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Original Article

Comparison of cold and tepid modified delnido cardioplegia on myocardial protection in open heart surgery patients

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Abstract

Objectives: Cardioplegia is a crucial component of myocardial protection during aortic cross-clamping and cardiopulmonary bypass. It has been reported to provide effective myocardial protection and improved clinical outcomes with enhanced surgical flow in adult cardiac procedures. This study investigates the efficacy and safety of cold-modified Del Nido cardioplegia versus tepid blood cardioplegia in adult cardiac surgery patients using Myotherm, a device mainly used in cardiac surgery to monitor and manage the myocardial temperature during surgery.

Methods: After obtaining approval from the ethics committee and establishing entry criteria that included age, type of heart surgery, and absence of cardioplegic contraindications, the researchers defined exclusion criteria-such as previous heart surgery or significant comorbidities. Seventy patients were randomly divided into two groups: Group A received a cold solution at 4°C(n=35), while Group B received a tepid solution at 28°C (n=35).The amount of cardioplegia was 10 to 15 cc/kg and was injected with a pressure of 70 to 90 mm Hg in an anterograde manner. The temperature of cardioplegia was also adjusted with a Myotherm device. The day before the surgery, a written consent form was obtained from the patients, and the patients were informed about the study method. The sampling method is a double-blind clinical trial to achieve minimal bias, ensuring the reliability of the results and reducing influences on it. This study was conducted in Afshar Hospital in Yazd during 2023 and 2024.

Results: There were no significant differences between the two groups in terms of the need for an intra-aortic balloon pump (p=1.0), intraoperative and postoperative inotropic support (p=0.26), and postoperative pacemaker (p=0.49). Also, there were no significant differences between the two groups in terms of troponin I level after surgery (p=0.50), left ventricular ejection fraction after discharge (p=0.34), time to return of spontaneous heart rhythm (*P*=0.25)**,** cross-clamp time (*P*=0.30), cardiopulmonary bypass time (*P*=0.07)**,** and length of stay in the ICU (*P*=0.21).

Conclusions: The result showed that both techniques provide similar results. Although the time of cross-clamp and cardiopulmonary bypass was shorter in the group using tepid solution, these differences were not statistically significant. In other words, cold and tepid solutions are equally effective and safe to protect the myocardium, and doctors can use both types of solutions during open heart surgery**.**

Keywords: Myocardial protection, CPB, Cold and Tepid Modified Del Nido cardioplegia, Myotherm

Introduction

Single-dose del Nido cardioplegia (DNC) has been widely used in congenital heart surgery for over 20 years, proving safe and effective in pediatric patients by enabling a secure period of cardiac arrest lasting up in adults to 120 minutes [1,2]. Recent studies have shown its effectiveness in providing safe myocardial protection in open-heart surgery patients [3-7]. The standard DNC consists of one fully oxygenated patient with whole blood mixed with four parts Plasma-Lyte A. It is given as a single dose every 90 minutes at a temperature of 8-12°C [1]. However, many clinicians have altered this traditional formula [8-12].In our modified del Nido cardioplegia protocol, cardioplegia was administered at a 4:1 blood-to-crystalloid ratio. Group A received it at 4°C, while Group B received it at 28°C, every 60 minutes. This study aimed to compare the efficacy and safety of cold-modified del nido cardioplegia (CMDNC) versus tepid-modified del nid cardioplegia (TMDNC) to protect the myocardium in open heart surgery patients using the Myotherm device in adult patients undergoing heart surgery.

Abbreviation, acronyms & symbols

Aortic cross clamp	= ACC
Blood cardioplegia	= BC
Coronary artery bypass grafting	= CABG
Cold blood cardioplegia	= CBC
Cross clamp	= CC
Cold modified Del Nido cardioplegia	= CMDNC
Cardiopulmonary bypass	= CPB
Diabetes mellitus	= DM
Del Nido cardioplegia	= DNC
Ejection fraction	= EF
Hematocrit	= HCT
Intra-aortic ballon pump	= IABP
Intensive care unit	= ICU
Tepid modified Del Nido cardioplegia	= TMDNC

Materials and Methods

This clinical trial, approved by the university ethics committee, aimed to evaluate the efficacy and safety of two groups of patients undergoing elective open heart surgery with the assistance of a cardiopulmonary bypass machine. The code of ethics: IR.SSU.MEDICINE.REC.1402.337.

Study Design and Methodology

A prospective, randomized controlled trial design was implemented, appropriate for the research question addressing treatment outcomes in cardiac surgery. The participants included 70 adult patients scheduled for elective open-heart surgery. They were randomly assigned to two groups: 35 patients received CMDNC and 35 TMDNC.

Patient Selection Criteria

Inclusion criteria comprised participants aged 18 years or older who were candidates for elective open heart surgery, exhibiting an ejection fraction (EF) greater than 25%. Exclusion criteria included patients with a history of prior heart surgery or myocardial infarction, those undergoing emergency or re-surgery, recent acute coronary syndrome, those who required inotropic or vasopressor support preoperatively, and those needing a second aortic cross-clamping. Before inclusion, patients underwent comprehensive preoperative evaluations, which included cardiac function tests, echocardiograms, and general health assessments to ensure their suitability and safety in participating in the study.

Surgical Protocol

The surgical procedures were performed by experienced cardiac surgeons following established protocols for open heart surgery.

Before the removal of aortic cross-clamping, all patients received a standardized preoperative medication regimen comprising 100 mg of 2% lidocaine and 2 grams of 50% magnesium sulfate.

Data Collection and Measurement

The primary endpoint of this study was the assessment of hemodynamic stability post-surgery, measured through continuous monitoring of cardiac output and systemic vascular resistance. Secondary endpoints included the duration of mechanical ventilation and postoperative complications, evaluated through regular postoperative assessment by the cardiac care team. The primary endpoint of this study was the evaluation of hemodynamic stability during and after surgery, measuring through continuous monitoring of arterial blood pressure, central venous pressure, cardiac output, and systemic vascular resistance. Secondary endpoints included ICU length of stay and postoperative complications, which were assessed through regular postoperative evaluation by the cardiac care team. Statistical analyses were performed to compare outcomes between the two groups, using appropriate tests to evaluate differences in means and proportions, ensuring a robust examination of the intervention's effectiveness.

Operational technique

The researchers used a standard general anesthesia protocol for all patients. This protocol included preoperative assessment, laboratory tests, informed consent, patient fasting, premedication, monitoring, induction of anesthesia, airway managers, maintenance of anesthesia, and fluid management. The researchers performed all procedures with a median sternotomy and, in all procedures, established cardiopulmonary bypass (CPB)using an extracorporeal circulatory circuit with lactated Ringer's solution and retrograde autologous priming to reduce hemodilution and allogeneic transfusion. If needed, freshly concentrated erythrocyte suspensions (≤ 7 days of storage) were added to the initial pump volume to maintain a hematocrit level greater than 25% during CPB. Mean arterial pressure (MAP) was kept at 60-70 mm Hg. Systemic temperature was allowed to decrease to 32±1°C. Rewarming of the patients was started a few minutes before cross-clamp (CC) removal. Table 2 illustrates the surgical data of the patients.

Table1. Patient demographics

variable	Group A (CMDNC) cold modified del nido cardioplegia n=35	Group B (TMDNC) tepid modified del nido cardioplegia n=35	P-value
Age (Years)	58.17 ± 15.94	76.62 ± 90.35	0.45
Sex (M/F)	26/9	26/9	1.0
Diabetes mellitus	11	9	0.79
CAD	21	20	
MR	4	5	
AI	6	5	
PAPVC	1	1	0.92
CAD+MR	0	1	
CAD+AI	2	1	
MR+AI	1	2	
Preoperative EF	46.28 ± 10.66	45.42 ± 9.50	0.52
Preoperative troponin I	17.67 ± 33.36	20.53 ± 64.11	0.50

Continuous variables are presented as the mean ± standard deviation and were compared by "Independent-samples t-test". x2 or Fisher's exact test was used for categorical variables.M, male/ F, female/ CAD, coronary artery disease/ MR, mitral regurgitation/ AI, aortic insufficiency/ PAPVC, partial anomalous pulmonary venous connection.

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Table2. Patients operative data

variable	Group A (CMDNC) cold modified del nido cardioplegia n=35	Group B (TMDNC) tepid modified del nido cardioplegia n=35	P-value
Cardiac rhythm recovery time	3.95 ± 2.95	4.09 ± 2.02	0.25
Use of pacemaker	0	2	0.49
Use of IABP	1	1	1.00
Inotropic support	11	6	0.26
Cross-clamp time	65.77 ± 26.11	59.22 ± 20.27	0.30
CPB time	104.67 ± 28.43	93.97 ± 27.06	0.07
ICU stay(days)	2.54 ± 1.46	2.88 ± 1.64	0.21
Troponin I at 7^{th} d	787.94 ± 802.44	601 ± 207.02	0.50
EF(percent)	46.14 ± 8.32	44.57 ± 8.07	0.34

Continuous variables are presented as the mean ± standard deviation and compared by "Independent-samples t-test. x2 or Fisher's exact test was used for categorical variables.
IABP, intra-aortic balloon pump
CPB, cardiopulmonary bypass
ICU, intensive care unit
EF, ejection fraction

Cardioplegia Strategy

Based on the temperature of cardioplegia, patients were randomly divided into cold (4°C, group A, number = 35) and tepid (28°C, group B, number = 35) groups. MDNC made by combining one part of oxygenated blood and four parts of a crystalloid solution, was performed anterogradely in the aortic root with a pressure of 70-90 mmHg through the root cannula or direct infusion into the ostial coronary arteries and Cardiac arrest was induced. The temperature was adjusted (4 degrees in the cold and 28 degrees in the warm group) using a Myotherm device (cardioplegia delivery system). Myocardial protection was achieved through the administration of CMDNC or TMDNC. Local hypothermia was not utilized. Table 3 provides the composition of the cardioplegia solution.

Table3. Composition of modified del nido cardioplegia solution

Blood to crystalloid ratio	1:4
Base solution	Saline (0.9% NaCl)
Manitol 20%	3.2 g
Magnesium sulphate	2.5 g
NaHCO3	13 mEq/L
Potassium	26 mEq/L
Lidocaine 2%	130 mg
Temperature of cardioplegia	4°C and 28°C

Modified Cold and Tepid Del Nido Cardioplegia Strategy

In this type of del Nido cardioplegia, 0.9% normal saline was used instead of plasma-lite A. Cardiac arrest was initially induced with a dose of 10-15 ml/kg up to a maximum of 1000 ml for patients over 50 kg. The Cardioplegia solution was delivered anterogradely. A retrograde dose was not used.

Primary Endpoints

Clinical manifestations of myocardial damage, such as the late return of spontaneous cardiac rhythm, need for inotropic support, need for pacemaker support, need for IABP support, postoperative left ventricular ejection fraction (LVEF) measured by echocardiography (day before discharge), and Troponin I levels were evaluated.

Secondary Endpoints

The study's secondary endpoints included assessing postoperative clinical outcomes, CBP time, ACC time, and ICU length of stay.

Statistical Analysis

All statistical analyses were performed using SPSS Version 23.0 (IBM Corp. Released 2023. IBM SPSS Statistics for Windows, Version 29.0.2.0 Armonk, NY: IBM Corp). The normality distribution of continuous variables was examined by the Kolmogorov-Smirnov test, and summarized by mean ± standard deviation for data with normal distribution and by median (interquartile range) for data with non-normal distribution. Qualitative variables were presented by frequencies and percentages. The chi-square or Fisher's exact test was used to compare categorical variables between two groups. The independent t-test and Mann-Whitney U test were utilized to compare continuous variables between two groups with normal and abnormal distribution, respectively. The significance level of 0.05 was considered for all statistical tests.

Results

Demographics and Baseline Clinical Profile

The comparison of demographics and baseline clinical characteristics demonstrated no significant differences between the cold-modified del Nido cardioplegia (CMDNC) and tepid-modified del Nido cardioplegia (TMDNC) groups. Both cohorts exhibited comparable demographic profiles, preoperative baseline data, and clinical attributes, ensuring a well-matched comparison for the subsequent analysis.

Primary Endpoints

The assessment of primary endpoints revealed no significant differences in clinical outcomes between the CMDNC and TMDNC groups. Specifically, the need for inotropic support was similar (p=0.26), as was the requirement for pacemaker support (p=0.49) and intra-aortic balloon assistance (p=1.00). Furthermore, postoperative left ventricular ejection fraction (LVEF) before discharge showed no significant difference (p=0.34), and peak postoperative troponin I levels were comparable between the groups (p=0.50). These findings suggest that both cardioplegia techniques provide similar levels of myocardial protection and postoperative cardiac function.

Secondary Endpoints

In examining secondary endpoints, the TMDNC group tended toward a shorter median aortic cross-clamp (ACC) time (55 minutes for TMDNC vs. 62 minutes for CMDNC). However, this difference did not reach statistical significance (p=0.30). Similarly, there was a trend for shorter cardiopulmonary bypass (CPB) time in the TMDNC group (93 minutes vs. 103 minutes for CMDNC), with p=0.07, indicating a potential benefit of the tepid approach. However, neither of these findings was statistically significant. Additionally, both groups had an identical median ICU stay of 2 days (P=0.21), further reflecting the clinical equivalence of the two cardioplegia strategies considering postoperative recovery. The findings suggest that CMDNC and TMDNC are equally safe and effective in providing myocardial protection during adult cardiac surgery, with no significant differences in key clinical outcomes.

Discussion

This study introduces single-dose TMDNC as a safer alternative to CMDNC for adult patients undergoing cardiac surgery. Both groups showed similar clinical outcomes considering intra-aortic balloon pump support requirement, postoperative peak troponin levels, perioperative inotropic support, pacemaker support requirement, and postoperative left ventricular ejection fraction (LVEF) at discharge.TMDNC was associated with significantly reduced aortic cross-clamp (ACC)

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and cardiopulmonary bypass (CPB) times compared to CMDNC.The findings suggest that single-dose TMDNC may be a safer option, as it does not compromise clinical outcomes while improving surgical efficiency. The results indicate that TMDNC can be effectively implemented without negatively affecting critical postoperative outcomes. The reduction in ACC and CPB times with TMDNC suggests that this approach may facilitate faster surgical procedures, potentially leading to shorter hospital stays and lower healthcare costs. Additionally, the comparable outcomes in both groups highlight the feasibility of TMDNC as a standard practice in cardiac surgery, emphasizing its safety and efficiency. This study's findings support previous research indicating that TMDNC offers advantages over CMDNC in surgical efficiency and safety. The present literature emphasizes the risks of prolonged CPB times and their correlation with negative postoperative outcomes. This study further underscores that effective monitoring techniques can help reduce surgical times and enhance patient outcomes. Conversely, some studies advocate for CMDNC due to its established protocols and the familiarity of surgical teams with this approach. Additionally, traditional methods may provide more comprehensive monitoring, which can be safer in complex cases. Moreover, the debate surrounding TMDNC and CMDNC also raises essential considerations relating to resource allocation and training. While TMDNC has demonstrated potential for improved efficiency, the implementation of such techniques necessitates a commitment to ongoing education and skill development for surgical teams. Furthermore, the variability in patient populations and surgical complexities must not be overlooked. Certain cases may benefit more from the established protocols of CMDNC, particularly in scenarios where the surgical team is well-versed in its nuances. This familiarity can lead to quicker decision-making and potentially better outcomes in high-stakes situations. Ultimately, the choice between TMDNC and CMDNC should be guided by a careful assessment of individual patient needs the specific surgical context, and the capabilities of the surgical team. Collaborative discussions among multidisciplinary teams can help tailor the approach to maximize safety and efficacy. Future studies should continue to explore the long-term implications of these techniques, focusing on patient outcomes across diverse surgical settings to establish better guidelines for the best practices. In conclusion, while previous studies provide a foundation for implementing CMDNC, the current research suggests that TMDNC may offer a promising alternative without compromising patient safety or clinical outcomes. Further multicenter trials with larger sample sizes and longer follow-up periods are warranted to validate these findings and establish TMDNC as a standard practice in cardiac surgery.

The Rationale for 4:1 Blood to Crystalloid Ratio

Blood cardioplegia (BC) offers numerous advantages over crystalloid solutions. It is nutrient-rich, providing essential fatty acids and glucose, the original energy sources for adenosine triphosphate in different metabolic states. BC helps replenish energy stores during ischemic arrest, supplies endogenous buffers and antioxidants and exhibits favorable rheological properties [13]. Compared to crystalloid cardioplegia, BC reduces hemodilution and transfusion needs, enhances oxygen delivery due to hemoglobin content, minimizes myocardial edema formation, and offers superior myocardial protection in high-risk and energy-depleted hearts. In our MDNC protocol, a 4:1 blood-to-crystalloid ratio is employed, leveraging the benefits of BC [13].

The Rationale for Tepid Temperature

Cardioplegia temperature selection is a crucial factor to safeguard the integrity of the heart muscle during surgical procedures. The choice typically offers three temperature options for administration: cold cardioplegia(ranging between 4-10°C), tepid cardioplegia(around 28-30°C), or normothermic cardioplegia (maintained at 34-37°C),each presenting distinct advantages and disadvantages. Careful consideration of these temperature ranges is essential as they directly impact the effectiveness of myocardial protection, influencing outcomes post-surgery and recovery processes [14]. The optimal temperature for cardioplegia is still controversial within the medical field. Several studies have revealed that hypothermia can cause a decrease in basal metabolism and oxygen consumption in the whole body. Specifically on the myocardium, cold cardioplegia significantly affects oxygen consumption decrease, due to a general reduction in metabolic activity that helps protect the heart muscle during surgical procedures. Research into the ideal temperature for cardioplegia continues with a focus on maximizing the benefits of hypothermia while

ensuring the safety and efficacy of the procedure [14]. Hypothermia can protect the heart during cardiac arrest. It can also harm the myocardium by slowing enzymatic and cellular repair processes, inhibiting ion pump function, raising the risk of myocardial swelling, reducing the effectiveness of certain drugs, increasing plasma viscosity, and impairing red blood cell flexibility. Hypothermia's effect on heart enzymes can delay myocardial recovery after removing the cross-clamp [14]. In a cold alkalotic cardioplegia solution, the oxygen dissociation curve shifts left due to higher hemoglobin oxygen affinity, which reduces oxygen supply to the myocardium, where the main oxygen source is the dissolved oxygen in the solution [14]. Blood Cardioplegia's benefits peak at 37°C and are influenced by temperature. Lower temperatures can diminish these advantages. Warm cardioplegia was introduced to maximize benefits, counteract hypothermia's harmful effects, sustain aerobic metabolism during ischemia, shorten rewarming and perfusion time (and thus CPB time), and mitigate systemic hypothermia's adverse effects. Blood Cardioplegia has been meticulously studied and proven to showcase its maximum benefits precisely at the optimal temperature of 37°C. It is essential to understand that the efficacy of these benefits correlates to temperature variations, with lower temperatures potentially compromising the advantages that this technique offers. In light of these findings, warm cardioplegia techniques were innovatively developed and introduced. These warm solutions serve a dual purpose: they seek to maximize the advantages imparted by Blood Cardioplegia, but they also act as a strategic countermeasure against the detrimental effects of hypothermia. Furthermore, the implementation of warm cardioplegia strategies aims to sustain the critical process of aerobic metabolism even in the face of ischemic conditions. Additionally, this approach effectively reduces the time required for rewarming and perfusion, resulting in shorter Cardiopulmonary Bypass (CPB) durations. Doing so, not only optimizes the overall efficiency of the cardiac surgical procedure but also helps in attenuating the harmful impacts of systemic hypothermia that may otherwise arise. [14]. Warmed blood cardioplegia improves metabolic and functional recovery of the myocardium in various experimental models [14]. Higher temperature increases myocardial requirements and may make maintaining complete electromechanical quiescence challenging. The myocardium's tolerance to ischemic is reduced in a normothermic heart, rendering it susceptible to ischemic injury if there is an interruption or maldistribution of the cardioplegic solution. Despite some reports of decreased ischemic tolerance with warm cardioplegia, studies indicate that a single dose can preserve the myocardium for up to 40 minutes [15-17]. Minatoya et al. [15] discovered that intermittent warm blood cardioplegia allowed 30 minutes of safe ischemia during coronary bypass surgery. Tepid cardioplegia, which involves the administration of a moderately warm solution to the heart during surgery, was developed to combine the advantages of warm cardioplegia with a reduction in the drawbacks associated with both warm and cold cardioplegia techniques. By implementing a mildly warm temperature, tepid cardioplegia aims to provide essential myocardial protection without subjecting the heart to the potential risks of extreme temperatures. This technique seeks to balance the benefits of warm cardioplegia in cellular metabolism and myocardial functions while mitigating the fundamental complications, such as myocardial stunning, that may arise from utilizing excessively cold or warm solutions. Tepid cardioplegia offers a promising alternative seeking to optimize cardiac surgical outcomes by harnessing the advantages of both warm and cold cardioplegia while minimizing their respective shortcomings [14]. Hayashida et al. [18] reported that reducing heart temperature from 37°C to 29°C did not alter myocardial oxygen consumption, indicating maintained mitochondrial function. Tepid cardioplegia led to reduced anaerobic lactate and acid release during arrest, preserving myocardial function. Immediate myocardial recovery and superior myocardial protection were noted with tepid cardioplegia compared to warm and cold cardioplegia [18]. In a study by Ramani et al. [19], a single dose of 4:1 Blood Cardioplegia with lidocaine at 20°C effectively safeguards the myocardium. Various factors impact myocardial temperature, such as blood return pathways, perfusate temperature during CPB, ambient conditions in the operating room and heat transfer from nearby tissues. Myocardial temperature increases during the post-clamp period following cold cardioplegia, approaching systemic temperature until the next cardioplegia dose. Thus, the myocardial protective effect of hypothermia diminishes over time, notably in patients administered single-dose cardioplegia.In another study conducted by Rao et al.[20], patients were cooled to 32°C and administered DNC at 4°C. Within 40 minutes after initial cardioplegia delivery, the transseptal probe temperature reached about 25°C, with the right ventricular temperature slightly

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higher at around 30°C [20]. In a study by Momin et al. [21], Patients received a single dose of DNC. The researchers systemically cooled them to 32°C, with right atrial temperatures above 25°C at 30 minutes post-induction. Boldt et al. [22] reported rewarming of the heart to approximately 25°C 30 minutes after the induction with cold (4°C) cardioplegic solution. Boldt et al. used topical cooling and cooled the patients down to 34°C. Daily et al. [23] observed myocardial rewarming from 18°C to 22°C within 20 minutes after implementing a cold cardioplegic solution. The researchers cooled the patients to 28°C. In another study, Okamoto et al.[24], a 10°C increase in myocardial temperature was observed after a 30-minute interval preceding the second dose of cardioplegic solution during normothermic CPB. Then, the researchers warmed the hearts to around 25°C. These findings suggest that the effectiveness of cold cardioplegia in protecting the heart diminishes over time, especially in patients receiving a single dose. After the initial dose, the heart remains warm for approximately 45 out of 90 minutes in such patients. Given the safety of single-dose cardioplegia in prolonged ischemia, subjecting the heart to 45 minutes of tepid cardioplegia during an ischemic period could be safe and advantageous.

Modified Del Nido Cardioplegia in Clinical Practice

Previous studies have shown that using DNC provides effective myocardial protection in many cardiac surgeries, even in complex procedures with extended ACC time [3-5]. Nevertheless, only a few studies evaluated the safety of MDNC in adults undergoing cardiac surgery. A few studies have reported several modifications of DNC, including the base solution, blood-to-crystalloid ratio, temperature, re-dosing interval, and constituents [8-12]. Yammine et al. [8] compared modified del Nido cardioplegia to standard Blood cardioplegia in adult heart surgeries. MDNC contained 0.9% NaCl, 8 mEq/L magnesium sulfate 50%, 30 mEq/L potassium chloride, and 100 mg/L lidocaine 1%. Blood to crystalloid ratio was 8:1. Patients with over 60 minutes of cross-clamping received standard Blood cardioplegia. MDNC excluded sodium bicarbonate and mannitol. The study did not provide temperature details. The study suggested lidocaine-based cardioplegia as a safe option for the initial 60 minutes of aortic cross-clamp in adult patients. Stamou et al. [10] modified the traditional DNC by using whole-blood microplegia as the base solution, removing the crystalloid portion, and administering DNC additives in whole blood. They assessed the safety of MDNC in high-risk patients during cardiac surgery compared to low-risk patients using the same cardioplegia protocol.MDNC with 24 mEq/Lt potassium chloride, 6 mL of 2% lidocaine, 2.5 g/L of 25% mannitol, 2.7 g of 50% magnesium sulfate, 8.6 mEq/L of sodium bicarbonate, and 970 mL of oxygenated blood was administered every 90 minutes at 6°C. The study confirmed the safety of MDNC in high-risk patients and prolonged operations. The researchers also compared their MDNC approach with lidocaine-containing CBC [9]. They found similar clinical outcomes. Kantathut et al. [11] discovered that using MDNC with lactated Ringer's solution as the base solution instead of Plasma-Lyte-A provided comparable or better myocardial protection in adult cardiac surgery patients compared to standard Cold Blood cardioplegia. The 1:4 ratio of oxygenated pump blood to cardioplegia solution with traditional additives was administered every 90 minutes at 4°C. Gallo et al. [12] Gallo and colleagues (2012) detailed the successful application of a specialized formulation during donor heart implantation in four individuals. Specifically, a unique combination of 4 parts blood to 1 part crystalloid, also known as Cold Modified Del nido cardioplegia (CMDNC), was administered. The researchers used a normal-R solution as a carrier for a novel approach to cardiac preservation. Noteworthy in this formulation was the elevation in potassium chloride content to 35 milliequivalents per liter, surpassing the conventional concentration observed in typical cardioplegia solutions. Ensuring proper myocardial protection and minimizing ACC and CPB durations are crucial to improving perioperative results. A single dose of cardioplegia has been shown to decrease ACC, CPB, and operative durations, thereby improving surgical efficiency [3-5]. Administering extra doses of cardioplegia during surgery can disrupt the procedure and lead to longer ACC, CPB, and operative times, especially in patients receiving multiple doses. The present study revealed that although multiple-dose normothermic cardioplegia was related to shorter ACC and CPB durations comparing the Cold Blood cardioplegia group, the difference did not result in better clinical outcomes.

Strengths and Limitations of the Study

Strengths

This study conducts a comparative analysis of TMDNC and CMDNC, offering crucial insights into their safety and efficacy. The extensive data on postoperative outcomes bolsters the reliability

of the findings, while the emphasis on key clinical parameters ensures the study's relevance to cardiac surgery practitioners.

Limitations

Since the researchers conducted the study in a single center, the findings may not be generalizable to other contexts. Furthermore, focusing on low-risk patients may not reflect results for high-risk populations. Consequently, while this study provides valuable insights, it may not fully reflect potential outcomes in high-risk groups or cardiac alternatives.

Conclusion

This study compared the efficacy and safety of cold-modified del Nido cardioplegia (CMDNC) and tepid-modified del Nido cardioplegia (TMDNC) for myocardial protection in adult cardiac surgery. The results showed that both techniques provided similar outcomes regarding inotropic support, pacemaker needs, intra-aortic balloon use, postoperative left ventricular ejection fraction (LVEF), and peak postoperative troponin I levels. Although the TMDNC group exhibited trends toward shorter median aortic cross-clamp and cardiopulmonary bypass times, these differences were not statistically significant. Given the comparable clinical outcomes, these conclusions may be generalizable to the Iranian population, where healthcare contexts and patient demographics are similar to those in the study. The findings suggest that both CMDNC and TMDNC are equally effective and safe for myocardial protection in adult cardiac surgery, offering valuable insights for clinicians in Iran and similar settings. Clinicians are encouraged to consider both CMDNC and TMDNC as viable options for myocardial protection during cardiac procedures. Future research should involve larger sample sizes and diverse patient populations to validate these findings and evaluate the long-term outcomes of each technique, enhancing the understanding of cardioplegia strategies and their impact on patient care in cardiac surgery.

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