2
Renal dysfunction	9	9.8

IABP: Intra-Aortic Balloon Pump; GI: Gastrointestinal

The exclusion criteria were as follows: patient age lower than 50 and higher than 75, existence of preoperative medically treated renal disease or chronic obstructive pulmonary disease, existence of preoperative hematological dysfunction, preoperative warfarin and/or fibrinolytic agent treatment, acute myocardial infarction with emergent surgery, re-operations for CABG, concomitant valve and/or vascular surgery, existence of preoperative atrial fibrillation, intraoperative or early postoperative deaths, intra-aortic balloon pump implantations, off-pump CABG operations, left ventricle ejection fraction equal or worse than 35%, postoperative severe neurologic and/or other systemic complications, reoperations for early massive bleeding after surgery.

Results

We targeted to present an interaction line between CCT and Troponin I levels after surgery. A major postoperative systemic complication or death resulted with exclusion of the patient from the study. We summarized our preoperative and operative data in Table 1 for the study group.

Saphenous vein was used for coronary bypass in all patients and LIMA was used for most patients. Postoperative bleeding levels decreased gradually after the second day, and 4 patients required revision for bleeding.

Table 3: Mean Troponin I for all 3 periods.

Blood samples taken 3 period Troponin I levels	Mean troponin I levels (ng/mL)
Before cross clamping	0.04 ± 0.7
After cross clamping (during operation)	2.2 ± 1.9
Postoperative first day	2.4 ± 1.8

Table 4: Comparison of prolonged cross clamp times and troponin I levels.

Cross clamping time Troponin I levels	During operation troponin I levels (CPB+CC)	Postoperative first day troponin I levels
< 40 (min)	2.1 ± 1.1	1.9 ± 0.6
40-50 (min)	2.2 ± 1.2	2.3 ± 1.4
50-60 (min)	5. 7 ± 1.5	5.4 ± 1.9
60-70 (min)	7.0 ± 2.1	6.8 ± 1.8
> 70 (min)	7.1 ± 2.4	7.1 ± 2.1

Postoperative data and complications were presented in Table 2. Neurological dysfunction was observed in 4 patients. These dysfunctions (such as transient ischemic attack, agitation, orientation problems) did not cause postoperative patient morbidity and mortality as ischemic stroke. Infections associated with sternotomy and mediastinal region were observed in 9 patients. In these patients, sternum revision was performed in only 3 patients. In 3 other patients, the infection was improved by vacuum-assisted closure. The other 3 patients disappeared with antibiotic treatment and dressing.

Two patients died in the postoperative period. These two patients had EF 35% and multi-vessel disease. Although IABP and bilateral inotropic support, patients died in the first postoperative week in ICU. Gastrointestinal bleeding occurred in 2 patients in the early period and paralytic ileus in 1 patient. Nasogastric catheterization, oral feeding discontinuation and transfusion were improved in 3 patients. Nine patients had different degrees of renal dysfunction. In 8 of these patients, creatine values increased to 1.5 mg/dL to 2.0 mg/dL. Renal function improved with fluid replacement without dialysis. In 1 patient, anuri appeared creatine levels increased to 3 mg/dL levels. Dialysis was performed 2 times a week for 1 month postoperatively. After 1 month, renal dysfunction regressed and the patient was discharged.

Troponin I levels taken 3 times were evaluated postoperatively. Table 3 shows the mean results of troponin I for samples taken in all 3 periods. As shown in Table 3, the mean troponin I levels of the patients were within the normal range before the cross-clamp was inserted. After entering the CPB and inserting the cross clamp (during operation), it is observed that the average of troponin I levels increased. On the first postoperative day, the mean results of the troponin I levels were similar to those obtained during operation (cross-clamped). In addition, we compared the levels of troponin I in the operative and postoperative periods with cross-clamp times. Table 4 shows the comparison of cross-clamp times with troponin I levels during operation (CPB + cross-clamp) and postoperative first day. The highest cross-clamp time was 92 mins, the lowest was 31 mins. The mean cross-clamp time was 55.1 ± 23.6. There was no difference in the levels of troponin I during the operation and postoperative first day. The mean values were similar. However, troponin I levels were also increased as cross clamp times increased. The mean of the troponin I levels in both the operation and the postoperative first day were higher in the prolonged cross clamp periods (Table 4). These results also showed that the increase in troponin levels was seen more in cross-clamp times of more than 50 mins (Figure 1).

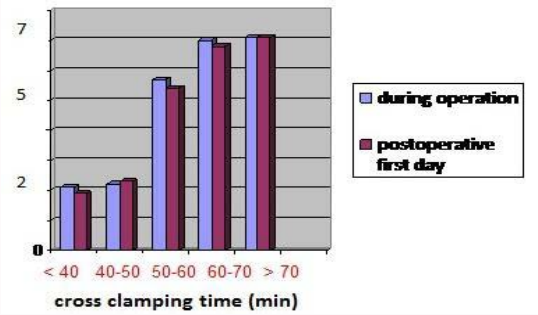

Figure 1: The graph of cross-clamp time with troponin I levels.

Discussion

There is a well described set of serum markers connected with myocardial damage in several clinical conditions including Acute Myocardial Infarction (AMI), myocarditis, polymyositis, low exercises capacity, sepsis, multiorgan insufficiency, severe pulmonary embolism and/or tachycardia, cardiogenic shock, heart failure and/or cardiomyopathy [1-3]. These serum markers include troponins, creatinine kinase and its isoenzyme types, sedimentation levels, lactate dehydrogenase, aspartate transaminase, ischemia-modified albumin, natriuretic peptide, and glycogen phosphorylase isoenzyme BB and myoglobin.

Troponin has different subunits as Troponin C, Troponin T and Troponin I. Troponin is a product of actin and myosin filament degradation. In physiological point of view, Troponin consists of three different proteins and is a segment of both skeletal and cardiac muscle. It plays a key role on muscle contraction stimulated by action potential, sarcoplasmic reticulum and calcium through actin and tropomyosin. Troponin I specifically interacts with actin to hold this tropomyosin complex by muscle activity. Troponin I and Troponin T have been called "cardiac troponins" because they provide valuable evidence for cardiac conditions. Troponin I is studied as the most sensitive and specific evaluation method by several publications in this manner. Troponin I is a prominent indicator of myocardial cell damage and myocardial cellular ischemia released through the cytosolic structures of myocytes [4,5].

Chaikhouni et al. [6] presented a study about the relations between CABG operations and Troponin levels in similar algorithm as our study. He claims the postoperative Troponin levels to be an independent predictive model of short and long-term mortality. In their study group of 333 patients, 77 patients had a Troponin value over 10 mg/ml (Group II). Group II reported to have more cardiac (13%) and non-cardiac (12%) complications, postoperatively. These postoperative complications were stroke, bleeding, arrhythmia, infarction, pleural effusion, renal insufficiency, wound infection, confusion and gastrointestinal conditions. Chaikhouni also showed a higher mortality rate in this Group II in 6.5% when compared to the other group with lower postoperative Troponin levels in 0.4%. Our results also showed that cross-clamp had negative effects on troponin levels such as other studies [2,4,5]. In addition, it was determined that long cross clamp times increased at troponin levels compared to other short cross clamping times. In this case, it has been shown that the clinical problems related to cardiac cell damage and subsequent negative cardiac condition may be higher.

In another similar study, Sadony et al. [7] used Troponin I plasma levels for the diagnosis and measurement of perioperative myocardial injury in patients who had undergone coronary artery bypass surgery in 119 patients. He reported that the prognostic effects of Troponin I on various types of myocardial injury, including transmural infarction, were 100% sensitivity and 97% specific. In this study, it has been reported that all patients undergoing coronary artery bypass surgery have a myocardial damage.

In spite of many studies, the relationship between cross clamp duration and Troponin levels is still not fully elucidated. The aim in our study was to prove this correlation and to determine the cross clamp time, which resulted in a much greater increase of Troponin levels. So, we tried to determine the safe time interval for cross-clamp. According to the results of our study, we concluded that the cross clamp time is a safer time for surgeons in cases with shorter than 50 mins. In our study, a reasonable increase in troponin was observed in short cross clamp times, while a significant increase in troponin values was observed in longer periods. We found very high levels of troponin levels in some of our patients with long cross-clamp times that may cause severe myocardial damage. Cross-clamp times were greater than 50 mins in these patients with multi-vessel disease that we lost in our postoperative period. These high levels of troponin have been shown as an indicator of cardiac failure and our patients have been lost due to heart failure. In other words, high cross-clamp durations cause significant increases in morbidity and mortality.

Cardioplegia application, which is among the cardiac protection options during the operation, has an important role in reducing myocardial cell damage. The application of antegrade cardioplegia due to proximally coronary lesions may be ineffective in the diffuse protection of the heart muscle. Therefore, continuous retrograde cardioplegia solutions instead of intermittent play an effective role in the prevention of cardiac cell damage. Especially in patients with significant proximal coronary lesions, retrograde cardioplegia and short cross-clamp times are important in achieving successful surgical and low myocardial cell damage [4-6]. However, since we have created a working principle that provides the same characteristics for all patients, we have generated similar patient data by performing the same preoperative and operative applications for all patients. To evaluate the relationship between cross clamp time and troponin, we had to choose the same surgical principles as the patients with the same characteristics. We also tried to prevent such additional pathological conditions that could cause myocardial cell damage such as rhythm problems, bleeding, low oxygen values, blood pressure, and electrolyte changes during and after surgery as soon as possible. As a result of these evaluations, further research is needed to show myocardial cell damage as a marker of cross-clamp and troponin I levels. Because, myocardial cell damage can be affected by many factors. Preoperative status of the patient, the severity of coronary lesions and their localization, and the degree of cardiac injury in cases of additional cardiac diseases may be different and may change the results [8,9]. As we mentioned above, we chose as much similar patients as possible in creating this study and tried to apply the same surgery and methods in the operation.

Conclusion

Higher levels of Troponin I have higher heart tissue damage in all aspects. Among patients who underwent elective coronary artery bypass graft surgery, there is a direct and linear relationship between aortic cross clamp duration and postoperative Troponin I levels. A cross clamp time exceeding an average of 50 mins leads to increases in troponin levels, which is the most important finding indicating the high myocardial cell damage.

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