Journal of The Cardiovascular Thoracic Anaesthesia and Intensive Care Society

GKDA Derg 2022;28(2):135-143
DOI: 10.14744/GKDAD.2022.71501

Research Article / Araştırma

Evaluation of the Effect of Del Nido and Cold Blood Cardioplegia on Renal Functions in the Surgery of Congenital Heart Diseases

Konjenital Kalp Hastalıkları Cerrahisinde Del Nido ve Soğuk Kan Kardiyoplejisinin Böbrek Fonksiyonlarına Etkisinin Değerlendirilmesi

Fatma Ukil Işıldak,[1] Yasemin Yavuz,[1] Sedat Arısüt,[1] Abdullah Arif Yılmaz[2]

[1]**Department of Anesthesia and Reanimation, Istanbul Provincial Health Directorate, Kartal Kosuyolu High Speciality Training and Research Hospital, Istanbul, Türkiye**

İstanbul İl Sağlık Müdürlüğü, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İstanbul, Türkiye

[2]**Department of Cardiovascular Surgery, Istanbul Provincial Health Directorate, Kartal Kosuyolu High Speciality Training and Research Hospital, Istanbul,Türkiye**

İstanbul İl Sağlık Müdürlüğü, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerahisi Anabilim Dalı, İstanbul, Türkiye

ABSTRACT

Objectives: We aimed to evaluate the effect of del Nido (DN) and cold blood (CB) cardioplegia on renal functions in children undergoing cardiac surgery for congenital heart disease (CHD).

Methods: This study was conducted prospectively. One hundred and nineteen pediatric patients with Risk Adjustment for Congenital Heart Surgery (RACHS) scores below 3 were randomly assigned using allocation software to two groups (CB and DN cardioplegia) according to the type of cardioplegia solution used. The change of urea, creatinine, estimated glomerular filtration rate (eGFR), and renal near-infrared spectroscopy (NIRS) values before and after cardioplegia were the primary outcome measures of this study.

Results: Cardiopulmonary bypass (CPB) duration (p<0.001), ACC duration (p<0.001), and extubation time (p=0.032) were longer and the VIS-48th h (p=0.048) value was higher in the DN group. The pre-operative versus 48th h increase in urea were higher in the DN group (p=0.028). The increase in CPB duration was predictive for the increase in urea (p=0.009) and creatinine (p=0.004), and younger age was a predictor for the increase in urea (p=0.014) and decrease in eGFR (p=0.044).

Conclusion: Although CPB duration, aortic cross-clamp times, and extubation times are longer in DN cardioplegia recipients, it is as safe as blood cardioplegia in terms of ICU LOS, mortality rates, VIS-initial and VIS-24th h values, and changing renal NIRS, creatinine, eGFR, and urea values during surgery. There is a need for more extensive research on the use of DN cardioplegia in CHD surgery.

Keywords: Cardiac surgical procedures, cardioplegia, cardioplegic solutions, children, congenital heart disease

ÖZ

Amaç: Çalışmada, konjenital kalp hastalığı nedeniyle kalp cerrahisi geçiren çocuklarda del Nido ve soğuk kan kardiyoplejisinin böbrek fonksiyonlarına etkisinin değerlendirilmesi amaçlandı.

Yöntem: Bu çalışma, prospektif olarak gerçekleştirildi. "Risk Adjustment for Congenital Heart Surgery (RACHS)" skoru 3'ün altında olan 119 pediatrik hasta, gruplandırma yazılımı kullanılarak kardiyopleji solüsyonunun tipine göre rastgele iki gruba (soğuk kan ve del Nido kardiyoplejisi) ayrıldı. Kardiyoplejiden önce ve sonra üre, kreatinin, tahmini glomerüler filtrasyon hızı ve renal yakın kızılötesi spektroskopi değerlerinin değişimi bu çalışmanın birincil sonuç ölçütleriydi.

Bulgular: Del Nido grubunda kardiyopulmoner baypas süresi (p<0,001), aort kros klemp süresi (p<0,001) ve ekstübasyon süresi (p=0,032) daha uzun, VIS-48. saat (p=0,048) değeri daha fazlaydı. Preoperatif değerlere göre 48. saatte üre artışı del Nido grubunda daha yüksekti (p=0,028). Kardiyopulmoner baypas süresindeki artışın üre (p=0,009) ve kreatinin (p=0,004) artışını, daha genç yaşta olmanın ise üre artışı (p=0,014) ve tahmini glomerüler filtrasyon hızındaki düşüşü (p=0,044) öngördüğü belirlendi.

Sonuç: Del Nido kardiyopleji uygulanan olgularda kardiyopulmoner baypas süresi, aort kros klemp süresi ve ekstübasyon süresi daha uzun olmasına rağmen, del Nido kardiyopleji yoğun bakım ünitesinde yatış süresi, mortalite oranları, VIS-başlangıç ve VIS-24. saat değerleri ve cerrahi sırasında renal yakın kızılötesi spektroskopi, kreatinin, tahmini glomerüler filtrasyon hızı ve üre değerlerinin değişimi açısından kan kardiyoplejisi kadar güvenlidir. Del Nido kardiyoplejisinin konjenital kalp hastalığı cerrahisinde kullanımı konusunda daha kapsamlı araştırmalara ihtiyaç vardır.

Anahtar sözcükler: Çocuklar, kalp cerrahisi prosedürleri, kardiyopleji, kardiyoplejik solüsyonlar, konjenital kalp hastalığı

Please cite this article as: "Ukil Işıldak F, Yavuz Y, Arısüt S, Yılmaz AA. Evaluation of the Effect of Del Nido and Cold Blood Cardioplegia on Renal Functions in the Surgery of Congenital Heart Diseases. GKDA Derg. 2022;28(2):135-143".

Address for correspondence: Fatma Ukil Işıldak, MD. İstanbul İl Sağlık Müdürlüğü, Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İstanbul, Türkiye

Phone: +90 505 869 55 80 **E-mail:** ukilfatma@yahoo.com.tr

Submitted Date: February 26, 2022 **Accepted Date:** March 24, 2022 **Available Online Date:** June 10, 2022

Introduction

Congenital heart disease (CHD), one of the most frequently diagnosed congenital disorders, affects approximately 0.8-1.2% of live births worldwide.[1] Cardioplegia is an indication for cardiac surgery and is an indispensable and basic method of myocardial protection for patients of all ages whose hearts need to be stopped during surgery.[2] The main purpose of myocardial protection is to preserve myocardial function by minimizing myocardial metabolism during surgical repair and to stop the heart by creating a bloodless surgical field that will allow cardiac repair to be performed easily. Myocardial protection has been modified over time and different strategies and solutions have been proposed for clinical use. These strategies and solutions vary between countries, institutions, and even between different surgeons in the same institution. In addition to all these developments, the optimal cardioplegia strategy in terms of composition, route, and technique has not yet been scientifically explained.[3]

The del Nido (DN) cardioplegia solution was developed in the 1990s at the University of Pittsburgh.[4] This solution, which causes depolarizing arrest during open-heart surgery, has a more dilute structure than the conventional cardioplegia solution. The DN solution slows down energy consumption by reducing calcium accumulation during myocardial ischemia because it contains lidocaine and magnesium and contains Ca2+ in lower doses.[2]

In previous adult[5-12] and pediatric[13-15] age group studies, DN cardioplegia solution was reported to be safe and effective in cardiac surgery. It has been reported that different perfusion strategies used for cardiopulmonary bypass (CBP) may directly affect pediatric cardiac surgery outcomes.[16] Accordingly, it is important to evaluate the effects of cardioplegia solutions used on renal functions.

The aim of the study was to evaluate the effects of cold blood (CB) cardioplegia and DN cardioplegia solutions on renal functions in children undergoing open-heart surgery.

Methods

This study was conducted prospectively. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Local Ethics Committee approved the study protocol. The purpose and scope of the study were explained in detail to the parents or legal guardians of the patients, and written consent was obtained from those who agreed to participate in the study.

There were 119 pediatric patients aged between 1 and 120 months in the study group with Risk Adjustment for Congenital Heart Surgery (RACHS) scores of <3. Patients with elevation or failure in liver and kidney function tests, severe heart failure, those undergoing emergency surgery, requiring post-operative extracorporeal membrane oxygenator, and in the neonatal period were not included in the study. Patients were assigned to two groups using a randomizer software according to the type of cardioplegia solution used (CB group and DN group). The structure and dosage of the cardioplegia solutions used are summarized in Table 1. The cardioplegia delivery system consisted of a disposable tubing set, cardioplegia bag, cardioplegia reservoir, pump loop, and a cooling coil, as well as a temperature and pressure monitoring area.

The surgical procedures were performed by the same surgical and anesthesia teams using a standard general anesthesia protocol. CPB was used with systemic hypothermia in the heart opened using median sternotomy.

Pre-operative age, sex, height, bodyweight values, and intraoperative urine volume, intake extracted balance, central venous pressure, and blood gas lactate values of the patients were recorded. Pre-operative, post-operative 24 and 48 h creatinine, urea, renal near infrared spectroscopy (NIRS), and vasoactive inotropic score (VIS) values of the patients were recorded. In addition, the extubation time, intensive care unit (ICU) length of stay (LOS), hospital LOS, and the mortality rates of the patients were recorded. The changes in urea, creatinine, eGFR, and renal NIRS values before and after cardioplegia were the primary outcome measures of this study. The comparison between the cardioplegia choices used was made using the pre-operative, post-operative 24th h, and post-operative 48th h values of the measured parameters.

RACHS was used to determine the risk for each patient based on the surgical procedure performed. RACHS is easily applicable and was created to provide an understanding of the differences in mortality between patients undergoing congenital heart surgery. RACHS divides patients into six categories according to the type of surgical procedure to be performed. The higher the category level, the higher the risk of mortality and morbidity.[17] Patients in RACHS categories 1 and 2 were included in the study group.

VISs were calculated by recording the inotropic drugs used by the patients and their doses (VIS: Dopamine dose (mcg/kg/min)+dobutamine dose (mcg/kg/min)+ 100×adrenaline dose (mcg/kg/min)+10×milrinone dose (mcg/kg/min)+ 10,000×vasopressin dose (unit/kg/min) min))+100×noradrenaline dose (mcg/kg/min)).[18]

Height and weight measurements of the children were made using standard measuring instruments. Bodyweight

Table 1. Content and route of cardioplegia solutions

Variables	Cold blood cardioplegia	Del Nido cardioplegia
Route	Antegrade	Antegrade
Ingredients	0.5 mEq/kg 7.5% KCL	4 units of cristalloid* + 1 unit of blood
	0.5 mEq/kg $MgSO_4$	*500 mL isolyte, 8.2 mL mannitol 20%,
	1 mEq/kg $NaHCO_3$	6.6 mL magnesium sulfate 15%, 6.2 mL sodium bicarbonate 8.4%, 13 mL potassium chloride (1 mEq/mL), 3.2 mL lidocaine 2%
Dose	20 cc/kg first dose	20 mL/kg single dose
	10 cc/kg maintenance (repeated every 20 min)	

was measured in the horizontal plane by removing the clothes and diapers (if used) of the children. For older children, measurements were made by removing their clothes and allowing them to stand on a scale. While evaluating the height, children aged 0-2 years were placed on a flat surface without shoes and the measurement was made while they were in the lying position. Height measurements of older children were made in an upright position on a flat surface with their shoes removed. Body mass index (BMI) (kg/m^2) was calculated using height and body weight values.

Statistical Analysis

All analyses were performed using the SPSS v21 software package (SPSS Inc., Chicago, IL, USA). For the normality check, the Kolmogorov-Smirnov test was used. All of the continuous variables were non-normally distributed. Data are given as median (1st quartile-3rd quartile) for continuous variables and as frequency (percentage) for categorical variables. Between-group analyses of continuous variables were performed using the Mann-Whitney U-test. Repeated measurements were analyzed using Friedman's analysis of variance by ranks. Pairwise comparisons were performed using Bonferroni correction. Categorical variables were analyzed using the Chi-square test. Multiple linear regression analyses (stepwise selection) were performed to determine significant factors of the changes in renal injury markers. Two-tailed $p<0.05$ was considered statistically significant.

Results

Of the 119 children in the research group, 50 (42.02%) were girls and 69 (57.98%) were boys. The mean age of the children was 13.82±12.56 months, range, 6-18 months. The frequency of tetralogy of Fallot was significantly higher in the DN group ($p=0.036$). The CPB ($p<0.001$), ACC ($p<0.001$), and extubation times ($p=0.032$) were longer in the DN group. The VIS-48th h value was higher in the DN group ($p=0.048$) (Table 2).

In the CB ($p<0.001$) and DN ($p<0.001$) groups, the measurements of the renal NIRS value during the study period differed significantly. In the CB group, the pre-operative measurement value of the renal NIRS value was lower than in the other measurements. The renal NIRS value after CPB was higher than all except the post-operative value. The post-operative renal NIRS value was higher than the pre-CPB and CPB full flow values.

In the DN group, the pre-operative renal NIRS value was lower than all except before CPB. The renal NIRS value after CPB was higher than all except CPB full flow and post-operative values. The post-operative renal NIRS value was higher than all except the CPB full flow and post-CPB values. The CPB full flow renal NIRS value was higher than the pre-CPB value. Pre-operative and post-operative changes in renal NIRS values were similar between the CB and DN groups ($p=0.902$) (Table 3).

The measurement values of urea in the cardioplegia groups during the study showed a significant difference ($p<0.001$). In the CB group, the 24th and 48th h urea values were higher than the pre-operative and post-operative values. The 48th h urea value was higher than the pre-operative and post-operative urea values in the DN group. The pre-operative versus 48th h change in urea level were higher in the DN group ($p=0.028$) (Table 3 and Fig. 1).

The post-operative and 24th h creatinine values were higher than pre-operative and 48th h values in the CB group ($p<0.001$). In the DN group, pre-operative creatinine value was lower than all other values, and the 24th h creatinine value was higher than the 48th h creatinine value ($p<0.001$). The pre-operative-48th h creatinine change was similar between the groups ($p=0.122$) (Table 3 and Fig. 2).

In the CB group, the pre-operative eGFR value was higher than the post-operative and 24th h eGFR values. In this group, the 48th h eGFR values were higher than the post-operative and 24th h eGFR values ($p<0.001$). The pre-operative eGFR value was higher than other values in the DN cardioplegia group. The 48th h eGFR value of this group was higher than the 24th h value ($p<0.001$). The pre-operative and 48th h change of eGFR was similar in the CB and DN cardioplegia groups ($p=0.403$) (Table 3 and Fig. 3).

We performed multiple linear regression analyses to determine significant factors of the increase in urea levels. We

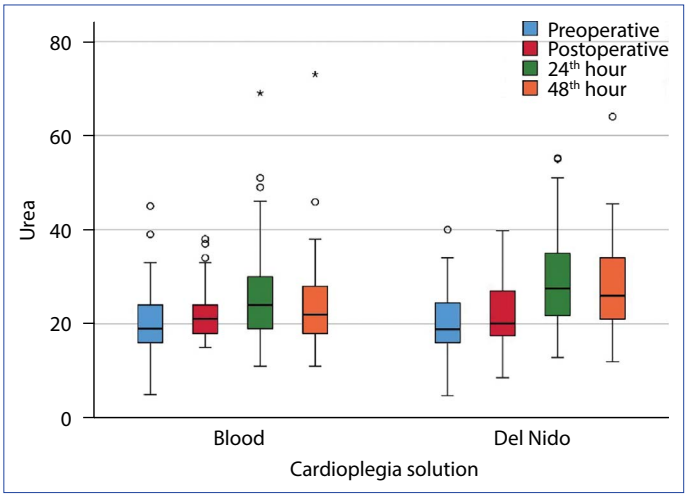

Figure 1. Urea levels according to the groups.

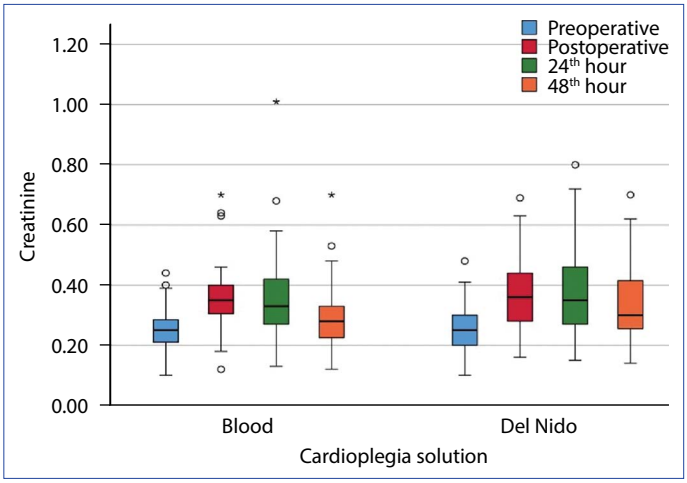

Figure 2. Creatinine levels according to the groups.

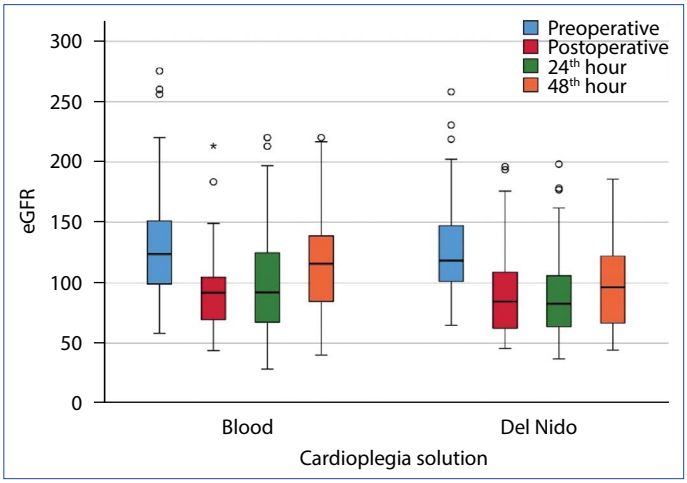

Figure 3. eGFR according to the groups.
eGFR: Estimated glomerular filtration rate.

found that a longer duration of CBP (p=0.009) and lower age (p=0.014) were associated with a greater increase in urea levels. Other variables included in the model, sex (p=0.162), BMI (p=0.061), RACHS (p=0.783), cardioplegia solution type (p=0.396), and aortic cross-clamp (ACC) time (p=0.104) were found to be non-significant (Table 4).

We performed multiple linear regression analyses to determine significant factors of the increase in creatinine levels. We found that a longer duration of CBP (p=0.004) was associated with a greater increase in creatinine levels. Other variables included in the model, age (p=0.081), sex (p=0.475), BMI (p=0.262), RACHS (p=0.183), cardioplegia solution type (p=0.508), and ACC time (p=0.090) were found to be non-significant (Table 5).

We performed multiple linear regression analyses to determine significant factors of the decrease in eGFR. We found that lower age (p=0.044) was associated with a greater decrease in eGFR. Other variables included in the model, sex (p=0.660), BMI (p=0.439), RACHS (p=0.353), cardioplegia solution type (p=0.300), duration of CBP (p=0.107), and ACC time (p=0.188) were found to be non-significant (Table 6).

Discussion

Inadequate myocardial protection can cause myocardial stunning, cell apoptosis, and infarction. Although the search for an ideal cardioplegic solution has been ongoing since the beginning of cardiac surgery, there are no guidelines on the use of any specific solutions.[4] The DN cardioplegia solution seems to be very efficient both in terms of myocardial protection and cost.[4] In this study, we evaluated the results of DN and blood cardioplegia in terms of clinical parameters and renal functions.

In newborns and infants, higher VIS after cardiothoracic surgery is one of the important factors evaluated in the process of congenital heart surgery in terms of prolonging ICU and hospital stay and negatively affecting clinical outcomes.[19] In cases where DN cardioplegia is used, less myocardial damage and lower coronary vascular resistance develop during reperfusion, and superior functional recovery occurs after cardioplegic arrest.[20] Therefore, it is expected that the ACC and CPB times will be shorter and the needed inotropic support will be less in patients undergoing DN cardioplegia. In the study of Işıldak et al.,[21] it was reported that DN cardioplegia provided shorter ACC and CPB times and lower post-operative VIS compared with blood cardioplegia in pediatric patients undergoing surgical repair for CHD. Rushel et al.[22] reported that DN cardioplegia was associated with reduced CPB and ACC times during tetralogy of Fallot repair. In another study comparing DN and blood cardioplegia in pediatric cardiac surgery, it was reported that VIS values at transfer to the ICU and at 24 h were lower in the DN group.[20] In a study by Charette et al.,[13] it was reported that the groups treated with single-dose DN cardioplegia and modi-

Table 2. Summary of patients' characteristics according to the groups

Variables	Cardioplegia solution				p
	Cold blood (n=63)		Del Nido (n=56)		
	n	%	n	%	
Age, months	10	6-18	8	6-15.5	0.575
Sex					
Girl	30	47.62	20	35.71	0.260
Boy	33	52.38	36	64.29	
Height, cm	70 (63-80)		69.5 (62.5-79.5)		0.717
Weight, kg	7.8 (5.6-11)		7.9 (6.2-9.4)		0.955
Body mass index, kg/m^2	14.72 (13.53-16.48)		15.55 (12.77-17.18)		0.668
Diagnosis					
Atrial septal defect	12	19.05	4	7.14	0.103
Ventricular septal defect	36	57.14	23	41.07	0.117
Atrioventricular septal defect	6	9.52	11	19.64	0.189
Tetralogy of Fallot	9	14.29	18	32.14	0.036
Pulmonary stenosis	6	9.52	7	12.50	0.822
Others	11	17.46	6	10.71	0.431
RACHS					
Category 1	10	15.87	4	7.14	0.234
Category 2	53	84.13	52	92.86	
Duration of CPB, minutes	75 (56-105)		122.5 (91-151.5)		<0.001
Duration of ACC, minutes	56 (34-75)		89.5 (67.5-115.5)		<0.001
Extubation time, hours	7.5 (4-19)		11 (6-21)		0.032
Length of stay in ICU, hours	48 (24-94)		72 (45-96)		0.161
Vasoactive-inotropic score					
Initial	8 (7-11)		8 (7-11)		0.724
24th h	6 (0-8)		6.5 (5-8)		0.126
48th h	0 (0-5)		5 (0-6.5)		0.048
Length of stay in hospital, days	6 (4-8)		7 (5-9)		0.308
Mortality	0	0.00	0	0.00	N/A

Data are given as median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables.
RACHS: Risk Adjustment for Congenital Heart Surgery; CPB: Cardiopulmonary bypass; ACC: Aortic cross-clamp.

fied adult multiple-dose cardioplegia solutions were similar in terms of CPB and ACC duration. In a study that compared conventional blood cardioplegia and DN cardioplegia in pediatric cardiac surgery, it was reported that CPB and ACC durations were similar in the two groups.

It has been reported that the VIS values at the time of transfer to the ICU and at the 24th h are lower in the DN group.[20] In another study comparing conventional blood cardioplegia and DN cardioplegia in congenital heart surgery, it was reported that the groups were similar in terms of CPB and ACC durations and inotropic scores.[15] In the present study, the DN cardioplegia group had longer ACC and CPB times and higher VIS-48th h values than the blood cardioplegia group. However, the results of the DN cardioplegia group were similar to the CB cardioplegia group in terms of VIS-initial and VIS-24th h values. The results we found for the DN group are quite different from those of other studies. The fact that the frequency of children with tetralogy of Fallot was significantly higher in the DN cardioplegia group may be among the reasons for this difference. However, possible differences in diagnosis, age, and practice of treating physicians of patients included between the studies may have affected the results.

In this study, no difference was found between the CB and DN cardioplegia groups in terms of ICU LOS, hospital LOS, and mortality distribution. The extubation time was longer in children treated with DN cardioplegia solution. In a study comparing DN and blood cardioplegia in children undergoing pediatric heart surgery, it was reported that the extubation time was longer in the DN cardioplegia group, and the groups were similar in terms of ICU and hospital LOS, similar to our results. In the same study, it was

Table 3. Summary of patients' measurements according to the groups

Variables	Cardioplegia solution				p
	Cold blood (n=63)		Del Nido (n=56)		
	n	%	n	%	
Renal NIRS					
Pre-operative	78	74-84[a]	79	75-81[a]	0.977
After induction of anesthesia	85	80-90[bc]	83	80-89[bc]	0.431
Before CPB	84	80-90[b]	82	78.5-87[ab]	0.057
CPB, full flow	85	80-89[b]	86	83-90.5[cd]	0.175
CPB, 34 degree	88	84-90[bc]	84	79-89[bc]	0.010
After CPB	92	86-95[d]	88.5	84-91.5[d]	0.022
Post-operative	89	83-93[cd]	88	82.5-93.5[d]	0.718
p (within groups)	<0.001		<0.001		
Urea					
Pre-operative	19	16-24[a]	18.8	16-24.44[a]	0.759
Post-operative	21.1	18-24[a]	20.1	17.5-27[a]	0.831
24th h	24	19-30[b]	27.5	21.77-35[b]	0.038
48th h	22	18-28[ab]	26	21-34[b]	0.016
p (within groups)	<0.001		<0.001		
Creatinine					
Pre-operative	0.25 (0.21-0.29)[a]		0.25 (0.20-0.30)[a]		0.968
Post-operative	0.35 (0.30-0.40)[b]		0.36 (0.28-0.44)[bc]		0.556
24th h	0.33 (0.27-0.42)[b]		0.35 (0.27-0.46)[c]		0.364
48th h	0.28 (0.22-0.34)[a]		0.30 (0.26-0.42)[b]		0.090
p (within groups)	<0.001		<0.001		
eGFR					
Pre-operative	123.90 (97.18-151.43)[a]		118.55 (101.09-147.37)[a]		0.639
Post-operative	91.78 (68.83-105.25)[b]		84.51 (62.45-108.83)[bc]		0.280
24th h	92.04 (67.38-125.87)[b]		82.60 (63.85-106.00)[c]		0.140
48th h	115.64 (83.93-140.13)[a]		96.34 (66.67-122.15)[b]		0.038
p (within groups)	<0.001		<0.001		
Urine output, mL					
Intraoperative	340 (205-500)		365 (212.5-540)		0.678
1st day	800 (600-1000)		727 (517.5-861)		0.145
2nd day	715 (600-895)		700 (500-827.5)		0.212
Urine output, mL/kg/hr					
1st day	4.13 (3.30-5.12)		3.68 (2.90-5.06)		0.316
2nd day	3.91 (2.92-4.94)		3.68 (2.75-4.5)		0.297
Fluid balance					
1st day	0 (−150-50)		27 (−86-100)		0.192
2nd day	20 (−100-60)		50 (−25-100)		0.080

Data are given as median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables. Same letters denote the lack of statistically significant difference between repeated measurements. NIRS: Near-infrared spectroscopy; CPB: Cardiopulmonary bypass; eGFR: Estimated glomerular filtration rate.

reported that no mortality was observed.[21] Similarly, in a study conducted with adult patients, it was reported that the duration of intubation was significantly longer in the DN group, but the blood and DN cardioplegia groups were similar in terms of ICU and hospital LOS.[23] Panigrahi et al.[20] reported that mechanical ventilation, and ICU and hospital LOS were similar in the conventional blood and DN cardioplegia groups in pediatric cardiac surgery. Pourmoghadam et al.[15] reported that the hospital LOS and mortality rates were similar between groups that underwent DN and blood cardioplegia in pediatric cardiac surgery. According to our results, although the DN cardioplegia solution was found

Table 4. Significant factors of the increase in urea levels, multiple linear regression analysis

Variables	Unstandardized β	Standard error	Standardized β	p	95.0% confidence interval for β	
(Constant)	2.876	2.605		0.272	-2.283	8.036
CPB	0.053	0.020	0.235	0.009	0.014	0.093
Age	-0.195	0.078	-0.220	0.014	-0.349	-0.041

Dependent variable: Increase in urea levels (pre-operative vs. 48th h), R^2=0.111, F=7.258, p=0.001. CPB: Cardiopulmonary bypass.

Table 5. Significant factors of the increase in creatinine levels, multiple linear regression analysis

Variables	Unstandardized β	Standard error	Standardized β	p	95.0% confidence interval for β	
(Constant)	-0.006	0.026		0.812	-0.057	0.045
CPB	0.001	0.000	0.263	0.004	0.000	0.001

Dependent variable: Increase in creatinine levels (pre-operative vs. 48th h), R^2=0.069, F=8.687, p=0.004. CPB: Cardiopulmonary bypass.

Table 6. Significant factors of the decrease in eGFR, multiple linear regression analysis

Variables	Unstandardized β	Standard error	Standardized β	p	95.0% confidence interval for β	
(Constant)	28.838	5.594		<0.001	17.759	39.916
Age	-0.611	0.300	-0.185	0.044	-1.205	-0.016

Dependent variable: Decrease in eGFR (pre-operative vs. 48th h), R^2=0.034, F=4.141, p=0.044. eGFR: Estimated glomerular filtration rate.

to be associated with longer myocardial ischemic times, it did not seem to cause an increase in ICU and hospital LOS and mortality values. It may be said that DN cardioplegia can be used as safely as blood cardioplegia in CHD surgery.

Early detection of post-surgical acute kidney injury (AKI) can reduce morbidity and mortality from AKI with appropriate intervention. Furthermore, surgical success can be increased by administering treatment for the underlying condition causing AKI. Serum creatinine and urea levels are the most commonly used parameters for diagnosing AKI.[24] However, due to the delayed rise of these parameters, there is a need to investigate different parameters that may predict AKI in the early period. Monitoring of NIRS allows real-time monitoring of tissue saturation non-invasively. Renal NIRS has been shown to be significant in predicting the development of AKI after pediatric cardiac surgery in the early post-operative period.[25] In studies evaluating the effects of the DN cardioplegia solution and blood cardioplegia on renal functions in adults, it was reported that no difference was found between the groups in terms of acute renal failure.[26-29] In the present study, we evaluated the renal function outcomes of DN and CB cardioplegia in children who underwent open-heart surgery for CHDs. In the present study, the changes in renal NIRS, creatinine, and eGFR were similar in the pre-operative and post-operative 48th h groups in the DN and CB cardioplegia groups. The increase in urea during surgery was higher in children who received DN cardioplegia. However, the type of cardioplegia solution used was not one of the independent determinants of the increase in urea. The increase in CPB duration was an independent predictor of the increase in urea and creatinine. Younger age was a determinant of an increase in urea and a decrease in eGFR, independent of other factors. The use of DN cardioplegia in pediatric cardiac surgery is safe in terms of renal functions including urea, renal NIRS, creatinine, and eGFR changes. No other study could be found in the literature on the effect of DN and CB cardioplegia on renal functions in children who underwent open-heart surgery due to CHDs.

Limitations

This study has several limitations. One is that the study was conducted in a single center with a limited number of patients. This prevents the generalizability of the results to the population. Another limitation was that patients with higher RACHS scores were not included in the study. Therefore, our results cannot be generalized to higher-risk pediatric age groups. The heterogeneous nature of the patients in our study group with a wide range of CHD diagnoses is another limitation that limits the comparability of the groups.

Despite these, our study is remarkable in that it is the first to share detailed results about renal functions of DN and CB cardioplegia in children undergoing surgery for CHDs.

Conclusion

DN cardioplegia provides effective cardioplegic arrest required for congenital heart surgery in the pediatric age group. It can be said that DN cardioplegia is as safe as blood cardioplegia in pediatric congenital heart surgery in terms of ICU and hospital LOS, mortality, VIS-initial and VIS-24th h values, and pre-post-operative change of renal NIRS, creatinine, eGFR, urea values, and pre- and post-operative change in renal NIRS, creatinine, eGFR, and urea values. Although CPB, ACC, and extubation times are longer in recipients of DN cardioplegia, it seems that this effect does not lead to an adverse outcome in terms of renal functions and other clinical parameters. It would be beneficial to conduct more comprehensive, randomized controlled and multicenter studies to detect differences in clinical outcomes related to DN cardioplegia and blood cardioplegia.

Disclosures

Ethics Committee Approval: The study was approved by The Kartal Kosuyolu High Speciality Training and Research Hospital Clinical Research Ethics Committee (Date: 08/12/2020, No: 2020/13/393).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – F.U.I., Y.Y.; Design – Y.Y., S.A.; Supervision – S.A., A.A.Y.; Fundings – A.A.Y., Y.Y.; Materials – F.U.I.; Data collection &/or processing – Y.Y., F.U.I.; Analysis and/or interpretation – S.A., A.A.Y.; Literature search – F.U.I., A.A.Y.; Writing – F.U.I., S.A.; Critical review – S.A., A.A.Y.

Etik Kurul Onayı: Çalışma Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu tarafından onaylandı (Tarih: 08/12/2020, Numara: 2020/13/393).

Hasta Onamı: Hastalardan yazılı onam alınmıştır.

Hakem değerlendirmesi: Dışarıdan hakemli.

Çıkar Çatışması: Çıkar çatışması bulunmamaktadır.

Finansal Destek: Yazarlar bu çalışmanın herhangi bir finansal destek almadığını beyan etmişlerdir.

Yazarlık Katkıları: Fikir – F.U.I., Y.Y.; Tasarım – Y.Y., S.A.; Denetmeler – S.A., A.A.Y.; Kaynaklar – A.A.Y., Y.Y.; Malzemeler – F.U.I.; Veri Toplanması ve/veya İşlemesi – Y.Y., F.U.I.; Analiz ve/veya Yorum – S.A., A.A.Y.; Literatür Taraması – F.U.I., A.A.Y.; Yazıyı Yazan – F.U.I., S.A.; Eleştirel İnceleme – S.A., A.A.Y.

References

1. Wu W, He J, Shao X. Incidence and mortality trend of congenital heart disease at the global, regional, and national level, 1990-2017. Medicine (Baltimore) 2020;99:e20593.
2. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital. J Extra Corpor Technol 2012;44:98–103.
3. Caneo LF, Matte GS, R Turquetto AL, Pegollo LMC, Amato Miglioli MC, T de Souza G, et al. Initial experience with del nido cardioplegia solution at a pediatric and congenital cardiac surgery program in Brazil. Perfusion 2021:2676591211020471.
4. Sanetra K, Pawlak I, Cisowski M. Del Nido cardioplegia - what is the current evidence? Kardiochir Torakochirurgia Pol 2018;15:114–8.
5. Ad N, Holmes SD, Massimiano PS, Rongione AJ, Fornaresio LM, Fitzgerald D. The use of del Nido cardioplegia in adult cardiac surgery: A prospective randomized trial. J Thorac Cardiovasc Surg 2018;155:1011–8.
6. Yerebakan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, et al. Del Nido Cardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: A propensity matched comparison. J Cardiothorac Surg 2014;9:141.
7. Timek T, Willekes C, Hulme O, Himelhoch B, Nadeau D, Borgman A, et al. Propensity matched analysis of del nido cardioplegia in adult coronary artery bypass grafting: Initial experience with 100 consecutive patients. Ann Thorac Surg 2016;101:2237–41.
8. Smigla G, Jaquiss R, Walczak R, Bonadonna D, Kaemmer D, Schwimer C, et al. Assessing the safety of del Nido cardioplegia solution in adult congenital cases. Perfusion 2014;29:554–8.
9. Ota T, Yerebakan H, Neely RC, Mongero L, George I, Takayama H, et al. Short-term outcomes in adult cardiac surgery in the use of del Nido cardioplegia solution. Perfusion 2016;31:27–33.
10. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. J Thorac Cardiovasc Surg 2015;149:626–36.
11. Guajardo Salinas GE, Nutt R, Rodriguez-Araujo G. Del Nido cardioplegia in low risk adults undergoing first time coronary artery bypass surgery. Perfusion 2017;32:68–73.
12. Sorabella RA, Akashi H, Yerebakan H, Najjar M, Mannan A, Williams MR, et al. Myocardial protection using del nido cardioplegia solution in adult reoperative aortic valve surgery. J Card Surg 2014;29:445–9.
13. Charette K, Gerrah R, Quaegebeur J, Chen J, Riley D, Mongero L, et al. Single dose myocardial protection technique utilizing del Nido cardioplegia solution during congenital heart surgery procedures. Perfusion 2012;27:98–103.
14. Kotani Y, Tweddell J, Gruber P, Pizarro C, Austin EH 3rd, Woods RK, et al. Current cardioplegia practice in pediatric cardiac surgery: A North American multiinstitutional survey. Ann Thorac Surg 2013;96:923–9.

15. Pourmoghadam KK, Ruzmetov M, O'Brien MC, Piggott KD, Plancher G, Narasimhulu SS, et al. Comparing del Nido and conventional cardioplegia in infants and neonates in congenital heart surgery. Ann Thorac Surg 2017;103:1550–6.
16. Medikonda R, Ong CS, Wadia R, Goswami D, Schwartz J, Wolff L, et al. Trends and updates on cardiopulmonary bypass setup in pediatric cardiac surgery. J Cardiothorac Vasc Anesth 2019;33:2804–13.
17. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. J Thorac Cardiovasc Surg 2002;123:110–8.
18. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11:234–8.
19. Davidson J, Tong S, Hancock H, Hauck A, da Cruz E, Kaufman J. Prospective validation of the vasoactive-inotropic score and correlation to short-term outcomes in neonates and infants after cardiothoracic surgery. Intensive Care Med 2012;38:1184–90.
20. Panigrahi D, Roychowdhury S, Guhabiswas R, Rupert E, Das M, Narayan P. Myocardial protection following del Nido cardioplegia in pediatric cardiac surgery. Asian Cardiovasc Thorac Ann 2018;26:267–72.
21. Isildak FU, Yavuz Y. Comparison of Del Nido and blood cardioplegia in pediatric patients undergoing surgical repair for congenital heart disease. Pediatr Cardiol 2021;42:1388–93.
22. Rushel KZ, Hoque A, Alamgir MK, Islam MZ, Hasan KA, Rahman MR, et al. Comparative study between the use of multidose standard cardioplegia and long acting Del Nido cardioplegia during Intracardiac repair for tetralogy of fallot in pediatric patients. Mymensingh Med J 2018;27:610–6.
23. Kavala AA, Turkyilmaz S. Comparison of del Nido cardioplegia with blood cardioplegia in coronary artery bypass grafting combined with mitral valve replacement. Braz J Cardiovasc Surg 2018;33:496–504.
24. Lu HY, Ning XY, Chen YQ, Han SJ, Chi P, Zhu SN, et al. Predictive value of serum creatinine, blood urea nitrogen, uric acid, and β2-Microglobulin in the evaluation of acute kidney injury after orthotopic liver transplantation. Chin Med J (Engl) 2018;131:1059–66.
25. Hazle MA, Gajarski RJ, Aiyagari R, Yu S, Abraham A, Donohue J, et al. Urinary biomarkers and renal near-infrared spectroscopy predict intensive care unit outcomes after cardiac surgery in infants younger than 6 months of age. J Thorac Cardiovasc Surg 2013;146:861–7.e1.
26. Hamad R, Nguyen A, Laliberté É, 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.
27. Kuserli Y, Turkyilmaz S, Turkyilmaz G, Kavala AA. Comparison of del Nido cardioplegia and blood cardioplegia in aortic root surgery. Heart Surg Forum 2020;23:E376–84.
28. Luo H, Qi X, Shi H, Zhao H, Liu C, Chen H, et al. Single-dose del Nido cardioplegia used in adult minimally invasive valve surgery. J Thorac Dis 2019;11:2373–82.
29. Lafci A, Gokcinar D, Budak AB, McCusker K, Dag O, Günaydin S. Comparison of metabolic effects of del Nido cardioplegia, blood cardioplegia, and St. Thomas cardioplegia solutions in adult patients undergoing isolated minimally invasive aortic valve replacement surgery. Turk J Clin Lab 2018;9:260–5.