ANTEGRADE VERSUS ANTEGRADE / RETROGRADE CARDIOPLEGIA FOR MYOCARDIAL PROTECTION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

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ABSTRACT

Objective: Nonhomogeneous distribution of cardioplegia antegradely in severe coronary artery stenosis and evolving acute myocardial infarction has been demonstrated experimentally. Administration of cardioplegia retrogradely causes homogeneous distribution and offers a good alternative for myocardial protection.

Methods: Thirty five consecutive patients with three vessel-disease undergoing elective coronary artery bypass grafting were prospectively randomized to receive either antegrade cold blood cardioplegia alone (Group A, n: 17) or antegrade/retrograde cold blood cardioplegia (Group B, n: 18). The patients in group B received cardioplegia half dose antegradely and then the other half dose was given retrogradely. In both groups, following the induction dose of cold blood cardioplegia, 500 ml cold blood maintenance cardioplegia every 20 minutes and terminal warm blood cardioplegia were applied before the removal of the aortic cross clamp antegradely in group A and retrogradely in group B.

Results: Baseline patients characteristics did not differ in both groups. Myocardial temperature measured following the induction cardioplegia; was significantly higher in group A than in group B ($p \leq 0.05$). After 10 minutes of reperfusion, the rise in myocardial oxygen extraction and myocardial lactate extraction was higher in group A than in group B ($p \leq 0.02$). CK-MB and Troponin-T levels at the postoperatively 12th hour were significantly higher in group A than in group B ($p < 0.05$). Eight patients in group A, and 4 patients in group B inotropic support was used because of the low cardiac output (p: NS). However, when compared the inotropic score of the two groups, it was significantly higher in group A than in group B (2.1±0.6 in group A, 1.2+0.5 in group B $p < 0.04$). In four patients in group A, 5 patients in group B atrial fibrillation, and in 5 patients in group A, 2 patients in group B ventricular extrasistole were observed (p:NS).

Conclusion: Antegrade/retrograde cardioplegia performs better protection and faster recovery than the antegrade cardioplegia alone.

Key Words: Antegrade, Retrograde, Protection, CABG

INTRODUCTION

Optimal myocardial protection is required for the homogeneous delivery of the cardioplegic

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solution to all parts of the heart. This is especially important in the presence of critical coronary artery stenosis. Nonhomogeneous distribution of cardioplegia antegradely in severe stenosis and evolving acute myocardial infarction (AMI) has been demonstrated experimentally (1,2).

Administration of cardioplegia through the coronary sinus (CS) retrogradely causes homogeneous distribution and offers a good alternative for myocardial protection (3,4). However, the uniformity of myocardial protection with retrograde cardioplegia is still controversial. In many studies it is emphasized that; a large percentage of retrograde solution was shunted through the arteriosinusoidal system and thebesian veins into the ventricular cavities, thus causing inadequate protection of the right ventricle and posterior left ventricle (5,6).

The aim of this study was to evaluate the metabolic effects of antegrade cardioplegia (AC), and antegrade / retrograde cardioplegia (ARC) in low-risk patients with three vessel coronary artery disease undergoing coronary artery bypass grafting (CABG).

MATERIAL AND METHODS

Patient selection: Thirty five consecutive patients with three vessel disease undergoing elective CABG were prospectively randomized to receive either AC alone (Group A, n: 17) or ARC (Group B, n:18). Patients with unstable angina pectoris, emergency procedures, reinterventions, concomitant procedures such as; valve replacement were not included in the study. Preoperative data are summarized in Table I.

Table I: Baseline patients' characteristics

	Group A (n:17)	Group B (n:18)	P
Age (yr)	59.8±7.6	64.0±7.5	NS
Gender (male)	14	12	NS
Diabetes mellitus	8	5	NS
Hypertension	9	12	NS
Smoking	9	9	NS
LVEDP (mmHg)	14.4±10.1	12.3±5.0	NS
EF %	58.8±10.0	62.7±14.3	NS
VPS	8.2±1.1	8.1±1.7	NS

LVEDP: Left ventricle enddiastolic pressure, EF: Ejection fraction, VPS: Ventricular performance score, NS: Not significant

Surgical Procedure: The same surgical team performed all operations. Standard median sternotomy, full heparinization, aortic and two-stage venous cannula were inserted. Cardiopulmonary bypass (CPB) was performed with membrane oxygenator and non-pulsatile roller pump. Moderate hypothermia (rectal temperature 30-32 °C) was used and 2.4 lt/min/m2 flow rate was maintained during bypass. In group A cold blood cardioplegic solution was infused in the aortic root at a pressure of 60 mmHg and 150 mL/min flow rate, 15 ml/kg in dose. In group B before the cardiopulmonary bypass (CPB) a self-inflating balloon cannula was placed via transatrial in the CS using blind insertion technique. The patients in group B received cardioplegia half dose antegradely and the other half dose was given retrogradely at a pressure of 40 mmHg. In both groups, following the induction dose of cold blood cardioplegia (+4 °C, 15 mL/kg, potassium level: 20mEq/lt), 500 mL cold blood maintenance cardioplegia (+4 °C, potassium level: 10 mEq/lt) every 20 minutes and terminal warm blood cardioplegia (37°C) were applied before the removal of the ACC antegradely in group A and retrogradely in group B. Topical iceslush was used in all patients to support the myocardial protection. At the end of the first cardioplegic dose, myocardial temperature was measured with needle thermistor probes in the right ventricle free wall (RVFW), inferior wall (IW), septum and left ventricle posterolateral wall (LVPW). All the distal anastomoses were performed on ACC. In all operations, conduit for bypass were included saphaneous veins or LIMA or combination of two. The first distal anastomosis was performed with vein graft to the right coronary artery, and was completed with LIMA to LAD anastomosis in both groups. Following each vein anastomosis, 200 mL cold cardioplegia was perfused through the vein to test the anastomos quality. Proximal anastomoses were performed on the ascending aorta on a side-biting aortic clamp. After myocardial reperfusion, spontaneous recovery of the electromechanical activity of the heart and the need for temporary pacing were also recorded. Operative variables are summarized in Table II.

Table II: Operative variables

	Group A	Group B	P
CCT (min)	37.3±7.5	37.3±8.0	NS
CPBT (min)	66.5±10.6	67.7±8.8	NS
Graft per case	3.6±0.7	3.3±0.8	NS
Spontan.defibrillation	12	14	NS
Myocar. temp. (°C)			
RVFW	13.5±2.2	10.5±3.0	<0.02
Septum	17.0±2.4	13.8±2.5	<0.04
Inferior	18.1±1.5	15.6±2.6	<0.05
LVPW	17.5±1.6	15.8±3.4	NS

CCT: Cross clamp time, CPBT: Cardiopulmonary bypass time,
RVFW: Right ventricle free wall,
LVPW: Left ventricle posterolateral wall

Coronary Sinus Sampling: Coronary sinus sampling was done in both groups to measure the myocardial oxygen and lactate extraction. Blood samples were taken simultaneously from the arterial or blood cardioplegia line at the beginning of the CPB and 10 min. after the cross-clamp release. The samples were analyzed for PO2, PCO2, O2 saturation, O2 content, lactate content and Hb. The temperature difference was taken into consideration and corrected during calculation. The following formulas were used to calculate myocardial O2 and lactate extraction. Myocardial O2 extraction (MOE) = O2 content of arterial blood - O2 content of CS blood (CIBA-corning 288 blood gas system), myocardial lactate extraction (MLE) = blood cardioplegia lactate content - CS lactate content (Spinreact - Cobas Mira Plus - Roche).

Cardiac enzyme release and myocardial infarction: Before the operation and at 4 hours and 12 hours after the operation creatin kinase - isoenzyme MB (CK-MB) and troponin-T were measured in all patients. Diagnostic criteria for peroperative myocardial infarction were new Q waves of 0.04 mm or more or a reduction in R waves of more than 25% in at least 2 leads in electrocardiography (ECG) or CK-MB level more than 50 IU/L.

Inotropic support score: In the peroperative or early postoperative period patients were considered to have low cardiac output (LCO) whenever the systolic blood pressure was lower than 90 mmHg and mix venous 02 saturation lower than 60% despite adequate preload and optimal afterload. Inotropic support score was done due to the dose, the number and the using time of the inotropic agents (Grade 1: Dopamine 3μg/kg/min, Grade 2: Dopamine ≥5 μg/kg/min more than 24 hours, Grade 3: Using double inotropic agents such as; Dopamine ≥5 μg/kg/min + Adrenalin ≥1 μg/kg/min or triple inotropic agents such as; Dopamine ≥5μg/kg/min + Adrenalin ≥1 μg/kg/min + Dobutamine ≥5 μg/kg/min more than 48 hours).

Statistical Analysis: Data are expressed as means and standard deviations. Continuous and discrete variables were compared using analysis of variance and $\chi 2$ analyses, respectively. A multivariate analysis was performed for comparison of preoperative and intraoperative data between groups. A p value of less than 0.05 was considered significant.

RESULTS

Baseline patient characteristics: Mean age was 59.8 ± 7.6 years in group A and 64.0 ± 7.5 years in group B. Gender and incidence of hypertension, diabetes mellitus, smoking were similar in both groups. Furthermore, the parameters of the left ventricular function did not differ significantly in the groups. Ventricular performance score (VPS) is a scoring system of left ventricular function due to wall motions of seven segments at the left and right oblique ventriculography (normal: 1, hypokinesia: 2, akinesia: 3, diskinesia: 4, aneurysm: 5).

Operative variables: Number of graft per case, ACC time, CPB times were similar in both groups. Following removal of the ACC spontaneous recovery of electromechanical activity of the heart in group A was lower than in group B (12/17 in group A, 14/18 in group B p: not significant). Myocardial temperature was significantly higher in RVFW, IW and septal segments of the heart in group A than in group B ($p \leq 0.05$) (Table II).

Coronary sinus samples: There were no differences in preischemic MOE and MLE values in both groups. However, after 10 minutes of reperfusion the rise in MOE and MLE (Figs 1, 2) were higher in group A than in group B ($p \leq 0.02$)

Cardiac enzyme release and myocardial infarction: Postoperative levels of all enzymes were above normal or preoperative levels but no significant differences between the two groups were found for the preoperative and at the first postoperative measurement values. CK-MB and troponin-T levels at the postoperatively 12th hour (Table III) were significantly higher in group A than in group B ($p<0.05$). Peroperative MI was detected in 1 patient in group A, and none in group B (p: not significant).

Low cardiac output: For eight patients in group A, and 4 patients in group B inotropic support was used because of the LCO (p:not significant). However, when compared the inotropic score of the two groups (Table IV), was significantly higher in group A than in group B ($p<0.04$).

Cardiac arrhythmia: In four patients in group A, and 5 patients in group B atrial fibrillation (AF) was observed during the hospital stay (p: not significant). Also ventricular extrasistole (VES) needing therapy occurred 5 patients in group A and 2 patients in group B (p: not significant).

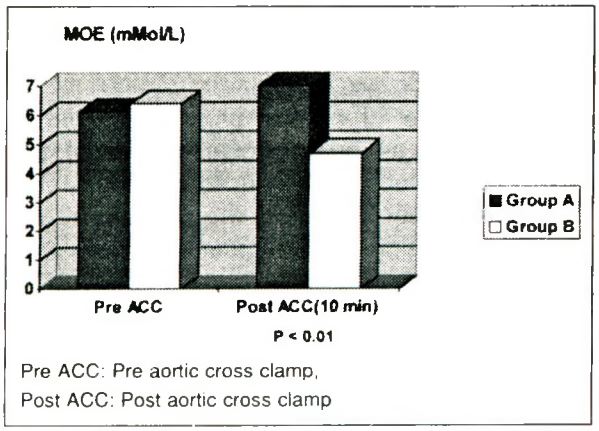
Table III: Cardiac enzyme release

	Group A	Group B	P
CK-MB (IU/L)			
Preoperative	1.7±0.8	1.3±0.5	NS
Postoperative 2th h	21.4±6.4	19.3±6.4	NS
Postoperative 12th h	18.0±13.0	9.3±2.4	<0.04
Troponin-T (μg/L)			
Preoperative	0.03±0.05	0.02±0.03	NS
Postoperative 2th h	0.5±0.4	0.5±0.2	NS
Postoperative 12th h	0.7±0.5	0.3±0.1	<0.05

Table IV: Complications

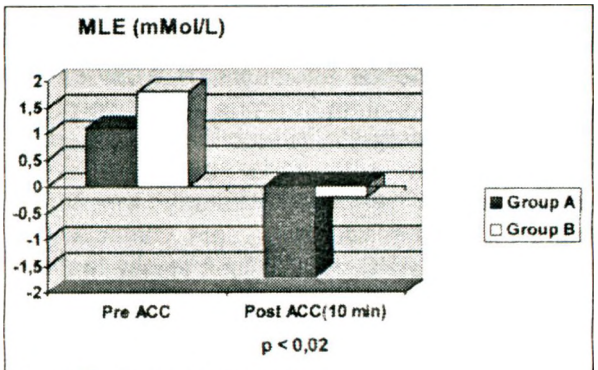
	Group A	Group B	P
LCO	8	4	NS
Inotropic score	2.1±0.6	1.2±0.5	<0.04
MI	1	0	NS
AF	4	5	NS
VES	5	2	NS

LCO: Low cardiac output, MI: Myocardial infarction.
AF: Atrial fibrillation, VES: Ventricular extrasistole



Pre ACC: Pre aortic cross clamp,
Post ACC: Post aortic cross clamp

Fig.1: Myocardial oxygen extraction (MOE)



Pre ACC: Pre aortic cross clamp,
Post ACC: Post aortic cross clamp

Fig.2: Myocardial lactate extraction (MLE)

DISCUSSION

Today, systemic hypothermia, cardioplegic arrest and topical hypothermia are essentials of conventional myocardial protection in open-heart surgery. Critical coronary artery stenoses may prevent the homogeneous distribution of the cardioplegic solutions. With the increasing use of LIMA to the occluded LAD artery; direct antegrade perfusion of cardioplegia beyond the stenoses is technically impossible (7). Retrograde infusions may deliver cardioplegic solution beyond obstructed coronary arteries and may improve subendocardial perfusion (8,9). However, in many studies inadequate protection of the right ventricle with retrograde cardioplegia was noted (5,6,10).

Spontaneous recovery of electromechanical activity of the heart following removal of the ACC has been used as an indicator of myocardial protection (11). In this study no difference was

found in both groups (12/17 in group A and 14/18 in group B, p: NS).

Likely, the level of cardiac enzyme release is being thought as an essential marker of the myocardial protection (12-14). In our study, CK-MB and troponin-T level at the postoperatively 12th hour was significantly higher in group A than in group B ($p<0.05$). This result shows faster myocardial recovery was constituted with ARC.

Also homogeneous and adequate cooling of the heart could be accepted as an indicator of homogeneous cardioplegic delivery. In this study myocardial temperature had been measured following the induction dose of cardioplegia and was found significantly lower in three segments (RVFW, IW, Septal segments, $p<0.05$) of the heart in group B than in group A. As we noted before the adequate protection of the right ventricle with retrograde cardioplegia is controversial. But in our study the lower myocardial temperatures of right ventricle was observed with ARC. It is difficult to say that the right ventricle is always inadequately protected with retrograde cardioplegia, on the contrary of adequate protection of left ventricle. Retrograde cardioplegia has a mixed effect: more homogeneous distribution of the cardioplegic solution to the left ventricular microcirculation, especially in patients with critical coronary artery stenoses, (2,4,9,15) and causes the endocavitary cooling of the right ventricle with cardioplegic solution diverted from the arterial network through the thebesian veins and arterio-venous shunts (16). Therefore we believe that; combined ARC with infusion of the cardioplegic solution after the right coronary artery anastomoses via the graft will protect the right ventricle adequately.

Myocardial biopsy samples were not taken in this study, but it has been shown that in patients with three vessel disease and a significant stenosis in the LAD, the preservation of energy-rich phosphates during ischemic cardiac arrest is better with retrograde than with antegrade cardioplegia (17).

Regarding the metabolic study performed on the coronary sinus blood samples, the level of MOE and MLE did not differ significantly preoperatively. However, 10 min. after reperfusion the rise in MOE and MLE levels was significantly higher in group A than in group B ($p<0.02$). These metabolic study results show that better myocardial protection was obtained by ARC than solely by AC.

Eight patients in group A, and 4 patients in group B needed inotropic support because of LCO (p: not significant). The inotropic score of group A was significantly higher ($p<0.04$) than in group B (2.1 ± 0.6 vs. 1.2 ± 0.6).

In conclusion; despite the small numbers of included patients, in this study the overall myocardial protection was satisfactory in both groups. There was no early mortality and no severe cardiac morbidity (such as; prolonged LCO, intractable arrhythmia) during the hospital stay. But some indicators of myocardial protection (such as; spontaneous defibrillation of the heart, cardiac enzyme release, myocardial cooling) were against the efficacy of AC. Therefore, ARC should be preferred, especially in patients with three vessel coronary artery disease undergoing CABG.

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