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Antegrade versus Retrograde Blood Cardioplegia in Left Main Coronary Artery Disease Patients Underwent CABG

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ABSTRACT

Background: Cardioplegia is used to protect the heart from ischemic insult. In left main coronary artery disease, free and homogenous spread and chemical preservation of antegrade cardioplegia is limited. Other option is to bypass the left main stenosis by giving retrograde cardioplegia.

Objective: This study aimed to compare the postoperative cardiac function, and clinical outcome between antegrade and retrograde blood cardioplegia in left main coronary artery disease patients who underwent CABG.

Patients and methods: A randomized retrospective observational comparative study that was done in Beni-Suef University. The study included 40 patients with left main coronary artery disease who had elective isolated on pump CABG between June 2017 to June 2022, of them 20 patients had antegrade cardioplegia and the other 20 had retrograde cardioplegia. **Results:** There was no statistical significance difference between both groups regarding patients' demographics, baseline clinical data, preoperative investigations, operative and postoperative data, except in more inotropic support usage (P value 0.024) and more post-operative elevation of cardiac enzymes (P value 0.028) in antegrade cardioplegia group. Regarding postoperative morbidities there was no statistically significant difference between both groups. Also, there was no complication form retrograde cardioplegia cannula and no mortality in our study group. **Conclusions:** There is no difference between antegrade and retrograde cardioplegia in left main coronary artery disease patient who underwent CABG except for higher rate of postoperative elevation of cardiac enzymes and more patients required inotropic support with antegrade cardioplegia, without any difference in the incidence rate of postoperative morbidity and mortality between both groups.

Keywords: Left main stenosis, Antegrade cardioplegia, Retrograde cardioplegia, On pump, CABG, CPB.

INTRODUCTION

Nowadays, there is a great advance in cardiac surgery in general, and coronary artery bypass grafts (CABG) operation in specific. Different methods of myocardial preservations were used during cardiopulmonary bypass (CPB) when used in these types of surgeries. There is a high rate worldwide for cardiac surgery, in USA alone there is approximately 300,000 cardiac surgery per year [(1)].

In terms of coronary architecture, the aortic root gives rise to the two main coronary arteries, the left coronary artery from the left coronary sinus and the right coronary artery from the right coronary sinus. These arteries supply oxygen- and nutrient-rich blood to various regions of the myocardium [(2)]. The A-V groove in the coronary sinus, which drains through the Thebesian valve and must be crossed during the insertion of a coronary sinus catheter, serves as the primary venous drainage route for the myocardium. The small, medium, great, and oblique cardiac veins are drained by the coronary sinus. Additional pathways for myocardial drainage comprise the Thebesian veins, which empty into the right ventricle (RV), and the anterior cardiac veins, which empty into the right atrium (two to five veins) [(3, 4)].

When we start CPB cardioplegia is used to decrease O_2 and nutrient needs of the myocardium, and to protect the heart from ischemic insult. For the preservation of the myocardium, the cardioplegia must be delivered correctly and simultaneously to every area of the heart [(5)].

So, we can use antegrade blood cardioplegia through the aortic root to the coronary ostia, but in left main coronary artery disease, free and homogenous spread of chemical preservation of the cardioplegia solution is limited [(6, 7)].

On the other hand, before initiation of CBP, retrograde cardioplegia catheter might be inserted into the coronary sinus through the right atrium, so cardioplegia is being delivered in retrograde manner through the coronary sinus, bypassing the left main coronary artery stenosis [(8)].

In certain cases, the right internal jugular can be percutaneously used to introduce the coronary sinus catheter (perfect hands required). Taking into consideration a special case of a persistent left superior vena cava (PLSVC), before insertion of retrograde cardioplegia cannula, we should revise the systemic venous drainage of the body. In PLSVC the venous drainage of the left side of head, neck and left upper limb is returning through PLSCV into the coronary sinus, so while infusing the retrograde cardioplegia, it diffused into systemic venous system, so in this special case retrograde blood cardioplegia is contraindicated [(9)].

There is a conflict on which is better for myocardial protection in left main ischemic heart disease during CABG surgery, as some studies see that antegrade cardioplegia is good for non-occluded coronaries. But in occluded coronaries, there is cardioplegia maldistribution [(10)], which may lead to perioperative myocardial injury (PMI) that may affect

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myocardial postoperative recovery and left ventricular (LV) function [11]. So, some studies suggested using retrograde cardioplegia which can bypass the coronary stenosis and occlusion and can give homogeneous cardioplegia distribution to the coronaries so avoid PMI and LV impairment post CABG [12].

On the other hand, some studies showed that there are risks and disadvantage from using retrograde cardioplegia as it may cause suboptimal distribution to the RV because the anterior cardiac veins are not connected directly to the coronary sinus, which may affect RV protection and postoperative function [13, 14]. Also, there is difficulty that may cause coronary sinus injury during insertion, or insertion in improper position, which may lead to maldistribution of the cardioplegia away from the coronary sinus to the right atrium that affect myocardial preservation. Also, it needs proper monitoring to the perfusion pressure (PP) as too low PP affect the myocardial protection and too high PP can cause coronary sinus rupture [15, 16]. If retrograde cardioplegia is used alone at the beginning for arresting the heart it has a delayed action [17, 18]. Thus, our study aimed to compare the postoperative cardiac function advantage, disadvantage and the outcome of both antegrade and retrograde cardioplegia in left main coronary artery disease patients who underwent CABG.

PATIENTS AND METHODS

A randomized retrospective observational comparative study that was conducted in Beni-Suef University. Patients' data were collected from patients who had left main CABG surgery during 5 years between June 2017 to June 2022, where 40 patients had left main (>50% stenosis) ischemic heart disease, underwent elective isolated on pump CABG operation whether with antegrade cardioplegia or retrograde cardioplegia. Of them, 20 had antegrade cardioplegia and the other 20 had retrograde cardioplegia.

Patients were divided into two groups according the type of cardioplegia used in the surgery: Group A included 20 patients that were operated using antegrade cardioplegia, and group B that included 20 patients who were operated using retrograde cardioplegia.

Inclusion criteria: Patients with CAD (left main > 50%), underwent elective on pump CABG operation whether with antegrade or retrograde cardioplegia.

Exclusion criteria: Patients with EF below 40%. Re-do CABG surgery. Off pump CABG surgery converted to on pump. Minimal invasive CABG.

Urgent or emergency operation. Patients with ischemic or non-ischemic mitral regurgitation. Patients with combined procedure e.g., other valves & aorta surgeries. Also, patient with chronic non cardiac disease e.g., hepatic dysfunction, renal dysfunction.

Preoperative evaluation data were obtained from all patients in both groups including:

1. Medical history, clinical examination findings and identified risk factors.
2. Demographic data (Name, Age, sex, residency, BSA and comorbidities).
3. Clinical data: Dyspnea (NYHA classification), angina, consciousness, blood pressure and pulse.
4. Full Laboratory study (Full labs including cardiac enzymes).
5. Chest x ray.
6. Electrocardiogram (ECG) abnormalities.
7. Transthoracic echocardiography findings [EF%, LV and RV function, mitral valve (morphology, MVA, VC, regurgitation & etc.), other valves pathology, PASP, LA dimensions, PLSCV].
8. Cardiac catheterization (associated lesions with left main > 50%).
9. Spirometry result.

Pre-operative preparation and anesthetic technique: The protocol of pre-operative preparation was the same for all patients in both groups.

Type of anaesthesia used: There was no significant difference between both groups where general anaesthesia was used in all patients. Transesophageal echocardiography (TOE) was used in both groups intraoperatively. All our patients were transferred to the ICU post-operatively on mechanical ventilation.

Surgical technique: All our study group patients were operated through full sternotomy incision.

Group "A" (antegrade cardioplegia): Heart lung machine was used with all cardioplegia doses were given in the form of warm blood antegrade cardioplegia with mild hypothermia (temperature drifting to 34-35 °C).

Group "B" (retrograde cardioplegia): Heart lung machine was used where first dose of cardioplegia started through warm blood antegrade cardioplegia with mild hypothermia (temperature drafting to 34-35 °C). Then, cardioplegia is continued through retrograde cardioplegia cannula. The maintenance doses were given through retrograde cardioplegia cannula.

Operative data:

Data collected for both groups: Cross clamp time, operative time, urine output, T `

Post-operative data:

Data collected for both groups: Adding or weaning of inotropes, post-operative hemodynamics and post-operative elevation of cardiac enzymes, chest X-ray, ECG changes or abnormal Echo findings. Also, post-operative blood loss and timing of ICT removal, re-exploration or not (for bleeding or revision of the

grafts), mechanical ventilation duration, ICU and hospital stay duration, morbidity or mortality and OPD abnormal clinical or laboratory findings (if available).

Ethical consent: An approval of the study was obtained from The Human Research Ethical Committee of Faculty of Medicine, Beni-Suef University (FMBSUREC/09072023/Wahba). Following receipt of all information, signed consent was provided by each participant. The Helsinki Declaration was adhered to at every stage of the study.

Statistical analysis

Data were coded, processed, and analyzed using SPSS pack version 24.0. Quantitative data were expressed as means ± SD (age, BMI, and Cardiopulmonary bypass time). Qualitative data were expressed as numbers and percentage (%) (Comorbidities & operative complications). P value ≤ 0.05 was considered significant in testing relationships between variables.

RESULTS

Patient included in our study group were divided into two groups according the type of cardioplegia used in the surgery: Group A included 20 patients that were operated using antegrade cardioplegia and group B that included 20 patients who were operated using retrograde cardioplegia. Both groups' baseline clinical data and patients' demographics were gathered, and there was no statistically significant difference between the two groups (Table 1).

Table (1): Patients' demographics and baseline clinical data.

		Group A (20)	Percentage	Group B (20)	Percentage	P value
Age (year)	Mean ±SD	57.1±10.4		58.3±10.2		0.19
Sex	Male	11	55%	12	60%	0.2
	Female	9	45%	8	40%	0.21
BMI (kg/m^2)	Mean ±SD	27.8±2.3		27.6±2.6		0.23
Smoker	Smoker	11	55%	10	50%	0.25
Chest disease	Chronic (COPD,asthma)	9	45%	8	40%	0.21
Chronis disease	Diabetes mellitus	11	55%	10	50%	0.25
	Hypertension	12	60%	13	65%	0.29
	Dyslipidaemia	4	20%	5	25%	0.22
	Previous MI	5	25%	6	30%	0.19
	Previous percutaneous coronary intervention	6	30 %	4	20%	0.11
New York Heart Association class	**II**	6	30%	7	35%	0.18
	III	10	50%	10	50%	1
	IV	4	20%	3	15%	0.21

Patients' preoperative investigations results data were collected for both groups and there was no statistical significance difference between both groups (Table 2).

Table (2): Patients' preoperative investigations results.

		Group A (20)	Percentage	Group B (20)	Percentage	P value
CBC	Chronic Anaemia	1	5%	2	10%	0.28
ECHO	Left ventricular ejection fraction (40-50%)	3	15%	2	10%	0.3
Coronary angiography (number-percentage)	Number of					
	1 vessel disease	1	(5%)	2	(10%)	0.28
	2 vessels disease	6	(30%)	7	(35%)	0.18
	3 vessels disease	13	(65%)	11	(55%)	0.16
Euroscore II	Mean ±SD	2.3±1.4		2.5±1.1		0.23

Regarding operative data there was no significant difference between both groups regarding post-bypass hemodynamics, cross clamp and cardiopulmonary bypass time, total surgery time, intraoperative urine output, IAB pump insertion, intraoperative blood loss, blood transfusion and usage of arterial grafts other than left internal mammary artery (LIMA). There was no complications form retrograde cardioplegia cannula in our study group. But there was a statistically significant difference between both groups regarding more inotropic support usage that were used in group A (Table 3).

Table (3): Operative data.

	Group A (20)	**Group B (20)**	**P value**
Post bypass Hemodynamic Heart rate (beats/min) MAP (mmHg)	 87± 4 76.3± 1.4	 86± 5 77.2± 1.5	 0.32 0.29
CL time (min)	63.1 + 2.3	61.7 ± 2.5	0.31
CPB time (min)	84.6+ 3.1	85.8 ± 2.9	0.28
Urine output (ml /hour) (mean ± SD)	120.3±47.1	122.1±39.7	0.38
IAB pump (number-percentage)	1(5%)	1(5%)	1
Inotropic support	7(35%)	3(15%)	0.024
Blood loss (ml) (mean ± SD)	327.3±107.5	325.9±110.2	0.34
Blood transfusion (units) (mean ± SD)	2.5±0.7	2.4±0.9	0.32
Total surgery timetable (mean ± SD) (min.)	240.4 ± 38.2	241.2± 41.3	0.31
Arterial grafts used (number-percentage) LIMA RIMA RADIAL Artery	 20(100%) 5(25%) 3(15%)	 20(100%) 5(25%) 2(10%)	 1 1 0.3

IAB intra-aortic ballon pump, LIMA left internal mammary, RIMA right internal mammary; CL, aortic cross clamp; CPB cardiopulmonary bypass.

During surgery while weaning from cardio-pulmonary bypass, 3 (15%) patients required DC shock and 1 (5%) patient required temporary pace maker in group A in comparison with group B where there were 3 (15%) patients required DC shock and 2 (10%) patient required temporary pace maker during surgery, which showed no statistical significant difference between both groups. All patients in both groups were sent to the intensive care unit on MV.

Regarding the length of MV, when extubation was performed, postoperative blood loss and transfusion, re-examination for bleeding, ICU stay, ECG abnormalities including ischemic changes and arrhythmia, and abnormal ECHO findings, there was no statistically significant difference between the two groups. Regarding the temporary impairment of contractility that happened in both groups, it was for both LV and RV not only for the RV, so retrograde cardioplegia effect on RV impairment does not happen in our group study, but there was statistically significant difference between both groups regarding post-operative elevation of cardiac enzymes, which was much more in group A (Table 4).

Table (4): Postoperative data.

	Group A	**Group B**	**P value**
MV duration (hours) Mean ± SD	6.5±1.2	6.4±1.3	0.28
Blood loss (ml) Mean ± SD	470±72.5	468±74.1	0.31
Blood transfusion (unit) Mean ± SD	2.4±0.7	2.5±0.6	0.29
ICU stay (day) Mean ± SD	2.2±0.6	2.4±0.4	0.32
Re-exploration for bleeding or graft revision	1(5%)	1(5%)	1
Post-Operative elevation of cardiac enzymes ECG changes Ischemic changes Arrhythmia abnormal ECHO findings (temporary impairment of contractility)	8(40%) 0 1(5%) 2(10%)	4(20%) 0 1(5%) 2(10%)	0.028 1 1

Regarding postoperative morbidities, there was no statistically significant difference between both groups. Also, there was no mortality in our study group (Table 5).

Table (5): Morbidity and mortality.

	Group A (20)	Group B (20)	P value
Morbidity			
Renal complication -AKI Dialysis -Temporary -Permanent	 1(5%) 0 0	 1(5%) 0 0	 1
IABP ICU application	1(5%)	1(5%)	1
Myocardial infarction	0	0	
New onset atrial fibrillation (AF)	1(5%)	1(5%)	1
Superficial wound infection	1(5%)	2(10%)	0.28
Deep wound infection	0	0	
Arrhythmias	1(5%)	1(5%)	1
Stroke	0	0	
Pneumonia (ARDS)	2(10%)	1(5%)	0.28
ICT insertion for pleural effusion	3(15%)	2(10%)	0.3
Mortality	0 (0%)	0 (0%)	

DISCUSSION

With the great advancement in the cardiac surgery techniques, still myocardial protection is one of the most debated issues with different studies showing different outcomes. There are different techniques to operate the heart of which beating heart, cross camp fibrillation and cardioplegia, which may be blood and non-blood cardioplegia, warm or cold and given through antegrade, retrograde only or both together antegrade and retrograde together.

The principle of cardioplegia in cardiac surgery is to have a temporary cardiac arrest with good myocardial protection during the cardiac surgery to preserve the myocardium and regain its normal contractility after surgery with the least damage possible.

The most common route used in giving cardioplegia is antegrade route, which is given in the aortic root through aortic root cannula, then distribute smoothly and equally through the coronaries to the whole myocardium. A lot of studies showed its beneficial effect in open heart but in ischemic heart disease where the coronaries showed different degrees of stenosis and occlusion that impair cardioplegia distribution with severe coronaries stenosis so it may be harmful to the myocardium and may cause PMI [(19)]. To overcome that retrograde cardioplegia can be given through retrograde cardioplegia cannula in the coronary sinus and spread to the whole myocardium through the venous network. **Pratts** [(20)] was the first who thought about protecting the myocardium from ischemia through giving retrograde cardioplegia including oxygenated blood through the venous system, and was applied for the first time by **Blanco *et al.*** [(21)] in 1956 then was used in many cardiac centres.

Menasche *et al.* [(22)] was the first who compared retrograde cardioplegia versus antegrade cardioplegia in aortic valve replacement (AVR) surgery and showed no difference between both routes of cardioplegia regarding post-operative cardiac output, hemodynamic stability, and incidence of right and left ventricular infarction. Also, **Menasche *et al.*** [(23)] had a retrospective observational study that was done on a big number of patients who had isolated CABG or AVR surgery who had just retrograde cardioplegia and their study group had less or similar mortality rates like that in other studies for antegrade cardioplegia. Although, the coronary sinus is not directly related to the anterior cardiac veins that drain the RV, this might have an impact on the distribution of retrograde cardioplegia, **Kaukoranta *et al.*** [(24)] had study on small group had CABG surgery and received antegrade or retrograde cardioplegia and showed significant RV ischemic changes in retrograde cardioplegia group without any postoperative complications observed.

A lot of studies had been done on small patient number for evaluation of the outcome of retrograde cardioplegia, but most of them were not comparative with antegrade cardioplegia outcome and were only for retrograde cardioplegia outcome. Only few studies were comparative between antegrade and retrograde cardioplegia outcome one of them is our study. In our study, there was no statistical significant difference between both groups regarding patients' demographics, baseline clinical data and preoperative investigations results. Also, there was no statistical significance difference between both groups regarding operative data including post-bypass hemodynamic, cross clamp and cardiopulmonary bypass time, total surgery time, intraoperative urine output, IAB pump insertion, intraoperative blood loss, blood transfusion and usage of arterial grafts other than LIMA. There were no complications form retrograde cardioplegia cannula in our study group, but there was a statistically significant difference between both groups regarding more inotropic support usage that were used in antegrade cardioplegia group (P value 0.024). There was no statistically significant difference between both groups regarding the duration of MV and timing of extubation, postoperative blood loss and transfusion, re-exploration for bleeding, ICU stay, ECG changes including ischemic changes and arrhythmia and abnormal ECHO findings. Regarding the temporary impairment of contractility that happened in both groups, it was for both LV and RV not only for the RV, so retrograde cardioplegia effect on RV impairment did not happen in our group study. But there was statistically significant difference between both groups regarding post-operative elevation of cardiac enzymes, which was much more in antegrade cardioplegia group (P value 0.028). Regarding postoperative morbidities there was no statistically significant difference between both groups. Also, there was no mortality in our study group.

In comparison with other studies that compared both types of cardioplegia, our outcome was like that of **Radmehr *et al.*** [14] where they reported that there is statistically significant decrease (16.5% less) in inotropic requirement in retrograde versus antegrade cardioplegia in CABG surgery. **Candilio *et al.*** [25] had a retrospective study that showed reduced incidence of PMI in patients who had first time CABG with combined antegrade and retrograde cardioplegia group than in the isolated antegrade cardioplegia group.

CONCLUSION

There was no difference between antegrade and retrograde cardioplegia in left main patient undergoing CABG except for higher rate of postoperative elevation of cardiac enzymes and more patients required inotropic support with antegrade cardioplegia, without any difference in the incidence rate of postoperative morbidity and mortality between both groups.

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