ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

COMPARISON OF ANTEGRADE WITH ANTEGRADE/RETROGRADE CARDIOPLEGIA FOR MYOCARDIAL REVASCULARIZATION IN CORONARY ARTERY BYPASS GRAFTING

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ABSTRACT

Background: Cardioplegia aimed to protect myocardial function during cardiac surgery and facilitate surgical procedures providing a quiet and bloodless operative field. Integrated cardioplegia offers superior myocardial protection of left ventricular free wall and septum compared with antegrade mode of cardioplegia delivery.

Objective: To compare the post-operative myocardial protection indicators of antegrade cardioplegia and antegrade/retrograde cardioplegia during surgery in patients undergoing coronary artery bypass grafting surgery.

Study Design: Prospective Cohort Study

Setting: Department of Cardiac Surgery, National Institute of Cardiovascular Diseases, Karachi.

Duration: 3rd August 2019 To 2nd February 2020

Material and Methods: 80 patients underwent CABG with antegrade/retrograde cardioplegia (exposed Group) and 80 patients with antegrade cardioplegia (unexposed Group) were included. Post inotropic Support and retained postoperative ejection fraction were obtained. Comparison between exposed and unexposed group was done applying chi-square test or fisher exact test. P-value ≤0.05 was considered as significant.

Results: The mean postoperative ejection fraction was 50.43±9.25% in exposed group while in unexposed group it was 45.06±7.35% respectively. Total 52.5% patients were retained postoperative ejection fraction in exposed group and 26.3% patients in unexposed group while inotropic support were required for 72% patients in exposed and 25% in unexposed group. Significant association of study group with retained postoperative ejection fraction and inotropic support.

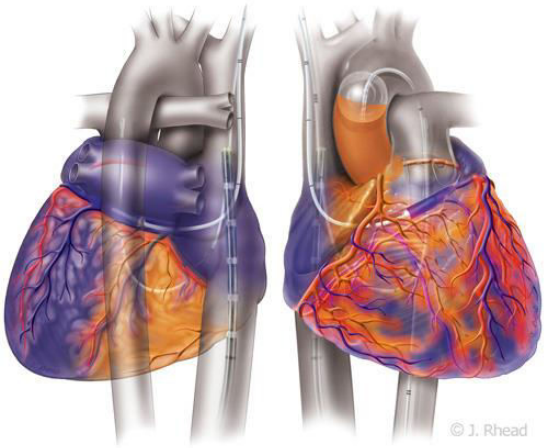
Conclusion: The retained postoperative ejection fraction in exposed group was more as compared to unexposed group. The inotropic support was required less in unexposed groups as compared to exposed group.

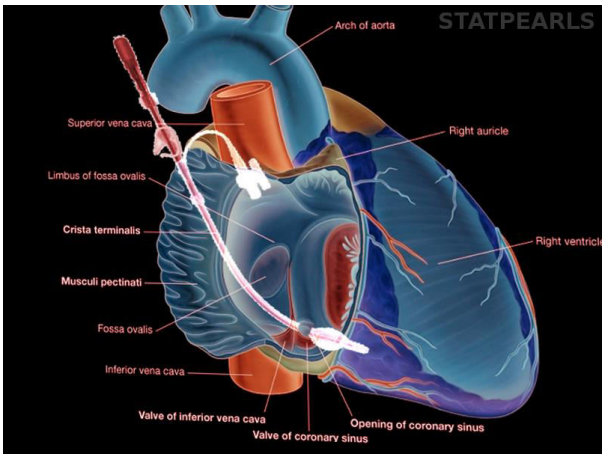
INTRODUCTION:

Cardioplegia represents the most important strategy aimed to protect myocardial function during cardiac surgery and to facilitate surgical procedures providing a quiet and bloodless operative field.[1] Initially, cardioplegia was introduced as an agent for hypothermic hyperkaliemic arrest. Blood was then found to be an important vehicle for delivery of potassium cardioplegia.[3] Integrated cardioplegia offers superior myocardial protection of the left ventricular free wall and septum compared with the antegrade mode of cardioplegia delivery.

Cardioplegia allows for the regeneration of cellular energy stores and the repair of reversible injuries to the myocardium during the period of electromechanical quiescence. This restoration improves metabolic and short-term functional recovery and decreases mortality in cardiac surgery. However, controversy still surrounds the principles for choosing the optimal type of cardioplegia that can provide the desired level of myocardial protection[2].

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021



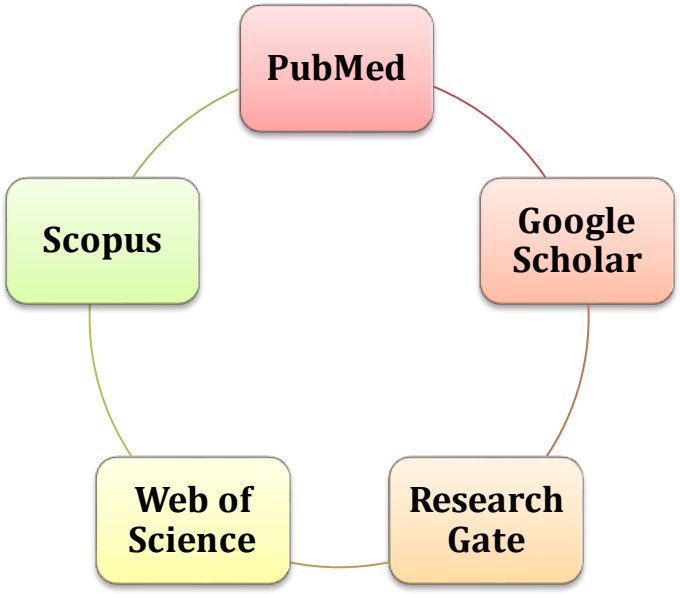


Studies compared antegrade/retrograde and antegrade cardioplegia on myocardial function following CABG and reported need of inotropic agent in 8.2% vs. 24.5% of the patients respectively. Similarly, retained postoperative ejection fraction (either did not change or increased 5 to 15%) was observed in 51.1% vs. 23.1% of the patients respectively[3].

No clear guidelines are available for choosing the optimal route of cardioplegia, no study has been conducted for the Pakistani population. And due to difference is disease prevalence and anatomy, we expect to see variations and differences in our results for Pakistani population. Therefore, this study is designed with aim to compare the indicators of myocardial protection in two methods[4].

LITERATURE REVIEW:

Literature was searched for the appropriate studies from the online databases of the PubMed, Scopus, Web of science and Google scholar published.



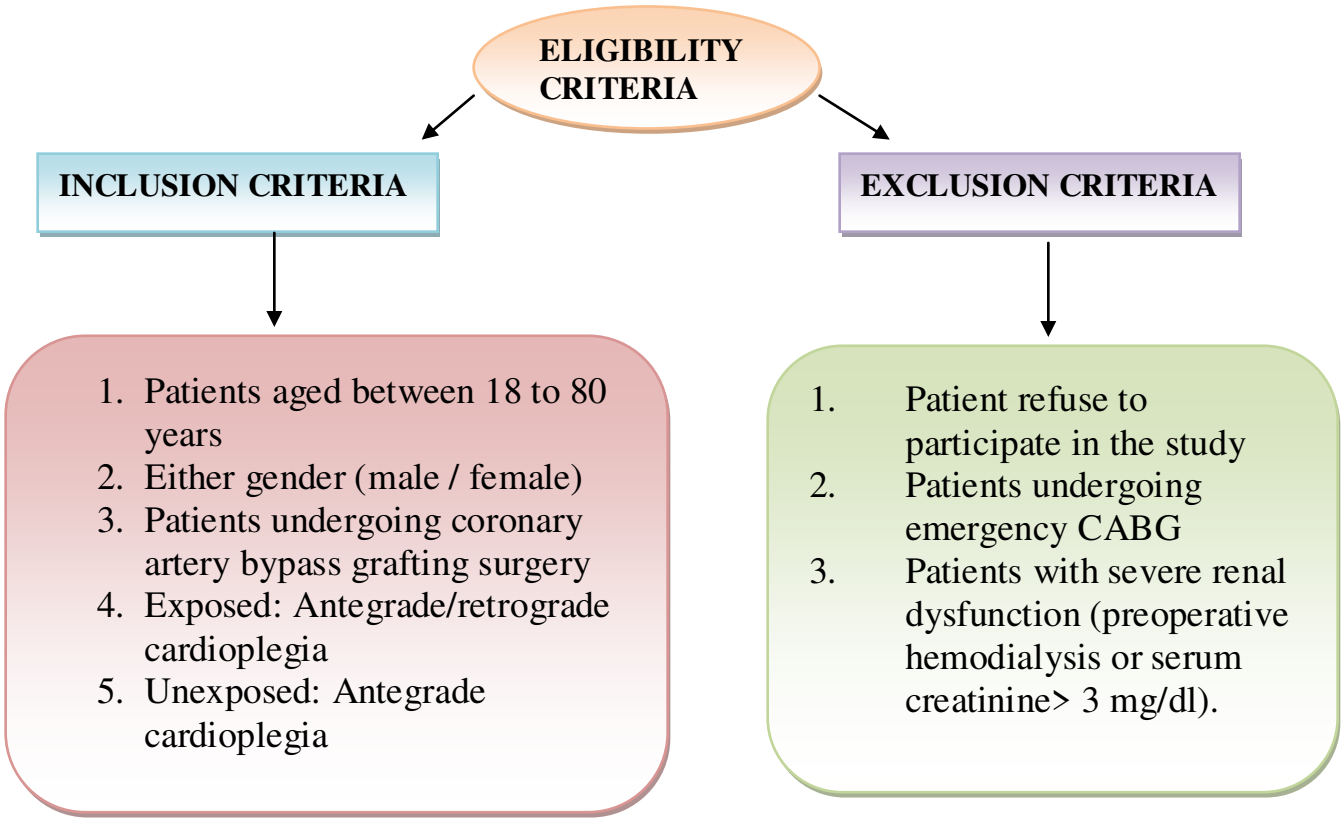
The pathophysiology of coronary artery disease was established in 1876 by Adam Hammer when he postulated that angina (imbalance of coronary perfusion supply and demand) was caused by interruption of coronary blood supply

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

and that myocardial infarction occurred after the occlusion of at least one coronary artery[6]. In 1950, at McGill University in Montreal, QC, Canada, Vineburg and Buller were the first to implant the internal mammary artery (IMA) into the myocardium to treat cardiac ischemia and angina. In 1953, D. W. Gordon Murray reported placement of arterial grafts in the coronary circulation[4].

The 1960s saw great advances in coronary artery surgery. Goetz et al. are credited with performing the first successful human coronary artery bypass operation in 1961. In 1962, Proudfit et al. produced the first practical cardiac angiography visualizing the coronary arteries. In the 1980s, the prevalence of CABG increased and safety improved. Thoracoscopic harvesting of the left IMA was reported in 1998 and minimally invasive and robotic surgical approaches were also developed Currently, the number of CABG is declining from a peak of 519,000 operations in 2000 to an estimated 300,000 cases in 2012[5].

MATERIAL AND METHODS:



Approval of ethical review committee of NICVD was taken prior to the data collection. Informed consent was taken by the principal investigator from all patients before surgery[6]. Required number of patients underwent CABG with antegrade/ retrograde cardioplegia were recruited consecutively as exposed Group. For exposed group initial dose were infused in the aortic root (pressure, 60 mm Hg; flow-rate, 150 mL/min). After initial dose, when asystole occurred, the aortic root was vented by the antegrade cardioplegic catheter and 200 mL of cardioplegia was infused into the coronary sinus at a pressure of 40 mmHg. Later, 200 mL of cardioplegic solution was infused into the coronary sinus every 30 minutes of aortic cross-clamping[7]. And similarly, required number of patients undergoing CABG with antegrade cardioplegia was recruited consecutively as Unexposed Group 2. For unexposed group the cardioplegic solution was infused in the aortic root with an aortic cross-clamp on the distal aorta (pressure, 60 mm Hg; flow-rate, 150 mL/min).After initial dose, when asystole occurred, another 200 mL of cardioplegic solution was infused. Later, 200 mL of cardioplegic solution was infused into the aortic root after every 30 minutes of aortic cross-clamping[8].

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

Demographic profile of the patients were recorded like gender, age (years), weight (kg), height (cm), and BMI (kg/m^2). Risk profile such as diabetes mellitus, family history of ischemic heart disease, hypertension, smoking, and obesity were recorded as per the operational definitions. Single protocol was used for anesthesia induction and maintenance for all patients[9].

Echocardiography was performed at 24 hour postoperative and postoperative ejection fraction (%) was recorded for all the patients. Post-operative myocardial protection indicators such as need for Inotropic Support and retained postoperative ejection fraction were obtained[10].

STATISTICAL ANALYSIS:

Data were entered and analysis using SPSS version-21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Shapiro-Wilk test was applied to check the hypothesis of normality for quantitative (continuous) variables such as age (years), weight (kg), height (cm), BMI (kg/m^2), pre and post-operative ejection fraction (%).[13]Comparison of categorical outcome variables, such as Inotropic Support and retained postoperative ejection fraction, between Exposed Group and Unexposed Group was made by applying chi-square test or fisher exact test. Effect modifiers like age groups, gender, diabetes mellitus, family history of ischemic heart disease, hypertension, smoking, and obesity were controlled through stratification. Post stratification chi-square test or fisher exact test was applied. Two sided p-value of ≤ 0.05 was taken as criteria of statistical significance[11].

RESULTS:

The frequency of retained post operative ejection fraction according to exposed and unexposed groups[12]:

Gender	Retained Postoperative Ejection Fraction	STUDY GROUP		TOTAL	P-Value
		Exposed	Unexposed		
Male	**Yes**	31 (67.4)	15 (32.6)	**46**	0.001*
	No	33 (38.4)	53 (61.6)	**86**	
	TOTAL	**64**	**68**	**132**	
Female	**Yes**	11 (64.7)	6 (35.3)	**17**	0.315**
	No	5 (45.5)	6 (54.5)	**11**	
	TOTAL	**16**	**12**	**28**	

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

The frequency of inotropic support according to exposed and unexposed groups for hypertension[13]:

Hypertension	Inotropic Support	STUDY GROUP		TOTAL	P-Value
		Exposed	Unexposed		
Yes	**Yes**	7 (30.4)	16 (69.6)	**23**	0.062**
	No	45 (52.3)	41 (47.7)	**86**	
	TOTAL	**52**	**57**	**109**	
No	**Yes**	1 (20)	4 (80)	**5**	0.099**
	No	27 (58.7)	19 (41.3)	**46**	
	TOTAL	**28**	**23**	**51**	

The frequency of inotropic support according to exposed and unexposed groups for diabetes mellitus[14]:

Diabetes Mellitus	Inotropic Support	STUDY GROUP		TOTAL	P-Value
		Exposed	Unexposed		
Yes	**Yes**	3 (33.3)	6 (66.7)	**9**	0.403**
	No	28 (48.3)	30 (51.7)	**58**	
	TOTAL	**31**	**36**	**67**	
No	**Yes**	5 (26.3)	14 (73.7)	**19**	0.010*
	No	44 (59.5)	30 (40.5)	**74**	
	TOTAL	**49**	**44**	**93**	

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

DISCUSSION:

Optimal myocardial protection requires uniform delivery of cardioplegic solution throughout the heart. Coronary artery disease may cause maldistribution of cardioplegic solutions, which may result in inadequate and ineffective protection of vulnerable cardiac muscle.[17] The infusion of cardioplegic solution through the aortic root is a common delivery method used by cardiac surgeons. This method produces rapid diastolic arrest and good preservation of myocardial function. However, in patients with advanced coronary artery disease, and particularly in patients with left anterior descending coronary artery occlusion, this approach can result in uneven distribution of cardioplegic solution to the myocardium. This limitation of antegrade perfusion can be overcome by direct graft perfusion (performing proximal grafting before aortic clamping and administering cardioplegia after each distal graft is completed) or through coronary sinus retrograde cardioplegia[15].
Other investigators have examined the safety and effectiveness of retrograde cardioplegia in CABG and have found that it is associated with more even cooling of the myocardium, a decreased need for postoperative inotropic support, and a greater number of patients in sinus rhythm postoperatively. Other studies have suggested that retrograde cardioplegia is associated with more effective myocardial cooling, better preservation of myocardial cellular structures, improved left ventricular diastolic compliance after AVR, and less depression of ventricular contractility.[16]

Loop and co-authors compared antegrade and combined antegrade/retrograde blood cardioplegia delivery with antegrade crystalloid cardioplegia and found that, when adjusted for patient risk, both types of blood cardioplegia reduced morbidity, mortality, and cost. Combined antegrade/retrograde blood cardioplegia reduced major morbidity and mortality more than did antegrade blood cardioplegia alone, especially in patients at the highest risk. Importantly, these authors concluded that the method of delivery had no impact on 1-year survival or event-free survival.[17]

Noyez and colleagues evaluated 60 patients who underwent 3-vessel myocardial revascularization and found that when considering patients with left anterior descending coronary artery (LAD) occlusion, retrograde delivery was superior to antegrade delivery[21]. In patients with LAD occlusion, left ventricular stroke work index (LVSWI) decreased more significantly, high energy phosphates were less preserved, and septal temperature was higher with antegrade delivery of cardioplegic solution. However, the authors were unable to demonstrate better preservation of left ventricular myocardial function when LAD occlusion was not considered independently.[18]

A study by Misare and colleagues, who evaluated warm blood cardioplegia in swine and found improvements in global and ischemic-zone systolic function with retrograde delivery systems. These comparisons of antegrade and retrograde delivery systems have been supported in clinical trials by Arom and Emery, who demonstrated decreased requirements for inotropic support (9% vs 42%) and temporary pacemaker use (27% vs 51%) in the group receiving retrograde delivery during CABG[19, 20].

Studies suggested that retrograde and combined antegrade/retrograde delivery systems for myocardial preservation may offer benefits during myocardial revascularization. These benefits include measurable improvements in biochemical and cellular markers and in cardiac performance variables. Improved intramyocardial pH, preservation of high-energy phosphates, better protection of myocardial cellular structure, improved septal cooling, increased left ventricular diastolic compliance, and improved ventricular contractility have all been associated with retrograde cardioplegia[20].

CONCLUSION:

It can be concluded by the study findings that postoperative ejection fraction was more in exposed group as compared unexposed group. The retained postoperative ejection fraction in exposed group was also high as compared to unexposed group. The inotropic support was required less in unexposed groups as compared to exposed group. Further, the difference was also found significant. One may assume that a combined antegrade/retrograde approach is appropriate for patients with an increased risk[21].

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

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