Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 6
Open Access

Results of Combined Antegrade and Retrograde Versus Antegrade Cardioplegia in Complex Coronary Artery Bypass Surgeries

Ahmed Ibrahim Abdelwahhab, Elhussein Mohamed, Mahmoud Khairy, Ahmed Elminshawy
Cardiothoracic Surgery department, Faculty of Medicine, Assiut University, Egypt
Corresponding author Husseinmoh24@gmail.com

Cite this paper as: Elhussein Mohamed (2024) Results of Combined Antegrade and Retrograde Versus Antegrade Cardioplegia in Complex Coronary Artery Bypass Surgeries. *Frontiersin Health Informatics, 13(6*), 1036-1043

Abstract
Background*: Myocardial protection during complex coronary artery bypass surgery, especially for the right ventricle, faces challenges due to severe coronary lesions that hinder antegrade cold cardioplegia delivery, potentially causing asymmetric myocardial cooling, postoperative left and right ventricular dysfunction. The ongoing debate over optimal cardioplegia routes and compositions continues to influence myocardial protection outcomes in ischemic heart disease. We aimed to compare simultaneous antegrade-retrograde cardioplegia with antegrade cardioplegia in complex coronary artery bypass surgeries.*
Results*: One hundred twenty-eight patients were randomized into two groups: Group A (n=64) received antegrade cardioplegia only, and Group B (n=64) received ante-retrograde cardioplegia. Both groups were compared for demographic characteristics, pre- and postoperative echocardiographic data, bypass and ischemic times, number of grafts, serum lactate levels at 1 and 24 hours, and inotropic support. No substantial differences were found between the two groups in terms of demographic characteristics, with the exception of weight (P=0.0058) and BMI (P=0.0375). Significant differences were observed in the duration of inotropic support (P<0.001), while pre- and postoperative echocardiographic data, bypass time (P=0.9321), ischemic time (P=0.8296), and number of grafts (P=0.236) remained comparable. However, serum lactate levels at 1 hour (P<0.001) and 24 hours (P=0.0142) differed significantly which is lower in Ante-retrograde group than Antegrade group. Notably, both the Antegrade and Ante-Retrograde groups exhibited significantly lower serum lactate levels at 1 and 24 hours (P < 0.001 for both).*
Conclusions*: The ante-retrograde group had shorter inotropic support duration and significantly lower serum lactate levels at 1 hour and 24 hours, suggesting better myocardial perfusion and metabolism recovery, indicating improved cardiac function with ante-retrograde cardioplegia.*
Keywords*: Antegrade Cardioplegia, Retrograde Cardioplegia, Coronary artery bypass, Surgical outcomes*

Introduction

Myocardial protection, particularly of the right ventricle, can be inadequate during coronary artery bypass surgery when severe coronary lesions obstruct the antegrade delivery of cold cardioplegia **[1].** Asymmetric myocardial cooling has been linked to postoperative right ventricular dysfunction, contributing to morbidity and mortality **[2].** Retrograde coronary sinus perfusion, introduced in 1956 to aid aortic valve surgery, was adapted in 1967 for coronary artery bypass surgery and has recently garnered renewed interest **[3].**
Fabiani and colleagues have developed an innovative technique for delivering retrograde cardioplegia through the right atrium, eliminating the need for direct coronary sinus cannulation and reducing risks of coronary sinus rupture and inadequate right ventricular perfusion **[4, 5].** Unlike antegrade delivery, retrograde cardioplegia via the right atrium achieves more uniform left ventricular cooling, unaffected by coronary artery occlusive disease **[6].**
The optimal route for cardioplegia delivery in ischemic heart disease remains controversial. Cardiothoracic surgeons and anesthesiologists debate the efficacy of different routes and compositions of cardioplegic solutions, given the critical role of myocardial protection in surgical outcomes **[7].** Since Lillchei and colleagues introduced the retrograde route through the coronary sinus in 1956, numerous studies have investigated its effectiveness in valve surgeries, with renewed interest in the late 1970s for coronary surgery **[8].**

Concerns have been raised about the adequacy of right ventricular preservation with retrograde perfusion. Some studies suggest that combined antegrade and retrograde routes offer myocardial preservation comparable to antegrade cardioplegia alone, while others report significant benefits of the retrograde route over antegrade administration **[9].**

The aim of this study was to compare simultaneous antegrade-retrograde cardioplegia with antegrade cardioplegia in complex coronary artery bypass surgeries.

Methods

The study was conducted on patients diagnosed with ischemic heart disease and multi-vessel disease, indicated for coronary artery bypass grafting (CABG), from January 2020 to January 2022. These patients were divided into two groups based on specific inclusion and exclusion criteria. The research design was a prospective, double-blinded, randomized controlled trial (RCT) conducted at Assiut University Cardiac Hospital.

Inclusion criteria for the study subjects were: patients aged above 50 years, with a left ventricular ejection fraction between 30% and 60%, and diagnosed with left main stem coronary artery disease. Exclusion criteria included patients with double valve disease or other valve diseases, those with mitral or aortic valve disease associated with congenital heart disease, patients who had undergone prior heart surgery, those requiring emergency operations, and patients with poorly controlled diabetes mellitus.

Randomization was done by computer-generated random list, the allocation sequence is concealed from researchers and participants to prevent selection bias. This is achieved through sequentially numbered sealed envelopes.

All patients underwent detailed history taking, physical examinations, and laboratory investigations. History taking included age, gender, medical history, and past surgical history. Physical examinations involved checking vital signs (blood pressure, heart rate, respiratory rate), measuring weight and height, and conducting a local chest examination. Laboratory investigations comprised a complete blood picture, coagulation profile, renal and hepatic function tests. Serum lactate levels were also assessed using ELISA.

Transthoracic Echocardiography: Echocardiographic assessments were performed using a Vivid 5S ultrasound machine (General Electric). The patient was positioned in the left decubitus position, and a 2.5 to 3.5 MHz probe was placed in the intercostal spaces to minimize bone scattering. Measurements included left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic diameter (LVEDD), and left ventricular ejection fraction (EF). EF was calculated as EF = (EDV - ESV) / EDV x 100%.

Preoperative and study population: One hundred twenty-eight patients who had undergone CABG surgery for severe coronary artery disease, with 90% or greater stenosis in the left anterior descending artery (LAD), a sizeable obtuse marginal (OM) branch of the circumflex and a dominant right coronary artery (RCA) or its posterior descending branch (PDA) were selected so as to form 2 equal groups with comparable demographic features. cold crystalloid cardioplegia is prepared for two groups with technique of administration described later.

Operative Technique: Standard anesthetic and surgical procedures were used. The chest was opened via a median sternotomy incision, and both the aorta and right atrium were cannulated using a single double-stage venous cannula. Heparinization was performed at 3-5 mg/kg heparin sulfate to achieve an activated clotting time of at least 400 seconds. Patients were then connected to a heart-lung machine with a membrane blood oxygenator, and systemic hypothermia was induced, reducing body temperature to 28-30°C. The aorta was clamped, cardioplegia was administered, and the pericardium was irrigated with ice-cold saline. Distal anastomoses were performed during aortic cross-clamping, and proximal anastomoses were completed post-declamping. Hemodynamic stability was confirmed before decannulation, with heparin neutralized using protamine sulfate.

Cardioplegia Technique:.

In antegrade cardioplegia: For antegrade cardioplegia, a cannula containing a side-port for venting and a side-arm for pressure monitoring in the aortic root was used. The cannulation site was also used for deairing after declamping and as a site for proximal anastomosis. Aortic root pressure was kept between 80 and 100 mm Hg. Cardioplegia solution chilled to 4°C was infused in a dose of 15 mL per kg body weight initially and repeated every 15 minutes in a dose of 10 mL per kg.

In combined antegrade retrograde cardioplegia: Buckberg cardioplegia cannula with a self-inflating balloon, semirigid stylet and a handle was used. A coronary sinus catheter with a manually inflated balloon (DLP catheter) was introduced via a closed transatrial cannulation method. The cannula was inserted in the coronary sinus through a 4/0 polypropylene purse string suture placed low in the right atrium, near the junction with the inferior vena cava and it was withdrawn through a rubber tourniquet.

The catheter was guided to the mid-portion of the coronary sinus and inflated with 2-3 mL of isotonic solution. This cannula has a side-arm for pressure monitoring in the coronary sinus. Half of the initial dose was given antegradely with aortic root pressure of 80 to 100 mm Hg and the other half was given retrogradely with coronary sinus pressure ranging between 30 and 50 mm Hg. The pressure in the coronary sinus was not allowed to exceed 50 mm Hg. All subsequent doses were given retrogradely through the coronary sinus.

Cardioplegic infusions were interrupted when necessary to permit adequate coronary visualization. After the completion of each distal anastomosis, each vein graft was attached to a manifold to permit cardioplegic delivery through each completed vein graft and into the coronary sinus from a single pump head.

During subsequent distal anastomoses, cardioplegic solution was administered into the coronary sinus and into each completed vein graft with the aortic root vented. Proximal anastomoses were performed after the left internal thoracic artery graft was opened.

Postoperative Follow-Up: Postoperative follow-up included assessing the duration of inotropic support, vasoactive inotropic score (VIS), and monitoring serum lactate levels. Additionally, transthoracic echocardiography was performed to evaluate cardiac function.

The VIS was calculated as follows: dopamine dose (µg/kg/min) + dobutamine dose (µg/kg/min) + 10 × milrinone dose (µg/kg/min) + 100 × epinephrine dose (µg/kg/min) + 100 × norepinephrine dose (µg/kg/min) + 10,000 × vasopressin dose (U/kg/min).

Research aim: To compare the efficacy of simultaneous antegrade-retrograde cardioplegia versus antegrade cardioplegia in complex coronary artery bypass surgeries, specifically in the preservation of myocardial function.

Research outcomes:

Primary outcome: Duration of inotropic support.

secondary outcome: Ejection fraction, Mean and peak vasoactive inotropic score, Serum lactate at 1 and 24 hours between two groups.

Sample Size Calculation

The sample size was calculated using G*Power software (version 3.1.9.2). Assuming a power of 80% ($\beta = 0.20$) and a significance level of 0.05 (two-sided), the sample size was determined to detect a medium effect size (Cohen's d = 0.52) in the duration of inotropic support between the two groups using an independent samples t-test. Based on these assumptions, a minimum of 60 participants per group was required to ensure sufficient power to detect the expected difference. Four participants were added to each group to compensate for probable dropouts as shown in (Fig.1) .

Data Management and Analysis: Data were collected, reviewed for completeness, and analyzed using appropriate statistical methods. Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range (IQR) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages.

Group comparisons were conducted using the independent samples t-test for normally distributed continuous variables, the Mann-Whitney U test for non-normally distributed continuous variables, and the paired t-test for repeated measures. The Chi-square test was used to compare categorical variables.

Statistical significance was set at a P-value < 0.05. All analyses were performed using SPSS version 20.

Results

The study is conducted on one hundred twenty eight patients indicated for CABG divided into two equal groups with sixty four patients in every group. Four patients were removed from Ante-retrograde group due to their death before the operation and considered as dropouts. (Fig. 1)

Baseline Characteristics

The Antegrade group had a higher weight compared to the Ante-Retro group (P = 0.0058). BMI was also significantly lower in the Ante-Retro group compared to the Antegrade group (P = 0.0375). Non-significant parameters included age (P = 0.7954), gender distribution (P = 0.1413), and height (P = 0.5367). (Table 1)

Pre and Post-Operative Echocardiographic Data

There was no significant difference between the two groups regarding pre and post-operative echocardiography data. (Table 1)

Operative and Post-Operative Parameters

The number of grafts showed no significant difference between the two groups (P=0.236). The duration of inotropic support was significantly shorter in the Ante-Retro group (P < 0.001). Serum lactate levels were significantly lower in the Ante-Retro group at both 1 hour (P < 0.001) and 24 hours (P = 0.0142). Non-significant parameters included bypass time (P = 0.9321), ischemic time (P = 0.8296), mean 24-hour VIS (P = 0.8925), and peak 24-hour VIS (P = 0.4536). (Table 2-3)

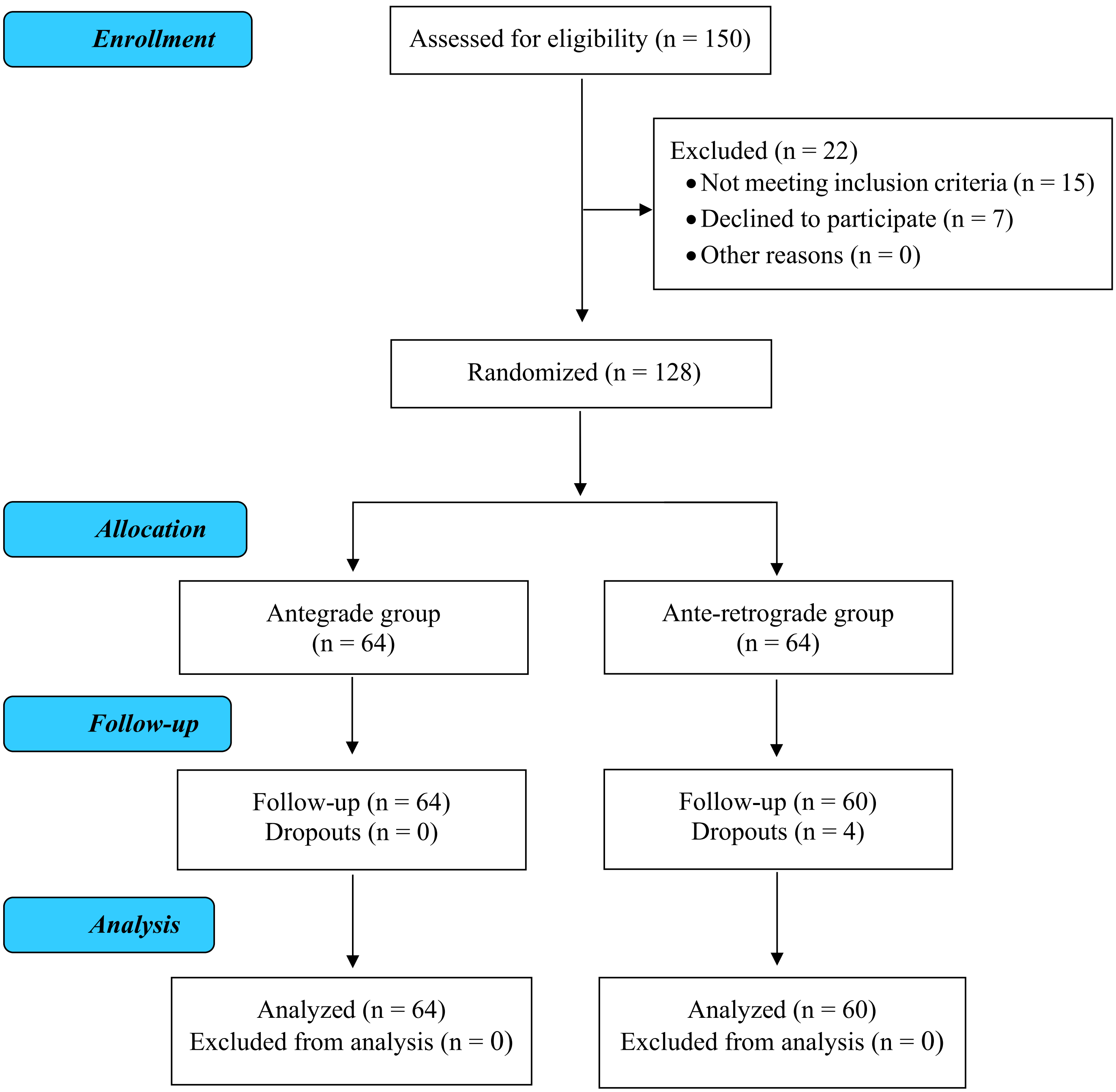

Fig. 1. CONSORT flow diagram of the participants.

Table (1): Demographic and echocardiography data among included patients:

	Antegrade Group (N = 64)	Ante-Retro Group (N = 60)	P. Value
Age (Years)	61.09 ± 3.11	61.15 ± 2.86	0.7954
Gender			
Male	31 (48.44%)	37 (61.67%)	0.1413
Female	33 (51.56%)	23 (38.33%)	
Weight (Kg)	89.23 ± 5.99	85.65 ± 6.5	0.0058*
Height (m)	1.72 ± 0.12	1.73 ± 0.08	0.5367
BMI (Kg/m^2)	30.53 ± 4.7	28.88 ± 3.98	0.0375*
Pre-operative echocardiography			
LVESD	3.11 ± 0.26	3.13 ± 0.22	0.4355
LVEDD	4.42 ± 0.38	4.41 ± 0.39	0.5991
EF	52.38 ± 3.76	53.03 ± 3.91	0.4091
Post-operative echocardiography			
LVESD	3.11 ± 0.26	3.13 ± 0.22	0.4355
LVEDD	4.42 ± 0.38	4.41 ± 0.39	0.5991
EF	52.41 ± 3.86	53.58 ± 4.02	0.1351

BMI: Body Mass Index, LVESD: Left Ventricular End Systolic Diameter, LVEDD: Left Ventricular End Diastolic Diameter, EF: Ejection Fraction
*P < 0.05: significant, P > 0.05: non-significant

Table (2): Operative data and follow up among included patients:

	Antegrade Group (N = 64)	Ante-Retro Group (N = 60)	P. Value
Number of grafts			
2	28 (43.7%)	20 (33.3%)	0.236
3	36 (56.2%)	40 (66.7%)	
Operative data			
BYPASS TIME	103.84 ± 10.46	104.65 ± 8.1	0.9321
Ischemic time (Min)	81.38 ± 10.32	81.95 ± 8.28	0.8296
Follow up			
Serum Lactate 1 hour	5.28 ± 0.91	3.01 ± 0.64	<0.001*
Serum Lactate 24 hour	1.42 ± 0.26	1.3 ± 0.2	0.0142*
Inotropic support			
Duration of inotropic support (hour)	7.23 ± 1.23 7 (6 -8)	6.05 ± 1.12 6 (5 -7)	<0.001*
Mean 24 hours VIS	1.76 (1.16 - 2.76)	1.68 (1.43 - 2.12)	0.8925
Peak 24 hours VIS	9 (7 - 11)	8 (7 - 9)	0.4536

VIS: Vasoactive Inotropic Score
*P < 0.05: significant, P > 0.05: non-significant

Table (3): Serum lactate for same group in 1 and 24 hours

	Group 1 n=64	Group 2 N=60
Serum Lactate 1 hour	5.28 ± 0.91	3.01 ± 0.64
Serum Lactate 24 hour	1.42 ± 0.26	1.3 ± 0.2
p-value	<0.001*	<0.001*

*P < 0.05: significant, P > 0.05: non-significant

Discussion

In our study, patients in the Ante-Retro group exhibited favorable outcomes compared to the Antegrade group. Notably, the Ante-Retro group demonstrated significantly lower body weight (P = 0.0058) and BMI (P = 0.0375). While age, gender, and height did not differ significantly between the groups, the Ante-Retro group experienced significantly lower serum lactate levels at both 1 hour (P < 0.001) and 24 hours (P = 0.0142) postoperatively. Moreover, this group required shorter durations of inotropic support (P < 0.001) and inotropes (P < 0.001).

These findings diverge from some previous studies. For instance, Onorati et al. **[10]** and Franke et al. **[11]** reported similar preoperative and postoperative ejection fractions (EF) between antegrade and antegrade/retrograde cardioplegia groups. Similarly, Elwatidy et al. **[12]** observed non-significant differences in postoperative EF between various cardioplegia techniques, including antegrade and antegrade/retrograde.

However, other studies have supported the potential benefits of combined antegrade and retrograde cardioplegia. A clinical trial indicated better preservation of left ventricular stroke work index in patients receiving retrograde cardioplegia **[13]**. Retrospective analyses have suggested superior myocardial protection with combined antegrade and retrograde delivery **[14, 15].**

In line with our findings, Hılm İ Tokmak oğlu et al. **[17]** reported a higher rise in myocardial lactate extraction in the antegrade group compared to the combined group after 10 minutes of reperfusion. However, Olivier Jegaden et al. **[18]** did not find significant differences in serum lactate levels between the two groups, which might be attributed to the smaller sample size in their study.

The discrepancy between our findings and some previous studies may be attributed to several factors. One possible explanation is the unique patient population in our study. Patients with severe left ventricular hypertrophy may benefit from more homogeneous cardioplegic distribution, as achieved with combined antegrade and retrograde delivery. However, this approach can pose technical challenges, such as obscuring the surgical field during distal coronary anastomosis **[16].**

Retrograde cardioplegia requires careful attention to infusion pressures to prevent myocardial edema and endothelial injury. Hirata et al. **[13]** emphasized the importance of precise anatomical knowledge for effective cardioplegia administration.

While experimental studies have yielded mixed results comparing antegrade and retrograde cardioplegia methods **[14, 15]**, our clinical findings suggest that combined antegrade and retrograde cardioplegia may offer advantages in terms of myocardial protection and postoperative outcomes.

Limitations of our study include lack of comprehensive assessment of long-term outcomes, including mortality, morbidity, and quality of life, which is essential. While the study demonstrated short-term advantages for the ante-retrograde group, it's unclear whether these benefits persist in the long term. Another limitation is small sample group which we prefer a larger multicenter study would be required to recruit thousands of patients.

Conclusions

Our study compared cardiac surgery outcomes using antegrade versus ante-retrograde cardioplegia. Despite baseline differences in weight and BMI, demographic parameters, preoperative echocardiographic measures, operative data, and pre-discharge echocardiographic findings were similar between groups. However, postoperatively, the ante-retrograde group showed a shorter duration of inotropic support indicating better cardiac function recovery, and significantly lower serum lactate levels at 1 hour and 24 hours suggesting improved myocardial perfusion and metabolism., implying potential advantages of ante-retrograde cardioplegia over traditional antegrade methods.

List of abbreviations

BMI	Body Mass Index
VIS	Vasoactive Inotropic Score
CABG	Coronary Artery Bypass Grafting
LVESD	Left ventricular end-systolic diameter
LVEDD	Left ventricular end-diastolic diameter
EF	Left ventricular ejection fraction
EDV	End diastolic volume
ESV	End systolic volume

References

[1] Whittaker A, Aboughdir M, Mahbub S, Ahmed A, Harky A. Myocardial protection in cardiac surgery: how limited are the options? A comprehensive literature review. Perfusion. 2021;36(4):338-51. https://doi.org/10.1177/026765912094265
[2] Kot TKM, Chan JSK, Froghi S, Lau DHH, Morgan K, Magni F, et al. Warm versus cold cardioplegia in cardiac surgery: A meta-analysis with trial sequential analysis. JTCVS open. 2021;6(1):161-90. https://doi.org/10.1016/j.xjon.2021.03.011
[3] Mazine A, Lee MM, Yau TM. Myocardial Protection During Cardiac Surgery. Evidence-Based Practice in Perioperative Cardiac Anesthesia and Surgery. 2021:423-32. https://doi.org/10.1007/978-3-030-47887-2_34
[4] McNichols B, Spratt JR, George J, Rizzi S, Manning EW, Park K, et al. Coronary artery bypass: review of surgical techniques and impact on long-term revascularization outcomes. Cardiology and Therapy. 2021;10(1):89-109. https://doi.org/10.1007/s40119-021-00211-z
[5] Kawago K, Yoshida Y, Shiraiwa S, Honda Y, Sakakibara K, Kaga S, et al. Pitfalls of retrograde cardioplegia cannulation: left atrium dissection. The Annals of Thoracic Surgery. 2020;110(5):e381-e394. https://doi.org/10.1016/j.athoracsur.2020.04.019
[6] Jabeen S, Arif A, Bukhari SR, Umair M, Akbar S, Yunus A, et al. Correlation of Post-Operative Outcomes in patients undergoing CABG Receiving Antegradecardioplegia alone Versus Combined Antegrade Plus Retrograde Cardioplegia: A Prospective Review. Pakistan Journal of Medical & Health Sciences. 2023;17(04):156-162. https://doi.org/10.53350/pjmhs2023174156
[7] Bradić J, Andjić M, Novaković J, Jeremić N, Jakovljević V. Cardioplegia in open heart surgery: age matters. Journal of Clinical Medicine. 2023;12(4):1698-1715. https://doi.org/10.3390/jcm12041698
[8] Athanasuleas CL, Buckberg GD. Cardioplegia strategies. State of the Art Surgical Coronary Revascularization. 2021:211.
[9] Amaç B, Bağış MZ. Comparison Of Antegrade And Antegrade/Retrograde Blood Cardioplegia Applications In Cardiopulmonary Bypass Accompanıed Cardiac Surgery. Abant Medical Journal.13(1):16-23. https://doi.org/10.47493/abantmedj.1377193
[10] Onorati F, Renzulli A, De Feo M, Santarpino G, Gregorio R, Biondi A, et al. Does antegrade blood cardioplegia alone provide adequate myocardial protection in patients with left main stem disease? The Journal of Thoracic and Cardiovascular Surgery. 2003;126(5):1345-51. https://doi.org/10.1016/S0022-5223(03)00736-0
[11] Franke U, Wahlers T, Cohnert TU, Koenig J, Rath NF, Wirsing M, et al. Retrograde versus antegrade crystalloid cardioplegia in coronary surgery: value of troponin-I measurement. The Annals of thoracic surgery. 2001;71(1):249-53. https://doi.org/10.1016/S0003-4975(00)02145-7
[12] Elwatidy AM, Fadalah MA, Bukhari EA, Aljubair KA, Syed A, Ashmeg AK, et al. Antegrade crystalloid cardioplegia vs antegrade/retrograde cold and tepid blood cardioplegia in CABG. The Annals of thoracic surgery. 1999;68(2):447-53. https://doi.org/10.1016/S0003-4975(99)00359-8

[13] Hirata N, Sakai K, Ohtani M, Sakaki S, Ohnishi K. Assessment of myocardial distribution of retrograde and antegrade cardioplegic solution in the same patients. European journal of cardio-thoracic surgery. 1997;12(2):242-7. https://doi.org/10.1016/S1010-7940(97)00119-X

[14] Jiang X, Gu T, Shi E, Wang C, Xiu Z, Zhang G, et al. Antegrade versus continuous retrograde del Nido cardioplegia in the David I operation. Heart, Lung and Circulation. 2018;27(4):497-502. https://doi.org/10.1016/j.hlc.2017.02.037

[15] Brant S, Rosenbaum D, Cobert M, West L, Jessen ME, Peltz M, editors. Effects of antegrade and retrograde machine perfusion preservation on cardiac function after transplantation in canines. Transplantation proceedings. 2014; 46(5): 1601-1605. Elsevier. https://doi.org/10.1016/j.transproceed.2014.03.006

[16] ÇİÇEK MC, GÖRMÜŞ N, DURGUT K, KAYRAK M, TOKER A, GÖRMÜŞ İS, et al. Comparison of effect of antegrade with combined antegrade/retrograde cardioplegia on inflammatory response and left ventricular systolic function in coronary bypass surgery: a prospective randomized study. Turkish Journal of Clinics and Laboratory. 2018;9(3):179-84. https://doi.org/10.18663/tjcl.432111

[17] Tokmakoğlu, H., Kandemir, Ö., Yorgancıoğlu, C., Zorlutuna, Y. (2016). ANTEGRADE VERSUS ANTEGRADE* / RETROGRADE CARDIOPLEGIA FOR MYOCARDIAL PROTECTION IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING. Marmara Medical Journal, 14(3), 154-159.

[18] Olivier Jegaden, MD, Armand Eker, MD, Pietro Montagna, MD, Jean Ossette, MD, Christian Vial, PhD, Jeanine Guidollet, PhD, and Philippe H. Mikaeloff, MD. Antegrade/Retrograde Cardioplegia in Arterial Bypass Grafting: Metabolic Randomized Clinical Trial. Ann Thorac Surg 461 "1995;59:456-61 https://doi.org/10.1016/0003-4975(94)00863-3