

Myocardial Protection with multiport antegrade cold blood cardioplegia and continuous controlled warm shot through vein grafts during proximal ends anastomosis in conventional coronary artery bypass graft surgery

Muhammad Sher-i-Murtaza, Hafiz Muhammad Farhan Ali Rizvi, Mirza Ahmad Raza Baig, Waqas Hamid, Haider Zaman

Abstract

Objective: To evaluate the benefits of simultaneous aortic root and vein graft cold blood cardioplegia and continuous controlled warm blood perfusion through vein grafts during proximal aortocoronary anastomosis in conventional coronary artery bypass graft surgery in patients with multi-vessel coronary artery disease.

Methods: The prospective randomised study was conducted at Chaudary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan, from April 2013 to June 2014, and comprised patients of isolated conventional coronary artery bypass graft surgery. The patients were randomised into 2 groups; Group I had patients in whom multiperfusion set was used for cardioplegia and continuous warm blood perfusion through vein grafts during proximal ends anastomosis, and Group II had patients in whom routine aortic root antegrade cardioplegia was used with no warm blood perfusion during proximal anastomosis of vein grafts. Data was analysed using SPSS 20.

Results: There were 434 patients in the study, with Group 1 having 215(49.5%) being the study group, and Group II having 219(50.5%) being the Control group. The groups showed no significant difference in the number of grafts, and aortic cross-clamp time ($p>0.05$ each). Total bypass time was significantly prolonged in the Control Group ($p=0.001$). Incidence of intra-operative arrhythmias, peri-operative myocardial infarction, need for inotropic support and intra-aortic balloon counter-pulsation and operative mortality were significantly higher in the Control group ($p<0.05$ each).

Conclusions: Simultaneous aortic root and vein graft cold blood cardioplegia and continuous controlled warm blood perfusion was beneficial for myocardial protection and early patient outcome.

Keywords: Coronary artery bypass graft surgery, Myocardial protection, Cardioplegia, Multi perfusion adapter. (JPMA 66: 53; 2016)

ClinicalTrials.gov identifier: NCT02303704

Introduction

Conventional coronary artery bypass graft (CABG) surgery using cardiopulmonary bypass (CPB) circuit and cardioplegia with aortic cross-clamp is still the commonest technique used for coronary grafting. Currently, more than 80% patients undergo conventional CABG in the United States¹ and also at our institution. Despite all advancements in techniques of myocardial protection, perioperative myocardial damage is still the most important cause of cardiovascular events and mortality after technically successful CABG.^{2,3} Optimal myocardial protection may be achieved by proper energy preservation of ischaemic myocardium by reducing ischaemia time and providing an adequate, homogeneous distribution of cardioplegia to all parts of myocardium,^{4,5} complete revascularisation and energy restoration by warm shot before the removal of aortic cross-clamp.⁶

Aortic root antegrade cold blood cardioplegia is a commonly used method for myocardial protection. Tight stenosis in the native coronary arteries limits the delivery of antegrade cardioplegia solution distal to critical lesions and hampered myocardial preservation.^{7,8} Retrograde cardioplegia through the coronary sinus can be used as additive for myocardium protection during CABG to overcome this limitation of antegrade cardioplegia. Isolated retrograde cardioplegia is associated with inadequate protection of right ventricle (RV) and part of interventricular septum.⁹⁻¹¹

However, it is notable that to cannulate coronary sinus for retrograde cardioplegia is technically demanding, especially for young surgeons, has definite learning curve, and is associated with complications and failure.^{12,13}

To overcome the limitation of aortic root antegrade cardioplegia in patients with severe coronary artery disease (CAD), we used simultaneous aortic root and vein graft cold blood cardioplegia, calling it 'multiport antegrade cold blood cardioplegia', which is a safe and simple technique without complications.

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Department of Cardiac Surgery, Chaudary Pervaiz Elahi Institute of Cardiology, Multan, Pakistan.

Correspondence: Muhammad Sher-i-Murtaza. Email: sherm.cpeic@gmail.com

The current study was planned to analyse the effects of multiport antegrade cold blood cardioplegia on myocardial protection along with continuous controlled warm blood perfusion through veins graft during proximal ends anastomosis in conventional CABG surgery in patients having multi-vessel disease.

Patients and Methods

The prospective randomised controlled study was conducted at the Cardiac Surgery Department of Chaudary Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan, from April 2013 to June 2014. The CPEIC is a tertiary care cardiac centre and over 600 coronary artery bypass surgeries are performed annually.

The sample size for this study was calculated using level of significance (α) of 5% and power of the test ($1-\beta$) 80%. The calculated sample size was 80 individuals. After approval from the institutional ethics committee, patients undergoing isolated conventional CABG were included. Excluded from the study were cases of redo CABG, those who required 2 or less than 2 grafts, patients who had major postoperative neurological complications like stroke, 2nd arterial graft along with left internal mammary artery (LIMA), patients who need CABG within a week of ST-elevation myocardial infarction (STEMI) or non-ST-elevation myocardial infarction (NSTEMI) and patients with calcified or diseased aorta in which case single cross-clamp technique was used for proximal aorto-coronary anastomosis.

Draw randomisation technique was used to assign individuals to Study and Control group. We made 112 sets, each set containing four patients. The staff nurse on duty was requested to pick up the two folded papers from four containing hidden identity of the patients. The patients chosen by draw were included in the Study group, while others were placed in the Control group.

Group I, which was the Study group, had patients who received multiport antegrade cardioplegia and continuous controlled warm blood perfusion through vein grafts, and Group II, the Control group, had patients who underwent routine conventional CABG with antegrade aortic root cardioplegia without warm blood perfusion.

All operations were carried out by two consultant surgeons at our institution. In all patients 3mg bromazepam was given orally as a premedication on the eve of surgery. intravenous (IV) morphine, midazolam and propofol was used to induce anaesthesia, and doses were adjusted according to the response of the patients, and was maintained with sevoflurane/isoflurane.

Atracurium bromide (1mg/kg) was given before endotracheal intubation.

In all patients, standard CPB was established using an ascending aortic arterial cannula and a two-stage single venous cannula in the right atrium. Heparin was administered in a dose of 400-450IU/Kg before cannulation to maintain activated clotting time (ACT) more than 480 seconds. The body temperature was lowered to about 30-32°C. Ice slush was used to achieve local cooling of the heart. In all patients cold blood cardioplegia was used to achieve cardiac arrest. Complete arrest was achieved with an initial cardioplegia dose of 10-15 ml/kg and was maintained by giving 5-7ml/kg of cardioplegia in repeated doses after each graft or after 20 minutes. Cold blood cardioplegia was given by using cardioplegia delivery system, including heat exchanger in both groups. A cardioplegia delivery cannula with a separate vent line was used for cardioplegia delivery to the aortic root (antegrade method). Cardiac index was maintained between 2.0 and 2.4 L/min/m² to maintain a mean arterial pressures of 55-70 mm of Hg. In Group I, a multiple perfusion set (Figure-1) was used to deliver cardioplegia simultaneously in aortic root and vein grafts. After the distal anastomosis of each vein graft had been completed, the proximal ends were connected to the free branch of the multi-perfusion set. In this way, simultaneous intermittent antegrade graft cardioplegia was administered in addition to aortic root cardioplegia - named multiport antegrade cardioplegia. LIMA and saphenous vein grafts were used as conduits. LIMA was anastomosed to left anterior descending (LAD) artery, while other coronary vessels received greater saphenous vein grafts as conduits.

Just before the removal of the aortic cross-clamp, warm blood shot (normo-kalaemic) was started through multi-perfusion set attached to cardioplegia cannula in the aortic root and vein grafts in Group I. As contraction of heart started, the multiport limb attached to cardioplegia cannula was off and cross-clamp was removed. The warm perfusion through the vein grafts was continued at controlled pressures of about 50-70 mmHg, flow rate of 10-30ml/min/graft and temperature of 35-37°C (Figure-2). Proximal anastomosis was performed in both groups using partial occluding clamp.

The necessity of inotropic support and the choice of inotropic drugs to be administered on weaning from CPB were determined by a cardiac anaesthetist team blinded to and independent of the study. Peak post-op creatinine kinase myocardial band (CKMB) levels were noted within 36 hours after surgery. The designated reference value for detection of myocardial damage

were >125 IU/L for CKMB.

Patient characteristics were entered prospectively in the electronic database system of the hospital (CASCADE DATABASES, Lahore, Pakistan). The data not included in the database was entered separately in Microsoft Excel Spreadsheet (MS Excel, version 2007, Microsoft Co. USA). Statistical analysis was carried out using SPSS 20. Numeric variables were summarised using means and standard deviation. The groups were compared using Independent sample t-test and Mann Whitney U test for numeric variables. Chi-square test and Fisher's exact test were used to compare categorical variables. The significance of differences between the groups was expressed using $p < 0.05$.

Results

Of the 448 patients initially approached, 14(3%) were excluded for not meeting the criteria. The 434(97%) patients were divided into two groups; Group I with 215(49.5%) patients was the Study group, while Group II with 219(50.5%) was the Control group. There were no significant difference regarding preoperative characteristics i.e. age, risk factors of CAD, extent of CAD disease, carotid artery disease, renal function and pre-operative CKMB levels between the groups ($p > 0.05$ each).

There were more patients with left ventricle (LV)

Table-1: Pre-operative Variables.

Name of Variable	Group I with multiport (Study Group)	Group II without multiport (Control Group)	P Value
No. of Patients	215	219	
Age (years)	54.97±8.44	53.62±9.60	0.12 (N.S)
Gender male, Female (%)	186 (86.5), 29 (13.5)	192 (87.7), 27 (12.3)	0.72 (N.S)
Diabetic history (%)	40.5	38.4	0.65 (N.S)
Smoking history (%)	42.3	40.6	0.72 (N.S)
History of Hypertension (%)	47.4	47.0	0.93 (N.S)
Family History (%)	12.6	10.0	0.41 (N.S)
History of Carotid Artery Disease			
Normal, mild,			
moderate severe (%)	76.3, 19.1, 1.9, 2.8	77.6, 17.4, 1.8, 3.2	0.97 (N.S)
Pre-op Creatinine levels (mg/dl)	1.01±0.22	1.00±0.24	0.81 (N.S)
Pre-op CKMB* Levels (IU/L)	20.40±11.68	20.35±11.59	0.96 (N.S)
Category of Disease			
TVD, DVD, TVD+LMS† (%)	88.8, 5.6, 5.6	86.8, 10.5, 2.7	0.07 (N.S)
Ejection Fraction (%)	49.49±11.29	51.12±9.96	0.11 (N.S)
L.V‡ Function Grades 1, 2, 3 (%)	59.1, 21.4, 19.5	66.2, 19.2, 14.6	0.26 (N.S)
Parsonnet score	4.38±3.42	3.73±2.88	0.03 (Sig.)
Add-euro Score	1.13±1.17	1.15±1.24	0.92 (N.S)
Log-euro Score	1.36±0.62	1.34±0.58	0.63 (N.S)

*CKMB indicates Creatinine kinase Myocardial Band, † TVD Tripple vessel disease, DVD Double Vessel Disease, TVD+LMS Triple Vessel Disease combined with Left Main Stem Disease, ‡ L.V Left Ventricle.

Table-2: Operative and Post-operative variables.

Name of Variable	Group I with multiport (Study Group)	Group II without multiport (Control Group)	P Value
Bypass time (min.)	115.90±25.90	125.73±34.53	0.001 (Sig.)
X-Clamp* time (min.)	67.44±15.57	70.19±17.51	0.08 (N.S)
No. of Grafts (mean+S.D)	3.46±0.61	3.42±0.56	0.42 (N.S)
Adrenaline on weaning (ug/kg/min)	0.047±0.018	0.064±0.82	0.06 (N.S)
Nor-adrenaline on weaning (ug/kg/min)	0.035±0.016	0.089±0.50	0.17 (N.S)
Dobutamine on weaning (ug/kg/min)	3.41±1.70	4.20±2.24	>0.0001 (Sig.)
Post-op CKMB† Levels (IU)	71.70±41.50	92.66±88.10	0.002 (Sig.)
Duration of Support (hours)	6.22±10.27	11.21±16.73	>0.0001 (Sig.)
Ventilation time (hours)	5.80±8.04	10.00±26.68	0.03 (Sig.)
Hospital stay time (days)	6.11±1.55	6.73±2.46	0.002(Sig.)
MI‡ by enzymatic Criteria (%)	7.5	13.2	0.05 (Sig.)
IABPS (%)	4 (1.9)	14 (6.4)	0.02 (Sig.)
Spontaneous Rhythm (%)	94.4	86.3	0.004 (Sig.)
Coronary End-arterectomy (%)	4.7	5.9	0.55 (N.S)
Graft Revised or augmented (%)	1.9	2.3	1.0 (N.S)
Operative Mortality (%)	0.50	4.1	0.02 (Sig.)

*X-clamp indicates Cross Clamp, †CKMB Creatinine Kinase-Myocardial Band, ‡MI Myocardial Infarction, §IABP Intra-aortic Balloon Pump, SD: Standard deviation.

dysfunction in Group I but it was not statistically significant ($p > 0.05$). Regarding preoperative operative mortality risk stratification scoring systems, there were statistically significantly higher risk patients according to parsonnet scoring system in Group I ($p = 0.03$) (Table-1).

Operative and postoperative results showed that there was no significant difference regarding number of vessels revascularised, need for coronary artery endarterectomy because of severity of distal disease and aortic cross-clamp time in the two groups ($p > 0.05$ each). The mean CPB time was significantly lower in Group I ($p < 0.05$). After aortic declamping, spontaneous rhythm was achieved without electrical defibrillation in Group I patients ($p = 0.004$) (Table-2).

The need, duration and dose of pharmacological inotropic support and intra-aortic balloon counterpulsation were significantly higher in Group II ($p < 0.05$). The mean length of ventilation and hospital stay time were significantly lower in Group I ($p < 0.05$).

Post-op peak CKMB level was significantly higher in the Control group ($p = 0.002$). Incidence of peri-operative myocardial infarction (MI) according to enzymatic criteria was also significantly higher in Group II ($p < 0.05$). Operative mortality was also significantly higher in Group II ($p = 0.02$).

Multiperfusion adapter without vent port



Multiperfusion adapter with vent port

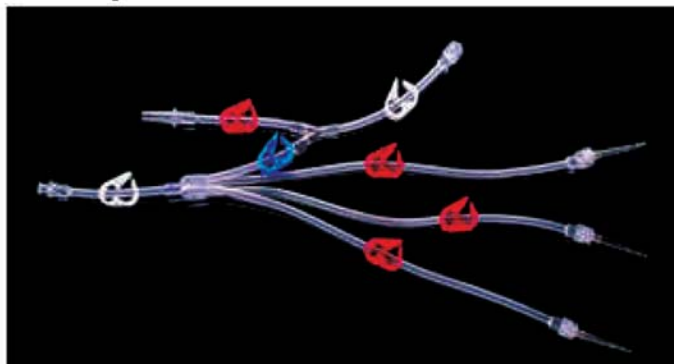


Figure-1: (A) Multi-perfusion set without vent port. (B) Multi-perfusion set with vent port.

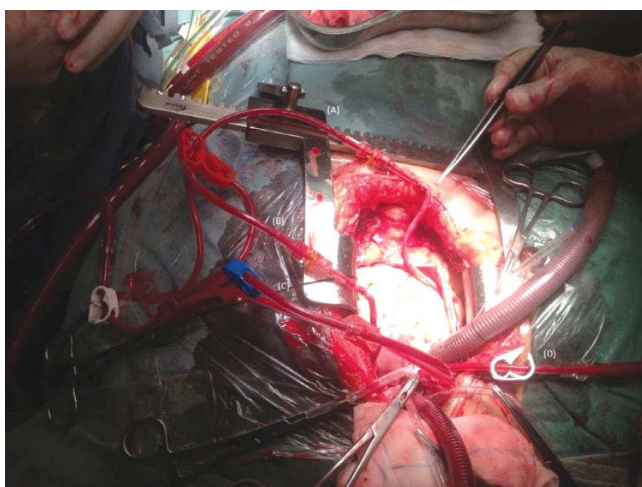


Figure-2: Use of multi-perfusion set, port C is connected with Antegrade Aortic root cardioplegia cannula, while ports A and B are connected with venous grafts via vessel tip cannulae, and port D is connected with vent port of aortic root cardioplegia cannula.

Discussion

With advancement in technology and experience of interventionist approaches and sometime because of patient preference for minimal invasive procedures, percutaneous coronary intervention is the modality of treatment for CAD patients who are referred for CABG usually with severe multi-vessel CAD. Hence, surgery and myocardial protection is becoming more challenging for coronary surgeons. The principle of coronary surgery in conventional CABG is to have nearly complete revascularisation of all ischaemic areas that require adequate visualisation in a quiet, bloodless operative field by using simple and safe cardio-protective techniques to avoid per-operative myocardial damage and post-

operative deterioration in cardiac function.

AT present, combined antegrade and retrograde cardioplegia is considered the standard for myocardial protection.¹⁴ However, aortic root antegrade cardioplegia is a commonly used method for myocardial protection because of its simplicity and safety. The multiport cardioplegia technique used in the present study facilitates antegrade selective cardioplegia perfusion by means of free grafts following each distal anastomosis in addition to antegrade cardioplegia administered from the aortic root. This technique also supplies blood to the ischaemic myocardium during construction of the proximal graft anastomosis, promoting early reperfusion and rapid recovery of grafted ischaemic myocardial regions, thus reducing ischaemic time. It is also observed that during patch anastomosis of long open coronary endarterectomies like open endarterectomy of LAD, when because of increased time of cardioplegia dose or return of cardiac activity which may jeopardise myocardial protection, cardioplegia through aortic root is not feasible without surgical interruption because of the position of heart. The cardioplegia can be infused through vein grafts without surgical interruption. The name of technique of simultaneous antegrade and vein graft cardioplegia as multiport antegrade cardioplegia was never used before and we have used it for the first time.

The idea of continuous controlled warm perfusion at the time of proximal aortocoronary anastomosis was derived from perfusion assisted direct CABG used in off-pump CABG surgery. Some studies have concluded that early graft perfusion preserves myocardium in multivessel CAD in patients undergoing off-pump CABG.¹⁵⁻¹⁷ We utilised this concept and technique in conventional CABG during proximal aortocoronary anastomosis to restore and build

the energy before putting load on energy depleted- ischaemic heart.

Literature review revealed that very little work has been done on the technique of myocardial protection used by us and there is conflicting results in the published studies.

The graft perfusion was first described in 1987,¹⁸ and suggested that selective graft perfusion provides early and uniform cooling to ischaemic zones identified by intramyocardial temperature probes and can also provide uniform warm blood reperfusion during construction of the proximal anastomosis. It concluded that this technique is beneficial in patients presenting with acute and on-going ischaemia and those having tight left main coronary artery stenosis.

One study¹⁹ showed no advantage of antegrade perfusion of vein grafts along with antegrade aortic root cold blood cardioplegia in low-risk patients. Studies²⁰⁻²¹ on simultaneous aortic root and vein graft cardioplegia do not prove any beneficial effects on myocardial protection. However, in both these studies the sample size was very small, low-risk patients were included and patients with poor LV were excluded and they did not perfuse the vein grafts with warm blood at the time of proximal anastomosis.

The results of our study are very similar to an earlier study²² which randomised controlled study on 96 patients with 48 patients in each group on the effect of antegrade graft cardioplegia combined with passive graft perfusion in on-pump CABG and found that the release of cardiac troponin I (cTn-I) was significantly less in patients who received passive graft perfusion, indicating superior myocardial preservation.

The CPB time, need for defibrillation on removing cross-clamp, inotropic support on weaning was significantly low in the Study group. It also concluded that RV protection was better with this technique. The beneficial effect in that study was accentuated in patients with poor LV and patients with near total occlusion of right coronary artery. The difference between the two studies is that they used passive perfusion of grafts and we used perfusionist assisted active warm blood perfusion of all grafts keeping in mind that it is controlled and better¹⁷ and blood can be enriched.

The findings of our study suggest that selective antegrade graft cardioplegia delivery along with aortic root can provide superior myocardial protection because of more homogeneous distribution of cardioplegia solution and warm blood reperfusion through vein grafts to areas of critical coronary artery stenosis or complete coronary

artery occlusion.

Together, these factors result in lower ischaemia time and minimise ischaemic-reperfusion injury. Early resuscitation of ischaemic myocardium with warm blood minimises the risk of post-ischaemic myocardial dysfunction. The technique used in the study may prove beneficial in lowering mortality and morbidity after CABG surgery in patients with multi-vessel CAD.

Conclusions

This Multiport antegrade cold blood cardioplegia and continuous controlled warm blood shot through aortic root and vein grafts during construction of proximal anastomosis is a beneficial technique for myocardial protection and early patient outcome. The method may well be adopted as a routine in patients with severe multi-vessel CAD undergoing conventional CABG.

Acknowledgment

We are grateful to CPEIC, Multan, for financial assistance.

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