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Relationship between central venous oxygen saturation and post-operative cardiac Troponin I in Coronary Artery Bypass Grafting- Observational prospective study

Saeed Khademi[1], Shahrbanoo Shahbazi[1], Mohammad Ghazinour[2] and Mohsen Rezaee*[3]

[1]Shiraz Anesthesiology and Intensive Care Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran
[2]Cardiac Surgery Department, Shiraz University of Medical Sciences, Shiraz, IR Iran
[3]Student research committee, FASA University of medical science, FASA, IR Iran
**Corresponding Author: Mohsen Rezaee M.D, Mohsenrezaee86@gmail.com*

ABSTRACT

Heart is one of the susceptible organs which could be damaged during Coronary Artery Bypass Grafting because of hypoperfusion. Cardiac Troponin I is a sensitive marker which increases immediately after myocardial damages due to poor coronary blood supply. Decrease in central venous oxygen saturation has also been demonstrated in various conditions especially myocardial infarction. The present study aimed to evaluate relationship between central venous oxygen saturation and post-operative cardiac Troponin I in Coronary Artery Bypass Grafting, and find its relations to post-operative laboratory and clinical outcomes. This prospective study was conducted on 53 patients who underwent elective CABG. After anesthesia induction, measurement of Scvo2 was done by central venous catheter after surgery and arterial blood samples were taken for measuring Troponin I before and 24 hours after surgery. The correlation between Scvo2 and other variables was assessed using non-parametric tests, such as Spearman correlation and Mann-Whitney test. Besides, P<0.05 was considered as statistically significant. Among the 53 study patients, 29 (54.8%) were male and 24 (45.2%) were female, with the mean age of 61.02±10.42 years. The results showed an inverse association between Scvo2 and cardiac Troponin I that was checked after the operation (P=0.012, r=-0.348). The study results revealed a reverse relationship between Scvo2 and Troponin I. Therefore, we can conclude that changes in Scvo2 can predict the probability of myocardial damage and cardiac prognosis in early postoperative period. Future longitudinal and cohort studies are recommended to be conducted to follow the patients for long-term outcomes.

Keywords: Troponin I, Coronary artery bypass grafting, Central venous saturation, Relationship, Infarction

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INTRODUCTION

Tissue hypoperfusion is one of the serious concerns of cardiac anesthesiologist during cardiac surgery, especially Coronary Artery Bypass Grafting (CABG). Tissue perfusion can be measured through several methods, such as measurement of Saturation of venous oxygen (Svo2) with Pulmonary Artery Catheter (PAC) which is inserted in the pulmonary artery, but this method is very invasive and costly[1]. Another method is measurement of serum lactate level during Cardiopulmonary Bypass (CPB)[3, 4]; however, a study has reported that serum lactate level is not a sensitive marker [5]. Central venous saturation shows the equal condition between tissue oxygen demand and oxygen delivery, also oxygen demand is based on the metabolic state of tissue and oxygen delivery is determined by

cardiac output and efficacy and availability of carriers in blood stream [6,7]. Measurement of central venous oxygen Saturation (Scvo2) is yet another method which is performed by positioning the tip of the central venous catheter in the superior vena cava just before to its junction with right atrium. Several experimental studies have shown a relationship between Scvo2 changes and tissue oxygenation impairment. The Scvo2 level monitoring during and after cardiac surgery is reported to be associated with patients' outcome [8,9]. Heart is one the susceptible organs which could be damaged in patients who underwent CABG surgery especially during cardiopulmonary bypass, because of hypoperfusion and hypoxemia. During cardiac surgery possible myocardial damages due to functional or structural changes may be occurs, and some biomarkers like Creatine Kinase-MB (CK-MB) release from cardiomyocytes after ischemia. Also myofibrillar proteins such as Troponin I and T, heart-type fatty acid binding protein (hFABP), high sensitivity C-reactive protein (hs-CRP) and myoglobin used widely in research and clinics but the major concern is that about half-time required to detect measurable amount of these markers in peripheral blood after probable cardiac damages during CABG[10]. Nevertheles, cardiac Troponin I is more sensitive and available marker than others, which start increasing immediately after myocardial damages due to poor coronary blood supply and peaks at 18-24 hours and levels stay elevated for 10 days. Recent trials have shown a significant correlation between increased postoperative troponin values and increased mortality and morbidity. On the other hand[11], decrease in Scvo2 has also been demonstrated in various conditions especially myocardial infarction. Thus, Scvo 2 could be a predictor for the subsequent events which might occur in end-organs, such as heart. The present study aims to evaluate the correlation between Scvo2, as a prognostic marker, and troponin I and other clinical indices after CABG surgery.

MATERIALS AND METHODS

2.1 Methods:

This observational prospective cross-sectional study was conducted in the department of cardiac surgery in Shahid Faghihi educational hospital affiliated to Shiraz University of Medical sciences, Shiraz, Iran. After approval the proposal of this study in ethic committee of Shiraz university of Medical Sciences and obtaining written informed consents, checklists were filled for all the patients by a nurse-anesthetist. The checklists contained the patients' demographic characteristics, left ventricular cardiac Ejection Fraction (EF) before surgery, weight, height, and Body Mass Index (BMI) and history of smoking (patients who smoke cigarette more than 5 pack-year were considered smoker).. Overall, 64 patients who were candidate for elective CABG were enrolled into this study. Inclusion criteria were 3 vessels coronary disease patients who needed elective CABG with age between 20 and 75 years old and EF more than 40%. The exclusion criteria of the study were emergency CABG, renal failure, Chronic Obstructive Pulmonary Diseases (COPD) with Forced Expiratory Volume in 1 second (FEV1) <50%, redo cardiac surgery, any liver diseases, CABG combined with valve surgery or aortic procedures and carotid surgery, pregnancy, and being in poor conditions such as sepsis or septic shock. Poor control diabetic patients who had HbA1c>7%, patients with cardiac tamponade and refractory hypotension who had not any responses to drugs and patients with advanced coronary artery disease were excluded.

All patients received 10 mg Oxazepam the night before surgery. Peripheral venous access and then radial artery cannula were inserted (under local anesthesia and sedation) before induction of anesthesia. Then, blood sampling was done for evaluating Troponin I level as a baseline cardiac marker. Midazolam 0.1 mg/kg, sufentanil 0.5-1 μg/kg, morphine 0.1 mg/kg, pancuronium 0.1-0.15 mg/kg, and thiopental 1-2 mg/kg were used to induce anesthesia. In addition, anesthesia was maintained with Isoflurane 0.5-1.5% and all the patients were ventilated with an oxygen-air mixture (50%-50%) to maintain an end-tidal CO_2 of 35 to 45 mmHg. FiO2 was equal for all participants (Fio2=50%) during maintenance of anesthesia.

Also, all patients underwent nonpulsatile, normothermic (34-36°C) CPB with intermittent cold blood cardioplegia for cardiac quiescence. The extracorporeal circuit was primed with 1000-1500 mL of Ringer's solution and 250-500 mL of 6% voluven solution. Besides, the mean Blood Pressure (MBP) was maintained between 60 and 90 mmHg with pump flow rate of 2 to 2.4 L/min/m2 (by stoker S5, 2010 Germany) throughout CPB. Immediately after induction of anesthesia and tracheal intubation, a Central Venous Catheter (CVC), a triple lumen spectrophotometer catheter, was inserted in the right internal jugular vein and was adjusted for central venous pressure monitoring and to obtain a sample for measuring Scvo 2 before CPB and 30 minutes after pump termination.

The patients' Blood pressure (BP), Heart Rate (HR), and Central Venous Pressure (CVP) were continuously monitored from before anesthesia induction up to 30 minutes after pump termination. In case of uncontrolled hypertension, nitroglycerin (TNG) was used to maintain BP during the surgery. Moreover, in case of hemodynamic instability (mean arterial pressure <60 mm Hg) at the termination of CPB, an inotropic agent (epinephrine) 0.05 µg/kg/min was started and the infusion rate was increased as needed.

The patients who had blood transfusion, needed 1 to 6 packed cell that were produced 10 to 20 days prior to administration (storage time= 10-20 days). Storage solution of packed cell was: CPDA-1(citrate, phosphate, dextrose, and adenine-1). Hematocrit was maintained 20%-24% during pump time and >26 at termination time and after termination of CPB and >30% during Intensive Care Unit (ICU) admission in both male and female. Blood sugar was checked every 30 minutes during operation and controlled between 120mg/dl to 180 mg/dl.

Blood sampling from arterial line for evaluating Troponin I level as primary outcome was done before surgery and 24 hours after end of surgery. Also, secondary outcomes such as intubation period (or time to extubation), ICU admission time, hospital admission time, duration of receiving inotrope, biochemical indices such as total billirubin and creatinin changes, and episodes of arrhythmia which means any new non-sinus rhythms such as atrial fibrillation or flutter, ventricular tachycardia or fibrilaton that cause hemodynamic instability in whom needed any interventions to rescue from arrhythmia were recorded after surgery.

2.2 Statistic:

According to Shapiro test P-value, $Scvo_2$ as an independent variable was not normal; therefore, non-parametric tests such as Spearman correlation and Mann-Whitney test were used to assess the correlation between $Scvo_2$ and other variables. Descriptive data were reported as mean ± SD. Besides, $P<0.05$ was considered as statistically significant. All the analyses were performed using the SPSS statistical software, version 19 (SPSS Inc. Chicago I11).

RESULTS

In this study, 11 participants were excluded due to off pump during surgery, insufficient blood sampling, and recurrent bleeding after surgery. Thus, the data of 53 patients were analyzed. Among these patients, 29 (54.8%) were male and 24 (45.2%) were female, with the mean age of 61.02±10.42 years. Besides, the patients' mean BMI was 24.98±4.11 which had no relationship with $Scvo_2$ (P=0.194, r=-0.191). In addition, their mean duration of ICU admission was 3.27±1.93 days. The patients' demographic characteristics have been summarized in Table 1. Troponin I level was 0.38±1.43befor surgery and 4.25±5.67 24 hours after termination of pump. .According to the results, the mean range of $Scvo_2$ was 75.17%±11.6 (93%-42%). Additionally, an inverse association was found between $Scvo_2$ and cardiac Troponin I level that was checked after the operation (P=0.012, r=-0.348). Also, a significant reverse association was observed between $Scvo_2$ and Troponin I changes before and after the surgery (P=0.022, r=-0.316). In our cases the mean pump time was 74.67±20.72 with a mean cross clump time of 41.90±12.49.

Table 1: Demographic and descriptive characteristics of the study patients

Items	N	Mean	Std. Deviation
Age	52	61.02	10.42
Ejection Fraction[a]	50	48.14	11.05
Body Mass Index(BMI)	48	24.98	4.11
Height[b]	48	162.21	8.13
Weight[c]	50	65.32	12.90
Intubation period[d]	52	12.15	8.02
Intensive Care Unit(ICU) period[e]	51	3.27	1.93
Hospital admission period[e]	50	5.28	1.73
Inotrope usage[d](Epinephrine)	53	21.49	21.14

a :Ejection Fraction of heart before surgery %,
b:Centimeter, c : Kilogram, d : Hour e : Day,

There was also an inverse association between Scvo2 and pump time (duration of using pump in CABG) (P=0.001, r=-0.431). Moreover, a significant correlation was found between Scvo2 changes and gender (P=0.004). However, no significant relationships were observed between Scvo2 and demographic characteristics (more details described in Tables 2 and 3). Also, no significant relationship was detected between hospital admission period and Scvo2 (P=0.364, r=- 0.133). The correlations between Scvo2 and ICU admission and intubation periods have been presented in Table 3.

Table 2: The correlation between $Scvo_2$ and other variables

Variables	$Scvo_2$	
	r-value	P-value
Pump time	**-.431**	**0.001**
Troponin I before surgery	0.014	0.924
Troponin I after surgery	**-.348**	**0.012**
Intubation period	0.115	0.420
ICU admission period	-0.124	0.390
Inotrop usage	-0.140	0.321
Troponin changes	**-0.316**	**0.022**
Creatinin	-0.146	0.301
Total Billirubin	0.093	0.511
Packed cell receiving	-.0140	0.321

Relationships were evaluated with Spearman correlation test
P-value was significant <0.05

Table 3: correlation between $Scvo_2$ and demographic variables

Variables		$Scvo_2$	
		Mean rank	P-value
Arrhythmia	Yes	23.86	0.268
	No	28.68	
Gender	Male	31.93	**0.004**
	Female	19.65	
Smoking	Yes	27.50	0.794
	No	26.20	

P-value was significant <0.05; Relationships were evaluated with Mann-Whitney Test.

DISCUSSION

This present study aimed to evaluate the relationship between Scvo2 and tissue specific variables, such as Troponin I level, as tissue oxygen perfusion markers. Some studies have shown that Scvo2 evaluation during and after cardiac surgeries is not useful for critically ill patients, but it can be used for many conditions to evaluate tissue perfusion[12-15]. Sevenmarker et al reported that the risk of premature death increase over 3 years after CABG in patients with central venous saturation <75%[16]. In short term period there is relationship between morbidity and mortality indices and SVO2 [17.18]. Poloen et al reported outcome improved in the patients who had SVO2 more than 70% during operation [19]. Litton et al reported that PaO2 and PaCO2 perfusion index and central venous pressure were a predictor of low ScvO2 in patients after cardiac surgery [20].

The current study demonstrated a reverse relationship between Scvo2 and cardiac Troponin I level as a cardiac perfusion marker. Accordingly, when Scvo2 decreased, myocardial perfusion and oxygenation were impaired and myocardial damages occurred, eventually increasing cardiac Troponin I level after CABG. Nevertheless, there are no data in the literature regarding checking Troponin I level as a prognostic cardiac marker after CABG. Our study results also revealed a reverse association between Scvo2 and Troponin I changes before and after the surgery, which could be due to tissue perfusion structurally or functionally changes during the surgery. Troponin I is one of the special markers only released from myocardium. Nauli et al. [21] reported that troponin I even 30 days after surgery could predict heart failure and low cardiac output syndrome in the patients undergoing elective CABG. Considering the correlation between troponin level and Scvo2 reported in the present study, the patients undergoing CABG are suggested to be monitored with Scvo2 because it is less invasive and less costly and can be used as a predictor for myocardial damages instead of checking during CABG.

The current study findings indicated a reverse association between Scvo2 and pump duration. Accordingly, as pump duration increased, Scvo2 decreased after surgery. This phenomenon might occur due to hypothermia and possible hypoperfusion during prolong pump time that can cause subsequent impairment of tissue oxygenation and decrease in Scvo2. Although we evaluated patients only who had on pump surgery and any relationships which existed were in on pump group, but Malik et al reported that on pump CABG group with cardioplegic arrest causes more myocardial damage than does off pump CABG[22].

In this study, no significant relationship was observed between Scvo2 and ICU admission period, intubation period, and hospital admission duration. Similar results were also obtained by Laine et al. [23]. Hence, Scvo2 changes might not be associated with morbidity and length of hospital stay.

Our study had some limitations. One of the study limitations was that the patients could not be followed for long time due to their poor cooperation. Therefore, future longitudinal and cohort studies are recommended to follow the patients for better evaluation both short- and long-term secondary outcomes, such as EF and quality of life.

CONCLUSION

We can conclude that changes in Scvo2 can predict the probability of myocardial insult due to any hypoxemic reasons which cause cardiomyocytes damages and cardiac prognosis in early postoperative period, so maintaining central venous oxygen saturation above upper normal limit during CABG should be a serious concern to decrease tissue hypoxia especially cardiac muscle and subsequent complications. Also if the patients had low Scvo2 during CABG which didn't rise to normal range despite any effort, intensive post-operative monitoring needed.

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Conflict of Interest
Not declared

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