Comparison of De Ritis Rate for Del Nido Versus Blood Cardioplegia in Patients Who Underwent Coronary Artery Bypass Graft Under Cardiopulmonary Bypass

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Abstract

Aim: Within the scope of this research, we aimed to compare the liver function tests, liver enzymes and De Ritis ratio of patients given Del Nido cardioplegia and blood cardioplegia in coronary heart surgery.

Methods: This retrospective study included a total of 80 patients who underwent cardiopulmonary bypass (CPB) guided coronary heart surgery with 40 Del Nido cardioplegia solutions and 40 blood cardioplegia solutions. CPB-guided coronary heart surgery patients given Del Nido cardioplegia solution were determined as the first group (Group 1), and patients given blood cardioplegia were determined as the second group (Group 2).

Results: Preoperative and postoperative aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, and gamma-glutamyl transferase (GGT) levels of the groups were similar ($p>0.005$). AST, ALT, total bilirubin, direct bilirubin, and GGT levels were similar in CPB output ($p>0.005$). The De Ritis ratio of the groups was similar on the preoperative and postoperative 1st day ($p=0.072$; $p=0.687$, respectively), and the rate of ritis at CPB output was higher in group 2 ($p=0.003$). The requirement for defibrillation was higher in group 1 ($p=0.044$).

Conclusions: The Del Nido cardioplegia solution may be superior to blood cardioplegia in coronary artery bypass graft (CABG) cases accompanied by CPB regarding the De Ritis ratio.

Keywords: *Cardiopulmonary bypass, coronary artery bypass graft, del nido cardioplegia, blood cardioplegia, de ritis rate*

1. Introduction

Myocardial protection during diastolic arrest and cardiopulmonary bypass (CPB) in cardiac surgery has been an important area of interest. However, the optimal cardioprotective strategy and ideal cardioplegia solution are still debated. Cardioplegia is an integral method of myocardial protection, which is required to prevent cardiac arrest in open-heart surgery[1]. The immobile heart reduces the likelihood of air embolism during open procedures on the left side of the heart and provides a surgical space. Cross-clamping eliminates continuous coronary blood flow to the myocardium, providing a bloodless surgical field and increasing visibility[2, 3]. Del Nido cardioplegia in adults as a single dose prevents interruption of the surgery. It has been reported that intraoperative peak glucose value surgery, shortening cross-clamp time, duration of CPB, and total and insulin requirement are lower with Del Nido cardioplegia, which has prognostic importance. Additionally, this technique has a lower incidence of atrial fibrillation (AF) and a decrease in the need for defibrillation[4]. Del Nido cardioplegia involves a base Plasma-Lyte A solution with an electrolyte composition similar to an extracellular fluid[5]. It is delivered with 20% by volume of fully oxygenated patient blood, which supports aerobic metabolism for a limited period and provides buffering properties to promote anaerobic glycolysis[6].

Blood cardioplegia is achieved by adding autologous patient blood taken from the cardiopulmonary bypass circuit to crystalloid cardioplegia solution in different ratios (8:1, 4:1, 2:1). The advantages of blood cardioplegia include providing an oxygenated environment, limiting haemodilution, having high buffering capacity, having ideal osmotic properties, and having many endogenous antioxidants[7].

Liver function abnormalities are common in heart failure patients. In the past, increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values in heart failure patients were attributed to low perfusion. In contrast, the decreased AST/ALT ratio was attributed to damage secondary to increased venous congestion observed in heart failure. Hence, the De Ritis ratio (AST/ALT ratio) may be utilized as a predictive marker in cardiac events such as heart failure, acute coronary syndromes, and acute myocardial

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infarction[8–10]. Additionally, a high De Ritis ratio was reported as an independent risk factor of mortality and adverse cardiovascular events in coronary artery disease patients[9, 10].

The plasma AST and ALT levels are within normal limits in the healthy population. These parameters are usually affected in chronic hepatitis, coronary heart disease, impaired renal function, and due to several medications. The previous literature elaborated that it is more convenient to calculate both AST and ALT as a composite parameter rather than using any single of them.

Within the scope of this research, we aimed to compare the liver function tests, liver enzymes and De Ritis ratio of patients given Del Nido cardioplegia and blood cardioplegia in coronary heart surgery (Coronary artery bypass graft – CABG).

2. Materials and methods

This study is a retrospective cohort clinical study.

2.1. Ethics Approval

The study was conducted in accordance with the principles of the Declaration of Helsinki. In this study; before the study, approval was obtained from the institution where the study will be conducted (Şanlıurfa Mehmet Akif İnan Training and Research Hospital) and the local ethics committee (Harran University Clinical Research Ethics Committee) (Date: 10.04.2023 - Approval no: HRÜ/23.06.04). As this was retrospective research, no informed consent has been obtained from participants.

2.2. Population of the Research

In this study, retrospectively, CPB-guided coronary heart surgery (CABG replacement) was performed between 01/04/2022-01/04/2023, and after applying the exclusion criteria, 80 patients, for whom 40 del nido cardioplegia solutions and 40 blood cardioplegia solutions were used, were consecutive sequential included.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.CPB-guided coronary heart surgery patients given Del Nido cardioplegia solution were determined as the first group (Group 1), and patients given blood cardioplegia were determined as the second group (Group 2).Demographic data, preoperative, intraoperative, and early postoperative data of the patients were obtained from the hospital database.

2.3. Exclusion and Inclusion Criteria

Patients with medication use or treatment that may affect liver enzymes before surgery (i.e. cholesterol and antifungal medications, some rheumatism medications, antibiotics such as tetracycline, cortisone, some depression medications and simple painkillers containing paracetamol), chronic liver patients, AF history, those with heart valve pathology, those with aortic valve insufficiency or stenosis, those with mitral valve insufficiency or stenosis, those with known systemic inflammatory disease, those who underwent emergency surgery or re-operation, and chronic hemodialysis patients were excluded from the study. After applying the exclusion criteria, consecutive patients who underwent CPB-guided isolated CABG replacement surgery were included in the study.

2.4. Surgical Approach

Standard coronary heart surgery techniques were implemented. Following median sternotomy, arterial cannulation was performed through the ascending aorta, and venous cannulation was performed through a single venous two-stage venous cannula from the right atrium. The left mammary artery graft was utilized in all cases. A saphenous vein was applied to other coronary grafts. All patients underwent complete revascularization.

2.5. Cardiopulmonary Bypass (Perfusion) Method

Patients' blood flow rates during extracorporeal circulation were determined according to body surface areas (2.4 L/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. A 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 active clotting time (ACT) was kept at 480 seconds and above, and 1200 mL of balanced solution (isolyte), 150 mL of 20 % mannitol, 5000 units of heparin and 2 g of cefazolin were used as the primarily.

2.6. Blood Cardioplegia Solutions

An isothermic blood cardioplegia solution (32oC) was used. The initial cardioplegia dose was 15 mL/kg (full dose) as the solution amount, and maintenance doses were administered as half dose every 20 minutes. Full dose (first dose) cardioplegia solution was prepared by adding 7.5 % potassium chloride (patient's blood gas K+ value + K+ mL to be added = 25 mL), 5 mL 15 % magnesium sulfate, 10 mL 8.4 % sodium bicarbonate into oxygenated patient blood. 7.5 % potassium chloride (patient's blood gas K+ value + K+ mL to be added = 7 mL), 5mL of 15 % magnesium sulfate, and 5mL of 8.4 % sodium bicarbonate were added to the oxygenated patient blood in maintenance doses.

2.7. Del Nido Cardioplegia Solution

Modified Del Nido cardioplegia solution was used at +4 oC. A single dose as the solution amount was used as 20 mL/kg with a maximum dose of 1000 mL. In cases with aortic cross-clamp (ACC) time of more than ninety minutes, a maintenance half dose was administered at 60 minutes. The solution was prepared by adding 17 mL 20% mannitol, 14 mL 15 % magnesium sulfate, 13 mL 8.4 % sodium bicarbonate, 27 mL 7.5 % potassium chloride, and 6.5 mL 2 % Lidocaine into a balanced isolating solution (ratio: 8/10) and oxygenated patient blood (ratio: 2/10).

2.8. Statistical Analyses

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data mean, and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the "Independent Sample T–test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

3. Results

The demographic and intraoperative data of the groups: age, gender, number of CABG, height, weight, body surface area (BSA), flow, perfusion time, aortic cross clamp (ACC) time, ejection fraction (EF) percentage, fluid given during CPB, amount of urine during CPB, erythrocyte suspension (ES) transfusion during CPB, extubation time, length of stay in the intensive care unit (ICU) and length of hospital stay were similar (p>0.005) (Table 1).

The preoperative AST, ALT, total bilirubin, direct bilirubin and gamma glutamyl transferase (GGT) levels of the groups were similar and there was no statistically significant difference between the groups (p=0.651; p=0.751; p=0.421; p=0.053; p=0.585, respectively) (Table 2). AST, ALT, total bilirubin, direct bilirubin and GGT levels measured at CPB output of the groups were similar and there was no statistically significant difference between the groups (p=0.676; p=0.075; p=0.663; p=0.305; p=0.735, respectively) (Table 2).

Table 1

Comparison of demographic, preoperative, intraoperative and postoperative parameters of the groups

		Group-1 (N=40)	Group-2 (N=40)	p
Age (years) (Mean±SD)		60.75±9.60	61.87±8.54	0.462
Gender (n, %)	Female	19, (47.5%)	22, (55%)	0.675
	Male	21, (52.5%)	18, (45%)	
Number of CABGs (n, %)	I	2, (5%)	2, (5%)	0.857
	II	8, (20%)	6, (15%)	
	III	17, (42,5%)	17, (42,5%)	
	IV	13, (32.5%)	15, (37.5%)	
Height (cm) (Mean±SD)		165.42±8.85	165.35±9.20	0.692
Weight (kg) (Mean±SD)		79.02±13.33	79.47±12.66	0.880
BSA (m2) (Mean±SD)		1.88±0.18	1.89±0.17	0.810
Flow (L) (Mean±SD)		4.53±0.42	4.49±0.39	0.718
Perfusion Time (min) (Mean±SD)		102.75±29.48	110.48±45.74	0.154
ACC Time (min) (Mean±SD)		79.42±31.32	81.75±35.01	0.399
EF% (Mean±SD)		50.80±7.84	50.65±7.68	0.853
Delivered Liquid (ml) (Mean±SD)		2221.40±521.18	2064.60±660.97	0.307
Urine Amount (ml) (Mean±SD)		1893.80±411.87	1658.80±575.89	0.162
Int. Blood Trans. (unit) (Mean±SD)		1.05±1.15	1.30±1.26	0.196
Extubation Time (Hour) (Mean±SD)		6.52±2.02	6.45±2.67	0.244
ICU Time (days) (Mean±SD)		3.10±0.96	3.05±1.06	0.482
Length of hospital stay (Mean±SD)		9.37±3.25	9.32±3.39	0.581

Mean±SD: Mean±standard deviation; n, %: number, percentage; CABG: Coronary artery bypass graft; BSA: Body surface area; ACC: Aortic cross-clamp; EF %: Ejection fraction percentage; Int. Blood Trans.: Intraoperative blood transfusion; ICU: Intensive care unit.

Table 2

Comparison of preoperative, intraoperative and postoperative parameters of the groups

	Group-1 (N=40) (Mean±Sd)	Group-2 (N=40) (Mean±Sd)	p
Preoperative AST	23.92±14.58	23.24±15.58	0.651
Preoperative ALT	30.74±20.48	27.51±20.18	0.751
Preoperative Total Bilirubin	0.53±0.29	0.52±0.23	0.421
Preoperative Direct Bilirubin	0.18±0.09	0.92±0.71	0.053
Preoperative GGT	37.65±34.91	33.65±33.79	0.585
CPB Output AST	27.00±13.29	24.76±13.93	0.676
CPB Output ALT	68.32±67.43	51.62±34.02	0.075
CPB Output Total Bilirubin	0.65±0.35	0.64±0.36	0.663
CPB Output Direct Bilirubin	0.18±0.18	0.21±0.19	0.305
CPB Output GGT	29.75±21.37	27.25±21.53	0.735
Postoperative Day 1 AST	53.70±77.58	41.77±59.83	0.228
Postoperative Day 1 ALT	117.70±218.94	85.74±161.88	0.127
Postoperative Day 1 Total Bilirubin	1.04±1.11	0.94±0.82	0.208
Postoperative Day 1 Direct Bilirubin	0.51±0.68	0.45±0.47	0.273
Postoperative Day 1 GGT	36.52±21.67	31.47±18.25	0.214

Mean±SD: Mean±standard deviation; n, %: number, percentage; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transferase.

AST, ALT, total bilirubin, direct bilirubin and GGT levels measured at CPB output of the groups were similar and there was no statistically significant difference between the groups (p=0.228; p=0.127; p=0.208; p=0.273; p=0.214, respectively) (Table 2).

The AST/ALT ratio of the groups was similar on the preoperative and postoperative 1st day, and there was no statistically significant difference between the groups (p=0.072; p=0.687, respectively) (Figure 1). The rate of De Ritis ratio was higher in the CPB output in group 2, with a statistically significant difference (p=0.003) (Figure 1). Perioperative pacemaker requirement, inotropic requirement, intra-aortic balloon pump (IAPP) requirement, acute renal failure (ARF), and mortality rates of the groups were similar (p=0.244; p=0.139; p=1.000; p=0.139; p=1.000, respectively). However, the need for defibrillation was higher in group 1 (p=0.044) (Table 3).

Table 3

Comparison of ritis rates and perioperative outcomes of the groups

		Group-1 (N=40)	Group-2 (N=40)	p
Preoperative AST/ALT Rate (Mean±SD)		0.88±0.44	1.11±1.15	0.072
CPB Output AST/ALT Rate (Mean±SD)		0.49±0.18	0.85±1.23	0.003
Postoperative Day 1 AST/ALT Rate (Mean±SD)		0.61±0.25	0.57±0.25	0.687
Pacemaker Requirement, (n, %)	• Yes	2, (5%)	1, (2.5%)	0.244
	• No	38, (95%)	39, (97.5%)	
Defibrillation Requirement, (n, %)	• Yes	18, (45%)	13, (32.5%)	0.044
	• No	22, (55%)	27, (67.5%)	
Inotrope Requirement, (n, %)	• Yes	37, (92.5%)	35, (87.5%)	0.139
	• No	3, (7.5%)	5, (12.5%)	
IABP Requirement, (n, %)	• Yes	1, (2.5%)	1, (2.5%)	1.000
	• No	39, (97.5%)	39, (97.5%)	
ARF, (n, %)	• Yes	5, (12.5%)	3, (7.5%)	0.139
	• No	35, (87.5%)	37, (92.5%)	
Mortality, (n, %)	• Yes	0, (0%)	0, (0%)	1.000
	• No	40, (100%)	40, (100%)	

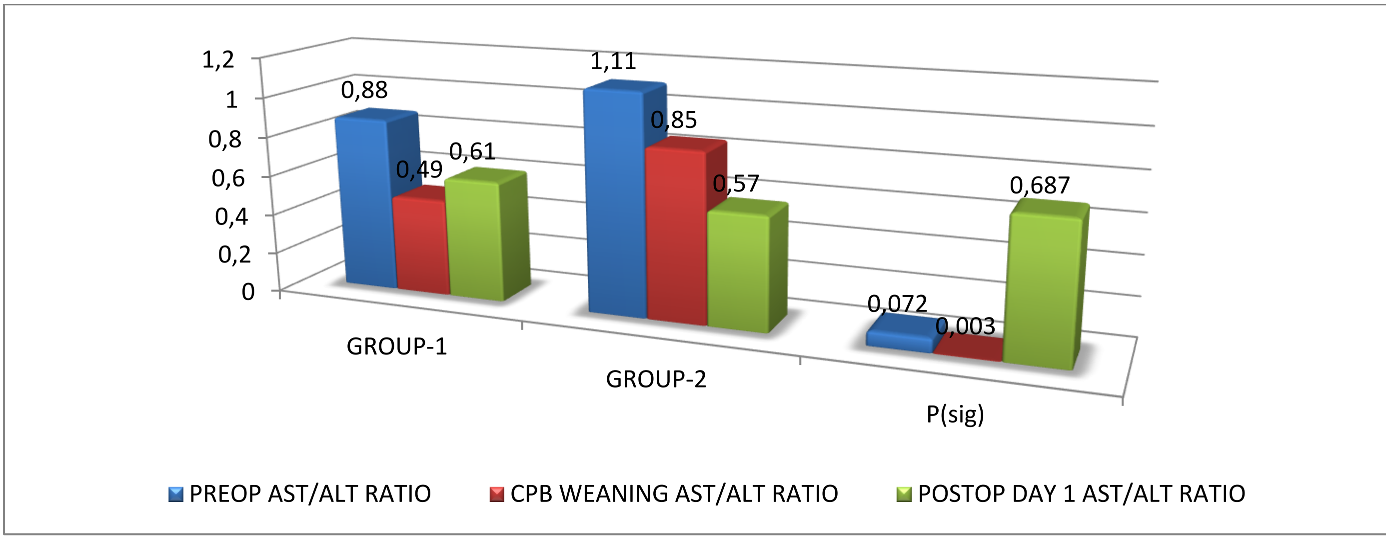
Mean±SD: Mean±standard deviation; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CPB: Cardiopulmonary bypass; IABP: Intra-aortic balloon pump; ARF: Acute renal failure.

4. Discussion

The AST/ALT ratio is also associated with an increased risk of cardiovascular disease. It can also be used as a simple independent determinant of left ventricular functional status in patients with heart failure and reduced ejection fraction. Furthermore, after the risk factors are eliminated, a high AST/ALT ratio can be evaluated as an independent indicator of future cardiovascular mortality[11]. In this research, AST/ALT was compared to evaluate the superiority or equivalence of two different cardioplegia solutions and was similar on the preoperative and postoperative 1st day in the patient groups who underwent both cardioplegia methods. At CPB output, it was observed that AST/ALT was significantly higher in the blood cardioplegia group. This suggested that Del Nido cardioplegia might be superior to blood cardioplegia. In addition, the results of liver function tests (AST, ALT) and liver enzymes (total bilirubin, direct bilirubin and GGT) at different times were similar in the two groups. Nonetheless, examining the perioperative results, it was observed that the required for intracardiac defibrillation was significantly higher in the group using Del Nido cardioplegia. Several studies indicated that each of the liver aminotransferases was inversely and independently associated with the risk of cardiovascular disease. It was also stated that it did not provide a significant improvement in the risk assessment of cardiovascular diseases beyond traditional cardiovascular disease risk factors[12].

Figure 1

Graphical analysis of the ritis rates of the groups



These results could be interpreted as the advantages of the study. The AST/ALT ratio was indicated as a risk factor for cardiovascular diseases in previous literature[13]. In one of these studies, the correlation between AST/ALT ratio and peripheral arterial disease (PAD) was investigated in the hypertensive population. In their study, they analyzed the data of 10.900 patients with hypertension and found that 350 (3.2 %) of these patients had PAD. The risk of PAD increased with the AST/ALT ratio. Additionally, a higher AST/ALT ratio (≥1.65) was associated with the risk of PAD in Chinese adults with hypertension. This led to the idea that a high AST/ALT ratio could be an appropriate, cost-effective, and beneficial tool for assessing the risk of atherosclerosis[14]. In our study, we used AST/ALT as a marker for postoperative results in cardiac surgery using two different cardioplegia solutions.

In another study, it was stated that the elevated AST/ALT ratio was associated with all-cause death and cancer. Chen W. et al.[15] investigated the correlation of the AST/ALT ratio as a possible determinant of mortality and cancer incidence. They found that both serum ALT and AST levels increased in patients with chronic disease, but the AST/ALT ratio decreased in general. In that study, they also claimed that cancer cases had a higher baseline rate (median = 1.15, IQR: 0.91-1.44) than non-cancer cases (median = 1.23, IQR: 0.96-1.54). They reported that a high AST/ALT ratio increased the risk of all-cause mortality. Thus, the AST/ALT ratio may be a potential biomarker for evaluating healthy conditions and long-term mortality, especially for cancer and its prognosis[15]. These findings indicated Del Nido cardioplegia might be a safer alternative than blood cardioplegia. Zhou J. et al.[16] investigated the AST/ALT ratio as an important determinant of prostate cancer incidence and found that the increased AST/ALT ratio predicted increased cancer incidence[16]. However, controversial data exists in the literature[17].

Liver function enzymes such as AST and ALT could be utilized as biomarkers that reflect disease severity in several chronic liver diseases. More recently, Weng SF et al.[18] reported that high AST/ALT ratios were independently associated with an increased risk of developing cardiovascular disease in men within ten years but not in women. They also stated that the AST/ALT ratio provides greater benefits in predicting cardiovascular diseases in individuals with high ALT levels[18]. These data supported our outcomes. Weng SF et al.[18] also concluded that the AST/ALT ratio should not be included in risk estimation tools in cardiovascular diseases. Furthermore, they stated that those with a high AST/ALT ratio may represent a higher risk that may be beneficial, especially when ALT is elevated, which may lead to the assumption that Del Nido cardioplegia is superior.

Liu Y. et al.[19] investigated the relationship between AST/ALT ratio and arterial stiffness in a cross-sectional study in a Japanese population without fatty liver. In their study, they observed that the relationship between AST/ALT ratio and arterial stiffness was not linear. However, an AST/ALT ratio greater than 13.1 (per 0.1 change) was positively associated with arterial stiffness[19]. Feng X. et al.[20] investigated the relationship between AST/ALT ratio and cardiovascular disease mortality in peritoneal dialysis patients. They found that peritoneal dialysis patients with high AST/ALT ratio levels might be at a significant risk of cardiovascular disease mortality[20]. In our study, since the CPB output AST/ALT ratio was higher in the blood cardioplegia group, Del Nido cardioplegia was considered superior.

Studies on GGT reported that GGT levels did not provide promising results in predicting the first cardiovascular events[21]. However, the fact that the two cardioplegia solutions were similar in comparing perioperative outcomes, our study suggested that the two cardioplegia solutions might have similar results.

When evaluating the two cardioplegia solutions in terms of perioperative results, it is possible to say that Del Nido cardioplegia is superior when we consider the value of the De Ritis rate, which is a predictor for liver damage, at the time of CPB exit, while the need for defibrillation is disadvantageous in the Del Nido cardioplegia solution group. In addition, in clinical use, the fact that del Nido cardioplegia is a single dose (additional half dose if needed), whereas blood cardioplegia requires administration every twenty minutes may cause a separate loss of time for the surgical team, interrupting the operation and prolonging the duration of CPB, and is a disadvantage in terms of a separate workload for the perfusionist. However, when evaluated in terms of liver function tests and liver enzymes, it can be considered that the two cardioplegia methods show equivalent results.

4.1. Limitations of the Study

The limitations of this study are that it is single-centered and retrospective. Moreover, only the cases with CABG replacement 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.

5. Conclusion

According to the results of this study, the effects of Del Nido cardioplegia solution and blood cardioplegia on liver function tests and liver enzymes were similar in CABG performed under CPB guidance. However, AST/ALT ratio at CPB discharge was higher in the blood cardioplegia group; therefore, del Nido cardioplegia may be considered superior to blood cardioplegia. The need for intracardiac defibrillation was a disadvantage for del Nido cardioplegia. In conclusion, although the effects of the two cardioplegia solutions on the liver showed similar results, del nido cardioplegia may be superior in terms of De Ritis rate.

Statement of ethics

In this study; before the study, approval was obtained from the institution where the study will be conducted (Sanliurfa Mehmet Akif Inan Training and Research Hospital) and the local ethics committee (Harran University Clinical Research Ethics Committee) (Date: 10.04.2023 - Approval no: HRÜ/23.06.04). As this was retrospective research, no informed consent has been obtained from participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author Contributions

BA is the major contributor to the writing of the manuscript. BA, MZB and MP are involved in the design, conception, data collection and analysis of the study. All authors read and approved the final version of the manuscript.

Availability of data and materials

The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Consent for publication

The original article is not under consideration by another publication, and its substance, tables, or figures have not been published previously and will only be published elsewhere.

References

1.Carvajal C, Goyal A, Tadi P. Cardioplegia. 2023 Jul 24. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 32119350.

2.Bradić J, Andjić M, Novaković J, Jeremić N, Jakovljević V. Cardioplegia in Open Heart Surgery: Age Matters. J Clin Med. 2023;12(4):1698. doi:10.3390/jcm12041698.
https://doi.org/10.3390/jcm12041698

3.Chan J, Oo S, Butt S, et al. Network meta-analysis comparing blood cardioplegia, Del Nido cardioplegia and custodiol cardioplegia in minimally invasive cardiac surgery. Perfusion. 2023;38(3):464-72.
https://doi.org/10.1177/02676591221075522

4.Waterford SD, Ad N. Del Nido cardioplegia: Questions and (some) answers. J Thorac Cardiovasc Surg. 2023;165(3):1104-8.
https://doi.org/10.1016/j.jtcvs.2021.11.053

5.Zhai K, Cheng X, Zhang P, et al. Del Nido cardioplegia for myocardial protection in adult cardiac surgery: a systematic review and update meta-analysis. Perfusion. 2023;38(1):6-17.
https://doi.org/10.1177/02676591211031095

6.Fresilli S, Labanca R, Monaco F, et al. Del Nido Cardioplegia in Adult Cardiac Surgery: Meta-Analysis of Randomized Clinical Trials. J Cardiothorac Vasc Anesth. 2023;37(7):1152-9.
https://doi.org/10.1053/j.jvca.2023.02.045

7.Ahmed AA, Mahboobi SK. Warm Blood Cardioplegia. 2023 Jun 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 32644345.

8.Steininger M, Winter MP, Reiberger T, et al. De Ritis Ratio Improves Long-Term Risk Prediction after Acute Myocardial Infarction. J Clin Med. 2018;7(12):474.
https://doi.org/10.3390/jcm7120474

9.Ndrepepa G, Holdenrieder S, Kastrati A. Prognostic value of De Ritis ratio in patients with acute myocardial infarction. Clin Chim Acta. 2022;535:75-81.
https://doi.org/10.1016/j.cca.2022.08.016

10.Wang K, Chen Z, Zeng D, Ran M. Impact of the De Ritis Ratio on the Prognosis of Patients with Stable Coronary Artery Disease Undergoing Percutaneous Coronary Intervention. Med Sci Monit. 2022;28:e937737.
https://doi.org/10.12659/MSM.937737

11.Muzurović E, van der Lely AJ, Gurnell M. AST to ALT Ratio and Peripheral Arterial Disease in a Hypertensive Population-Is There a Link?. Angiology. 2021;72(10):905-7.
https://doi.org/10.1177/00033197211004387

12.Kunutsor SK, Bakker SJ, Kootstra-Ros JE, Blokzijl H, Gansevoort RT, Dullaart RP. Inverse linear associations between liver aminotransferases and incident cardiovascular disease risk: The Prevend study. Atherosclerosis. 2015;243(1):138-47.
https://doi.org/10.1016/j.atherosclerosis.2015.09.006

13.Liu H, Ding C, Hu L, et al. The association between AST/ALT ratio and all-cause and cardiovascular mortality in patients with hypertension. Medicine (Baltimore). 2021;100(31):e26693.
https://doi.org/10.1097/MD.0000000000026693

14.Liu H, Zha X, Ding C, et al. AST/ALT Ratio and Peripheral Artery Disease in a Chinese Hypertensive Population: A Cross-Sectional Study. Angiology. 2021;72(10):916-22.
https://doi.org/10.1177/00033197211004410

15.Chen W, Wang W, Zhou L, et al. Elevated AST/ALT ratio is associated with all-cause mortality and cancer incident. J Clin Lab Anal. 2022;36(5):e24356.
https://doi.org/10.1002/jcla.24356

16.Zhou J, He Z, Ma S, Liu R. AST/ALT ratio as a significant predictor of the incidence risk of prostate cancer. Cancer Med. 2020;9(15):5672-7.
https://doi.org/10.1002/cam4.3086

17.Kobayashi D, Yamamoto K, Kimura T, Shimbo T. Aspartate aminotransferase/alanine aminotransferase ratio and subsequent cancer development. Cancer Med. 2022;11(3):798-814.
https://doi.org/10.1002/cam4.4473

18.Weng SF, Kai J, Guha IN, Qureshi N. The value of aspartate aminotransferase and alanine aminotransferase in cardiovascular disease risk assessment. Open Heart. 2015;2(1):e000272.
https://doi.org/10.1136/openhrt-2015-000272

19.Liu Y, Zhao P, Cheng M, et al. AST to ALT ratio and arterial stiffness in non-fatty liver Japanese population:a secondary analysis based on a cross-sectional study. Lipids Health Dis. 2018;17(1):275
https://doi.org/10.1186/s12944-018-0920-4

20.Feng X, Wen Y, Peng FF, Wang N, Zhan X, Wu X. Association between aminotransferase/alanine aminotransferase ratio and cardiovascular disease mortality in patients on peritoneal dialysis: a multi-center retrospective study. BMC Nephrol. 2020;21(1):209.
https://doi.org/10.1186/s12882-020-01840-7

21.Kunutsor SK, Bakker SJ, Kootstra-Ros JE, Gansevoort RT, Dullaart RP. Circulating gamma glutamyltransferase and prediction of cardiovascular disease. Atherosclerosis. 2015;238(2):356-64.
https://doi.org/10.1016/j.atherosclerosis.2014.12.045