**Use of del Nido Cardioplegia Solution in Adult Aortic Surgery**

Eris C1, Engin M1, Erdolu B1, As AK1

**1. Cüneyt Eriş, MD. Assoc Prof. (Corresponding author)**

1University of HealthSciences, Bursa Yuksek Ihtisas Training and Research Hospital, Department of Cardiovasculer Surgery, Mimar Sinan Town. Emniyet Street. Yıldırım / BURSA, Turkey **E-mail:** dr\_ceris@hotmail.com **Phone:** +90224 295 50 00 **Fax:** +90224 275 67 67

Orcid ID: 0000 0003 0573 5690

**2. Mesut Engin, MD.**

1University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Department of Cardiovasculer Surgery, Mimar Sinan Town. Emniyet Street. Yıldırım / BURSA, Turkey **E-mail:**[mesut\_kvc\_cor@hotmail.com](mailto:mesut_kvc_cor@hotmail.com)

Orcid ID: 0000 0003 2418 5823

**3. Burak Erdolu, MD.**

1University of Health Sciences, Bursa Yuksek Ihtisas Training and ResearchHospital, Department of Cardiovasculer Surgery, Mimar Sinan Town. Emniyet Street. Yıldırım / BURSA, Turkey **E-mail:**[kalpcerrahi@gmail.com](mailto:kalpcerrahi@gmail.com)

Orcid ID: 0000 0002 4679 8682

**4. Ahmet Kağan AS, MD.**

1University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Department of Cardiovasculer Surgery, Mimar Sinan Town. Emniyet Street. Yıldırım / BURSA, Turkey **E-mail:** ahmetkagan\_as@hotmail.com

Orcid ID: 0000 0001 8098 4393

**Abstract**

**Background:** The aim of the present study was to compare the operative and early postoperative results of the use of del Nido Cardioplegia solution (dNCS) with traditional blood cardioplegia (BC) in adult aortic surgery.

**Methods:** A retrospective single-center study was performed on 118 patients who underwent aortic surgery with cardiopulmonary bypass (CPB) between January 2016 and June 2020. Patients were divided in to two groups according to the type of cardioplegia solution used during the operation. Cardiac arrest was achieved in Group 1 (n:65) with traditional BC and in Group 2 (n=53) with dNCS. Operative and postoperative outcomes of the patients were compared between the two groups.

**Results:**Patient demographic characteristics were similar between the two groups. dNCS group showed significantly lower aortic cross-clamp (ACC) time (87,5 vs 73,3 min; P=0.001), cardioplegia volume (P<0.001), defibril­lation (P=0.006), drenaige amount (P=0.026) and inotropic support need (P=0.046). Also dNCS group had significantly lower high sensitive troponin I (hsTnI) values at 6th (P=<0.001) and 24th (P=0.017) hours. Hematocrit levels at hours 6 and 24 were significantly higher in dNCS (P=0.001).Time of intensive care unit stay, duration of extubation and length of hospital stay times were similar in both groups. There was no significant difference in terms of postoperative ejection fraction values (P=0.714).

**Conclusion:**Compared with conventional BC, dNCS provided beter myocardial protection with significantly shorter ACC times, reduced need for intraoperative defibrillation, postoperative lower hsTnI levels and comparable early clinical outcomes for adult patients undergoing aortic surgery. dNCS is a safe and efficient alternative to the traditional BC solution in adult cardiac surgery.

**Keywords:** Cardioplegic solutions, Myocardial protection, Aortic surgery, Cardiopulmonary bypass

**INTRODUCTION**

One of the most important criteria for a successful open heart surgery is to maintain the vitality of the myocardium sufficiently and effectively during cardiopulmonary bypass (CPB). Numerous cardioplegia solutions exist with different compositions to provide myocardial protection. However, there is no standard for the optimal or ideal composition and delivery technique [1].

Cardioplegia solutions are crystalloid or blood-based solutions with various chemical compounds. Blood cardioplegia (BC), which is the mixture of the subject’s oxygenated blood(80%) and a crystalloid solution (20%), is the most widely used cardioplegia model [2]. However, dNCS provides long-term cardiac protection with a single dose administration and has been used safely in pediatric cardiac surgery since the early 1990s [3].

In many studies conducted in recent years, very successful and encouraging results have been reported also in adult cardiac surgery operations using dNCS. The basic advantage of dNCS is single-dose application for subjects who underwent procedures of less than 90 minutes duration. Del Nido cardioplegia is a calcium-free, potassium-based and modified depolarizing cardioplegic solution[4]. It contains lidocaine, a membrane-stabilizing agent that increases sodium-channel blockade and together with its magnesium content act as a calcium antagonist [5].

In recent years, the use of dNCS in adult cardiac surgery has attracted considerable attention, with reported successful and safe results, and an increasing number of case reports have been made in this regard. However, these cases generally include uncomplicated cases such as a single valve with preserved ventricular function or coronary artery bypass surgery. The number of studies including comparative results in the case group such as complex aortic or aortic root surgery is quite limited.

The aim of the present study is to compare the operative and early postoperative results of the use of dNCS with traditional BC in adult aortic surgery.

**METHODS**

# The study was planned, and approval of the Bursa Yuksek Ihtisas Education and Research Hospital Ethics Committee was obtained (2011-KAEK-25 2020/07-12) and written informed consent was obtained from all patients. As a surgical team, we started using dNCS at the beginning of 2018. In this study,118 consecutive patients who had undergone aortic surgery procedures with cardiopulmonary bypass (CPB) between January 2016 and June 2020 at our hospital were included in the study retrospectively. All operations were performed by the same surgical team. Surgical indications were determined according to European Society of Cardiology Guidelines on the diagnosis and treatment of aortic diseases [6].

# According to the type of cardioplegia solution used during the operation, patients were divided into two groups. In Group 1 (BC group) (n:65) cardiac arrest was achieved with cold BC (at 4°C to 8°C, 10-15 mL/kg, approximately 1000 ml, at a pressure of 100-120 mm Hg, in 5 minutes) given antegradly. Cardiac arrest was sustained with BC (300 ml), which was applied every 15-20 minutes. Before the release of the ACC, approximately 500 mL warm BC (hot shot; 37° C) was administered only in this group of patients. In Group 2 (dNCS group) (n:53) a single-dose of dNCS (at 4°C to 8°C, 20 mL/kg in5 minutes at a 100 to 120 mm Hg pressure) was administered. If the total aortic cross-clamp (ACC) time was predicted to exceed 90 minutes, an additional half dose (500 ml) was given 60 minutes after the initial dose and if the total ACC time was predicted to exceed 120 minutes, a full dose dNCS was repeated after seventy-five minutes. In our dNCS group, 39% (n = 21) of the patients (11%, n = 6 fulldoses; 28%, n = 15 halfdoses) required an additionaldose of dNCS. No hot shotwasadministered in thisgroup. The compositions of both cardioplegia solutions are shown in Table 1.

Patients who underwent aortic surgery were included in the study. Exclusion criteria were under the age of 18, severe preoperative hemodynamic instability requiring high doses of inotropic drugs, ejection fraction (EF) <30%, previous cardiac surgery, dialysis dependent renal failure or severe liver disease (liver enzyme levels of greater than 10 times the upper limit of normal), anemic patients (preoperative hematocrit<20%), concomitant myotomy/ myectomy, emergency surgery, severe pulmonary hypertension, aortic dissection, infective endocarditis, patients with carotid artery disease requiring concomitant intervention.

Preoperative, operative and postoperative variables and results were obtained from our hospital's computerized database. Data collection was based on hospital clinicrecords, anesthesia records, perfusion records, and intensive care data and observational records. For each patient’s preoperative baseline characteristics, patient’s age, gender, body massi ndex (BMI), presence of diabetes mellitus, hypertension (HT), smoking history, hypercholesterolaemia, chronic obstructive pulmonary disease, European System for Cardiac Operative Risk Evaluation II (EuroSCORE II) values, pre-operative EF values, preoperative stroke historys’ were evaluated and compared between two groups.

Aortic cross-clamp times, perfusion times, cardioplegia volumes delivered, defibrilation needs, intraaortic balloon pump (IABP) requirements, needs for inotropic support(>5 μg/kg/min) more than 24 hours after surgery, postoperative drainage amounts, postoperative sixth and twenty-fourth hour hematocrit (Htc) values, use of blood products, perioperative electrocardiogram changes, development of new atrial fibrillation, the durations of intensive careunit (ICU) stays, durations of intubation time, discharge times and complications were compared. Also preoperative (at the time of induction of anesthesia), postoperative sixth and twenty-fourth hour high-sensitive troponin I(hsTnI) values, preoperative (at the time of induction of anesthesia) blood glucose and peak blood glucose during CPB also evaluated and compared between the groups.

All patients had continuous electrocardiographic monitoring at the ICU. Twelve-lead electrocardiographic recordings were performed preoperatively, postoperative first hour at ICU, daily for at least the first 3 postoperative days and at discharge day. Left ventricular EF, an indicator of cardiac functions, were compared preoperatively and postoperatively before discharge with two-dimensional echocardiography. Antegrade cerebral perfusion (ACP) was used with moderate hypothermia as a brain preservation method in all patients requiring aortic arch surgery.

High sensitive troponin I values were measured by a RocheCobas® 8000 analyser (RocheDiagnostics, Mannheim, Germany).

*Defining of Postoperative Complications*

Mortality: Mortality that occurs in the first 30 days during the postoperative period,Renal injury: Post-operative renal injury was determined according to Kidney Disease Improving Global Outcomes criteria and development of any stage of this criteria after operations was defined as renal injury, Cerebrovascular accident: Central neurological deficit lasting at least 24 hours after the operation, Infection: Mediastinal infection involving bone and muscle structures requiring reoperation, pneumonia or septicemia requiring antibiotherapy. Atrial fibrillation: It was defined as an irregular rhythm with the absence of discrete P waves in the 12-lead electrocardiogram, Bleeding: Postoperative drainage disrupting the hemodynamic stability and requiring reoperation, Respiratory failure: The need for ventilation lasting more than 48 hours after the operation.

*Statistical Analysis*

Statistical analyses were performed with the Statistical Package for the Social Sciences version 23.0, SPSS Inc, Chicago, Illinois, USA. Continuous variables are presented as means±standard deviations, where as categorical variables are presented as percentages. Inter-group comparisons were made by Student's t-test (for normally distributed data) or the Mann–Whitney U test (for non-normally distributed data). Categorical varieties were compared by the chi-square or Fisher'sexact test. A p value less than 0.05 was accepted as statistically significant for all comparisons.

**RESULTS**

Data from aortic surgery patients in whom traditional BC were used for cardiac arrest defined as Group 1 (*n* = 65); 44 (67.7%) males; age 65.3±8.3years; (range of 42–80 years). The data from the other group (*n* = 53); 40 (74%) males; age 66.4±7.5years; (range of 44–78 years)in whom dNCS were used for cardiac arrest defined as Group 2. There were no statistically significant differences between the two groups in terms of age, gender, presence of HT, hyperlipidemia, cerebrovascular event, BMI, diabetes mellitus, smoking, EF and preoperative Htc, creatinine, C reactive protein and hsTnI values. Demographic characteristics and preoperative data of all patients are presented in Table 2.

For operative parameters, the groups did not differ in terms of operation type, rates of ACP use and ACP time. The ACC times were significantly shorter in Group 2 compared to Group 1 (73.3 ± 20.7 vs 87.5 ± 23.2, P = 0.001) and the CPB times were also shorter, but there was no significant difference (114.4 ± 27.1 vs 123.9 ± 28.8, P = 0.071). Cardioplegia volume( 2773.8±453.8 vs 1323.9±368.5; p<0.001)and peak glucose levels (199±64.8 vs 165.7±39.9; P=0.001) during CPB were statistically lower in Group 2. At the time of ACC removal more cases in Group 1 significantly needed defibrillation to return to normal sinus rhythm compared with Group 2 (69.2% vs 44.4%; P=0.006) (Table 3).

Postoperative features of the patients are summarized in Table 4.There was no statistically significant difference between the two groups in terms of ventilation time, IABP use rates, postoperative EF, total ICU and hospital stay days. Chest tube drainage amounts, used packed blood products and need of inotropic support were higher in Group 1 (P=0.026, P<0.001, P=0.046, recpectively). High sensitivetroponin I levels at 6th and 24th hours ( 275.7±76.2 vs 203.5±68.6; P<0.001, 6th hour; 293.4±80.1 vs 253.1±101, P=0.017, 24th hour) were significantly lower in Group 2. And hematocrit levels at hours 6 and 24 were significantly higher in Group 2 (P<0.001, P=0.024, respectively).

Postoperative complications of the patients are presented in Table 5. Mortality, cerebrovascular event, infection, postoperative atrial fibrillation, bleeding revision and respiratory failure rates were similiar between two groups. Acute kidney injury (AKI) rates were higher in Group 1 (P=0.025).

**DISCUSSION**

Del Nido cardioplegia solution has been used effectively and safely in pediatric cardiac surgery for many years, and its use in adult cardiac surgery has been the focus of attention in recent years. Most previous studies have been conducted in selected groups; like aortic or mitral valve surgery or coronary bypass surgery with normal ventricular function and there are no adequate numbers of studies on the use of dNCS comparing other types of cardioplegia in multiple comorbid conditions or complex cardiac surgeries. In our study, we compared the operative and early postoperative results of using dNCS against BC in aortic surgery. As a result, we demonstrated that use of dNCS in aortic surgery appears to be safe and even more advantageous in many aspects than BC solution in adult cardiac surgery operations.

Myocardial protection in CPB is an essential component of open cardiac surgery. Therefore, the cardioplegia solutions used are very important. The dNCS contains an electrolyte composition similar to the extracellular fluid, which is mixed in a ratio of four parts crystalloid to one part fully oxygenated patient whole blood. It also contains additional additives for free-radical scavenging and pH buffering. In addition to the decrease in cellular calcium concentration, it also reduces myocardial excitability, cellular metabolism and energy consumption [7, 8]. Intracellular calcium ion accumulation during CPB is currently believed to be the most important factor in ischemia-reperfusion injury [9]. Lidocaine reduces excitability by providing membrane stabilization. It also prevents spontaneous myocardial contractions by blocking sodium channels and reduces troponin release [10]. Mannitol in its composition is effective in reducing cells welling and increasing oxygen-free radical scavenging [11].

Studies that compared dNCS and BC solutions reported that they offer similar myocardialprotection [12, 13] or that dNCS solution was providing beter myocardial protection [14]. A recent study published by, Kuserli et al.compared the results of the use of dNCS (36 patients) and conventional BC (36 patients) in aortic root surgery, in their propensity matched retrospective study. Perfusion times, cardioplegia volumes, defibrillation numbers, erythrocyte suspension and fresh frozen plasma usage rates were found to be significantly lower in patients who dNCS were delivered. There was no difference between the two groups in terms of postoperative inotropic needs, complication rates,and length of stays in the intensive care unit. In addition, left ventricular ejection fractions in the postoperative period were better in the dNCSgroup [15].

Marzouk et al. compared 131 consecutive adult patients who underwent open heart surgery with dNCS and 251 patients who were administered cold BC, determined with propensity scores. They found that perfusion times, operation times, total cardioplegia volumes, and peak glucose levels during cardiopulmonary bypass were significantly lower in patients who were administered dNCS. In addition, dNCS provides myocardial protection similar to intermittent cold blood cardioplegia (ejection fractions before discharge and postoperative troponin values ​​(immediately after surgery, 1st day, 4th day) were similar) and it can be used safely in all adult cardiac surgery operations. In addition, they found that dNCS shortened the operative times [16]. In our study peak serum glucose levels during surgery with dNCS were significantly lower, likely owing to the nonglucose base of this cardioplegic solution.Also we found that the ACC time was significantly shorter in the dNCS group compared to the BC group (73.3 ± 20.7 vs 87.5 ± 23.2; p= 0.001), the CPB times were also shorter, but there was no significant difference (114.4 ± 27.1 vs 123.9 ± 28.8; p= 0.071).

In a metaanalysis, it was stated that dNCS had similar results to traditional cardioplegia and myocardial protection methods and was a good alternative to BC in routine adult cardiac surgery [17]. In an other recent meta-analysis that included 9 studies (4 that were conducted for adult valve surgery, 3 for coronary bypass surgery, and 2 for valve/coronary bypass or a combination of valve/ coronary bypass surgery) compared dNCS with conventional cardioplegia. Their results that are similiar to our study found dNCS reduced the CPB and ACC times. The cardioplegia volumes were lower, and the blood glucose levels were lower with dNCS. Lengths of hospital stay and mortality rates were not significantly different between the groups. Also, unlike our study,they found that dNCS shortened the intensive care unit stay, but myocardial enzyme levels and postoperative inotropic support needs were not significantly different between the dNCS and BC groups [2]. In our study, hsTnI levels were significantly lower at 6th and 24th hours in the dNCSgroup (P = 0.001; P = 0.071). We think that lower troponin I levels compared to BC group are associated with dNCS composition and lower ACC and CPB times.

Patients who received dNCS had higher rates of spontaneous return of normal rhythm and required fewer defibrillations to restore normal sinus rhythm [18]. In our study, the need for defibrillation was less in order to achieve a normal sinus rhythm in the dNCS group compared to the BC group (44.4% for dNCS and 69.2% for BC; P= 0.006). The reason for the need for less defibrillation or the higher rate of return to spontaneous sinus rhythm in the group receiving dNCS is thought to be due to differences in the composition of cardioplegia [13]. Reduced rate of ventricular fibrillation presumably protects myocardium from further ischemia of electrical defibrillation [19].

Current large meta-analyzes comparing the results of a single dose with conventional techniques in adult cardiac surgery have revealed that the single dose strategy resulted a reduction in ACC and CPB times, resulted in less cardiac enzyme release and no significant difference on clinical outcomes. The use of dNCS resulted in a modest but significant reduction in ischemic times and cardioplegia volume requirements [17]. In some cases, cardioplegia delivery is technically more difficult, especially in aorticsurgery. Repeated doses of antegrade cardioplegia, especially in the aortic valve or aortic surgery, may cause potentially detrimental interruption to the surgical workflow and increase the risk of myocardial damage due to prolongation of perfusion times. In addition, the risk of tissue damage caused by cannulation of the coronary ostiums more than once while cardioplegia is given can be minimized with dNCS. It is generally accepted that a single dose antegrade dNCS provides safe and effective myocardial protection in adult open-heart surgery patients for an ACC duration of approximately 90-120 minutes [20, 21]. However, according to the previous studies regarding the use of dNCS in adult open heart surgery, the optimal timing of repeat dNCS dosing has been accepted, in the main, as between 60 and 90 minutes [22- 24]. In our dNCS study group, 39% (n = 21) of the patients (11%, n = 6 full doses; 28%, n = 15 half doses) required an additional dose of dNCS. The majority of patients had an ACC time <90 minutes, and only six patients in the dNCSgroup had an ACC time>120 minutes. In these six patients, an additional full dose of dNCS were administered. In patients who had aortic ACC time between 90-120 had half dose dNCS were administered.

Cardioplegia volume was statistically lower in the dNCS group (P<0.001).Another advantage of using single dose dNCS technique is that there is no volume overload and consequently less blood product transfusions are required in the postoperative period. The cardioplegia volume given in repeated doses techniques causes lower Htc values ​​during and after the operation. Htc levels at hours 6 and 24 were significantly higher in the dNCSgroup than in the BC group. Also use of dNCS resulted in less use of blood product transfu­sions than BC.

In our study, there was no significant difference between the patient groups in terms of postoperative complications, except AKI development. After cardiac operations, AKI is seen at a rate of 5-30% and the second most common cause of AKI in intensive care unit is cardiac operations. Many factors such as perfusion times, advanced age, use of positive inotropic agent sand blood transfusion play a role on the development of AKI [25]. In our study we detected statisticaly significant difference between the twogroups in terms of postoperative development of AKI (P= 0.025). The increased use of blood products and longer cross-clamp times in patients whom were given BC may have led to the development of AKI. Inaddition, in a study by Mukdad et al., another advantage of dNCS was demonstrated. They compared the incidence of microembolism during cardiac operations using multi-dose conventional BC (15 patients) and dNCS (15 patients). Microembolism was scanned by monitoring with transcranial Doppler ultrasonography and controlling the middle cerebral artery. In theirstudy, they found that the single-dose dNCS strategy resulted in less cerebral microembolism than traditional multi-dose cardioplegia. The authors stated that this could be due to cardioplegia given in fewer sessions [18]. Microembolism is an important risk factor for the development of AKI. Although wecould not perform Doppler scans in our study, we believe that this parameter should be incorporated into further studies.

There are also some concerns related to dNCS. One of the major problems is that the dNCS solution has about 300 variations of the formula with the same name but with different chemical combinations. In coronary artery disease, a uniform distribution is not guaranteed owing tot he presence of diffuse vessel disease and impaired microcir­culation. Residual potassium due to the high potassium content of dNCS may cause coronary vasoconstriction and consequently complicate myocardial ischemia [4]. Also dNCS has a low nutrient content of 21 kcal/L. An energy-depleted myocardium will be affected by low energy levels [26].

Finally, we think that as the clinical experiences of surgeons and clinics on the use of dNCS in adult cardiac surgery increases, they will feel more confident and will form their personal algorithms for ischemic periods. In our clinical experience, we prefer to use dNCS widely, especially in valvular and aortic surgery.

There were several limitations of our study. Firstly, the sample size was relatively small, and the study was retrospective and singlecentered. Other important limitation was the non-randomised design of the study, in spite of homogeneous patient distribution of groups regarding baseline clinical characteristics. Another limitation of the study was the exclusion of emergency and redosurgery cases.

As a conclusion, in the present study we found that dNCS appears to be safe and even more advantageous in many aspects than other cardioplegia solutions and techniques in adult cardiac surgery operations. In many studies, dNCS has been shown to reduce the aortic cross clamp time, cardiopulmonary bypass time and the volume of cardioplegia solution used, and is equivalent or a safer and superior cardioplegia solutionand technique in terms of myocardial protection than conventional BC. In conclusion, thecurrentstudyresultsshowedthat dNCS can be used as a safe and effective solution even in complex adult cardiac surgery like aortic surgery. However, further multicenter prospective randomized clinical trials are stil required.

**Conflict of Interest**

None

**Funding statement**

None

**Data availability**

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**Author Contributions**Hypothesis generation: CE, Concept/design: CE, ME, Data collection and processing: ME, BE, AKA, Analysis and interpretation: CE, ME, Literature search: CE, ME, BE, AKA, Drafting article: CE, ME, BE, AKA, Critical revision of article: CE, ME, BE, AKA, Approval of article: CE, ME, BE, AKA  
**References**

1.Ad N. Del Nido cardioplegia: ready for prime time in adult cardiac surgery? J Thorac Cardiovasc Surg. 2015;149(2):637-8.

2. Li Y, Lin H, Zhao Y, Li Z, Liu D, Wu X, et al. Del Nido cardioplegia for myocardial protection in adult cardiac surgery: a systematic review and meta-analysis. ASAIO J. 2018;64(3):360-7.

3.Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children’sHospital. J ExtraCorporTechnol. 2012;44(3):98-103.

4.Kim K, Ball C, Grady P, Mick S. Use of del Nido cardioplegia for adult cardiac surgery at the Cleveland Clinic: perfusion implications. J Extra CorporTechnol. 2014;46(4):317-23.

5.O’Brien JD, Howlett SE, Burton HJ, O’Blenes SB, Litz DS, Friesen CL. Pediatric cardioplegia strategy results in enhanced calcium metabolis mand lower serum troponin T. AnnThoracSurg 2009; 87: 1517-1523.

6. Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al; ESC Committee for Practice Guidelines. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2014 Nov 1;35(41):2873-926.

7. O’Blenes SB, Friesen CH, Ali A, Howlett S. Protecting the aged heart during cardiac surgery: the potential benefits of del Nido cardioplegia. J Thorac Cardiovasc Surg. 2011;141:762-70

8. Edelman JJ, Seco M, Dunne B, Matzelle SJ, Murphy M, Joshi P, et al. Custodiol for myocardial protection and preservation: a systematic review. Ann Cardiothorac Surg. 2013;2:717-28

9. Piper HM, Meuter K, Schäfer C. Cellular mechanisms of ischemia-reperfusion injury. Ann Thorac Surg 2003; 75: S644-8.

10. Ad N, Holmes SD, Massimiano PS, et al. Theuse of del Nido cardioplegia in adult cardiac surgery: A prospective randomized trial. J Thorac Cardiovasc Surg 2018;155:1011-8.

11. Dobson GP, Jones MW. Adenosine and lidocaine: a new concept in nondepolarizing surgical myocardial arrest, protection, and preservation. J Thorac Cardiovasc Surg 2004;127(3):794–805

12.Sorabella RA, Akashi H, Yerebakan H et al. Myocardial protection using Del nido cardioplegia solution in adult reoperative aortic valve surgery. J Card Surg 2014; 29: 445-49

13. Vistarini N, Laliberté E, Beauchamp P et al. Del Nido cardioplegia in the setting of minimally invasive aortic valve surgery. Perfusion 2017; 32: 112-17.

14. Kim JS, Jeong JH, Moon SJ, Ahn H, Hwang HY. Sufficient myocardial protection of del Nido cardioplegia regardless of ventricular mass and myocardial ischemic time in adult cardiac surgical patients. J ThoracDis 2016; 8: 2004-10.

15. Kuserli Y, Turkyilmaz S, Turkyilmaz G, Kavala AA. Comparison of del Nido Cardioplegia and Blood Cardioplegia in Aortic Root Surgery. HeartSurg Forum. 2020;23(3): E376-E384

16. Marzouk M, Lafreniere-Bessi V, Dionne S, Simard S, Pigeon C, Dagenais F, et al. Transitioning to Del Nido cardioplegia for all-comers: the next switching gear? BMC CardiovascDisord. 2020;20(1):215

17. An KR, Rahman IA, Tam DY, Ad N, Verma S, Fremes SE, et al. A systematic review and meta-analysis of del Nido versus conventional cardioplegia in adult cardiac surgery. Innovations (Phila). 2019;14(5):385-93.

18.Mukdad L, Toppen W, Sanaiha Y, et al. Incidence of Cerebral Microemboli in Single-Dose vs. Multidose Cardioplegia in Adult Cardiac Surgery. J Extra Corpor Technol. 2018;50(3):143‐148

19.Ristagno G,Wang T, Tang W, Sun S, Castillo C,Weil MH. High-energy defibrillation impairs myocyte contractility and intracellular calcium dynamics. Crit Care Med 2008;36(11, Suppl):S422–S427

20. Mishra P, Jadhav RB, Mohapatra CK, Khandekar J, Raut C, Ammannaya GK, et al. Comparison of del Nido cardioplegia and St. Thomas Hospital solution – two types of cardioplegia in adult cardiac surgery. Kardiochir Torakochirurgia Pol2016;13:295–9

21. Hamad R, Nguyen A, Laliberte´ E´ ,Bouchard D, Lamarche Y, El- Hamamsy I, et al. Comparison of del Nido cardioplegia with blood cardioplegia in adult combined surgery. Innovations (Phila) 2017;12:356–62.

22. Ota T, Yerebakan H, Neely RC, Mongero L, George I, Takayama H, et al. Short-term out comes in adult cardiac surgery in the use of del Nido cardioplegia solution. Perfusion 2016;31:27–33

23. Aksun M, Girgin S, Aksun S, Kestelli M, Bozok S, Yu¨ rekli I, et al. Comparison of intermittent antegrade cardioplegia and antegrade/retrograde continuous cardioplegia in terms of myocardial protection in cardiac surgery. Turk Gogus Kalp Dama 2015;23:26–31

24. Durandy YD. Is there a rationale for short cardioplegia re-dosing intervals? World J Cardiol 2015; 7: 658–664.

25. Harky A, Joshi M, Gupta S, Teoh WY, Gatta F, Snosi M. Acute kidney injury associated with cardiac surgery: a comprehensive literature review. Braz J CardiovascSurg. 2020;35(2):211-24

26. Valooran GJ, Nair SK, Chandrasekharan K, Simon R, Dominic C. del Nido cardioplegia in adult cardiac surgery—scopes and concerns. Perfusion 2016 31:6-14

**Table 1.** Del Nido Cardioplegia Solution (dNCS) and Blood cardioplegia (BC) Contents

| **Content** | **dNCS** | **BC** |
| --- | --- | --- |
| Base solution (mL) | Isolyte-S (1000)\* | Ringer lactate (1000) |
| Mannitol 20% (mL) | 17 | 0 |
| MgSO4 15%(mL) | 14 | 0 |
| NaHCO3 8.4% | 13 | 10 |
| KCL (mEq) | 26 | 16 |
| Lidocaine 2% (mL) | 6.5 | 0 |
| Blood/ Cardioplegia | 1/4 | 4/1 |

\*Original dNCS contains Plasma Lyte A

**Table 2. Demographic datas, preoperative features and preoperative laboratory variables of the patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1**  **(N= 65)** | **Group 2**  **(N= 54)** | **P value** |
| Age(years) | 65.3±8.3 | 66.4±7.5 | 0.470 |
| Male gender, n(%) | 44 (67.7%) | 40 (74%) | 0.398 |
| BMI (kg/m2) | 28.8± 5.5 | 28.2± 2.5 | 0.432 |
| Hypertension, n (%) | 50 (76.9%) | 37 (68.5%) | 0.304 |
| Hiperlipidemia, n(%) | 38 (58.4%) | 32 (59.2%) | 0.896 |
| Diabetes mellitus, n (%) | 27 (41.5%) | 21 (38.8%) | 0.714 |
| COPD, n(%) | 25 (38.4%) | 18 (33.3%) | 0.582 |
| Smoking, n (%) | 33 (50.7%) | 28 (51.8%) | 0.820 |
| CAD, n(%) | 9 (13.8%) | 8 (14.8%) | 0.795 |
| History of CVA | 3 (4.6%) | 2 (3.7%) | 0.704 |
| EuroSCORE II | 7.2±1.5 | 7.5±1.6 | 0.347 |
| Ejection fraction (%) | 51.3±8.3 | 52.7±7.3 | 0.561 |
| White bloodcell (103/µL) | 8.9±2.3 | 9.2±2.4 | 0.755 |
| Hematocrit (%) | 38.9±5.5 | 39.3±7.1 | 0.456 |
| Platelet (103/µL) | 252.5±56.9 | 247.2±59.4 | 0.578 |
| Creatinine, mg/dL | 1.1±0.3 | 0.99±0.28 | 0.376 |
| Urea  Glucose | 21.2±7.3 | 20.8±6.3 | 0.432 |
| C reactive protein (mg/dL) | 9.7± 11.6 | 10.4±10.4 | 0.320 |
| Troponin T, ng/L | 9±4.9 | 8.9±3.9 | 0.935 |

BMI: Body mass index, CAD: Coronary artery disease, CVA: Cerebrovascular accident, COPD: Chronic obstructive pulmonary disease, EuroSCORE II: European System for Cardiac Operative Risk Evaluation II

**Table 3: Operative variables of the patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1**  **N= 65** | **Group 2**  **N= 54** | **P value** |
| Bentall procerdure, n (%) | 32 (49.2%) | 27 (50%) | 0.884 |
| Asendan aort replacement, n (%) | 21 (32.3%) | 17 (31.8%) | 0.923 |
| Wheat procedure, n(%) | 10 (15.3%) | 9 (16.6%) | 0.849 |
| Total arcus replacement | 2 (3%) | 1 (1.8%) | 1.000 |
| Concomitant CABG | 6 (9.2%) | 3 (5.5%) | 0.654 |
| Use of ACP, n(%) | 26 (40%) | 20 (37%) | 0.741 |
| ACP time, minutes | 24.4 ±8.2 | 22.3 ±7.9 | 0.534 |
| Total perfusion time, minutes | 123.9±28.8 | 114.4±27.1 | 0.071 |
| Cross-clamp time, minutes | 87.5±23.2 | 73.3±20.7 | 0.001 |
| Need of defibrillation, n(%) | 45 (69.2%) | 24 (44.4%) | 0.006 |
| In CPB peak glikose | 199±64.8 | 165.7±39.9 | 0.001 |
| Cardioplegia volume (mL) | 2773.8±453.8 | 1323.9±368.5 | <0.001 |

ACP: Antegrade cerebral perfusion, CPB: Cardiopulmonary bypass

**Table 4: Postoperative features of the patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variables** | **Group 1**  **N= 65** | **Group 2**  **N= 54** | **P value** |
| Chest tube drenaige | 446.9±95.1 | 412±73.2 | 0.026 |
| Packed blood products (units) | 4.18±1.9 | 3.56±1.8 | <0.001 |
| Inotropic support, n(%) | 36 (55.3%) | 20 (37%) | 0.046 |
| Intraaortic balon pump need, n(%) | 3 (4.6%) | 2 (3.7%) | 1.000 |
| Troponin T, ng/L (6th hours) | 275.7±76.2 | 203.5±68.6 | <0.001 |
| Troponin T, ng/L (24th hours) | 293.4±80.1 | 253.1±101 | 0.017 |
| Hematocrit (6th hours) | 22.5±2.5 | 25.1±3.2 | <0.001 |
| Hematocrit (24th hours) | 24.6±2.8 | 25.8±2.7 | 0.024 |
| Ventilation time (hours) | 10.6±3.7 | 10.1±3.4 | 0.534 |
| Postoperative EF % | 49.7±8.2 | 50.3±7.5 | 0.714 |
| Total ICU stay (days) | 2.4±0.9 | 2.3±0.6 | 0.165 |
| Total hospitalstay (days) | 7.8±2.2 | 7.6±1.4 | 0.489 |

EF: Ejection fraction, ICU: Intensive care unit

**Table 5: Postoperativecomplications of thepatients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Complications** | **Group 1**  **N= 65** | **Group 2**  **N= 54** | **P value** |
| Mortality, n(%) | 2 (3%) | 2 (3.7%) | 0.851 |
| Cerebrovascular accident, n(%) | 2 (3%) | 1 (1.8%) | 0.671 |
| Infection, n(%) | 1 (1.5%) | 0 | 0.559 |
| Bleeding, n(%) | 4 (%6.1) | 3 (%5.5) | 0.868 |
| Atrial fibrillation, n(%) | 8 (12.3%) | 6 (11.1%) | 0.840 |
| Respiratory failure, n(%) | 1 (1.5%) | 1 (1.8%) | 0.895 |
| Renal injury, n(%) | 18 (27.6%) | 6 (11.1%) | 0.025 |