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Comparison of Antegrade and Antegrade/Retrograde Blood Cardioplegia Applications in Cardiac Surgery with Cardiopulmonary Bypass

Kardiyopulmoner Bypass Eşliğinde Yapılan Kardiyak Cerrahide Antegrad ile Antegrad/Retrograd Kan Kardiyoplejisi Uygulamalarının Karşılaştırılması

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Abstract

Objective: In the present study, it was aimed to determine the perioperative and postoperative early outcomes of coronary artery bypass grafting (CABG) operations with CPB by comparing intermittent antegrade and intermittent antegrade (Initial) combined with retrograde (Maintenance) blood cardioplegia applications.

Materials and Methods: 240 patients with similar characteristics who underwent CPB-guided CABG operation were included in the present study. Two groups were formed as Antegrade (Group 1) and Antegrade/retrograde (Group 2). In this context; the preoperative, intraoperative, and early postoperative results of the groups were compared.

Results: Gender, age, body surface area, flow, ejection fraction percentages, EuroSCORE and LMCA lesion presence values were similar in both groups ($p>0.05$). Cross-clamp time, total perfusion time, mean activated clotting time during CPB and perioperative drainage were similar in both groups ($p>0.05$). There was no statistically significant difference between the sodium, potassium, calcium, glucose, and lactate levels evaluated after CPB of the two groups ($p>0.05$). In addition, there was no statistically significant difference between the two groups in terms of defibrillation requirement, inotropic requirement, and IABP requirement after CPB ($p>0.05$).

Conclusion: Similar results were observed between antegrade cardioplegia alone and antegrade combined with retrograde cardioplegia in CPB-guided CABG operations. For this reason, we think that the antegrade cardioplegia technique alone will be more advantageous in terms of ease of application, not requiring additional invasive intervention, and eliminating the risks of the necessity of additional intervention. Furthermore, we think that the importance of case-based evaluation in cardioplegia techniques should not be ignored.

Keywords: Cardiopulmonary Bypass, Myocardial Perfusion, Antegrade, Retrograde.

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Öz

Amaç: Bu çalışmada KPB eşliğinde koroner arter bypass greft (KABG) replasmanı yapılan vakalarda aralıklı antegrad ile aralıklı antegrad (Başlangıç) ardından retrograd (İdame) yoldan kan kardiyoplejisi uygulamalarını karşılaştırarak perioperatif ve postoperatif erken dönem etkilerini saptamak amaçlandı.

Gereç ve Yöntemler: KPB eşliğinde KABG replasmanı yapılan benzer özelliklere sahip 240 hasta dahil edildi. Antegrad (Grup-1) ve Antegrad/retrograd (Grup-2) olmak üzere iki grup oluşturuldu. Grupların preoperatif, intraoperatif ve erken dönem postoperatif sonuçları karşılaştırıldı.

Bulgular: Her iki grubun; cinsiyet, yaş, vücut yüzey alanı, flow, ejeksiyon fraksiyon yüzdeleri, EuroSCORE ve LMCA varlığı değerleri benzerdi ($p>0,05$). Her iki grubun; kross klemp süresi, total perfüzyon süresi, KPB sırasındaki ortalama etkinleştirilmiş pıhtılaşma zamanı ve perioperatif drenaj miktarı benzerdi ($p>0,05$). İki grubun KPB çıkışında değerlendirilen sodyum, potasyum, kalsiyum, glukoz ve laktat düzeyleri arasında istatistiksel olarak anlamlı fark yoktu ($p>0,05$). Ayrıca iki grubun KPB çıkışındaki defibrilasyon ihtiyacı, inotrop ihtiyacı ve İABP ihtiyacı arasında da istatistiksel olarak anlamlı fark yoktu ($p>0,05$).

Sonuç: KPB eşliğinde yapılan KABG replasmanı operasyonlarında tek başına antegrad kardiyopleji uygulama yöntemi ile antegrad ardından retrograd kardiyopleji uygulama yöntemi arasında, benzer sonuçlar saptandı. Bu nedenle uygulama kolaylığı ek invazif girişim gerektirmemesi açısından ve ek girişim gerekliliğinin risklerinin ortadan kalkması nedeniyle tek başına antegrad kardiyopleji uygulama yönteminin daha avantajlı olacağını düşünmekteyiz. Ayrıca kardiyopleji uygulama yöntemlerinde olgu bazlı değerlendirmenin önemi de göz ardı edilmemesi gerektiğini düşünmekteyiz.

Anahtar Kelimeler: Kardiyopulmoner bypass, Miyokardiyal Perfüzyon, Antegrad, Retrograd.

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Introduction

Ischemic heart diseases (IHDs) are among the leading causes of death worldwide (1). These diseases often require surgical treatment with the cardiopulmonary bypass (CPB) technique. Cardiac surgery with CPB has been performed for many years. Extracorporeal circulation techniques are used in CPB procedure. For this purpose, the functions of the heart and lungs are stopped and a heart-lung machine that performs artificial circulation and respiratory functions is used (2).

The heart-lung machine provides a bloodless field for cardiac surgery. The heart-lung machine contains an extracorporeal circuit that provides physiological support, in which venous blood is drained into a reservoir, oxygenated, and returned to the body using a pump. Teamwork between the surgeon, perfusionist and anaesthetist is crucial for a successful CPB administration. However, it is the responsibility of each area of expertise to reduce the complications that may occur and to develop strategies against them (3).

The myocardium must be protected since the heart is stopped during CPB. Therefore, various protection methods are applied. The most used and preferred ones are hypothermia and pharmacological techniques. In the pharmacological method, the heart is aimed to be protected with cardioplegia solutions. Besides, different solutions, components, and routes of administration have been developed to optimize myocardial protection with cardioplegia solutions. These include cold and warm blood and crystalloid solution via antegrade, retrograde or combined cardioplegia delivery approach (4). There is debate regarding the most appropriate cardioplegia application method in myocardial protection due to the variety of cardioplegia solutions, application methods and patient groups. In this study, we compared antegrade and antegrade/retrograde cardioplegia solutions in coronary artery bypass grafting (CABG) operations.

The aim of this study is to determine the early perioperative and postoperative effects of blood cardioplegia by comparing intermittent antegrade and intermittent antegrade (initial dose) and then retrograde (maintenance doses) blood cardioplegia applications in CPB-guided CABG operations.

Materials and Methods

A total of 240 patients who underwent CPB-guided CABG operation between 01.01.2019 and 30.08.2022 were retrospectively included in our study. A website was used to calculate the sample size of the groups (https://www.stat.ubc.ca/~rollin/stats/ssize/n2.html). The type I error rate was accepted as a maximum of 5%, while the type II error rate was accepted as a maximum of 20%. The effect size of the study was determined as ≥0.5. Case data, operative techniques, clinical and laboratory results (preoperative, intraoperative, and postoperative haematological and biochemical parameters) were reviewed retrospectively. Preoperative data, intraoperative data, and postoperative data were gathered from patient files and hospital records.

Ethical Approval

Approval from the local ethics committee was obtained before the related study (Ethics Committee of Harran University Clinical Research Ethics Committee with the decision dated 03.10.2022 and numbered HRU/22.19.14.). The study was conducted in accordance with the principles stated in the Declaration of Helsinki.

Exclusion and Inclusion Criteria

Patients treated with amiodarone before surgery, patients with a history of atrial fibrillation (AF) (preoperative AF and paroxysmal AF patients were excluded to determine the postoperative AF that may develop due to the application methods), patients with severe aortic valve insufficiency with valve pathology, those with moderate or higher mitral insufficiency or known systemic inflammatory disease, those who underwent emergency surgery or reoperation, chronic haemodialysis patients, those with acute coronary syndrome and concomitant congenital heart disease were excluded from the study. After applying the exclusion criteria, patients who underwent isolated CABG surgery consecutively with CPB and who did not undergo additional intervention were included in the study.

Creating Groups

In the present study, two groups were formed to evaluate the early effects of antegrade and antegrade/retrograde blood cardioplegia. Group 1 included 120 patients whom were used intermittent antegrade isothermal blood cardioplegia at 32°C. Group 2 included 120 patients whom were used intermittent retrograde blood cardioplegia at maintenance doses after the first dose of antegrade isothermal blood cardioplegia at 32°C.

Surgical Approach

Standard surgical techniques were used. After midline sternotomy, arterial cannulation was performed through the ascending aorta, and venous cannulation was performed through the right atrium with a two-stage venous cannula. Left internal mammalian artery graft was used for left anterior descending artery anastomosis in all cases. Saphenous vein was used as a graft for anastomosis of other coronary arteries. All patients underwent complete revascularization.

Inotrope Requirement

Inotropic agents were used for reasons such as low cardiac output syndrome and acute hypotension following coronary artery bypass surgery. The inotropic agents consisted of noradrenaline, dopamine and dobutamine.

Cardiopulmonary Bypass (Perfusion) Method

Patients' blood flow rates during extracorporeal circulation were determined according to body surface areas (2.4 lt/min/m2). An oxygenator and tubing set suitable for the patient's weight and appropriate cannula diameters according to body surface areas were used. Membrane oxygenator/tubing sets with integrated arterial filters were used. Tubing set venous line diameter was used as 1/2 and the arterial line diameter was used as 3/8. 32oC hypothermia was applied to all patients during extracorporeal circulation. Arterial line pressures were maintained on average between 150-180 mmHg during CPB. By providing adequate anticoagulation, the activated clotting time (ACT) was kept at 480 seconds and above. 1200 ml of balanced solution (Isolyte), 150 ml of 20% mannitol, 5000 units of heparin and 2 g of cefazolin were used as the prime solution.

Cardioplegia Solution

Isothermic blood cardioplegia solution (32oC) was used. The initial cardioplegia dose was administered as kgx15ml (full dose) as the solution amount, and the maintenance doses were administered as half dose (1/2). In the preparation of the cardioplegia solution, oxygenated patient blood taken from the extracorporeal circulation equipment was mixed with potassium chloride, magnesium, and sodium bicarbonate.

Statistical Analyses

Statistical analyses were performed using SPSS® 16.0 computer program. Mean and standard deviations were calculated for continuous and ordinal data. Kolmogorov Smirnov test and Shapiro-Wilk test were used to evaluate normal distribution. Student t test and Mann Whitney U tests were used to evaluate normal and non-normally distributed data, respectively. Frequency and percentage analyses were performed for nominal data and Chi Square test was used for comparisons. A p value less than 0.05 was considered statistically significant.

Results

In this study, the demographic data of the groups included gender, age, body surface area (BSA), flow, ejection fraction percentages (EF%), EuroSCORE values, presence of left main coronary lesion (LMCA=Left Main Coronary Artery) and CABG counts (Table 1), while intraoperative data included cross-clamp time, total perfusion time, mean activated clotting time (ACT) during CPB and perioperative blood drainage amount, which were similar with no statistically significant difference between the two groups ($p>0.05$) (Table 2). There was no statistically significant difference between the sodium, potassium, calcium, glucose, and lactate levels evaluated at the CPB output of the two groups ($p>0.05$) (Table 1). Moreover, there was no statistically significant difference between the two groups in terms of defibrillation requirement, inotropic requirement, and IABP requirement at CPB output ($p>0.05$) (Table 2).

Table 1

Preoperative Data

		Group 1 (n=120)	Group 2 (n=120)	P
Gender (n, %)	Male	76, (63.3%)	70, (58.3%)	0.254
	Female	44, (36.7%)	50, (41.7%)	0.509
Age (years) (Mean±SD)		73.05±3.55	71.33±6.73	0.333
BSA (m2) (Mean±SD)		1.88±0.17	1.89±0.18	0.812
Flow (lt) (Mean±SD)		4.48±0.42	4.49±0.43	0.989
EF% (Mean±SD)		47.16±8.42	46.79±8.37	0.702
EuroSCORE (Mean±SD)		4.55±1.43	4.57±1.41	0.825
LMCA (n, %)	NO	74, (61.66%)	71, (59.16%)	0.792
	YES	46, (38.33%)	49, (40.83%)	0.396
Number of CABGs, (n, %)	II	12, (10%)	14, (11.66%)	0.381
	III	63, (52.5%)	58, (48.33%)	0.517
	IV	38, (31.66%)	39, (32.5%)	0.985
	V	7, (5.83%)	9, (7.5%)	0.253

Mean±SD: Mean±Standard Deviation; **n, %:** Number, percent; **BSA**: Body Surface Area; **EF%**: Ejection Fraction; **LMCA**: Left main coronary artery lesion, **CABG**: Coronary artery bypass graft.

Table 2

Intraoperative and Postoperative Data

		Group 1 (n=120)	Group 2 (n=120)	P
Kross Clamp Time (Minute) (Mean±SD)		59.75±17.78	63.80±15.40	0.096
Total Perfusion Time (Minute) (Mean±SD)		85.43±23.84	91.01±23.81	0.121
Mean ACT (Seconds) (Mean±SD)		659.02±136.94	682.54±150.76	0.170
Perioperative Drainage Amount (ml) (Mean±SD)		179.88±23.02	181.17±23.50	0.373
CPB output Na (mEq/L) (Mean±SD)		140.62±3.36	140.06±4.05	0.063
CPB output K (mEq/L) (Mean±SD)		4.41±0.45	4.43±0.39	0.739
CPB output Ca (mg/dL) (Mean±SD)		8.74±4.74	8.78±4.71	0.733
CPB output Glucose (mg/dl) (Mean±SD)		176.64±54.60	174.24±60.10	0.491
CPB output Lactate (mmol/L) (Mean±SD)		1.56±0.88	1.86±1.28	0.104
Defibrillation Requirement (n (%))	NO	78 (65%)	71 (59.2%)	0.212
	YES	42 (35%)	49 (40.8%)	0.425
Inotrope Requirement (n (%))	NO	13 (10.8%)	16 (13.3%)	0.346
	YES	107 (89.2%)	104 (86.7%)	0.693
IABP Requirement (n (%))	NO	111 (92.5%)	109 (90.8%)	0.408
	YES	9 (7.5%)	11 (9.2%)	0.816
Postoperative Drainage Amount (ml) (Mean±SD)		1113.80±307.67	1135.00±313.86	0.568
Extubation Time (Hour) (Mean±SD)		6.99±2.33	6.57±2.81	0.141
ICU Length of Stay (Hours) (Mean±SD)		31.20±7.29	32.85±8.67	0.599

Mean±SD: Mean±Standard Deviation; **n (%):** Number, percent; **ACT**: Activated Clotting Time; **IABP**: Intra-aortic Balloon Pump; **ICU**: Intensive Care Unit; **Na**: Sodium; **K**: Potassium; **Ca**: Calcium.

Discussion

Today, in addition to hypothermia, the pharmacological arrest method with coronary perfusion (cardioplegia) is used to perform cardiac operations by stopping the heart and providing a still and bloodless environment. Thus, the heart is safely stopped, the continuity of energy production is ensured, and the harmful effects of ischemia on the heart are prevented (5,6). Cardioplegic solutions are currently accepted and applied solutions to protect the myocardium during aortic clamping (7). These solutions have been proven to be reliable by various experimental studies and are intended to be distributed to all parts of the heart with their administration routes. Nonetheless, the main focus today is on their composition, temperature, administration times and routes of administration (8-10).

In order to provide adequate myocardial protection, the cardioplegic solution should be distributed evenly to all areas of the myocardium. For this purpose, cardioplegia can be administered directly from the coronary ostium or aortic root as antegrade and retrograde from the ostium of the coronary sinus (11). In this study, we aimed to compare antegrade and antegrade combined with retrograde cardioplegia solutions in CABG patients.

Among the advantages of this study is that no significant difference was determined between the antegrade technique and the antegrade combined with the retrograde technique as a way of applying cardioplegia solutions for myocardial protection in cardiac surgery accompanied by CPB. In cardiac surgery, time planning and minimizing the time of the patient's connection to the extracorporeal circulation equipment (Heart-lung machine) is of great importance. In this regard, we think that it would be more advantageous to prefer the antegrade technique as the cardioplegia application method to save time.

Retrograde cannulation as a cardioplegia route of administration requires additional invasive intervention to the heart as it is performed with an additional entry through the right atrium. Due to this additional cannulation and decannulation, bleeding control time increases and even carries a significant risk of haemorrhage. We think that the retrograde route of administration may even be disadvantageous for these reasons.

Hirata et al. (12) aimed to evaluate the myocardial distribution of cardioplegia solution given as antegrade and retrograde in the same type of patients. In their study, they initially gave cardioplegia induction as an antegrade and then retrograde. They evaluated the intramyocardial distribution of the cardioplegic solution they gave to patients with heart valve disease and coronary artery disease using myocardial contrast echocardiography during surgery. They stated that the retrograde cardioplegia solution was less homogeneously distributed in heart valve patients and was not delivered to the middle part of the interventricular septum in two-third of the patients. They expressed that the transmural myocardial distribution in the anterior, lateral and posterior walls of the left ventricle was similar in both application methods. In coronary heart disease patients, they showed that the cardioplegia solution given retrogradely in the coronary collateral state associated with the complete occlusion of the coronary arteries was well delivered, however, the cardioplegia solution was not delivered through the antegrade route. They stated that delivery could not be achieved in both application methods to the areas with myocardial infarction. Consequently, they stated that planning strategies for myocardial protection have important effects, so knowing the exact anatomy of the coronary artery and vein of the patients is necessary and important in the administration of cardioplegia in the adequate way (12). In our study, we believe that there is no difference between the results of both methods, so it would be more accurate and important to evaluate and determine the cardioplegia application technique individually for each patient.

In some studies, it is also argued that there are advantages at different points related to both cardioplegia application techniques (13-14). In their study, Jiang et al. (13) compared antegrade and continuous retrograde del Nido cardioplegia in David I operation. As a result of their study, they found that Troponin I level (TnI), creatine kinase myocardium band level (CKMB), left ventricular ejection fraction (LVEF), ventilation times, length of intensive care unit stay and length of hospital stay were similar in both groups. Nevertheless, they found that the lactate level was slightly higher in the antegrade group compared to the retrograde group. They found that the incidence of heart block was higher in the retrograde group. As a result of their study, they stated that antegrade and continuous retrograde del Nido cardioplegia could be used safely and effectively in David I operation, but continuous retrograde del Nido cardioplegia was associated with higher transient AV block rate and lower lactate level that did not require permanent pacing (13). Brant et al. (14) investigated the effects of antegrade and retrograde perfusion protection on cardiac function in dogs after transplantation in their experimental study. As a result of their study, they stated that functional protection was superior in the antegrade group at the beginning, yet retrograde group’s hearts functioned better after reperfusion (14).

Some studies argue that retrograde or antegrade and retrograde (combined) application techniques are superior to the antegrade application method alone (15-16). Cicek et al. (15) compared the effects of antegrade cardioplegia and antegrade-retrograde (combined) cardioplegia on inflammatory response and left ventricular systolic functions in coronary bypass surgery. In their study, they stated that the mean postoperative EF decrease was less in patients who were given cardioplegia with the combined method, and that TNF-α levels were lower and other results were similar. As a result, they thought that co-administration of retrograde and antegrade cardioplegia was more advantageous in terms of myocardial protection than antegrade cardioplegia (15). Franke et al. (16) compared the effect of retrograde (29 patients) and antegrade (29 patients) crystalloid cardioplegia on troponin-I value in coronary surgery with elective coronary artery bypass grafting. In their study, they stated that a significantly higher cardiac troponin-I concentration was observed in the antegrade group 24 hours after the aortic cross-clamping. Therefore, they thought that retrograde cardioplegia was advantageous in myocardial protection in ischemic heart disease (16). Unlike the results of our study, we think that the fact that they state that the retrograde method is advantageous is due to the fact that the result at a certain time was evaluated in a limited number of patients and on a single parameter.

Lee et al. (17) compared different myocardial protection techniques in aortic stenosis. In their study, they compared three groups: combined antegrade and retrograde cold blood cardioplegia, antegrade crystalloid cardioplegia using histidine-tryptophan-ketoglutarate (HTK) solution, and retrograde cold blood cardioplegia. They established that they obtained similar early and late clinical results in all three groups (17). In this study, we think that different cardioplegic solutions used outside the application routes also have an effect on similar results despite different application methods. Therefore, we believe that the evaluation of different routes of administration (antegrade, retrograde and combined) will yield more general results in studies using the same cardioplegia solution in similar patient groups.

Lebon et al. (18) compared combined antegrade and retrograde cardioplegia with endovascular coronary sinus catheterized retrograde cardioplegia in minimally invasive mitral valve surgery. As a result of their study, they stated that retrograde cardioplegia alone provided comparable myocardial protection to combined antegrade and retrograde cardioplegia in minimally invasive mitral valve surgery, yet retrograde administration was not sufficient to achieve asystole in one-fifth of their patients (18). As seen in this study, it was observed that retrograde application alone was disadvantageous, and the combined method was superior. In our study, it was seen that there was no difference between the antegrade technique and the combined technique, and they showed similar results. Thus, the antegrade technique alone bears greater importance as it has fewer procedures and bleeding risks.

In their study, Kaukoranta et al. (19) evaluated myocardial protection during antegrade and retrograde cardioplegia. They compared patients with similar characteristics who underwent the elective CABG operation procedure. As a result of their study, they stated that the postoperative course was smooth in both groups, but retrograde mild hypothermic blood cardioplegia led to metabolic changes compatible with right ventricular ischemia, therefore, caution should be exercised when providing retrograde normothermic blood cardioplegia in patients with right ventricular hypertrophy, poor right ventricular function or severe preoperative myocardial ischemia (19). We also think that preoperative and other variables should be evaluated in the selection of cardioplegia application methods.

Ozbek et al. (20) compared intermittent antegrade and continuous retrograde isothermic blood cardioplegia applications after a single dose of antegrade in isolated CABG operations. In their study, they concluded that antegrade and retrograde cardioplegia, which are among the myocardial protection techniques used in patients who underwent isolated coronary artery bypass grafting, showed very similar results and both methods could safely provide myocardial protection (20). This study, which is similar to our study, supports our results.

The limitations of the present study are that it is single-center and retrospective. Moreover, only the cases with CABG operations were included in our study. We believe that the inclusion of more multi-center groups with different cardiac diagnoses and more patients in the study will yield more comprehensive results.

Conclusion

Similar results were found between antegrade cardioplegia alone and antegrade combined with retrograde cardioplegia in CPB-guided CABG operations. For this reason, we think that the antegrade cardioplegia technique alone will be more advantageous in terms of ease of application, not requiring additional invasive intervention and eliminating the risks of the necessity of additional intervention. We think that this method will change daily clinical practice. In addition, we think that the importance of case-based evaluation in cardioplegia techniques should not be ignored.

Ethics Committee Approval: The study was approved by the Harran University Clinical Research Ethics Committee (date: 03.10.2022 and approval number: HRU/22.19.14).

Informed Consent: Consent was not obtained as it was a retrospective study.

Conflict of Interest: Authors declared no conflict of interest.

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