

ORIGINAL ARTICLE

Comparison of CKMB, Lactate Levels and Ejection Fraction with Warm and Cold Cardioplegia on First Post Operative Day in Elective CABG Cases

TUFAIL AHMAD¹, SOBIA SIDDIQUE², ABUBAKAR SADIQ³^{1,2}Resident Cardiac Surgery Armed Forces Institute of Cardiology AFIC /NIHD Rawalpindi³Resident Paeds Cardiology Armed Forces Institute of Cardiology AFIC /NIHD RawalpindiCorresponding author: Tufail Ahmad, Email: horizonstar89@gmail.com, Cell: 03001402333**ABSTRACT**

Objectives: The main objective of the study is to find the comparison of CKMB, Lactate levels and ejection fraction with warm and cold cardioplegia on first post OP day in elective CABG cases.

Material and methods: This cross sectional study was conducted in Armed forces institute of cardiology AFIC /NIHD Rawalpindi during 1st October 2022 to 30th November 2022. Data was collected with the permission of ethical committee of hospital. The study variables were included level of troponin I during intraoperative and post-operative period, time taken for cardiac standstill, CKMB, Lactate levels and ejection fraction with warm and cold cardioplegia, post-operative improvement in ejection fraction, number of days in ICU.

Results: The data was collected from 100 patients. There was no statistically significant difference between the two groups as regards bypass and cross clamp times. Mean age of group I patients was 61.3 ± 12.5 years and for group II patients was 67.4 ± 10.4 years. P value of serum lactate level is <0.01, which is statistically significant. All the patients had elevated lactate level but the range of increase in lactate level was seen in those who didn't take adenosine as compared to those who took adenosine.

Practical Implications: Enzymes play an important role in both cold and warm cardioplegia.

Conclusion: It is concluded that there is less cardiac enzymes release after the application of warm blood cardioplegia for myocardial protection in patients undergoing CABG as compared to cold crystalloid cardioplegia.

Keywords: Cardioplegia, CKMB, Troponin, CABG, Cold

INTRODUCTION

The use of cardiopulmonary bypass (CPB), cardioplegic arrest, and subsequent reperfusion of the heart causes a systemic inflammatory response and ischemia-reperfusion injury, which are responsible for significant postoperative morbidity. Cardioplegic arrest of the heart in diastole is induced and maintained by injecting a potassium rich fluid into the coronary arteries, reducing the heart's oxygen consumption by about 90%, when the fluid is administered at physiological temperature¹. The medium into which the potassium is mixed can be either blood or crystalloid solution. Both of these can be administered cold (4 °C–10 °C), which can further reduce oxygen consumption in the arrested heart. Management of patients with coronary artery disease (CAD) with reduced ejection fraction (EF) remains a challenge, despite the new advances in medical therapy and surgical revascularization².

Patients with low EF undergoing coronary artery bypass graft (CABG) (compared with patients with normal left ventricular (LV) function) are usually associated with higher need for inotropic support; intra-aortic balloon pump; longer hours of ventilation, intensive care unit (ICU), and hospital stay; and higher postoperative morbidity and mortality³. Various techniques for cardioplegia delivery have been developed to optimize myocardial preservation and to decrease ischemia reperfusion injury. The optimal cardioplegia temperature during CABG surgery has been one of the most important aspects of myocardial protection⁴.

Blood cardioplegia at physiological temperature will improve the postoperative outcome for better myocardial protection due to the improvement of oxygen availability. Also, blood will improve the oxygen carrying capacity and is less accompanied with hemodilution⁵. Although cold cardioplegia can lower myocardial oxygen consumption and demands, myocardial enzymes may inhibit and delay metabolic and functional cardiac recovery after surgery. Blood cardioplegia will inhibit proteins responsible for ischemia reperfusion-induced apoptosis than crystalloid cardioplegia⁶.

Blood cardioplegic solution releases only 50% of its total oxygen content when cooled to 20 °C, and only 37% to 38% when cooled to 10 °C, because of the leftward shift of the oxyhemoglobin dissociation curve with hypothermia.¹¹ In addition, normothermic cardioplegic arrest results in an oxygen requirement of 1.1 mL oxygen/100 g/min, greater than 90% reduction of baseline

values⁷. If oxygenated blood can reach the arrested myocardium, oxygen demand can be met via warm cardioplegia. Oxygen demand is reduced to less than 0.3 mL/100 g/min at 20 °C. However, reduction in intracellular concentrations of metabolites and high-energy phosphates and suboptimal recovery of contractile function after intermittent hypothermic cardioplegia suggests that anaerobic metabolism does not completely meet the substantially reduced metabolic needs of the arrested hypothermic heart⁸.

Despite of improvements in surgical and myocardial protection techniques, postoperative ventricular dysfunction after cardiac surgery is clinically not uncommon and well observed experimentally⁹. Insufficient cardioplegia results in anaerobic metabolism during cardiac arrest with subsequent heart failure. However, a more detailed knowledge is required about myocardial regulation processes in concentration of nutrients and information about interstitial fluid shifts due to perfusion of cardioplegic solutions. Numerous investigations on the effect of different cardioplegic solutions were published, but up to now, monitoring of the post ischaemic human myocardium is focussed only on global myocardial function, systemic haemodynamics and on indirect criteria to assess oxidative stress in the clinical setting¹⁰.

The main objective of the study is to find the comparison of CKMB, Lactate levels and ejection fraction with warm and cold cardioplegia on first post OP day in elective CABG cases.

MATERIAL AND METHODS

This cross sectional study was conducted in Armed forces institute of cardiology AFIC /NIHD Rawalpindi during 1st October 2022 to 30th November 2022. Data was collected with the permission of ethical committee of hospital.

Inclusion criteria

- Both male and female patients
- Age > 18 years

Exclusion criteria

- Patients with cerebrovascular disease and renal failure, single-vessel coronary disease, emergency and redo operation were excluded from the study.

Data collection

Data was collected with the permission of ethical committee of hospital. Patients were divided two groups:

- Group I: antegrade cold crystalloid cardioplegia with topical cooling
- Group II: antegrade warm blood cardioplegia

The study variables were included level of troponin I during intraoperative and post-operative period, time taken for cardiac standstill, CKMB, Lactate levels and ejection fraction with warm and cold cardioplegia, post-operative improvement in ejection fraction, number of days in ICU. The study population comprises 100 patients who underwent elective coronary artery bypass grafting (CABG) surgery. The patients was divided into two groups based on the administration of cardioplegia with adenosine and

without adenosine during surgery and postoperative changes in the two groups.

Statistical analysis: The data was collected and analyzed using SPSS version 20. All the values were expressed in mean and standard deviation.

RESULTS

The data was collected from 100 patients. There was no statistically significant difference between the two groups as regards bypass and cross clamp times. Mean age of group I patients was 61.3 ± 12.5 years and for group II patients was 67.4 ± 10.4 years. All the basic values were represented in table 01.

Table 1: Basic characteristics of patients selected in both groups

	All patients	Group I	Group II	P value
Age, yr	63.5 ± 12.1	61.3 ± 12.5	67.4 ± 10.4	< 0.001
History and cardiovascular risk factors				
Known diabetes, n (%)	82 (25)	45 (22)	37 (31)	
Abnormal glucose metabolism, n (%)	106 (32)	68 (33)	38 (32)	
Hypertension, n (%)	238 (73)	134 (64)	104 (88)	
Smoking habit, n (%)	106 (32)	81 (39)	25 (21)	
Family history, n (%)	179 (55)	111 (53)	68 (58)	
Previous CABG, n (%)	26 (8)	7 (3)	19 (16)	
Previous PCI, n (%)	43 (13)	13 (6)	30 (25)	
Previous AMI, n (%)	60 (18)	21 (10)	39 (33)	
Previous stroke, n (%)	11 (3)	5 (2)	6 (5)	
Total cholesterol (under treatment), mg/dL	124.3 ± 26.0	123.4 ± 26.3	125.8 ± 25.5	0.424
Metabolic syndrome, n (%)	204 (62)	124 (60)	80 (68)	
BMI	27.2 ± 4.3	26.9 ± 3.7	27.9 ± 5.2	0.090
Left ventricle ejection fraction, %	47.2 ± 10.3	47.8 ± 9.2	46.4 ± 12.0	0.222
Patients with LVEF < 40%, n (%)	85 (26)	43 (21)	41 (35)	
Patient with heart failure at initial admission, n(%)	37 (11)	15 (7)	22 (19)	

Table 02 shows the CKMB levels in both groups. As regards CK, and CK-MB enzymes, there was a statistically significant difference in the 3rd sample (after 24 h) between the two groups, with the lower level in Group II.

Table 2: Postoperative CKMB level (IU).

Enzyme	Group I	Group II	P value	Significance
Immediate postop.	21.9 ± 36.1	12.9 ± 29.9	0.65	Non-significant
12 h postop.	14.3 ± 4.3	14.1 ± 2.15	0.091	Non-significant
24 h postop.	14.93 ± 4.2	6.89 ± 3.1	0.001	Significant

Table 03 shows the Troponin I level (µg/L) among both groups. Troponin I release was significantly lower in warm cardioplegia Group II.

Table 3: Postoperative Troponin I level (µg/L).

Enzyme	Group I	Group II	P value	Significance
Immediate postop.	1.76 ± 0.32	1.26 ± 0.20	<0.05	significant
12 h postop.	6.20 ± 1.15	5.21 ± 0.48	<0.01	significant
24 h postop.	6.81 ± 1.26	4.15 ± 0.57	<0.01	significant

P value of serum lactate level is <0.01, which is statistically significant. All the patients had elevated lactate level but the range of increase in lactate level was seen in those who didn't take adenosine as compared to those who took adenosine

Table 4: Postoperative serum lactate levels (µg/L).

Enzyme	Group I	Group II	P value	Significance
Immediate postop.	2.76 ± 0.32	2.26 ± 0.19	<0.05	significant
12 h postop.	1.20 ± 1.15	1.21 ± 0.48	<0.01	significant
24 h postop.	1.81 ± 1.26	1.15 ± 0.91	<0.01	significant

DISCUSSION

Heart rate variability is used to assess the balance between vagal and sympathetic activity or autonomic disturbances in the heart rate which leads to cardiac arrhythmia and sudden death. In 1965

Hon and Lee first time noticed that 10-12 fetal distress is associated with change in heart beat intervals¹¹. HRV is accepted as clinical test when it was 13 confirmed that it is one of the strong and independent risk factors for cardiac arrhythmias and sudden death especially after acute myocardial infarction. Myocardial cell injury after cardiac surgery is unavoidable with the currently available hyperkalaemic cardioplegic solutions¹². Several modifications to the cardioplegic solutions were made to decrease this cellular injury¹³. The concept of warm blood cardioplegia was introduced in 1983, based on a study that found that normothermic arrested heart requires 80- 90% less oxygen than does the normal working heart and from reports that indicated that 'Hot Shot' has significantly positive effects on myocardial recovery. The deliberate use of intermittent antegrade warm blood cardioplegia was for the first time reported by Calafiore in a retrospective study. It has become the standard of care to administer antegrade blood cardioplegia for CABG procedures¹⁴.

Cardiac troponin I (cTn I) is one of the biomarkers used for risk assessment of several cardiac diseases and post cardiac surgery. It is released whenever myocardial injury occurs regardless of the mechanism of injury and its release post cardiac surgery was found to be associated with increased morbidity and mortality. Thus, high sensitivity cardiac cTn I is a marker of myocardial injury and it has a prognostic role in several cardiac pathologies and after cardiac surgeries¹⁵.

Jacquet et al. reported an average age 65.2 ± 8.5 in cold crystalloid group and 64.5 ± 9.6 in warm blood group, with female percentage of 27.5% in contrast to our study which had the female percentage of 13%¹⁶. A recent study by Zerriouh et al. reported a 35.6% of patients more than 70 year of age with 20.8% female ratio. Blood cardioplegia was introduced in the 1970s and provides superior myocardial protection compared with crystalloid cardioplegia [13]. A variety of methods are in use and subject to investigations in terms of delivery, pressure, time, and temperature of the cardioplegic solutions¹⁷. Different temperatures of the cardioplegic solution during induction were shown to have a significant impact on the metabolic activity of the heart. The optimal temperature is discussed controversially. In the beginning, reducing the metabolic activity of the heart was considered to play

a key role in protecting the myocardium from ischaemia. Hypothermic cardioplegia was first introduced in the 1960s. Several studies then appeared suggesting that hypothermic cardioplegia may damage the myocardium and vascular endothelium¹⁸.

CONCLUSION

It is concluded that there is less cardiac enzymes release after the application of warm blood cardioplegia for myocardial protection in patients undergoing CABG as compared to cold crystalloid cardioplegia. That indicates less myocardial cell injury associated with warm blood cardioplegia.

Recommendation

Decreased level of cardiac enzymes and lower inotropic requirement suggests that an optimal myocardial protection with less cellular damage is obtained with adenosine pre-treatment as adjunct to cold blood cardioplegia.

Conflicts of interest

There is no conflict of interest by authors.

Funding

There is no funding association for this study.

Ethical Approval

REFERENCES

1. Sabiston DC, William F. Rienhoff Jr. The coronary circulation. Johns Hopkins Med J. 1974;134:314-29.
2. Kishore LJ, Vinu CV, Abdul RMH, Sony PS. Comparison of troponin I level among the patients who underwent coronary artery bypass grafting with and without adenosine as an adjunct to blood cardioplegia. *Int Surg J* 2021;8:3069-74.
3. Rinne T, Laurikka J, Penttilä I, Kaukinen S. Adenosine with cold blood cardioplegia during coronary revascularization. *Journal of cardiothoracic and vascular surgery*. 2000;14(1):18-20
4. Jakobsen O, Næsheim T, Nergard K, Sørli, Steensrud T. Adenosine instead of supranormal potassium in cardioplegia: it is safe, efficient, and reduces the incidence of postoperative atrial fibrillation. A randomized clinical trial. *The journal of thoracic and cardiovascular surgery*. 2013.
5. Mahrose, R., Shorbagy, M.S., Shahin, K.M. et al. Warm blood cardioplegia versus cold crystalloid cardioplegia for coronary artery bypass grafting (CABG) in patients with low ejection fraction. *Ain Shams J Anesthesiol* 12, 18 (2020). <https://doi.org/10.1186/s42077-020-00069-8>
6. Cleland JG, Calvert M, Freemantle N, Arrow Y, Ball SG, Bonser RS, Chattopadhyay S, Norell MS, Pennell DJ, Senior R (2011) The Heart Failure Revascularization Trial (HEART). *Eur J Heart Fail* 13:227
7. Fan Y, Zhang AM, Xiao YB, Weng YG, Hetzer R (2010) Warm versus cold cardioplegia for heart surgery: a meta-analysis. *Eur J Cardiothorac Surg* 37(4):912–919
8. Guru V, Omura J, Alghamdi AA, Weisel R, Fremes SE (2006) Is blood superior to crystalloid cardioplegia? A meta-analysis of randomized clinical trials. *Circulation* 114(Suppl I):I-331–I-338
9. James TM, Nores M, Rousou JA, Lin N, Stamou SC. Warm Blood Cardioplegia for Myocardial Protection: Concepts and Controversies. *Tex Heart Inst J*. 2020 Apr 1;47(2):108-116. doi: 10.14503/THIJ-18-6909. PMID: 32603472; PMCID: PMC7328091.
10. Mallidi HR, Sever J, Tamariz M, Singh S, Hanayama N, Christakis GT et al. The short-term and long-term effects of warm or tepid cardioplegia. *J Thorac Cardiovasc Surg*. 2003;125(3):711–20.
11. Liakopoulos OJ, Kuhn EW, Choi YH, Chang W, Wittwer T, Madershahian N et al. Myocardial protection in cardiac surgery patients requiring prolonged aortic cross-clamp times: a single-center evaluation of clinical outcomes comparing two blood cardioplegic strategies. *J Cardiovasc Surg (Torino)* 2010;51(6):895–905
12. Ascione R, Caputo M, Gomes WJ, Lotto AA, Bryan AJ, Angelini GD, Suleiman MS. Myocardial injury in hypertrophic hearts of patients undergoing aortic valve surgery using cold or warm blood cardioplegia. *Eur J Cardiothorac Surg*. 2002;21(3):440–6.
13. Fan Y, Zhang AM, Xiao YB, Weng YG, Hetzer R. Warm versus cold cardioplegia for heart surgery: a meta-analysis. *Eur J Cardiothorac Surg*. 2010;37(4):912–9.
14. Abah U, Garfield Roberts P, Ishaq M, De Silva R. Is cold or warm blood cardioplegia superior for myocardial protection? *Interact Cardiovasc Thorac Surg*. 2012;14(6):848–55.
15. Baig MA, Sher-I-Murtaza M, Iqbal A, Ahmad MZ, Farhan Ali Rizvi HM, Ahmed N et al. Clinical outcomes of intermittent antegrade warm versus cold blood cardioplegia. *J Pak Med Assoc*. 2015;65(6):593–6.
16. Matsuura H, Lazar HL, Yang XM, Rivers S, Treanor PR, Shemin RJ. Detrimental effects of interrupting warm blood cardioplegia during coronary revascularization. *J Thorac Cardiovasc Surg*. 1993;106(2):357–61
17. Sirvinskas E, Nasvytis L, Raliene L, Vaskelyte J, Toleikis A, Trumbeckaite S. Myocardial protective effect of warm blood, tepid blood, and cold crystalloid cardioplegia in coronary artery bypass grafting surgery. *Croat Med J* 2005;46(6):879e88.