

CORRELATION OF POSTOPERATIVE CARDIAC TROPONIN I WITH LENGTH OF INTENSIVE CARE UNIT (ICU) STAY AFTER CORONARY ARTERY BYPASS GRAFT SURGERY(CABG)

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Contribution

AK,RT conceived the idea, planned the study and drafted the manuscript, collected data, AURK,TAZ did statistical analysis, drafted the manuscript and critically reviewed manuscript. All authors contributed significantly to the submitted manuscript.

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ABSTRACT

Objective: To determine the correlation of mean postoperative cardiac troponin I levels and mean duration of length of ICU stay in CABG surgery patients.

Methodology: A cross sectional study was carried out at the National Institute of Cardiovascular Diseases Karachi from November 2012 to May 2013. Patients were selected based on specified criteria utilizing non probability consecutive sampling. Twenty four hours after CABG surgery, cardiac troponin I levels were measured and the length of ICU stay was determined for each patient.

Results: Total number of patients were 87 including 58 male (66.67%) patients. Mean age of patient was 54.71 ± 6.92 years with troponin I levels of 0.47 ± 1.90 $\mu\text{g/l}$ and the length of ICU stay of 75.86 ± 43.59 hours. About 57(65.52%) patients had triple vessel coronary artery disease (CAD) and 30 (34.48%) patients had two vessel coronary artery disease. In our study the Pearson's correlation coefficient was $r = 0.766$ between mean postoperative cardiac troponin I levels and length of ICU stay in patients who underwent CABG surgery. The p value was less than 0.05 and the correlation was significant at 0.01 level.

Conclusion: The mean postoperative cardiac troponin I levels and mean duration of length of ICU stay in CABG surgery patients are highly positively correlated.

Key Words: Coronary artery bypass grafting, Troponin I, Intensive care unit, Cardiac Surgery.

INTRODUCTION

Coronary artery bypass graft (CABG) surgery is a common cardiac operation.¹ Revascularization of ischemic myocardium represents an effective treatment strategy shown to prolong survival in patients with coronary artery disease. CABG surgery itself induces perioperative myocardial ischemia and consequent myocardial damage, which in itself is an important determinant of increased postoperative morbidity and mortality, leading to longer postoperative stay in the ICU and the hospital.² Perioperative myocardial infarction occurs in 7–15% of patients after cardiac surgery and is associated with increased hospital length of stay, costs, and reduced short and long term survival.³⁻⁷

Until recently, creatinine kinase and its MB fraction (CKMB) were utilized to detect myocardial injury, but after surgical procedures the specificity of the assay to detect myocardial injury alone was questionable.^{8,9}

Traditionally, the combination of electrocardiography and increases in cardiac marker concentrations has been used to define acute myocardial injury. Recently, cardiac markers, particularly troponins, have become the new standard in diagnosing acute myocardial injury because of their superior sensitivity and specificity for cardiac tissue.¹⁰ Cardiac troponin I may be utilized as a gold standard for perioperative myocardial injury in CABG surgery patients. Cardiac troponin I peaks around 24 hours have been reported for patients suffering perioperative myocardial damage.¹¹⁻¹⁴

Measurement of troponin I permits the identification of even minor myocardial damage with high diagnostic accuracy¹¹. Troponin I is a sensitive biomarker introduced predominantly for risk stratification in patients with acute coronary syndrome and is the gold standard for identifying myocardial necrosis or infarction. The range of time to initial elevation in hours for cardiac troponin I is 3-12 hours. The mean times to peak elevations for cardiac troponin I is 24 hours. The times to return to normal range for cardiac troponin I is 5 to 10 days.

Incidence of prolonged ICU stay after on pump CABG surgery is 9.2%.¹⁵ Patients who stayed in the ICU for more than 72 consecutive hours postoperatively were classified as having a prolonged ICU stay, while patients staying 72 hours or less were classified as having a normal ICU stay.¹⁵

A study showed that cardiac Troponin I measured at 24 hours postoperatively after CABG surgery is a significant predictor of increased postoperative length of stay in the ICU ($p=0.012$) and hospital ($p=0.024$) and the correlation between postoperative troponin I (measured in micrograms/liter) measured at 24 hours after the end of CABG surgery and postoperative length of stay in the

intensive care unit (recorded in hours) is 0.3.¹⁶ Cardiac Troponin I concentrations >0.5 micrograms/liter are associated with prolonged ICU length of stay ($p<0.05$).¹⁶ Hence, use of a single postoperative 24 hour troponin I value to quantify perioperative myocardial damage identifies patients at greater risk of extended ICU and hospital stays. So this strategy could assist in allocation of patients to different management streams after CABG surgery.

A study showed that postoperative patients with raised serum troponin I were more likely to have cardiac related complications e.g. low cardiac output syndrome, requiring intra-aortic balloon pumps, acute renal failure, longer intubation times,, atrial fibrillation, worse ventricular function, myocardial damage and prolonged ICU stay and hospital stay.¹⁷⁻²⁰ Therefore, postoperative measurement of troponin I represents a promising means for risk stratification of patients undergoing CABG surgery.

We conducted a study with aim to evaluate the correlation of mean postoperative cardiac troponin I levels and mean duration of length of ICU stay in patients who underwent conventional on-pump CABG surgery.

METHODOLOGY

A cross sectional study was conducted at the Cardiac surgery department of the National Institute of Cardiovascular Diseases, Karachi from November 2012 to May 2013. All patients were admitted through outpatient department. The sampling technique utilized was non probability consecutive.

Patients included in the study were those who were: undergoing elective on pump CABG surgery, of both genders, age range of 45 years to 65 years, $\geq 70\%$ stenosis of two or more coronary arteries on angiography with the duration of coronary artery disease of less than one year, ejection fraction $\geq 50\%$ on echocardiography, normal levels of cardiac troponin I (≤ 0.5 micrograms/liter) measured preoperatively, known diabetic and hypertensive patients controlled on medications. The standard acceptable cut off limit of troponin I after CABG was less than or equal to five times the normal levels of cardiac troponin I (≤ 0.5 micrograms/liter) measured preoperatively.

Patients excluded from the study were those with chronic obstructive airway disease, myocardial infarction within 30 days, emergency CABG surgery, associated valvular or secondary structural defects like ventricular septal defects and mitral regurgitation lesions, chronic renal failure, chronic liver disease, patients on inotropes and intravenous nitrates before surgery, re-do coronary artery bypass graft surgery, previous stroke.

Once the patients met the inclusion criteria they were included in the study then informed written consent was

taken from the patients. CABG surgery was performed by consultant surgeons. After the end of on-pump CABG surgery, patient were shifted to the ICU for monitoring. Postoperative length of ICU stay time measurement (hours) was started once the patient was shifted to the ICU from the operating room after the end of CABG surgery. The patients who met the following criteria were shifted from the ICU to the ward: patients maintained breathing independently (arterial oxygen saturation greater than 95% on room air), acceptable blood pressure (systolic:100-130 mmHg, diastolic: 70-90 mmHg) maintained without inotropic support, a stable heart rate (greater than or equal to 80 and less than 100 beats per minute), sufficient neurological function (Glasgow Coma Scale 15/15), acceptable renal function (urine output >40 milliliters/ hour) and normal range of serum potassium levels (3.5-5.4 meq/L).

The demographics variables including the patients' name, age, gender, duration of disease, number of diseased coronary arteries, troponin I levels measured 24 hours at the end of CABG surgery and length of ICU stay was noted by the researcher and entered into the proforma. Confounding variables were controlled by restriction of taking only those patients meeting the inclusion criteria and through stratification of data. Bias was controlled by standardization of troponin I measurement technique and uniform source of information. SPSS 10 was used to analyze the data. Mean \pm standard deviation were calculated for: the age of the patients, troponin I levels measured 24 hours after the end of CABG surgery and length of ICU stay. Frequency and percentage were calculated for gender and number of

diseased coronary arteries. Pearson's correlation coefficient (r) was computed to determine the correlation of mean postoperative cardiac troponin I levels and length of ICU stay in patients who underwent on pump CABG surgery. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The sample size of this study was 87 patients. The mean age of the patients who underwent CABG surgery was 54.71 ± 6.92 years with the range of 45 to 65 years. The mean cardiac troponin I level twenty four hours following CABG surgery was 0.47 ± 1.90 micrograms/liter. The mean length of ICU stay following CABG surgery was 75.86 ± 43.59 hours (Table 1). There were 58 male patients (66.67%) and 29 female patients (33.33%) . About fifty seven patients (65.52%) had three vessel disease and thirty (34.48%) had two vessel disease . The mean length of ICU stay for female patients was 100.97 hours and 63.31 hours for males (Table 2). The mean length of ICU stay for patients in the age range of 45 to 55 years was 61.38 hours and the mean length of ICU stay for patients in the age range of 56 to 65 years was 97.37 hours (Table 3). The number of diseased coronary arteries revealed that the mean length of ICU stay for patients with two coronary arteries diseased was 53.60 hours while it was 87.58 hours for triple vessel disease (Table 4). Pearson's correlation coefficient ($r = 0.766$) was computed to determine the correlation of mean postoperative cardiac troponin I levels and length of ICU stay in patients who underwent CABG surgery. ($p < 0.01$) (Table 5).

Table 1: Demographic Variables of Study Population (n=85)

Variables	Mean \pm Standard Deviation
Age of patients (years)	54.71 \pm 6.92 years
Troponin I level 24 hours postoperatively (micrograms/liter)	0.47 \pm 1.90 micrograms/liter
Length of ICU stay (hours)	75.86 \pm 43.59 hours
Males	66.67 %
Females	33.33 %
Single vessel disease	34.48 %
Triple vessel disease	65.52 %

Table 2: Gender Stratification for Length of ICU Stay in Study Population (n=85)

Gender	Length of ICU Stay (hours)	
	Mean	Standard Deviation
Male	63.31 hours	20.45 hours
Female	100.97 hours	63.30 hours

Table 3: Age Stratification for Length of ICU Stay in Study Population (n=85)

Age (years)	Length of ICU Stay (hours)	
	Mean	Standard Deviation
45 to 55 years	61.38hours	25.78hours
56 to 65 years	97.37 hours	54.90 hours

Table 4: Stratification of Number of Diseased Coronary Arteries with Length of ICU Stay in Study Population (n=85)

Number of Diseased Coronary Arteries	Length of ICU Stay (hours)	
	Mean	Standard Deviation
Two coronary arteries disease	53.60 hours	12.10 hours
Three coronary arteries disease	87.58 hours	49.37 hours

Table 5: Correlation Cardiac Troponin Level and ICU Stay in Study Population (n=85)

		Postoperative Cardiac Troponin I Level	Length of Intensive Care Unit Stay
Postoperative Cardiac Troponin I Level	Pearson Correlation	1	.766**
	Sig. (1-tailed)		.000
	n	87	87
Length of Intensive Care Unit Stay	Pearson Correlation	.766**	1
	Sig. (1-tailed)	.000	
	n	87	87

** . Correlation is significant at the 0.01 level (1-tailed).

DISCUSSION

Coronary artery bypass grafting surgery is a corner stone in the management of coronary artery disease but myocardial damage still complicates the postoperative course for a significant number of patients, necessitating longer in-hospital and ICU stays and leading to increased morbidity.²¹⁻²⁶ Cardiac troponin I is a valuable marker for the detection of postoperative cardiac events (including myocardial injury) in patients undergoing CABG surgery.²⁷ The efficacy and simplicity of a single cardiac troponin I after CABG surgery in identifying adverse outcomes may be of value in streamlining post CABG surgery patient care and postoperative management. Hence, identification of those patients at high risk of a complicated postoperative course is highly desirable.

Cardiac troponins I is a protein which is integral to the function of cardiac muscle. It is a very sensitive marker for the detection of myocardial damage, and the ability to assay troponin I serum levels accurately and quickly has revolutionized the concepts of minor myocardial injury and infarction. It is also a powerful prognostic indicator of future

adverse cardiac events. Rapid, whole blood assays are now available that can be done at the patient's bedside. The presence of myocardial injury is demonstrated by raised serum level of cardiac troponin I. In healthy adults virtually no cardiac troponin is demonstrable, so that every rise of the level of the heart-specific troponin in the blood means that there is myocardial damage. The range of time to initial elevation in hours for cardiac troponin I is 3-12 hours. The mean times to peak elevations for cardiac troponin I is 24 hours. The times to return to normal range for cardiac troponin I is 5 to 10 days.

Cardiac troponin I can be used as a predictor of postoperative morbidity in terms of extended ICU stay. Levels of postoperative cardiac troponin I may be used for the identification of patients at higher risk after CABG surgery, which in the future could enable more effective stratification of postoperative care. Our study prospectively assess the relationship of postoperative cardiac troponin concentrations with postoperative ICU length of stay and hence morbidity in CABG patients. Hence, risk stratification will enable surgeons to counsel the patients' families regarding patients' length of stay in the ICU and prognosis of

the patient.

In our study the mean age of the patients who underwent CABG surgery was 54.71 years. The majority of patients were males with the ratio of 2:1. Troponin I levels measured 24 hours after the end of CABG surgery were 0.47 ± 1.90 micrograms/liter. Our study determined the correlation of mean postoperative cardiac troponin I levels and mean duration of length of ICU stay in patients who underwent conventional on-pump coronary artery bypass graft (CABG) surgery and had normal levels of preoperative cardiac troponin I (≤ 0.5 micrograms/liter). The standard acceptable cut off limit of troponin I after CABG is less than or equal to five times the normal levels of cardiac troponin I (≤ 0.5 micrograms/liter) measured preoperatively²⁸⁻³⁰. In none of our patients the post operative troponin I levels reached ≥ 2.5 micrograms/liter.

Lower levels of postoperative cardiac troponin I have been reported in the off-pump CABG surgery as compared to the on-pump CABG surgery, indicating that the arrested heart coronary revascularization procedure causes more damage to the heart due to CPB than the off-pump myocardial revascularization surgery³¹.

In our study the mean length of ICU stay following CABG surgery was 75.86 ± 43.59 hours. Other studies showed that the mean length of stay in the ICU following CABG surgery was 91.2 hours and 88.80 ± 156 hours^{7,32}. In our study the mean postoperative cardiac troponin I levels and the mean duration of length of ICU stay in patients who underwent CABG surgery are highly positively correlated. Hence, the greater the level of mean postoperative cardiac troponin I levels the greater the mean duration of length of ICU stay in patients who underwent CABG surgery. Similar results were also obtained by other studies where a positive correlation was obtained between postoperative cardiac troponin I levels and mean duration of length of ICU stay in patients who underwent CABG surgery.^{16,33-35}

Although CABG surgery may be viewed as a common cardiac surgery procedure, minimizing adverse outcomes and minimizing the length of ICU and hospital inpatient stays associated with this procedure continues to be of importance for improving patient care and decreasing costs of treatment for CABG surgery. The use of a single biochemical test at 24 hours after CABG surgery to identify cardiac damage and predict adverse outcome has several benefits. Those patients who have the highest level of cardiac troponin I at 24 hours may warrant closer clinical attention to improve outcomes in this higher-risk group. The mechanisms such as demand ischemia, myocardial strain should be investigated to better tailor the therapeutical regimen in each patient.

The high efficacy and simplicity of a single cardiac troponin I measurement 24 hours after CABG surgery in identifying

adverse outcomes in our study support its routine use along with other similar variables in the future streamlining of post-CABG surgery care. When measured in the plasma, cardiac troponin I is considered to be a highly specific marker of myocardial cell damage. In the ICU setting, increased cardiac troponin I levels are quite common findings and when documented, intensivists should bear in mind that this laboratory finding holds an important prognostic role.

The variables that have been identified as being associated with increased length of ICU stay can be factored into patient management algorithms and may further enhance resource utilization in the cardiac surgery intensive care units. These measures could potentially be incorporated into risk stratification models and allow the identification of more severely affected patients who could undergo targeted clinical follow up to reduce adverse CABG surgery outcomes. The routine postoperative measurement of cardiac troponin I represents a promising means for risk stratification of CABG surgery patients.

Systemic inflammatory response measured by circulating cytokines is a result of surgical trauma during CABG surgery (conventional on-pump and off pump coronary artery bypass surgery) and cardiopulmonary bypass.³⁶⁻⁴⁰ A number of variables have been suggested which may be causative factors including reperfusion injury, aortic cross clamping time, myocardial ischemia during cardiopulmonary bypass and contact of blood with the bypass circuit. Cardiac troponin I has been used as a sensitive biomarker for risk stratification in patients with acute coronary syndrome and is the gold standard for identifying myocardial damage. CABG surgery related myocardial injury occurs in a significant number of patients, and that a cardiac troponin I test after CABG surgery could differentiate patients with significant revascularization injury.^{12,41-43}

Measurements of troponin I performed after CABG surgery as a biomarker of myocardial injury is a simple test that permits detection of patients at risk of complications and reduced survival.^{4,7,44-47} Identification of troponin I in the circulation may be due to two processes; it may reflect release from cytoplasmic stores or damage from the myocardial contractile apparatus and myofibrillar destruction.^{48,49} Although these two phenomena may occur simultaneously, cytosolic leakage may be a relatively benign early phenomenon and may not be associated with adverse outcomes. However, in contrast myocyte necrosis (early or late) may immediately worsen cardiac function or herald adverse ventricular remodeling and ultimately heart failure. The quantitative scale of injury and assessment of its prognostic impact are important to compare myocardial protective strategies and better design trials.

During on-pump CABG surgery with cardioplegic arrest the heart undergoes a period of ischemia. Myocardial injury may

occur due to inadequate myocardial protection. This may even lead to heart failure, requiring inotropic and mechanical (intraaortic balloon pump, left or biventricular assist devices) support or even death. Even in patients who have a seemingly normal recovery following CABG surgery, myocardial injury may occur and this may be evident in minor changes in cardiac function and the release of biomarkers of myocardial injury. Myocardial injury results in increased patient morbidity and mortality.^{4,44-46,50}

On multivariable analysis at thirty days, one year and three years, cardiac troponin I at 24 hours was an independent predictor of mortality in models incorporating EuroSCORE, inotrope requirements, surgical complexity, New York Heart Association class and estimated glomerular filtration rate.^{4,47,51} Hence, raised levels of troponin I predict an increased risk of complications and cardiac troponin I is helpful for early risk stratification in patients with myocardial injury.

With sampling up to 24 hours postoperatively, cardiac troponins offer a sensitivity higher than 95% and a specificity of 90%. The high specificity of cardiac troponins for myocardium makes false-positive elevations (i.e., an elevated cardiac troponin in the absence of myocardial injury) exceedingly rare. Rather, elevations in the absence of other clinical data consistent with myocardial injury usually represent true myocardial damage following cardiac surgery. Such damage may occur with forms of myocardial injury, such as in the setting of cardiac surgical procedure including coronary artery bypass grafting, aortic and mitral valve surgery and myocardial contusion. In patients with myocardial damage, an elevated cardiac troponin level conveys increased risk of postoperative complications in patients. Thus, troponin I is a very sensitive marker for the detection of myocardial injury in post cardiac surgery patients.

Identification of groups of patients at risk of increased morbidity and increased length of ICU stay by measurement of postoperative cardiac troponin I will allow for more aggressive and earlier secondary prevention therapy as well as more vigilant patient management in the ICU and follow up and could permit substantial cost savings in terms of hospital days saved through appropriate and efficient discharge planning.

LIMITATIONS

A limitation of our study is that it was carried out in a single cardiac surgery institution. This may limit the generalization of the results for a larger population.

CONCLUSION

The mean postoperative cardiac troponin I levels and mean duration of length of intensive care unit stay in patients who

underwent conventional coronary artery bypass graft(CABG) surgery are highly positively correlated.

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