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Delivering Cardioplegia Beyond Totally Occluded Native Coronary Arteries Through the Saphenous Bypass Vein Graft: Is It Really a Protective Technique?

Tam Tıkalı Nativ Koroner Arterlerde Safen Ven Baypas Grefti Yoluyla Kardiyopleji Verilmesi: Gerçekten Koruyucu Bir Teknik mi?

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ABSTRACT

Introduction: *Antegrade route may fail to provide homogenous cardioplegia distribution in patients with totally occluded coronary arteries. Cardioplegia via vein graft beyond occlusion is considered as an alternative approach to achieve better myocardial protection. In this study, we aimed to compare myocardial protection achieved with antegrade cardioplegia and antegrade plus vein graft cardioplegia in patients with totally occluded coronaries.*

Patients and Methods: *Consecutive 14 patients with at least one totally occluded coronary artery were randomly divided into two groups. Antegrade cardioplegia was used in group 1, antegrade plus vein graft cardiplegia was used in group 2. Creatine kinase, creatine kinase MB, lactate and troponine I levels were measured for myocardial damage monitorization. Samples were collected from the arterial line and coronary sinus simultaneously; at the beginning of the operation before extracorporal circulation institution (1), after completion of the distal anastomosis, immediately after "hot shot" cardioplegia infusion and aortic unclamping (2) and after removal of the side clamp (3). Measurements were repeated at the 6th (4), 12th (5), 24th (6) and 48th (7) postoperative hours from the peripheral arterial line. Groups were compared statistically.*

Results: *In this study, cardiac enzymes and transcoronary lactate gradient were found similar in each measurement.*

Conclusion: *Antegrade cardioplegia may achieve adequate myocardial protection in patients with totally occluded coronary arteries. Antegrade plus vein graft cardioplegia does not seem to provide any advantage in this spesific patient group.*

Key Words: *Cardioplegia; saphenous vein; coronary artery bypass.*

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ÖZET

Giriş: *Antegrad yol, tam tıkalı koroner arter hastalarında homojen kardiyopleji dağılımı sağlamada yetersiz kalabilir. Bu hastalarda tıkalı segmentin distaline ven greftiyle kardiyopleji uygulamak alternatif bir yöntem olabilir. Bu çalışmada, antegrad kardiyopleji uygulanan hastalarla antegrad kardiyoplejiyle eş zamanlı ven grefti kardiyoplejisi uygulanan tam tıkalı koroner arter hastalarını miyokardiyal koruma açısından biyokimyasal parametrelerle karşılaştırdık.*

Hastalar ve Yöntem: *En az bir koroner arteri tam tıkalı 14 hasta randomize olarak iki gruba ayrıldı. Grup 1'e antegrad kardiyopleji uygulanırken Grup 2'ye eş zamanlı antegrad ve ven grefti kardiyoplejisi uygulandı. Kreatin kinaz, kreatin kinaz MB, laktat, troponin I ölçüldü. Örnekler radial arter ve koroner sinüsten kardiyopulmoner baypastan önce (1), distal anastomozlar tamamlandıktan sonra (2), side klemp kaldırıldıktan sonra (3) arter ve koroner sinüsten, operasyon sonrası altıncı (4), 12. (5), 24. (6) ve 48. (7) saatlerde arterden alındı. Gruplar istatistiksel olarak kıyaslandı.*

Bulgular: *Gruplar arasında kardiyak enzimler ve transkoroner laktat gradiyenti açısından fark bulunmadı.*

Sonuç: *Antegrad kardiyopleji total tıkalı koroner arter varlığında yeterli miyokard koruması sağlayabilir. Antegrad ve ven greft kardiyoplejisi bu spesifik hasta grubunda bir avantaj sağlamamaktadır.*

Anahtar Kelimeler: *Kardiyopleji, safen veni, koroner arter baypas.*

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INTRODUCTION

Antegrade cardioplegia provides myocardial protection by delivering potassium enriched solutions via native coronary arteries. Theoretically, homogeneous cardioplegia distribution may not be achieved in the presence of totally occluded coronary arteries[1,2]. Nonhomogenous distribution of cardioplegia may lead to myocardial injury and left ventricular dysfunction. Although bloodless and arrested heart seems enough for surgery, in current practice, strong influence of cardioplegia to postoperative prognosis and outcomes is well known. Various studies considered alternative cardioplegia delivery methods for better myocardial protection. The vast majority of this studies investigated efficacy of retrograde cardioplegia simultanously with antegrade route or alone. Beside of studies have shown that retrograde cardioplegia results in better distribution, myocardial cooling and more complete recovery of function in the areas beyond the coronary occlusions, many studies reported no clear advantage in terms of myocardial protection with retrograde cardioplegia[1-4]. An alternative approach is delivering cardioplegic solutions beyond occlusion via vein grafts following distal anostomosis[5]. Hypothetically anostomosed veins should provide a more effective distribution of cardioplegia when compared to antegrade route only. Although suppositional effectiveness of this technique seems logical, randomised controlled studies are missing.

In this study, we aimed to compare two different cardioplegia methods (simultanous antegrade/vein graft cardioplegia or antegrade cardioplegia alone) for myocardial protection in patients with at least one totaly occluded coronary artery except left anterior descending artery.

PATIENTS and METHODS

All of our patients have signed an informed consent form and the study was approved by institutional ethics committee. Consecutive 14 patients, with at least one totally occluded coronary artery underwent on-pump coronary artery bypass grafting between May 2009 and August 2009. Patients were divided into two groups consecutively; in group 1 (n= 7) cardioplegia was delivered in the usual antegrade fashion, in group 2 (n= 7) cardioplegia was delivered via antegrade route and simultaneously from the sapheneous vein grafts after each distal anostomosis completion. Right coronary artery was totally occluded in six patients of group 1 but 5 of group 2. Circumflex artery was totally occluded in two patients of both groups. Left anterior descending artery was stenotic but not totally occluded in any patient. Left internal thoracic artery was used for left anterior descending artery anostomosis in each patient. Creatine kinase, creatine kinase MB, lactate and troponine I levels were measured for myocardial damage monitorization. Samples were collected from the arterial line and coronary sinus simultaneously; at the beginning of operation before extracorporal circulation institution (1), after completion of the distal anastomosis, immediately after 'hot shot' cardioplegia infusion and aortic unclamping (2) and after removal of the side clamp (3). Measurements were repeated at the 6^{th} (4), 12^{th} (5), 24^{th} (6) and 48^{th} (7) postoperative hours from the peripheral arterial line. Trans-coronary lactate gradient (TCLG) was calculated as the difference of coronary sinus and arteriel blood sample lactate values for each measurement intraoperatively.

Statistical Analysis

Statistical analysis were performed with the statistical package for the social sciences (SPSS) computer program, version 16.0 (SPSS, Inc., Chicago, III, USA). All data were expressed as mean±standart deviation. Results were analyzed with the Student t test or Mann-Whitney U test for quantitative data, and with the Chi-square or Fisher exact test (when Levene's test was significant) for categorical data. A p value of 0.05 was considered statistically significant.

Operative Technique

All patients underwent coronary artery bypass grafting surgery under cardiopulmonary bypass. LITA anostomosed to left anterior descending artery in all patients. Proximal anostomosis were done with aortic side clamping.

Cardioplegia Technique

Immediately after the aortic clamping, cold (9°C) blood cardioplegia (15 mL/kg, including 30 mEq/L KCl and 24 mEq/L $MgSO_4$ in the first injection; and 10 mL/kg, including 15 mEq/L KCl and 12 mEq/L $MgSO_4$ in the subsequent injections) was given via the aortic root under 70-80 mmHg pressure for at least two minutes in both groups. The cardioplegia was then repeated every 20 minutes, after the termination of distal anastomoses (irrespective to how many distal anastomoses were created, 20 minute time was waited for the next cardioplegia delivery) in all patients. However, the control group received the solution via the aortic root only, whereas the study group received via the aortic root and the free flow vessel cannulas (DLP #30003, Medtronic, MN, USA) attached to the proximal ends of the saphenous vein grafts. Multiple perfusion sets (DLP #14000, Medtronic, MN, USA) were used to connect the free flow vessel cannulas to the main cardioplegia line as side branches. Finally, all patients received 10 mL/kg warm (35°C) blood cardioplegia (hot shot) before the aortic cross-clamp was taken out.

RESULTS

Preoperative demographic datas were similar between groups. Mean age was 63.43 ± 9.79 in group 1 and 62.86 ± 8.47 group 2 (p= 0.91). No statistically significant difference was found in terms of; gender, smoking history, hypertension, hyperlipidemia and diabetes mellitus, preoperative ejection fraction, preoperative functional capacity and logistic Euroscore. Mean aortic cross clamp time was 83.86 ± 20.41 minute in group 1 and 84.14 ± 16.12 minute in group 2 (p= 0.97), partial bypass time 110.14 ± 33.22 in group1 and 108.22 ± 26.83 group 2 (p= 0.81). Mean proximal anostomosis number was 3.0 ± 0.57 in group 1 and 2.71 ± 0.48 in group 2 (p= 0.34) (Table 1). Mean volume of cardioplegic solution was 2234.39 ± 362.85 mL in group 1 and 2385.21 ± 401.39 mL in group 2 (p= 0.67). Central venous (S), coronary sinus (CS) and arterial (A) samples were compared for CK, CKMB, troponin I and lactate. All results were compared statistically. no difference was found between groups in any samples and any time (Figures 1-4). Cardiac enzyme changes were identical in both groups. Troponin I and CKMB gradually increased and reached to peak level at the 6^{th} postoperative hour in both groups (7.93 ± 4.68 ng/mL vs. 8 ± 6.25 ng/mL, p= 0.523 and 145 ± 33.54 U/L vs. 224 ± 53.15 U/L, p= 0.552). After than cardiac enzymes gradually decreased and normalized at postoperative 48^{th} hour in both groups. Notably, cardiac enzymes were measured higher but statistically in significant in group 2 in all time-points except of 2^{nd} samples (1.05 ± 0.33 ng/mL vs. 0.73 ± 1.16 ng/mL, p= 0.25). Similarly TCLG was lower but not significant of 2^{nd} samples in group 2 (1.75 vs. 0.86, p= 0.24).

DISCUSSION

Currently most of the cardiac surgery procedures are based on the generation of an asystolic-motionless heart by delivery of an optimal volume of cardioplegic solution for a good myocardial protection. Antegrade cardioplegia route is by far the most common method. Theoretically. non-homogeneous cardioplegia distribution and cooling may occur with antegrade route in the presence of severe native coronary artery stenosis[1,2]. Nonetheless antegrade cardioplegia is sufficient in terms of providing an arrested heart in the vast majority of patients even in the presence of advanced coronary artery disease. Noyez et al. showed importance of collateral circulation for homogenous cardioplegia distribution in patients with severe coronary artery stenosis[6]. In our study, we did not observe any difficulties in terms of achieving diastolic arrest by antegrade route so we did not use retrograde cardioplegia in any patients despite totaly occluded coronary arteries. As Noyez et al. declared we also concluded that coronary collateral circulation plays a critical role for myocardial protection[6].

As collateral arteries may be documented angiographically. echocardiography may also have predictive value

Table 1. Preoperative and operative characteristics of patients

	Group 1	Group 2	p
Age	63.43 ± 9.76	62.86 ± 8.47	0.91
Gender (male %)	100%	71.4 %	0.41
Diabetes mellitus	42.8%	42.8%	0.97
Hypertension	71.4%	85.7%	0.42
Hyperlipidemia	57.1%	85.7%	0.14
Smoking history	57.1%	85.7%	0.14
Functional capacity (NYHA)	1.94 ± 0.25	2.03 ± 0.37	0.31
Euroscore	2.41 ± 0.24	2.38 ± 0.31	0.67
Ejection fraction	52.71 ± 10.61	53.60 ± 9.84	0.44
AXC (minute)	83.86 ± 20.41	84.14 ± 16.12	0.97
CPB (minute)	110.14 ± 33.22	108.22 ± 26.83	0.81
Proximal anostomosis (n)	3 ± 0.57	2.71 ± 0.48	0.33

NYHA: New York Heart Association, AXC: Aortic Cross Clamp, CPB: Cardiopulmonary Bypass.

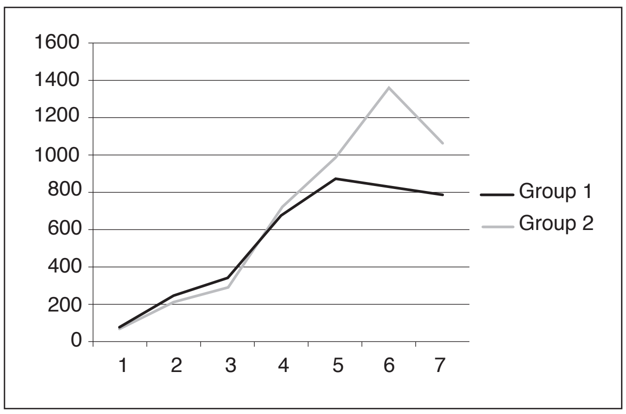

Figure 1. Change of creatine kinase in the arterial samples.

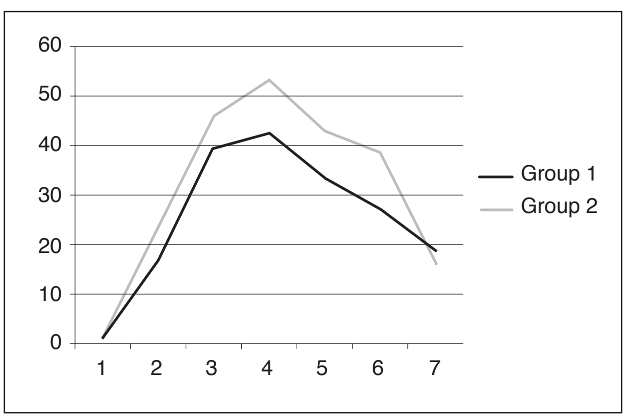

Figure 2. Change of CK-MB in the arterial samples.

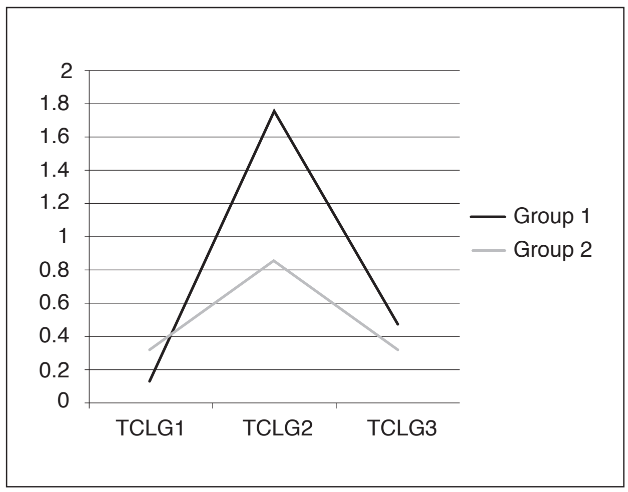

Figure 3. Changes of trans-coronary lactate gradient (TCLG).

in terms of cardioplegia distribution. At this point absence of akinetic area in preoperative echocardiogram becomes important. In our study preoperatively there were no akinetic segment in any patient. The collateral circulation may supply poor but enough cardioplegia distribution similarly.

Although there is no published data reporting patent arteries causing cardioplegia steal phenomenon in presence of severe stenosis of other arteries. Soltesz et al. in their animal study showed better cardioplegia distribution in the right ventricle when the left anterior descending artery was ligated(1). In practice blood flow runs to myocardial areas

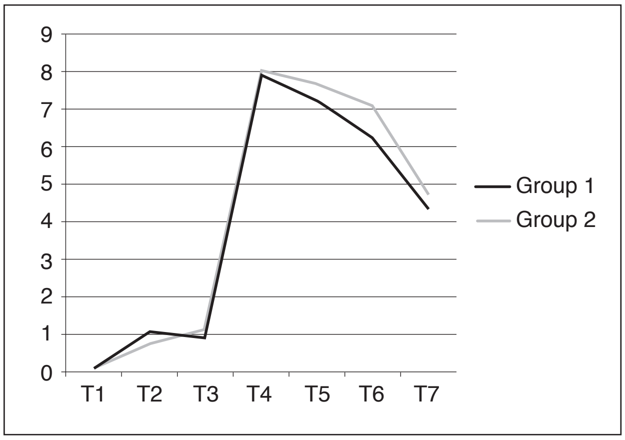

Figure 4. Changes of troponin I in the arterial samples.

with low pressure, thus cardioplegia tends to open arteries in spite of severely stenotic coronaries but bridging collateral arteries supply flow retrogradely to post occlusion myocardium.

Theoreticaly retrograde cardioplegia seems to overwhelm homogenous cardioplegia distribution problem although there are still clinical and surgical conflicts in terms of right ventricular protection during retrograde cardioplegia[7-12]. Currently general opinion is in favor of insufficiency of retrograde way to protect right ventricle because of thebesian veins directly draining to right atrium. Although we used antegrade cardioplegia in patients with totaly occluded right coronary artery in our control group, patients' postoperative electrocardiography and cardiac enymes showed no infarction or ischemia in any patient.

Although diastolic arrest and hypothermia reduce metabolic rate of the heart. cardioplegia ensures myocardial energy demand beyond arresting heart thus reducing its anabolic metabolism. In our results lactate values were not statisticaly significant between groups. But in time point two TCLG were markedly lower (1.75 vs. 0.86, p= 0.24). The second samples have been taken at the end of absolute ischemic time. Consequently. this samples reflects myocardial anabolic metabolism directly. In this context simultanous vein graft cardioplegia may provide better energy supplement than antegrade way olnly.

In conclusion, we emphasize that antegrade cardioplegia alone may provide adequate myocardial protection in patients with totally occluded coronary arteries. Although our study groups include limited patient numbers. simultanous antegrade/vein graft cardioplegia does not appear to provide better myocardial protection in this spesific patient subgroup.

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