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Original Article / Özgün Makale

Comparison of intermittent antegrade cardioplegia and antegrade/retrograde continuous cardioplegia in terms of myocardial protection in cardiac surgery

Kardiyak cerrahide miyokardiyal koruma açısından intermittant antegrad kardiyopleji ile antegrad/retrograd sürekli kardiyoplejinin karşılaştırılması

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ABSTRACT

Background: This study aims to compare intermittent antegrade cardioplegia and antegrade/retrograde continuous cardioplegia in terms of myocardial protection in cardiac surgery.

Methods: Hundred six patients who underwent cardiac surgery in our clinic between October 2010 and January 2011 were included in the study. Patients were divided into two groups as patients who received intermittent antegrade cardioplegia (group 1; 18 females, 14 males) and who received antegrade/retrograde continuous cardioplegia (group 2; 16 females, 58 males), and postoperative results were compared. Troponin-I, creatine kinase-myocardial band (CK-MB) levels, durations of cardiopulmonary bypass (CPB) and cross-clamping, total amounts of cardioplegia, and potassium utilization during the process were evaluated.

Results: According to our results, mean troponin-I and CK-MB levels were higher in group 1 than group 2. However, this difference was not statistically significant. While troponin-I and CK-MB values were correlated to durations of cross-clamping and CPB in group 1, troponin-I and CK-MB values were not correlated to durations of cross-clamping and CPB in group 2.

Conclusion: No correlation was detected between troponin I, CK-MB levels, and durations of CPB and cross-clamping in the group which received anterograde/retrograde continuous cardioplegia. Therefore, troponin-I and CK-MB levels were not affected and myocardial protection was better once effective myocardial protection was obtained by antegrade/retrograde continuous cardioplegia. Although antegrade/retrograde continuous cardioplegia provides better myocardial protection, aortic pressure must be monitored to be kept between desired levels during antegrade cardioplegia, and the retrograde cannula must be kept in the appropriate place during retrograde cardioplegia.

Keywords: Cardioplegia, coronary bypass surgery, myocardial injury, myocardial protection.

ÖZ

Amaç: Bu çalışmada kardiyak cerrahide miyokardiyal koruma açısından intermittant antegrad kardiyopleji ile antegrad/retrograd sürekli kardiyopleji karşılaştırıldı.

Çalışma planı: Ekim 2010 - Ocak 2011 tarihleri arasında kliniğimizde kardiyak cerrahi ameliyatı uygulanan 106 hasta çalışmaya alındı. Hastalar, intermittant antegrad kardiyopleji uygulananlar (grup 1; 18 kadın, 14 erkek) ve antegrad/retrograd sürekli kardiyopleji uygulananlar (grup 2; 16 kadın, 58 erkek) olmak üzere iki gruba ayrıldı ve ameliyat sonrası elde edilen sonuçlar karşılaştırıldı. İşlem sürecinde troponin-I, kreatin kinaz-miyokard bandı (CK-MB) düzeyleri, kardiyopulmoner baypas (KPB) ve kros klemp süreleri, kardiyopleji toplam miktarları ve potasyum kullanımı değerlendirildi.

Bulgular: Bulgularımıza göre, ortalama troponin-I ve CK-MB değerleri grup 1'de grup 2'den daha yüksekti. Ancak bu farklılık istatistiksel olarak anlamlı değildi. Grup 1'de troponin-I ve CK-MB değerleri kros-klemp ve KPB süresi ile korele iken, grup 2'de troponin-I ve CK-MB değerleri kros-klemp ve KPB süresi ile korele değildi.

Sonuç: Troponin-I, CK-MB düzeyleri ile KPB ve kros-klemp zamanları arasında anterograd/retrograd sürekli kardiyopleji uygulanan grupta korelasyon bulunmadı. Buna göre, antegrad/retrograd sürekli kardiyopleji ile efektif miyokardiyal koruma sağlandığında, troponin-I ve CK-MB değerleri etkilenmedi ve miyokardiyal koruma daha iyiydi. Anterograd/retrograd sürekli kardiyopleji daha iyi miyokardiyal koruma sağlasa da anterograd kardiyopleji sırasında aort basıncı istenen düzeylerde tutulabilmesi için monitörize edilmeli ve retrograd kardiyopleji sırasında da retrograd kanül doğru yerde tutulmalıdır.

Anahtar sözcükler: Kardiyopleji, koroner baypas cerrahi, miyokardiyal yaralanma, miyokardiyal koruma.

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The myocardium is sensitive to ischemia-reperfusion (IR) injury during cardiopulmonary bypass (CPB) surgery. Furthermore, surgically-induced IR seems to be a major contributor to morbidity and mortality after cardiac surgery. Hence, inadequate myocardial protection has become a major concern that should be eliminated in candidates for CPB surgery.[1-4]

Cardioplegia allows for the regeneration of cellular energy stores and the repair of reversible injuries to the myocardium during the period of electromechanical quiescence. This restoration improves metabolic and short-term functional recovery and decreases mortality in cardiac surgery. However, controversy still surrounds the principles for choosing the optimal type of cardioplegia that can provide the desired level of myocardial protection.[4,5] Therefore, the goal of this study was to observe and compare the cardioprotective efficacies of intermittent antegrade cardioplegia and continuous antegrade/retrograde cardioplegia during cardiac surgery with regard to myocardial protection.

PATIENTS AND METHODS

This study was comprised of two groups of patients. Group 1 consisted of 32 patients (18 females, 14 males; mean age 51.15±13.04 years; range 25 to 77 years) who received intermittent antegrade cardioplegia, and group 2 was composed of 74 patients (16 females, 58 males; mean age 54.78±13.29 years; range 27 to 74 years) who underwent continuous antegrade/retrograde cardioplegia.

Premedication was accomplished via the administration of oral diazepam (5 mg) the night before the operation, and in the operating theater, after the patients underwent electrocardiography (ECG) and pulse oxymetry, intravenous saline (10 mL/kg) was introduced. Arterial blood pressure monitorization was done via the cannulation of the radial artery in the non-dominant arm after confirming a negative result on the Allen test. General anesthesia was then induced with midazolam (0.03 mg/kg), fentanyl (1-2 µg/kg), and sodium thiopental (3-5 mg/kg), and intubation was carried out after the administration of rocuronium bromide (1 mg/kg). Subsequent to the onset of mechanical ventilation, central venous catheterization (through the right internal jugular vein) was performed, and pulmonary artery catheterization was done using a Swan-Ganz catheter (Edwards Lifesciences Corp., Irvine, CA, USA). In addition, the patients' temperatures were monitored via rectal and esophageal probes.

After performing a median sternotomy, the aorta and right atrium were cannulated, and anticoagulation was initially accomplished via the administration of heparin (300 U/kg), with the activated clotting time (ACT) values being maintained at above 450 seconds during the surgical period.

After the placement of the venous cannula in the right atrium and the arterial cannula in the ascending aorta, aortic cross-clamping was performed. Next, antegrade cardioplegia was carried out via a cannula located in the aortic root, whereas a retrograde cannula was placed in the coronary sinus for continuous isothermic cardioplegia. A 1000 mL solution consisting of 30 mEq potassium (K^+) 7.5%, 8.4% of 10 mEq sodium bicarbonate ($NaHCO_3$) and 15% of 12 mEq of a half ampule of magnesium sulfate ($MgSO_4$) was administered at a rate of 10-15 mL/kg for isothermic blood cardioplegia. The electrolyte composition and cardioplegia solution were regulated according to the cardiac activity, electrolyte composition, and urinary output.

For antegrade and continuous applications, isothermic cardioplegia was achieved by administering a 500 mL solution consisting of 4-10 mEq K^+ 7.5% and 8.4% of 4-10 mEq $NaHCO_3$ at a rate of 7-8 mL/kg.

Roller pumps (COBE Laboratories, Lakewood, CO, USA) and a venous reservoir (D-708 Simplex III, Dideco, Mirandola, Italy) were utilized during CPB, and the blood flow rate through the pump was 2-2.2 l/m^2. Both hypo- and hypertension were avoided, and the mean arterial blood pressure was kept at a range of between 50 and 80 mmHg. Nitroglycerine, sodium nitroprusside, ephedrine, and furosemide were used to maintain the appropriate blood pressure and urinary output during surgery, and at the end of the coronary artery bypass grafting (CABG) procedure, the heparin was neutralized with protamine at a proportion of 1:1.

The types of surgical procedures performed on our patients included CABG, valvular replacement, septal defect repair, and mass excision. In order to demonstrate the impact of cardioplegia on myocardial protection, blood samples were obtained two hours after the removal of the cross-clamp, and these were used to measure the troponin I and creatine kinase-myocardial band (CK-MB) levels. The total CPB and cross-clamp durations as well as the total amounts of cardioplegia and potassium utilized during this process were then noted and compared in both groups (Table 3).

Statistical analysis

All statistical analyses were performed using the SPSS version 15.0 for Windows software program (SPSS Inc., Chicago, IL, USA). The data were

Table 1. Preoperative patient data

	Group 1		Group 2		
	Mean±SD	Min.-Max.	Mean±SD	Min.-Max.	*p**
Age	51.15±13.04	25-77	54.78±13.29	27-74	0.413
Left ventricular ejection fraction	54.2±10.35	30-70	52.21±9.56	25-65	0.518
EuroSCORE	3.02±5.67	0.56-22.94	3.34±4.98	0.55-24.77	0.204
Aortic insufficiency degree	0.31±0.48	0-1	0.82±1.41	0-4	0.628
Coronary lesion	1.00±1.27	0-3	2.00±1.40	0-4	0.019*

SD: Standard deviation; Min.: Minimum; Max.: Maximum; * Indicates statistical significance.

given as mean ± standard deviation (SD) or median (minimum-maximum). The categorical variables were shown as the number of cases and percentages. In addition, independent samples t-test was used to evaluate the significance of the differences in normal distribution between the two groups, and the Mann-Whitney U test was used to analyze the statistical differences of the changing variables between the groups since these were not normally distributed. Furthermore, the categorical variants were evaluated using Pearson's chi-square or Fisher's absolute value chi-square test, and the results were considered to be statistically significant with a p value of <0.05.

RESULTS

An analysis of the data revealed that there were no statistically significant differences between the two groups with regard to age, degree of aortic insufficiency, preoperative left ventricular ejection fraction (LVEF), the European System for Cardiac Risk Evaluation (EuroSCORE) results (p=0.413, 0.628, 0.518, 0.204, respectively). However, the number of coronary lesions was statistically significantly higher in group 2 compared with group 1 (p=0.019) (Table 1). In addition, there was an increased number of patients with hyperlipidemia and previous myocardial infarction in group 2, and this was found to have statistical significance (p=0.016, 0.029, respectively). However, no statistically significant differences were identified between the other comorbid factors (p=0.898, 0.167, 0.349, 0.313, 0.175, 0.066, 0.090, 0.582, 0.485, respectively) in our study (Table 2), and none were found between the groups with regard to the CPB and cross-clamp durations (p=0.088, 0.678, respectively). The averages of the troponin I and CK-MB levels were higher in group 1 than in group 2, but the differences were not statistically significant (Table 3). Furthermore, while there was a correlation between troponin I and CK-MB levels and the CPB and cross-clamp times in group 1, the same correlation did not exist in group 2. Additionally, the total amounts of cardioplegia (p=0.001) and potassium (p=0.001) were statistically significantly higher in group 2 than in group 1 (Table 4).

Table 2. Patient comorbidities

	Group 1		Group 2		
	n	%	n	%	*p*
Diabetes mellitus	16	50.0	36	48.6	0.898
Hypertension	20	62.5	56	75.7	0.167
Hyperlipidemia	10	31.3	42	56.8	0.016*
Chronic obstructive pulmonary disease	6	18.8	8	10.8	0.349
Cerebrovascular disease	0	0.0	4	5.4	0.313
Carotid lesion	0	0.0	6	8.1	0.175
Peripheral arterial disease	4	12.5	2	2.7	0.066
Smoking	18	56.3	54	73.0	0.090
Renal disease	2	6.3	2	2.7	0.582
Previous myocardial infarct	2	6.3	18	24.3	0.029*
Previous cardiac operation	4	12.5	6	8.1	0.485
Total	32	30.18	74	69.81	

* Indicates statistical significance.

Table 3. Operative patient data

Group	Total amount of cardioplegia (mL)	Total amount of K^+ (mEq)	CPB duration (minutes)	Cross-clamp duration (minutes)	Troponin I	CK-MB
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Group 1	1700±860	41±11	74±29	46±24	5.75±7.9	34±33
Group 2	3759±1608	54±12	91±34	49±24	3.36±5.5	24±20
p	0.001*	0.001*	0.088	0.678	0.215	0.167

SD: Standard deviation; K^+: Potassium; CPB: Cardiopulmonary bypass; CK-MB: Creatine kinase-myocardial band; * Indicates statistical significance.

DISCUSSION

When myocardial protection is successful during cardiac surgery, its direct effect on postoperative cardiac function, recovery, and complications can be observed. Even though off-pump surgery has recently become more popular, the vast majority of coronary revascularization is still performed via an on-pump procedure.[1,5,6]

Reperfusion after cardioplegic arrest-induced myocardial ischemia may cause irreversible cellular changes,[2,5] and damage caused by reperfusion may occur in all cardiac operations requiring the temporary cessation of coronary circulation. This may contribute to the impairment of postoperative cardiac performance and eventually may lead to myocardial fibrosis that can occur after cardiac surgery.[4,6]

During cardioplegic arrest, the aim is to reduce cellular metabolism and boost cellular energy storage by avoiding myocardial damage. Furthermore, in response to the changes in temperature and composition of the cardioplegia, different perfusion procedures can be adopted to improve coronary distribution.[1,3,6-8] Warm and tepid blood cardioplegia is supposed to offer better protection for the cellular enzyme systems and reduce cellular swelling and myocardial edema.[1,3,6-10] The greatest hesitation for using the antegrade method is that it insufficiently preserves the myocardium distal to the site of coronary occlusion.[1,2,7,9] However, the antegrade/retrograde method allows for a better distribution of the cardioplegia throughout the myocardium, which is a distinct advantage.[1,9]

As in the study by Yilik et al.[11] we used a continuous retrograde isothermic blood cardioplegia solution under pressure to produce gravity after antegrade cardioplegia in group 2. This was done in order to prevent the detrimental effects of high pressure on the myocardium and cause less myocardial edema.[11]

Earlier studies carried out on adults revealed that the cases of the myocardium being threatened by global ischemia might be decreased via the meticulous control of reperfusion conditions.[1,2,4,7] Recent studies have also demonstrated that the route of delivery (ie., retrograde or antegrade) does not affect the degree of injury during cardioplegia.[4,5] However, it is known that retrograde perfusion allows for more effective subendocardial perfusion and that it provides more reliable myocardial protection than the antegrade route.[9]

When we analyzed the our datas, we found that one patient who underwent the Benthall operation that had a cross-clamp time of 90 minutes had a troponin I value of 0.07. We also discovered that another patient who underwent CABG with the cross-clamp applied for 44 minutes had a troponin I value of 0.35, and another, who also underwent CABG and had a 38-minute cross-clamp time, had a troponin I level of 21.5. In addition, one patient who underwent mitral valve replacement and tricuspid annuloplasty

Table 4. Correlation between troponin I and creatine kinase-myocardial band and the total amount of potassium and cardiopulmonary bypass and cross-clamp durations

Group	Troponin I	Total K^+	CPB duration	Cross-clamp duration
	p	*p*	*p*	*p*
Group 1				
CK-MB	0.000*	0.007*	0.001*	0.000*
Troponin I		0.008	0.002*	0.000*
Group 2				
CK-MB	0.000*	0.72	0.206	0.36
Troponin I		0.425	0.353	0.192

K^+: Potassium; CPB: Cardiopulmonary bypass; CK-MB: Creatine kinase-myocardial band; * Indicates statistical significance.

had a cross-clamp duration of 102 minutes and a troponin I level of 23.1. We also found a patient who underwent CABG with a cross-clamp time of 50 minutes who had a troponin I level of 80, and another who underwent the same operation as well as ascending aorta replacement that had a cross-clamp time of 122 minutes and a troponin I level of 0.37. These findings not only indicate that different types of operations can lead to different results but that the same type of operations can also yield varied results. This shows the importance of myocardial protection and cardioplegia. However, the appropriate application of the process is crucial. For example, undesired levels of aortic pressure during antegrade cardiolegia and inappropriate placement of the cannula and balloon during retrograde cardioplegia may cause problems when attempting myocardial protection.[12,13]

As a traditional method of myocardial protection, retrograde blood cardioplegia is preferable during aortic valve replacement. Nevertheless, controversy exists regarding whether or not this type of cardioplegia alone can offer efficient myocardial protection, especially when the right ventricle is involved.[4,5]

Considering the fact that most myocardial protection methods associated with coronary surgery are now more advanced, it is surprising that the optimal cardioplegia choice in patients with hypertrophic cardiomyopathy remains controversial.[4,5] Variations between ischemic and hypertrophic cardiac pathologies also show that the cardioplegic method developed for ischemic heart disease is not appropriate for hypertrophic hearts.[4,5]

Our study had several limitations. First, the relatively small number of patients in our series restricted the extrapolation of our results. If a larger patient population had been used, it is likely that statistical significance would have been reached. In addition, our results reflected an indirect measure of myocardial injury due to the lack of metabolic markers and biopsies. Furthermore, this study was not randomized. The two groups were separated by time, but there were no changes in the operative management protocols during the study period. While elevated biochemical markers and acute intracardiac hemodynamic changes can prove the existence of myocardial injury, in most cases, these are usually not reliable enough to anticipate the clinical results.

Hopefully, our results can help establish a standardized protocol that can be used against the deleterious effects of IR injury during CPB surgery.

Conclusion

Our study results indicated that continuous antegrade/retrograde cardioplegia seems to protect the myocardium better than intermittent antegrade cardioplegia. In addition, to ensure the safety of the procedure, monitorization of the ascending aorta pressure during cardioplegia along with localization of the retrograde cannula should be priorities.

Declaration of conflicting interests

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REFERENCES

1. Alex J, Ansari J, Guerrero R, Yogarathnam J, Cale AR, Griffin SC, et al. Comparison of the immediate post-operative outcome of two different myocardial protection strategies: antegrade-retrograde cold St Thomas blood cardioplegia versus intermittent cross-clamp fibrillation. Interact Cardiovasc Thorac Surg 2003;2:584-8.
2. Cohen G, Borger MA, Weisel RD, Rao V. Intraoperative myocardial protection: current trends and future perspectives. Ann Thorac Surg 1999;68:1995-2001.
3. Tan TE, Ahmed S, Paterson HS. Intermittent tepid blood cardioplegia improves clinical outcome. Asian Cardiovasc Thorac Ann 2003;11:116-21.
4. Ascione R, Suleiman SM, Angelini GD. Retrograde hot-shot cardioplegia in patients with left ventricular hypertrophy undergoing aortic valve replacement. Ann Thorac Surg 2008;85:454-8.
5. Lotto AA, Ascione R, Caputo M, Bryan AJ, Angelini GD, Suleiman MS. Myocardial protection with intermittent cold blood during aortic valve operation:antegrade versus retrograde delivery. Ann Thorac Surg 2003;76:1227-33.
6. Minatoya K, Okabayashi H, Shimada I, Tanabe A, Nishina T, Nandate K, et al. Intermittent antegrade warm blood cardioplegia for CABG: extended interval of cardioplegia. Ann Thorac Surg 2000;69:74-6.
7. Pelletier LC, Carrier M, Leclerc Y, Cartier R, Wesolowska E, Solymoss BC. Intermittent antegrade warm versus cold blood cardioplegia: a prospective, randomized study. Ann Thorac Surg 1994;58:41-8.
8. Landymore RW, Marble AE, Fris J. Effect of intermittent delivery of warm blood cardioplegia on myocardial recovery. Ann Thorac Surg 1994;57:1267-72.
9. Shirai T, Rao V, Weisel RD, Ikonomidis JS, Hayashida N, Ivanov J, et al. Antegrade and retrograde cardioplegia: alternate or simultaneous? J Thorac Cardiovasc Surg 1996;112:787-96.
10. Abah U, Garfjeld Roberts P, Ishaq M, De Silva R. Is cold or warm blood cardioplegia superior for myocardial protection?

Interact Cardiovasc Thorac Surg 2012;14:848-55.
11. Yilik L, Ozsoyler I, Yakut N, Emrecan B, Yasa H, Calli AO, et al. Passive infusion: a simple delivery method for retrograde cardioplegia. Tex Heart Inst J 2004;31:392-7.
12. Young JN, Choy IO. Aortic root pressure monitoring during antegrade cardioplegia administration. Ann Thorac Surg 1996;62:1213-4.
13. Manasse E, Barbone A, Gallotti R. How to determine the correct placement of the retrograde cardioplegia catheter. Interact Cardiovasc Thorac Surg 2002;1:28-9.