Effect of Antegrade direct hotshot Graft Perfusion in On-pump Coronary Artery Bypass Grafting

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ABSTRACT

Background: Cardiac ischemic time reduction and myocardium protection can be achieved by warm blood perfusion into arterial or venous grafts during proximal anastomosis construction in coronary artery bypass graft (CABG) as off-pump surgeries. However, there is few previous on-pump CABG surgery studies of the impact of warm arterial blood primary graft perfusion.

Objective: Our study aimed to investigate the positive benefits of warm arterial blood perfusion of grafted ischemic myocardial segments (through venous or arterial grafts during proximal graft anastomosis creation) on myocardium preservation.

Patients and Methods: One hundred and twenty patients were submitted to coronary artery bypass graft (CABG) as on-pump surgeries involving proximal graft anastomosis. They were allocated randomly into two equal groups. Group A undergone aortic root antegrade hotshot infusion. While in group B, the additional warm arterial blood bypass graft perfusion was performed before cross- clamp removal, followed by proximal anastomosis, which had been accomplished using partial aortic clamp.

Results: The requirement for the inotropic support and defibrillation throughout cardiopulmonary bypass (CPB) separation, total CPB duration inotropic support, IABP use, postoperative AF and MI as well as ICU and hospital stay were considerably lesser in group B when compared to group A.

Conclusion: As summarizing, there was a significant myocardium recovery impact from the addition of antegrade direct bypass graft perfusion to aortic root warm blood hotshot throughout proximal graft anastomosis during on pump CABG.

Keywords: Antegrade cardioplegia, Direct hotshot, Coronary artery bypass, Warm blood perfusion, Graft anastomosis, Myocardium recovery.

INTRODUCTION

Cardioplegia is a cardioprotective, as it is a necessary element of cardiopulmonary bypass. Also, the primary purpose of reducing myocardial oxygen demand by formation of electrical quiescence and making the heart more cooler to lower the ischemic consequences of being on bypass [(1)].

The injury of myocardial reperfusion after cardioplegic ischemic arrest is a significant predictor of adult and pediatric prolonged organ functional curing after open-heart surgery, morbidity, and mortality, with myocardial spectacular recovery and acute myocardial infarction cure. There were lot of cardioplegia application modes, which varied as antegrade one or retrograde one or the combination of antegrade and retrograde. Also, there are other types as intermittent or single shot cardioplegia. It may be cold (using warm introduction or not) or warm only [(2)].

According to the application route of antegrade and retrograde, antegrade perfusion is accomplished by inserting a cardioplegia line into the aortic root below the aortic cross-clamp and following anatomical paths and normal coronary circulation, while retrograde perfusion is accomplished by coronary sinus straight intubation. In the cardiac surgery situation, the myocardial recovery was achieved through alternating cold-blood antegrade cardioplegia and reperfusion after that with a terminal warm blood one (hot-shot introduction) [(3)].

This was achieved through warm versus cold cardioplegia in meta-analysis study of **Fan *et al.*** [(4)], which was accomplished via identifying 5,879 patients in 41 randomized controlled trials. There were non-significant difference in groups regarding surgery deaths, stay length, atrial fibrillation and incidence of stroke. Though, there was significant improve in index of heart (P < 0.00001), decrease in day 0 level of troponin (P = 0.006), and in peak level of CKMB (P = 0.002) after warm cardioplegia perfusion [(4)].

Mallidi *et al.* [(5)] prospective single center cohort study reported that by comparing cold cardioplegia in one group and tepid/warm cardioplegia in the other group through isolated CABG, the better warm cardioplegia outcomes were decreasing in death through surgery (from 2.5% to 1.6, P 0.027) and myocardial infarction (from 5.4% to 2.4, P <0.0001).

In addition, the Bristol Heart Institute where **Caputo *et al.*** [(6)] through a study on 35 patients stated that significant metabolic derangement happened in cardiac ischemic reperfused hearts after cold cardioplegia only compared to adding terminal warm hot shot introduction (P < 0.05) before the cross-clamp elimination.

Feng *et al.* [(7)] stated that graft perfusion in off pump CABG surgery can boost myocardial flow and minimize cardiac ischemia duration, resulting in stable systemic hemodynamics, an acceptable CI after surgery, and an improved surgical outcome.

Goncu *et al.* [(8)] found that in patients undergoing on pump CABG, hot shot given into the aortic root combined with early graft perfusion with warm blood resulted in less total by pass time need for inotropic

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support and postoperative AF and MI than in using only hot shot into aortic root.

According to this introductory patient series, grafted vessels perfusion with warm blood appears to help both off-pump and on-pump coronary artery bypass multi-vessel grafting by prompt grafted segments recovery, improving hemodynamic stability during the next anastomoses, and increasing grafting sequence flexibility [7, 9]. However, there is few previous studies of the primary graft perfusion impact through on-pump CABG by warm arterial blood. Our aim through this study was measuring the valuable impacts (on grafted ischemic myocardial segments) of early perfusion by warm arterial blood through proximal graft anastomosis, in on-pump CABG surgery.

PATIENTS AND METHODS

This retrospective clinical randomized study included 120 patients. These patients were receiving on-pump CABG surgery at Cardiovascular Surgery Department, Elkasr Elaini Hospital, Cairo University. This study was conducted between November 2018 and November 2019.

Inclusion criteria: On the basis of selective coronary angiography, patients who were fit to our study were identified with multi-vessel coronary artery disease (CAD) and the left ventricular ejection fraction (LVEF) equal to 30% or more than this after surgery.

Exclusion criteria: Single coronary artery disease, several or re-operations, significant hepatic or renal dysfunction, cerebrovascular disease history, significant carotid or aortic calcification and age more than 75 years. Additionally, patients who couldn't undergo left anterior descending coronary artery (LAD) bypass using LIMA, due to left internal mammary artery (LIMA) dysfunction were omitted.

Study treatments and data collection

120 patients were randomly allocated in two groups, 60 patients for each: Group A underwent aortic root antegrade hotshot infusion. While in group B, the additional warm arterial blood bypass graft perfusion was performed before cross-clamp removal, followed by proximal anastomosis being constructed using partial aortic clamp.

All patients' data (preoperative, intraoperative and postoperative) were included. Preoperative, on surgery day, day 1 and 5 postoperative, and immediately before discharge laboratory tests also were included. Preoperative and day 1 and 3 postoperative electrocardiogram (ECG) was got, and it may be repeated when wanted.

Preoperative and day 6 postoperative assessment of left ventricular function was performed using transthoracic two-dimensional to be identified as low (LVEF from 30 to 40%) or high (LVEF more than 40%). Dysrhythmias, conduction disorders and new ischemic events were assessed using ECG. In at least two leads, evidence of perioperative MI were identified by new Q waves of more than 0.04 ms or decrease more than 25% in R-waves [10]. Additionally, novel akinetic segments and cTn-I concentrations peak more than 3 ng/ml at twelve hours were recorded [11]. A cardiac surgeon and an anesthetist chosed inotropic drugs and its need through cardiopulmonary bypass (CPB) separation.

Surgical technique

All patients received standard anesthesia treatments and surgery and used median sternotomy to expose the heart and ascending aortic cannulation and two-stage venous cannulation of the right atrium for CPB. Also, a dose of 3 mg/kg heparin was received after LIMA ± RIMA preparation and radial arterial grafts or saphenous vein before CPB institution. In addition, during CPB procedure, the activated coagulation time was adjusted at more than 400 seconds.

In CPB, the ascending aorta was used for insertion of a cardioplegia delivery cannula with a separate vent line (DLP Medtronic, Grand Rapids, MI, USA). The extracorporeal circuit consisted of an oxygenator of Dideco D704 compact-flow system type (Dideco, Mirandola, Italy) and a pump of S3 roller type (Stöckert, Munich, Germany). A mean arterial pressure was maintained 60 – 70 mmHg by keeping the pump flow rate 2 and 2.4/min per m^2 surface area of the body. Additionally, Potassium solution was infused in warm blood intermittent antegrade cardioplegia every 20 minutes for myocardial recovery in both groups.

A LIMA was produced for all LADs but RIMA and radial grafts in artery or superior saphenous veins were produced for other vessels.

At the onset of the final distal anastomosis, arterial rewarming was commenced. All patients received antegrade final blood hotshot in intra-aorta. Also, the elimination of LIMA bulldog clamp was just before the elimination of cross-clamp in aorta. Therefore, an additional warm arterial blood was perfused into the grafts during the opening of the double cardioplegia cannula branch before the elimination of cross-clamp in aorta, in group B. All patients had proximal anastomosis by a partial clamp on beating heart following the elimination of cross clamp. Lastly, decannulation was performed once full hemodynamic stability was achieved, and protamine sulphate was used to neutralize heparin.

Ethical consent:

The approval of our study was attained from Cairo University Academic and Ethical Committee. All patients signed an informed consent forms that had been approved from the Institutional Ethics Committee of Cairo University. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis:

SPSS®, version 10.1 (SPSS Inc., Chicago, IL, USA) was utilized and data (means ± SD) were calculated. Fisher's exact or Pearson's χ^2 test were used for the assessment of categorical type of variables while Student's t-test or the Mann–Whitney U-test was utilized for continuous variables assessment. The statistical significance was evaluated by P-value to be equal or less than 0.05.

RESULTS

Descriptive statistics: One hundred and twenty patients submitted to randomized clinical trial, which was retrospective, received on-pump CABG procedure at duration from Nov. 2018 to Nov 2019. They were randomly allocated in two groups, 60 patients for each. Patients' demographic and preoperative characteristics in both groups are summarized in Table (1). There were no statistically significant differences between both groups. Most of the participants were males with more than 50 years old.

The majority of them had Euroscore of 3. About half of the participants were diabetic and hypertensive, while a minor percent of them had COPD and hyperlipidemia. The majority of them had history of previous MI and AF. Most of them had preoperative EF around 58%, and majority of them had three diseased vessels (Table 1).

Table (1): Demographic and preoperative characteristics of patients who underwent on-pump

		Group A		Group B	
Age (years)		53 ± 6		56 ±7	
Preoperative EF (%)		59 ±11		58 ±9	
No of diseased vessels		3 ±1		3 ±1	
		N	**%**	**N**	**%**
Sex	**Male**	54	45.0%	58	48.3%
	Female	6	5.0%	2	1.7%
Euroscore	**2**	18	15 %	23	19.16 %
	3	30	25 %	26	21.6%
	4	9	7.5%	10	8.4 %
	5	3	2.5 %	1	0.84 %
Diabetic	**No**	22	16.38%	26	21.7%
	Yes	38	33.62%	34	28.3%
HTN	**No**	20	16.7%	31	25.8%
	Yes	40	33.3%	29	24.2%
COPD	**No**	56	46.7%	60	50.0%
	Yes	4	3.3%	0	0.0%
Hyperlipidemia	**No**	55	45.8%	55	45.8%
	Yes	5	4.2%	5	4.2%
Previous MI	**No**	42	34.8%	47	39.2%
	Yes	18	15.2 %	13	10.8%
AF	**No**	55	45.8%	59	49.16%
	Yes	5	4.2%	1	0.84%

EF, ejection fraction, Euro SCORE, European System for Cardiac Operative Risk Evaluation; HTN, hypertension, COPD, chronic obstructive pulmonary disease. MI, myocardial infarction, AF, atrial fibrillation.

Comparative statistics

Features during surgery and clinical consequences after surgery for all patients were allocated in table (2). The mean required time for cross and partial clamp time in aorta showed insignificant difference in both groups, while the total bypass time was less in group B than in group A (p value < 0.001). Also, the mean of both hospital and intensive care unit stays length were significantly decreased in group B.

Table (2): Features during surgery and clinical consequences after surgery

Group Statistics	Groups	N	Mean	Std. Deviation	T. test P value
Aortic cross clamp time	A	60	80.30	21.63	Insignificant p value= 0.16
	B	60	75.97	9.58	
Partial clamp time	A	60	17.32	4.95	Insignificant P value = 0.466
	B	60	16.73	3.70	
Total bypass time	A	60	127.42	35.34	Significant P < 0.001
	B	60	106.20	11.66	
Preoperative EF	A	60	58.65	10.768	Not significant P value = 0.878
	B	60	58.37	9.383	
No of diseased vessels	A	60	2.9	0.796	Not significant P value = 0.060
	B	60	3.17	0.74	
ICU stay	A	60	4.38	2.598	Significant P < 0.001
	B	60	2.1	0.44	
Hospital stay	A	60	14.77	6.624	Significant P < 0.001
	B	60	8.3	1.69	

Table (3) showed that the greater number of patients who required DC shock were in group A (73.3%), while 8.3% in group B required DC shock (p < 0.001).

Table (3): CHI Square between groups regarding DC shock

Groups * DC shock Cross tabulation						
			DC shock		Total	P vale
			NO	YES		
Groups	A	Count	16	44	60	0.001
		% within groups	26.7%	73.3%	100.0%	
	B	Count	55	5	60	
		% within groups	91.7%	8.3%	100.0%	
Total		Count	71	49	120	
		% within groups	59.2%	40.8%	100.0%	

In group B patients, sinus rhythm came back naturally without electrical defibrillation after aortic declamping but did not in group A (P < 0.001) as illustrated in table (4).

Table (4): CHI Square of spontaneous recovery of sinus rhythm between both groups

Groups * Spontaneous recovery of sinus rhythm Cross tabulation						
			Spontaneous recovery of sinus rhythm		Total	P value
			NO	YES		
Groups	A	Count	44	16	60	0.001
		% within groups	73.3%	26.7%	100.0%	
	B	Count	5	55	60	
		% within groups	8.3%	91.7%	100.0%	
Total		Count	49	71	120	
		% within groups	40.8%	59.2%	100.0%	

In group A, there was significantly greater number of patients received inotropic support with higher dose compered to group B (P < 0.001) as demonstrated in table (5).

Table (5): CHI Square Inotropic support of both groups

Groups * Inotropic support Cross tabulation						
			Inotropic support		**Total**	**P value**
			NO	**YES**		
Groups	A	Count	12	48	60	0.001
		% within groups	20.0%	80.0%	100.0%	
	B	Count	51	9	60	
		% within groups	85.0%	15.0%	100.0%	
Total		Count	63	57	120	
		% within groups	52.5%	47.5%	100.0%	

Table (6) illustrated that in group B, there was significant reduction in balloon pump support necessity after surgery in intra-aorta (p =0.004).

Table (6): CHI Square of intra-aortic balloon pump support (IABP) in both groups

Groups * IABP Cross tabulation						
			IABP		**Total**	**P value**
			NO	**YES**		
Groups	A	Count	50	10	60	0.004
		% within groups	83.3%	16.7%	100.0%	
	B	Count	59	1	60	
		% within groups	98.3%	1.7%	100.0%	
Total		Count	109	11	120	
		% within groups	90.8%	9.2%	100.0%	

Data are n, n (%) or mean ± SD. IABP, intra-aortic balloon pump

Table (7) demonstrated that fewer patients in group B reported the onset of new AF in comparison with patients in group A (p< 0.001).

Table (7): CHI Square for new onset of AF in both groups

Groups * New onset AF Cross tabulation						
			New onset AF		**Total**	**P value**
			NO	**YES**		
Groups	A	Count	30	30	60	0.001
		% within groups	50.0%	50.0%	100.0%	
	B	Count	59	1	60	
		% within groups	98.3%	1.7%	100.0%	
Total		Count	89	31	120	
		% within groups	74.2%	25.8%	100.0%	

The optimal myocardial protection was evident from the observation of cTn-I release which was significantly reduced in group B. Similarly, there was statistical difference in having perioperative MI in both groups being less in group B, as shown in table (8). There were between day 3 and 15 two postoperative mortalities: one (2%) because of generalized sepsis and multi-organ dysfunction in group A and one (2%) caused by respiratory failure in group B. So, the rate of mortality difference between both groups was not statistically significant.

Table (8): CHI Square of perioperative MI in both groups

Groups * perioperative MI Cross tabulation						
			PERIOPERATIVE MI		**Total**	**P value**
			NO	**YES**		
Groups	A	Count	52	8	60	Significant
		% within groups	86.67%	13.33%	100.0%	
	B	Count	58	2	60	Significant
		% within groups	96.67 %	3 .33%	100.0%	
Total		Count	110	10	120	
		% within groups	91.66 %	8.34 %	100.0%	

DISCUSSION

Coronary surgeons are minded with the increasing attention of myocardium protection strategies. This protection can be achieved by the combination of two types of cardioplegia (antegrade and retrograde) [(12)].

In the cardiac surgery situation, the myocardial recovery achieved through alternating cold-blood antegrade cardioplegia reperfusion and after that terminal warm blood one shot (hot-shot introduction) [(3)]. In on- pump CABG, warm blood hot shots introduction through aortic root combined with the technique of direct hot shot graft perfusion made weaning from CPB easier and best curing of myocardial segments [(7)]. A number of studies determined that, the myocardium protection in multi-vessel CAD in patients received off-pump CABG was achieved by the direct warm blood graft perfusion [(7,9,13)].

The optimal myocardial protection was evident from the observation of cTn-I release, which was significantly reduced in group B. Similarly, there was statistical difference in having perioperative MI in both groups being less in group B. There were between day 3 and 15 two postoperative mortalities: one (2%) because of generalized sepsis and multi-organ dysfunction in group A and one (2%) caused by respiratory failure in group B. So, the rate of mortality difference between both groups was not statistically significant.

The technique used in our study and its results are similar to the study of **Goncu *et al.*** [(8)] regarding less total bypass time, need for inotropic support, new AF and perioperative MI, in the group which received hot shot in both aortic root and graft perfusion in comparison with the group receiving only hot shot into the aortic root alone. Similarly, **Onem *et al.***[(14)] reported in his study that early grafts and ischaemic myocardial areas warm blood perfusion, before the proximal anastomosis and removal of cross-clamp, reduced ischaemia–reperfusion rates and post-ischaemic myocardial dysfunction, and also significantly improved the myocardial deterioration.

Despite, the presence of the same circumstances of this study, there were different consequences due to slight differences in coronary artery stenosis degree and collateral blood flow. The deferential diagnosis between postoperative cardiac dysfunction after CPB injury, ischemia–reperfusion, direct surgical trauma, and preload and afterload maladjustment to contractile activity of myocardium was hard.

CONCLUSION

We had faith that in adding antegrade direct bypass graft perfusion to aortic root warm blood hot shot during proximal graft anastomosis may help prompt recovery of myocardium during CABG and reduction in postoperative mortality and morbidity especially in multi-vessel coronary artery stenosis patients.

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