Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2022 (30 Mar);36.28. https://doi.org/10.47176/mjiri.36.28

The Correlation of Lipid Peroxidation and Antioxidant Capacity on Perioperative Outcomes in On-Pump CABG in Adults

Naser Kachoueian[1], Farhad Gorjipour[2], Koroush Tirgarfakheri[3], Yaser Tolouei Tabar[3], Amirnaser Jadbabaie[1], Sepideh Bohlouli Ghashghaei[4], Kambiz Ghasemy[2], Sona Gorjipour[4], Meysam Mortazian[5*]

Received: 12 Jul 2021 Published: 30 Mar 2022

Abstract

Background: Cardiac surgeries in adults usually use cardiopulmonary bypass (CPB) for cardiac protection and provide a blood-free field for operation. However, due to changes in tissue perfusion and ischemia-reperfusion injury (IRI), there are some side effects for CPB operations. Lipid peroxidation and compromised antioxidant defense are consequences of IRI. This can, in turn, cause organ dysfunction and lead to unwanted biochemical and clinical changes.

Methods: In a cross-sectional study 107 patients with the ages of 35 to 79 years old matching the inclusion criteria with indication for elective on-pump CABG were studied. Renal function, serum malondialdehyde (MDA) and total antioxidant capacity (TAC), and clinical outcomes were studied until 24 hours after intensive care unit (ICU) admission. Correlations between MDA and TAC and other outcomes were tested. Between-group comparisons was one-way ANOVA with repeated measures was used for inferring changes in the plasma TAC and MDA levels, creatinine, and BUN over time. Correlations were investigated using regression models.

Results: Preoperative EF was inversely correlated with TAC at post- CPB time (r= -0.262, p= 0.031). Hyperlipidemia (HLP) was directly associated with higher MDA at post- CPB time (r= 0.267, p= 0.017. Cross-clamp and CPB duration were inversely correlated with the systemic MDA concentration at 24 hours post-ICU admission (r= -0.314, p= 0.005 and r= -0.312, p= 0.005, respectively). Preoperative TAC was inversely correlated with lactate at ICU admission (r= -0.294, p= 0.011). Creatine phosphokinase (CPK) and TAC were directly correlated with post-CPB time (r= -0.327, p= 0.006).

Conclusion: According to the findings, a direct correlation between TAC and myocardial protection during CPB exists. Reduced TAC during CPB is associated with elevation of muscle damage marker CPK. Preoperative HLP is associated with higher circulatory MDA content at the post-CPB time.

Keywords: Cardiac Surgery, Cardiopulmonary Bypass, Oxidative Stress, Total Antioxidant Capacity, Lipid Peroxidation

Conflicts of Interest: *None declared*
Funding: *This study was supported by Shahid Beheshti University of Medical Sciences.*

Cite this article as: Kachoueian N, Gorjipour F, Tirgarfakheri K, Tolouei Tabar Y, Jadbabaie A, Bohlouli Ghashghaei S, Ghasemy K, Gorjipour S, Mortazian M. The Correlation of Lipid Peroxidation and Antioxidant Capacity on Perioperative Outcomes in On-Pump CABG in Adults. *Med J Islam Repub Iran.* 2022 (30 Mar);36:28. https://doi.org/10.47176/mjiri.36.28

Introduction

Cardiopulmonary bypass (CPB) is used to maintain the blood supply of the body and also protect the myocardial

Corresponding author: *Dr Meysam Mortazian, m_mortazian@ajaums.ac.ir*

1. Department of Cardiac Surgery, Imam Hossein Educational Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Iranian Scientific Society of Extracorporeal Technology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran
3. Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran
4. Iran University of Medical Sciences, Tehran, Iran
5. AJA University of Medical Sciences Tehran Iran AJA University of Medical Sciences, Tehran, Iran

↑What is "already known" in this topic:
Oxidative stress is induced following ischemia/reperfusion injury and leads to various peri- and postoperative adverse outcomes including myocardial damage, systemic inflammatory response syndrome, remote organ damage, coagulation disorders, and brain edema. Preoperative history may be correlated with the schemia/reperfusion-induced oxidative stress during CPB.

→What this article adds:
Findings of the current study support correlation of the serum TAC and myocardial protection during CPB. Reduced TAC during CPB is associated with elevation of muscle damage marker CPK. Preoperative HLP is associated with higher circulatory MDA content at the post-CPB time. We suggest that control of lipid peroxidation during CPB may improve the postoperative outcomes, especially in patients with a history of HLP.

[DOI: 10.47176/mjiri.36.28]

tissue against ischemic injury through reducing metabolic demand (1). Despite its role in the protection against ischemic events, ischemia/reperfusion (I/R) injury occurs following the reestablis hment of the blood flow. Ischemia results in the enhanced anaerobic metabolism of the tissue. This, in turn, gives rise to high oxidative stress in the tissue, which overwhelms the capacity of the antioxidant defense system at the cellular and tissue level. Accumulation of the products of oxidation of cellular and components in the tissues incite systemic inflammatory response after reperfusion, re-establishment of the blood flow in the ischemic tissue (2, 3). In a vicious cycle, infiltration of the tissue by immune cells results in the enhancement of the oxidative and nitrosative stress that further induces an inflammatory response. Therefore, the elevation of circulatory proinflammatory cytokines and oxidative stress are post-CPB events that are known to contribute to the development of adverse outcomes of clinical significance (4). The clinical outcomes include changes in body temperature, renal dysfunction, arrhythmia, and dysrhythmias, and other outcomes which may increase the need for intensive care or hospitality. It is well established that elevated lipid peroxidation and impaired antioxidant capacity are major predictors of kidney injury in transplant settings. It has prognostic and diagnostic value for studying the graft dysfunction either in early and late graft rejection (5). Many approaches are suggested for intervening with an oxidative stress response to prevent tissue damage and improve outcomes following ischemia/reperfusion injury (3, 6-11). Evidence exists that MDA is elevated during CPB in patients undergoing coronary artery bypass grafting (CABG) surgery (12). Beyond the negative effect on the ischemic tissue, it may be associated with systemic inflammation and remote organ dysfunction (13, 14). The kidney is very sensitive to post-CPB adverse biochemical alterations I/R injury and systemic inflammatory response. Acute kidney injury (AKI) is one of the outcomes (complication) after cardiac surgery associated with serious morbidity. Temporary or irreversible kidney function loss is serious and difficult to manage condition (15) and its prevention in clinical settings is very important. Clinical markers such as serum level of creatinine (16) and blood urea nitrogen (BUN) are reliable markers for monitoring renal function and excretion of protein catabolism byproducts through the urinary system. However, these are not sufficient for stratifying the patients for late renal damage following operation-associated stress response. MDA is proven to be an early marker of early graft rejection in kidney transplant patients (11). Oxidative stress, as measured by oxidative protein immunostaining, is associated with post-CPB atrial fibrillation (17, 18). We hypothesized that oxidative stress parameters are potentially correlated with the clinical and biochemical peri- and postoperative outcomes and could be used as prognostic or diagnostic markers for patients' management. Therefore, we investigated the trend of total antioxidant capacity (TAC) and MDA as a marker of lipid peroxidation in CPB patients at three different times, pre-operation (after anesthesia induction), post-CPB (weaning from CPB), and 24 hours post-ICU, and correlation with peri- and postoperative outcomes in on-pump CABG operations.

Methods

Study design

In a cross-sectional study, 107 patients to undergo elective cardiac surgery with the cardio-pulmonary bypass (CPB) for (on-pump) CABG were recruited after informed consent in the present cross-sectional study. A convenient sampling method was applied. The available pool of patients referring to the department of cardiac surgery, Imam Hossein Educational Hospital, Shahid Beheshti University of Medical Sciences from the beginning of March 2018 until August 2019 were approached and sought to participate in the current study. Patients meeting the inclusion criteria and consenting to participate after being presented with the study information were recruited. Compliance with the ethical codes of the Helsinki declaration on medical studies including human subjects, was respected during the study. Inclusion criteria were age between 18 to 80 years, written informed consent, candidate for surgery for isolated CABG. Exclusion criteria were emergency surgery, pre-operative circulatory support with inotrope, chronic inflammatory systemic disease such as lupus erythematosus, rheumatoid arthritis, and diabetes, and asthma, renal and/or liver dysfunction. Kidney failure was defined as having a glomerular filtration rate (GFR) of below 15. Liver dysfunction was defined as abnormal levels of liver enzymes.

Operation procedure

Procedures for anesthesia induction and maintenance and operation have been previously described (19). In brief, pulse oximeter and ECG leads were monitored throughout the operation. A 20-gauge catheter was inserted for monitoring the arterial blood pressure. After induction of anesthesia, a triple-lumen catheter was placed into the right internal jugular vein for measuring central venous pressure.

All patients underwent the same anesthesia induction procedure with the same medications. Briefly, induction of anesthesia was through 10 – 15 µg/kg fentanyl and 0.1 mg/kg midazolam bolus. A bolus dose of 0.1 mg/kg pancuronium was administered to facilitate endotracheal intubation. A 5 µg/kg/hr fentanyl and 1 µg/kg/min midazolam were administered after tracheal intubation for anesthesia maintenance. Hemodynamic maintenance was applied using Phenylephrine infusion for hypotensive episodes when MAP or systolic pressure decreased below 40 and 80 mmHg, respectively. Tidal volume was set at 10 mL/kg of body weight-adjusted to respiratory rate, and target ETCO2 was set between 30 and 35 mmHg.

Heparin, 300 UI/Kg was administered before aortic cannulation to achieve activated clotting time (ACT) above 480 seconds. CPB was established in a standard manner with the use of a roller pump and non-pulsatile flow (about 2.4 L/m^2 BSA/min according to blood pressure and body temperature). During CPB, hematocrit was maintained between 25% and 30%. Hypothermia (body temperature maintenance at 30 – 32 °C) was applied. The hypotension correction was performed with Phenylephrine

[DOI: 10.47176/mjiri.36.28]

infusion, when MAP or systolic pressure ascended 40 and 80 mmHg, respectively.

A median sternotomy approach was used for surgery. The left internal mammary artery (with pedicle) and the greater saphenous vein were harvested. 10 ml/kg of Ringer solution was administered before surgery.

Blood samples for plasma TAC and MDA measurements were obtained from CV blood samples at the aforementioned times. Plasma was isolated from heparinized blood samples with centrifugation at 3000 rpm for 10 min, then plasma was isolated and snap-frozen using liquid nitrogen and stored at -80 °C until measurement of the desired parameters. TAC and MDA measurements were performed using commercial kits according to the suppliers' instructions (Navand Salamat, Urmia, Iran) by calorimetric methods. To measure other factors, blood samples were directly transferred to the clinical laboratory at the study center and were analyzed by Hitachi 917 and 912 RA 1000 (Hitachi, Tokyo, Japan) devices using clinical biochemistry reagents. Cross–clamping time, CPB duration, and the number of grafted vessels were also recorded.

Data collection

General demographic data, past medical history, and risk factors, and the peri-operative parameters such as duration of the operation, CPB, and the aortic cross-clamping were recorded. Acute renal disease (ARD) was defined according to blood creatinine; increasing less than 25% from base shows no ARD (20), increasing from 25% to 50% from base shows faint ARD (21), increasing from 50% to 100% from base shows moderate ARD (22), and increasing more than 100% shows severe ARD. The renal function impairment classification based on changes in the creatinine levels is described by others (20-23). ARD was defined by blood level of creatinine before surgery and 24-48 hours after operations.

Blood samples for measuring TAC and MDA were drawn at 1) after induction of anesthesia and before skin incision, 2) after CPB (after weaning from CPB), and 3) 24 hours after ICU admission. TAC and MDA were quantified in plasma for all these times using a standard spectrophotometric method with commercial assay kits Naxifer and Nalondi according to the manufacturer's guide (Navand Salamat, Urmia, Iran). Pre-operative renal function was estimated using the formula of Cockcroft and Gault (24). The volume of diuresis was recorded at the defined time points until 48 hours after the ICU admission.

Statistical analysis

Data analysis was performed using SPSS v18 (IBM Inc., CA, US). Continuous measurements were presented as mean±standard deviation (SD) for normally distributed data or median (interquartile range; IQR) for data with non-normal distribution. One-way ANOVA with repeated measures was used for inferring changes in the plasma TAC and MDA levels, creatinine, and BUN. Correlations were investigated using linear regression. The level of significance of 0.05 and the power of analysis of 0.8 were considered in the analysis.

Results

Patients' demographics and descriptive data and how they are correlated with circulatory TAC and the MDA are presented in Tables 1 and 2. Measurement of the circulatory TAC and MDA levels throughout the study demonstrated a minor change in circulatory levels of these mark-

Table 1. Demographic and background data of the sample population and their correlation with the TAC at three times, preoperative (TAC1), post-declamp (TAC2), and 24 hours after ICU admission (TAC3).

			(ρ) P Values	
Variable	Value (mean ± SD) or frequency%	TAC1	TAC2	TAC3
Age (years)	61.02±9.36	-0.45	-0.08	0.219
		0.697	0.508	0.057
Height (centimeters)	163.66±12.03	0.036	-0.024	-0.017
		0.757	0.844	0.884
Weight (kilograms)	74.83±14.49	-0.055	-0.207	-0.037
		0.637	0.088	0.753
Preoperative EF	45.87±9.91	-0.027	-0.262	-0.136
		0.821	0.03	0.247
Gender (male)	71 (65.1) %	-0.19	-0.122	-0.049
		0.097	0.312	0.674
Hypertension	(68) 63.6%	0.111	-0.018	0.064
		0.336	0.88	0.583
Diabetes	(50) 46.7%	0.123	-0.036	0.184
		0.258	0.767	0.113
Renal disease	(7) 6.5%	-0.22	0.12	-0.028
		0.055	0.32	0.811
Thyroid disorders	(7) 6.5%	-0.076	0.167	0.25
		0.512	0.164	0.029
CNS disorders	(2) 1.9%	0.035	-0.192	-0.105
		0.763	0.108	0.367
HLP	(29) 27.1%	0.098	-0.052	-0.071
		0.398	0.667	0.54
Addiction	(14) 13.1%	0.031	-0.048	0.059
		0.792	0.692	0.615

[DOI: 10.47176/mjiri.36.28]

Table 2. Demographic and background data of the sample population and their correlation with circulatory MDA at three times, preoperative (MDA1), post-declamp (MDA2), and 24 hours after ICU admission (MDA3).

		(r) P Values		
Variables	Value (mean ± SD) or frequency%	MDA1	MDA2	MDA3
Age (years)	61.02±9.36	-0.151	0.018	-0.092
		0.171	0.876	0.417
Height (centimeters)	163.66±12.03	0.027	-0.059	0.086
		0.807	0.608	0.452
Weight (kilograms)	74.83±14.49	-0.136	0.088	0.074
		0.219	0.447	0.514
Preoperative EF	45.87±9.91	0.166	0.053	-0.195
		0.134	0.646	0.085
Gender (male)	71 (65.1) %	-0.107	0.058	-0.071
		0.331	0.611	0.529
Hypertension	(68) 63.6%	-0.066	0.143	0.181
		0.551	0.21	0.108
Diabetes	(50) 46.7%	0.048	0.079	0.075
		0.662	0.491	0.507
Renal disease	(7) 6.5%	-0.057	-0.13	0.109
		0.605	0.254	0.335
Thyroid disorders	(7) 6.5%	0.087	0.022	-0.056
		0.43	0.849	0.622
CNS disorders	(2) 1.9%	-0.093	-0.018	0.026
		0.398	0.877	0.819
HLP	(29) 27.1%	0.057	0.267	-0.202
		0.604	0.017	0.073
Addiction	(14) 13.1%	-0.062	0.061	-0.097
		0.574	0.593	0.394

ers which were not statistically significant (Figs. 1 and 2). A significant inverse correlation was observed between preoperative EF and the total antioxidant capacity at separation from CPB (r= -0.262, p= 0.031) (Table 1).

Having a history of hyperlipidemia was associated with higher post-CPB circulatory MDA (r= 00.267, p= 0.017) (Table 2). Although no significant differences between perioperative parameters and the circulatory TAC level were observed (Table 3), there was a significant reverse correlation between aortic cross-clamp and CPB duration from one side and the MDA 24 hours after ICU admission from another side (r= -0.314, p= 0.005 and r= -0.312, p= 0.005, respectively) (Table 4).

The serum level of CPK after the operation was inversely correlated with the TAC at the post-CPB time (r= -0.283, p= 0.019). A similar trend was observed in the correlation between postoperative serum lactate and the TAC before operation (r= -0.294, p= 0.011) (Table 5). However, a similar trend was not observed between blood MDA levels and the biochemical parameters before, during, or after the operation (Table 6).

Discussion

In the current study, we measured the circulatory, antioxidant capacity and lipid peroxidation to understand the trends in these characteristics of the CPB and its potential correlation with the clinical and biochemical parameters in the course of patient management.

Among the preoperative characteristics, EF was inversely correlated with the TAC at the post-CPB time, and the

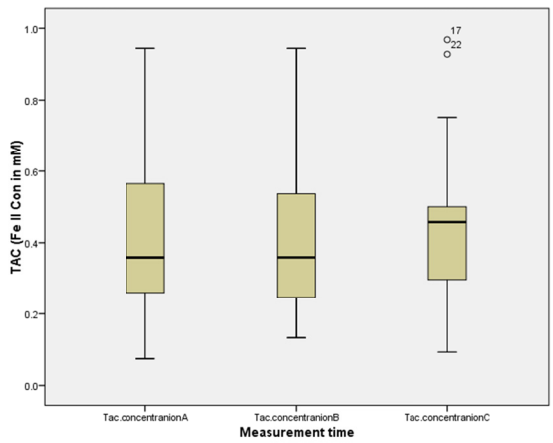

Fig. 1. Total antioxidant capacity (TAC) was measured in patients at three time points pre-operation, post-CPB, and 24 hours after ICU admission in plasma samples obtained by centrifuging of venous blood samples. The ferric reducing antioxidant power (FRAP) method was used for measuring the TAC.

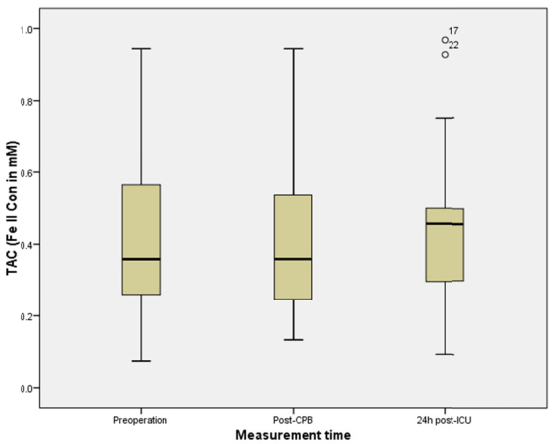

Fig. 2. Malondialdehyde (MDA) was measured in patients at three-time points pre-operation, post-CPB, and 24 hours after ICU admission in plasma samples obtained by centrifuging of venous blood samples. The Thiobarbituric acid reactive substances (TBARS) assay was used for measuring the MDA.

[DOI: 10.47176/mjiri.36.28]

Table 3. Peri- and postoperative clinical outcomes and the correlation of TAC at three times, preoperative (TAC1), post-declamp (TAC2), and 24 hours after ICU admission (TAC3).

Study variables	Mean± SD	Correlation coefficient and P-value		
		TAC1	TAC2	TAC3
Cross clamp time(min)	41.97±16.59	0.013	-0.138	0.027
		0.907	0.260	0.815
CPB (min)	74.75±25.31	0.026	-0.007	-0.012
		0.824	0.955	0.921
Operation time (hours)	5.078±1.086	-0.054	-0.055	0.036
		0.642	0.646	0.757
Mechanical Ventilation (hours)	18.91±54.04	-0.007	0.175	0.148
		0.955	0.151	0.217
ICU stay (days)	3.408±1.78	-0.063	-0.041	0.107
		0.593	0.739	0.370
Postop bleeding (cc)	530.93±411.01	0.167	0.143	0.167
		0.163	0.255	0.174

Table 4. Peri- and postoperative clinical outcomes and their correlation with circulatory MDA level at three times, preoperative (MDA1), post-declamp (MDA2), and 24 hours after ICU admission (MDA3).

	Mean± SD	Correlation coefficient and P-value		
		MDA1	MDA2	MDA3
Cross clamp time(min)	41.97±16.59	-0.092	0.060	-0.314
		0.409	0.604	0.005
CPB (min)	74.75±25.31	-0.061	0.022	-0.312
		0.582	0.847	0.005
Operation time (hours)	5.078±1.086	-0.196	0.097	-0.156
		0.074	0.396	0.166
Mechanical Ventilation (hours)	18.91±54.04	0.009	0.060	0.102
		0.938	0.597	0.380
ICU stay (days)	3.408±1.78	0.049	-0.139	0.014
		0.660	0.225	0.901
Postop bleeding (cc)	530.93±411.01	0.079	0.107	0.049
		0.497	0.361	0.675

correlation was inverse. It is probably reflecting the fact that lower EF is associated with inadequate perfusion and exposes the tissue to metabolic insufficiency and oxidative stress which activates the antioxidative response through a feedback mechanism. Therefore, causing the tissue to achieve better antioxidant protection against reperfusion injury following the reestablishment of the circulation to the cardiac tissue following cross-clamp removal (25). Similarly, a significant negative correlation between cross-clamp time and CPB time from one side and the MDA 24 hours after ICU admission from the other side could be justified according to the same rationale i.e. temporary higher oxidative stress may cause activation of the competent antioxidant defense system which in turn reduces the level of the oxidative stress and its marker MDA. However, to make conclusive comments regarding this justification, further studies are required. For example, the measurement of the activity of enzymes contributing to the antioxidant defense is very helpful in understanding the causes behind these events during and after the operation.

Patients with preoperative hyperlipidemia had higher levels of post-CPB circulatory MDA. It has been established that patients with hyperlipidemia have impaired antioxidant defense systems. According to previous studies, superoxide dismutase and glutathione peroxidase activities in hyperlipidemic patients have been demonstrated to be significantly lower than that in normolipidemic patients (26). Therefore, it is reasonable to attribute the higher MDA levels in hyperlipidemic patients to impaired or weak oxidative stress defense system.

The circulatory level of CPK after the operation was inversely correlated with the TAC at the post-CPB time. This finding supports the fact that an improved antioxidant defense system and higher antioxidative capacity moderates the negative effects of the reperfusion injury, therefore reducing the damage to the myocardial muscle. Indeed oxidative stress due to impaired antioxidant capacity and reduced TAC is the main contributor to the reperfusion injury-associated inflammatory response and tissue damage (27). A similar trend was observed when testing the correlation between postoperative circulatory lactate and the TAC before the operation which could be justified by the fact that lactate as a main metabolite and indicator of the anaerobic metabolism, is elevated following oxidative stress (28).

It appears that oxidative stress and lipid peroxidation has a complex interplay with other determinants of the reperfusion injury, including inflammation and tissue damage during CPB and may be correlated with subsequent adverse events. Impaired antioxidant defense is associated with postoperative adverse events and improving the antioxidant capacity by intervening with its determinants may prevent these adverse events.

[DOI: 10.47176/mjiri.36.28]

Table 5. Biochemical analysis was performed in patients and their correlation with TAC at three times, preoperative (TAC1), post-declamp (TAC2), and 24 hours after ICU admission (TAC3), are presented here.

Variables	Mean ±SEM or median (Q1-Q3)	(r) P Values		
		TAC1	TAC2	TAC3
Creatinine Pre Operation (mg/dL)	1.0 (0.9-1.2)	-0.013	-0.092	0.124
		0.911	0.450	0.287
Creatinine Post CPB (mg/dL)	0.9 (0.8-1.1)	-0.038	0.042	0.121
		0.747	0.731	0.304
Creatinine 24h (mg/dL)	1.0 (0.8-1.25)	-0.006	-0.003	0.059
		0.957	0.980	0.614
BUN Pre Operation (mg/dL)	18.0 (14.0-21.0)	0.057	0.218	0.216
		0.622	0.069	0.063
BUN Post CPB (mg/dL)	17.0 (14.0-20.0)	0.087	0.062	0.163
		0.456	0.611	0.166
BUN 24h (mg/dL)	19.0 (14.0-20.5)	0.041	-0.006	0.088
		0.724	0.958	0.456
Pre-Operation CPK	89.5 (56.0-137.0)	-0.177	-0.220	-0.208
		0.230	0.137	0.182
Post-CPB CPK	329.0 (231.5-526)	-0.046	-0.283	-0.054
		0.695	0.019	0.647
CPK 24h	698.5 (444.5-1100.0)	0.027	-0.057	-0.002
		0.820	0.643	0.985
Post-CPB lactate	1.80 (1.20-2.4)	0.008	-0.082	0.125
		0.945	0.499	0.287
ICU admission lactate	1.90 (1.20-2.90)	-0.294	0.002	-0.067
		0.011	0.990	0.576
Lactate 6 h postop	2.05 (1.40-3.50)	-0.106	-0.134	-0.144
		0.370	0.275	0.223

Table 6. Biochemical analysis was performed in patients and their correlation with circulatory MDA level at three times, preoperative (MDA1), post-declamp (MDA2), and 24 hours after ICU admission (MDA3), are presented here.

Variable	Mean ±SEM or median (Q1-Q3)	P Values (r)		
		MDA1	MDA2	MDA3
Creatinine Pre Operation (mg/dL)	1.0 (0.9-1.2)	0.065	0.050	0.211
		0.557	0.661	0.062
Creatinine Post CPB (mg/dL)	0.9 (0.8-1.1)	-0.058	0.146	0.189
		0.605	0.198	0.095
Creatinine 24h (mg/dL)	1.0 (0.8-1.25)	-0.069	0.102	0.205
		0.536	0.371	0.070
BUN Pre-Operation (mg/dL)	18.0 (14.0-21.0)	0.005	-0.167	0.136
		0.961	0.140	0.232
BUN Post CPB (mg/dL)	17.0 (14.0-20.0)	-0.072	-0.029	0.140
		0.519	0.799	0.217
BUN 24h (mg/dL)	19.0 (14.0-20.5)	0.014	-0.009	0.123
		0.899	0.936	0.284
Pre Operation CPK	89.5 (56.0-137.0)	-0.045	0.144	0.061
		0.751	0.304	0.667
Post-CPB CPK	329.0 (231.5-526)	-0.050	-0.075	-0.146
		0.654	0.514	0.202
CPK 24h	698.5 (444.5-1100.0)	0.197	0.093	0.035
		0.076	0.416	0.760
Post-CPB lactate	1.80 (1.20-2.4)	-0.005	-0.005	0.000
		0.965	0.966	1.000
ICU admission lactate	1.90 (1.20-2.90)	0.054	0.071	0.041
		0.629	0.539	0.720
Lactate 6 h postop	2.05 (1.40-3.50)	0.156	0.151	-0.209
		0.162	0.186	0.067

Conclusion

Higher level of oxidative stress is associated with adverse outcomes such as increased cardiac muscle damage in adult patients in CPB settings as evidenced by enhanced circulatory CPK level Findings hint that proper control of the oxidative stress is vital for the control of unfavorable clinical and pathological outcomes in these patients.

Acknowledgments

We would like to extend our warmest gratitude to the operation room staff for their cooperation during this study.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Azarfarin R, Dashti M, Totonchi Z, Ziyaeifard M, Mehrabanian M, Alizadehasl A, et al. Efficacy of the "head-up position" in returning

[DOI: 10.47176/mjiri.36.28]

cardiopulmonary bypass blood to the patient and reducing the required blood transfusion: A randomized trial. Iran Heart J. 2017;18(1):6-15.
2. Farsad BF, Janipour M, Totonchi Z, Gorjipour F, Oroji Omid S. Effects of Dexmedetomidine on surgical stress responses at patients under CABG. Biosci Biotechnol Res Asia. 2016;13(3):1537-45.
3. Gorjipour F, Dehaki MG, Totonchi Z, Hajimiresmaiel SJ, Azarfarin R, Pazoki-toroudi H, et al. Inflammatory cytokine response and cardiac troponin I changes in cardiopulmonary bypass using two cardioplegia solutions; del Nido and modified St. Thomas': a randomized controlled trial. Perfusion. 2017;32(5):394-402.
4. Zahler S, Massoudy P, Hartl H, Hähnel C, Meisner H, Becker BF. Acute cardiac inflammatory responses to postischemic reperfusion during cardiopulmonary bypass. Cardiovasc Res. 1999;41(3):722-30.
5. Fonseca I. Malondialdehyde as a Biomarker in Kidney Transplantation. In: Patel VB, Preedy VR, editors. Biomarkers in Kidney Disease. Dordrecht: Springer Netherlands; 2016. p. 849-73.
6. Gorjipour F, Totonchi Z, Gholampour Dehaki M, Hosseini S, Tirgarfakheri K, Mehrabanian M, et al. Serum levels of interleukin-6, interleukin-8, interleukin-10, and tumor necrosis factor-α, renal function biochemical parameters and clinical outcomes in pediatric cardiopulmonary bypass surgery. Perfusion. 2019:0267659119842470.
7. Gorjipour F, Hosseini-Gohari L, Ghavidel AA, Hajimiresmaiel SJ, Naderi N, Azar AD, et al. Mesenchymal stem cells from human amniotic membrane differentiate into cardiomyocytes and endothelial-like cells without improving cardiac function after surgical administration in rat model of chronic heart failure. J Cardiovasc Thoracic Res. 2019;11(1):35.
8. Tabaei AS, Mortazian M, Yaghoubi A, Gorjipour F, Manesh SA, Totonchi Z, et al. Modified Ultrafiltration in Coronary Artery Bypass Grafting: A Randomized, Double-Blinded, Controlled Clinical Trial. Iran Red Crescent Med J. 2018;20(5).
9. Asadi Y, Gorjipour F, Behrouzifar S, Vakili A. Irisin peptide protects brain against ischemic injury through reducing apoptosis and enhancing BDNF in a rodent model of stroke. Neurochem Res. 2018;43(8):1549-60.
10. Karimi AA, Asadi Y, Aboutaleb N, Gorjipour F, Malekloo R, Pazoki-Toroudi H. Improvement of Tissue Survival of Skin Flaps by 5α-Reductase Inhibitors: Possible Involvement of Nitric Oxide and Inducible Nitric Oxide Synthase. Iran Biomed J. 2015.
11. Fonseca I, Reguengo H, Almeida M, Dias L, Martins LS, Pedroso S, et al. Oxidative stress in kidney transplantation: malondialdehyde is an early predictive marker of graft dysfunction. Transplantation. 2014;97(10):1058-65.
12. Zakkar M, Guida G, Suleiman MS, Angelini GD. Cardiopulmonary Bypass and Oxidative Stress. Oxid Med Cell Longev. 2015;2015:8.
13. Wang H, Bloom O, Zhang M, Vishnubhakat JM, Ombrellino M, Che J, et al. HMG-1 as a late mediator of endotoxin lethality in mice. Science. 1999;285(5425):248-51.
14. Tsung A, Sahai R, Tanaka H, Nakao A, Fink MP, Lotze MT, et al. The nuclear factor HMGB1 mediates hepatic injury after murine liver ischemia-reperfusion. J Exp Med. 2005;201(7):1135-43.
15. Javidan AN, Shahbazian H, Emami A, Yekaninejad MS, Emami-Razavi H, Farhadkhani M, et al. Safety and efficacy of PDpoetin for management of anemia in patients with end stage renal disease on maintenance hemodialysis: results from a phase IV clinical trial. Hematol Rep. 2014;6(3).
16. Ostermann M, Joannidis M. Acute kidney injury 2016: diagnosis and diagnostic workup. Crit Care. 2016;20:299.
17. Ramlawi B, Otu H, Mieno S, Boodhwani M, Sodha NR, Clements RT, et al. Oxidative Stress and Atrial Fibrillation After Cardiac Surgery: A Case-Control Study. Ann Thoracic Surg. 2007;84(4):1166-73.
18. Jeganathan J, Saraf R, Mahmood F, Pal A, Bhasin MK, Huang T, et al. Mitochondrial Dysfunction in Atrial Tissue of Patients Developing Postoperative Atrial Fibrillation. Ann Thoracic Surg. 2017;104(5):1547-55.
19. Farsad BF, Janipour M, Totonchi Z, Gorjipour F, Omid SO. Effects of dexmedetomidine on surgical stress responses at patients under CABG. Biosci Biotechnol Res Asia. 2016;13(3):1537-45.
20. Tuttle KR, Worrall NK, Dahlstrom LR, Nandagopal R, Kausz AT, Davis CL. Predictors of ARF after cardiac surgical procedures. Am J Kidney Dis. 2003;41(1):76-83.
20. Tuttle KR, Worrall NK, Dahlstrom LR, Nandagopal R, Kausz AT, David CL. Predictors of ARF after cardiac surgical procedures. Am J Kidney Dis. 2003;41:76-83.
21. Andersson LG, Ekroth R, Bratteby LE, Hallhagen S, Wesslén Ö. Acute renal failure after coronary surgery-a study of incidence and risk factors in 2009 consecutive patients. Thorac Cardiovasc Surg. 1993;41(04):237-41.
22. Bove T, Calabro MG, Landoni G, Aletti G, Marino G, Crescenzi G, et al. The incidence and risk of acute renal failure after cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18(4):442-5.
23. Gueret G, Lion F, Guriec N, Arvieux J, Dovergne A, Guennegan C, et al. Acute renal dysfunction after cardiac surgery with cardiopulmonary bypass is associated with plasmatic IL6 increase. Cytokine. 2009;45(2):92-8.
24. Cockcroft DW, Gault H. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41.
25. Dogan A, Turker FS. The Effect of On-Pump and Off-Pump Bypass Operations on Oxidative Damage and Antioxidant Parameters. Oxid Med Cell Longev. 2017;2017:8271376-8271376.
26. Yang RL, Shi YH, Hao G, Li W, Le GW. Increasing Oxidative Stress with Progressive Hyperlipidemia in Human: Relation between Malondialdehyde and Atherogenic Index. J Clin Biochem Nutr. 2008;43(3):154-8.
27. Clermont G, Vergely C, Jazayeri S, Lahet J-J, Goudeau J-J, Lecour S, et al. Systemic free radical activation is a major event involved in myocardial oxidative stress related to cardiopulmonary bypass. Anesthesiology. 2002;96(1):80-7.
28. Christen S, Finckh B, Lykkesfeldt J, Gessler P, Frese-Schaper M, Nielsen P, et al. Oxidative stress precedes peak systemic inflammatory response in pediatric patients undergoing cardiopulmonary bypass operation. Free Radic Biol Med. 2005;38(10):1323-32.

[DOI: 10.47176/mjiri.36.28]