# Effect of Del Nido Cardioplegia Versus Plegisol Solution on Myocardial Protection in Cardiopulmonary Bypass

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AIM: This study aimed to compare the efficacy of the routinely used modified del Nido cardioplegia and Plegisol® solution in myocardial protection.

METHODS: In this retrospective study, patients who underwent cardiopulmonary bypass (CPB) guided cardiac surgery and received del Nido cardioplegia solution (Group 1) and Plegisol® solution (Group 2) were compared in terms of early clinical data and myocardial protection.

RESULTS: This study included 68 patients with similar demographic characteristics who received 38 modified del Nido cardioplegia and 30 Plegisol® solutions. Creatine kinase-myocardial bound (CK-MB) and cardiac troponin T (CTnT) levels on postoperative day 1 and CTnT levels on postoperative day 5 were higher in Group 2 and there was a significant difference between the groups (p = 0.025, p = 0.001, p = 0.001, respectively). In addition, the postoperative inotrope requirement and postoperative vasoactive-inotropic score were higher in Group 2 and there was a significant difference between the two groups (p = 0.004, p = 0.002, respectively).

CONCLUSIONS: In this study, the del Nido cardioplegia solution was found to be more advantageous regarding the need for intracardiac defibrillation and myocardial necrosis, although it showed similar results in some points when compared with the Plegisol® solution.

Keywords: cardiopulmonary bypass; del Nido cardioplegia; plegisol; myocardial protection

# Introduction

Heart diseases have an important place among the causes of morbidity and mortality worldwide [1]. Cardiopulmonary bypass (CPB) remains important in the surgical treatment of these diseases. A bloodless and immobilized environment is required for CPB-guided cardiac surgery. For this, the heart must be temporarily stopped during the operation. Various cardioplegia solutions are used to perform this procedure [2,3].

Cardioplegia is critical to reduce myocardial oxygen demand and minimize ischaemic damage during CPB. Cardioplegia provides this protection by stopping the electrical activity of the heart muscle and cooling it. In addition, it contributes to the success of the operation by keeping the surgical field bleeding and immobilised. Cardioplegia can be applied in many ways, such as antegrade and retrograde administration routes, solution content, temperature, indications, side effects, pharmacokinetics and pharmacodynamics [4].

Cardioplegia solutions may have various disadvantages as well as advantages. Myocardial ischemia during elective arrest and subsequent ischemia/reperfusion injury are the most important adverse effects of CPB and have not yet been fully resolved. To minimize the consequences of myocardial ischemia/reperfusion injury during cardiac surgery, some protective methods have been tried to be applied. The most important of these is cardioplegia administration [5]. However, there are differences in the application and types of cardioplegia, and discussions on this subject continue [5,6].

Cardioplegia methods commonly used for myocardial protection include del Nido cardioplegia and Plegisol® solution. Del Nido cardioplegia is an extracellular solution mixed with autologous blood from the extracorporeal circuit and is administered as a single dose. Several studies involving cardiac operations performed with del Nido cardioplegia show that it is a safer and superior cardioplegia solution and technique in terms of aortic cross-clamping time, total perfusion time, required cardioplegia solution volume, cardiac and many organ and biochemical parameters [6–9]. The term 'modified del Nido' refers to a varia-

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Original del Nido cardioplegia solution		Modified del Nido cardioplegia solution		
Content	Volume	Content	Volume	
Plasma-lyte A	1000 mL	Balanced electrolyte solution	1000 mL	
Mannitol 20%	16.3 mL	Mannitol 20%	17 mL	
MgSO4 50%	4 mL	MgSO4 15%	14 mL	
NaHCO3 8.4%	13 mL	NaHCO3 8.4%	13 mL	
KCL 2 mEq/mL	13 mL	KCL 1 mEq/mL (7.5%)	26 mL	
Lidocaine 1%	13 mL	Aritmal (lidocaine) 2%	6.5 mL	
Patient blood	200 mL (20% of del Nido	Patient blood	200 mL (20% of del Nido	
	cardioplegia solution)		cardioplegia solution)	

Table 1. Original and modified del Nido cardioplegia solution contents.

MgSO<sub>4</sub>, Magnesium Sulphate; NaHCO<sub>3</sub>, Sodium Bicarbonate; KCL, Potassium Chloride.

tion of the original del Nido cardioplegia solution originally developed for paediatric cardiac surgery but later adapted to adult patients [9–11]. The differences between the modified del Nido cardioplegia formulation used in our study and the original del Nido formulation are shown in Table 1 [9–11]. Plegisol®, which is a multidose solution, is an aqueous ion solution similar to extracellular fluid [12].

This study aimed to compare the efficacy of the routinely used modified del Nido cardioplegia and Plegisol® solution in myocardial protection.

# **Materials and Methods**

#### Type of Research

This study is a retrospective cohort-type clinical research. In this study, approval was obtained from the institution and the local ethics committee before the study (Harran University Clinical Research Ethics Committee) (Date: 27 May 2024 - Approval no: HRÜ/24.07.10). The study was conducted following the principles of the Declaration of Helsinki. Since only anonymized patient data was used and there was no risk or impact on patient care, informed consent was not required. This consent waiver was approved by the Institutional Review Board and Ethics Committee and complies with regulatory and ethical guidelines for retrospective studies.

#### **Research** Population

In this retrospective study, a total of 68 patients who underwent CPB-guided cardiac surgery (coronary artery bypass graft (CABG) replacement, mechanical mitral valve, and mechanical aortic valve replacement) between 1 January 2024 and 15 May 2024 were included. A total of 127 cardiac surgery operations were performed during this period. After the exclusion criteria, 68 consecutive patients were included in the study (Fig. 1).

The sample size of the groups in this study was calculated using a website at https://www.stat.ubc.ca/~rollin/stats/ssiz e/n2.html. Type I error rate was accepted as maximum 5% and Type II error rate was accepted as maximum 20%. The effect size of the study was determined as  $\geq 0.5$ .

#### Exclusion and Inclusion Criteria

Patients who underwent emergency surgery, patients with planned additional cardiac surgery such as aortic aneurysm or dissection, reoperations, patients with chronic autoimmune disease, systemic inflammatory disease, chronic renal and hepatic diseases, hematological disease, and history of atrial fibrillation (AF) were excluded. After applying exclusion criteria, adult patients aged 20–85 years who underwent consecutive CPB-guided cardiac surgery using Plegisol® or del Nido cardioplegia were included in the study (Fig. 1). Inclusion criteria also included that all included patients had complete clinical data.

#### Formation of Groups

In this study, patients who received del Nido cardioplegia solution in CPB-guided cardiac surgery operations were determined as the first group (Group 1) and patients who received Plegisol® solution were determined as the second group (Group 2).

#### Cardiopulmonary Bypass (Perfusion) Method

Extracorporeal circulation blood flow rates of the patients during CPB were determined according to their body surface areas (2.4 L/min/m<sup>2</sup>). Appropriate cannula diameters were used according to the body surface area of the patient. A membrane oxygenator with arterial filter integrated into the oxygenator was used. Tubing sets and membrane oxygenators suitable for the patient's age and weight were also used. Tubing set venous line diameter was 1/2 inch and arterial line diameter was 3/8 inch. All patients were subjected to 32 °C hypothermia during CPB. Arterial line pressures were maintained between 150-180 mmHg on average during CPB. Anticoagulation was monitored by active clotting time (ACT) and kept at 480 seconds and above. As prime solution, 150 mL of 20% mannitol, 5 thousand units of heparin and 2 g of cefazolin were used in 1200 mL of balanced solution (Isolayte).

#### Plegisol<sup>®</sup> Solution

Plegisol® solution +4 °C was used. Plegisol® was used as a ready-to-use market product in polyvinyl chloride (PVC)





#### Fig. 1. Flowchart of the study.

bags in plastic casings. The 1000 mL solution contained 6.43 mg sodium chloride, 0.176 mg calcium chloride dihydrate, 3.253 mg magnesium chloride (as magnesium chloride hexahydrate), and 1.193 mg potassium chloride granules. It was used by adding 20 mL of sodium bicarbonate with a ratio of 8.4% in each use. The initial dose of cardioplegia was 15 mL/kg (full dose) and maintenance doses were administered as half dose every 20 minutes.

#### Modified Del Nido Cardioplegia Solution

Modified del Nido cardioplegia solution was used at +4 °C. A single dose of 20 mL/kg solution was used with a maximum dose of 1000 mL. In cases with aortic cross-clamping time over 90 minutes, a maintenance half dose was administered at 60 minutes. The solution was prepared by adding 17 mL 20% mannitol, 14 mL 15% magnesium sulfate, 13 mL 8.4% sodium bicarbonate, 26 mL 7.5% potassium chloride, and 6.5 mL 2% aritmal (lidocaine) to a balanced isolate solution (ratio: 8/10) and oxygenated patient blood (ratio: 2/10).

### Data Collection

The data of patients who underwent CPB-guided cardiac surgery were recorded preoperatively, intraoperatively, and postoperatively after the exclusion criteria were applied. Demographic data, preoperative, intraoperative, and early postoperative data of the patients to be included in the study were recorded. Descriptive data of the groups with the obtained data: Age, gender, height, weight, body surface area (BSA), cigarette smoking, hypertension, chronic obstructive pulmonary disease (COPD), diabetes and hyperlipidaemia, preoperative ejection fraction percentage (EF%); Intraoperative data: Flow, aortic cross-clamp time, total perfusion time, and type of surgery performed (CABG, aortic valve, mitral valve) and preoperative variables: Intracardiac defibrillation requirement, pacemaker requirement, Intra Aortic Balloon Pump requirement, inotropic support requirement after cross-clamping and during intensive care unit (ICU) stay and length of hospital stay rate data were recorded. Biochemical parameters including creatine kinase-myocardial bound (CK-MB) and cardiac troponin T

(CTnT) levels, which are indicators of myocardial necrosis, and carbohydrate reactive protein (CRP) levels, which are indicators of inflammation, were recorded preoperatively, and on postoperative days 1 and 5.

In addition, the vasotropic inotropic score was used to evaluate the need for inotropic support. The vasotropic inotropic score is obtained by multiplying the doses of certain drugs (dopamine, dobutamine, epinephrine, milrinone, vasopressin and norepinephrine) by certain coefficients and summing them. A higher vasotropic inotropic score indicates the need for more intensive vasopressor and inotropic support. Vasotropic inotropic score was calculated according to the following formula.

Vasotropic inotropic score: [milrinone dose (mcg/kg/min  $\times$  10)] + [epinephrine dose (mcg/kg/min)  $\times$  100] + [norepinephrine dose (mcg/kg/min)  $\times$  100] + [vasopressin dose (u/kg/min)  $\times$  10.000] + [dopamine dose (mcg/kg/min)] + [dobutamine dose (mcg/kg/min)].

#### Statistical Analyses

Statistical analyses in this study were performed using the SPSS® 17.0 computer program (version 17.0, SPSS, Chicago, IL, USA). Means and standard deviations were calculated for continuous values. To assess normality distribution, Kolmogorov Smirnov test was used for the group with more than 30 patients and Shapiro-Wilk test was used for the group with less than 30 patients. Student's *t*-test (Independent sample *t*-test) and Mann-Whitney U tests were used to assess normal and non-normally distributed data. Frequency and percentage analyses were performed for nominal data and the Chi-square test and Chi-square corrected test were used for comparison. A 'p' value less than 0.05 was considered statistically significant.

#### Results

This study included 68 patients with similar demographic characteristics who received 38 modified del Nido cardioplegia (Group 1) and 30 Plegisol® solutions (Group 2). The groups had similar age (p = 0.516), gender (p = 0.446), type of surgical procedure (p = 0.892), height (p = 0.133), weight (p = 0.363), BSA (p = 0.341), cigarette smoking (p = 0.398), hypertension (p = 0.189), COPD (p = 0.899), diabetes (p = 0.649), hyperlipidaemia (p = 0.764), flow (p = 0.560), preoperative % EF (p = 0.066), total perfusion time during CPB (p = 0.265) and aortic cross-clamp times (p = 0.154) (Table 2).

Preoperative CRP, CK-MB and CTnT values of the groups were similar (p = 0.791, p = 0.643, p = 0.553, respectively). In addition, CRP levels on postoperative day 1 and day 5 and CK-MB levels on postoperative day 5 were similar (p = 0.702, p = 0.288, p = 0.503, respectively). However, CK-MB and CTnT levels on postoperative day 1 and CTnT levels on postoperative day 5 were higher in Group 2 and there was a significant difference between the groups (p = 0.025, p = 0.001, p = 0.001, respectively) (Table 3). In this study, pacemaker requirement (p = 0.741), intracardiac defibrillation requirement (p = 0.737), ICU inotrope requirement (p = 1.000) and Intra Aortic Balloon Pump (IABP) requirement (p = 1.000), ICU vasoactive-inotropic score (p = 0.429), extubation time (p = 0.138), ICU length of stay (p = 0.440) and hospital stay rates (p = 0.309) were similar among the early clinical outcomes of the groups. However, postoperative inotrope requirement and postoperative vasoactive-inotropic score were higher in Group 2 and there was a significant difference between the two groups (p =0.004, p = 0.002, respectively) (Table 4).

#### Discussion

Myocardial protection is of great importance in open heart surgery. In this study, we compared del Nido cardioplegia solution and Plegisol® solution, which are two different cardioplegies used for myocardial protection in CPBguided cardiac surgery. In our study, we found that the need for pacemaker, need for intracardiac defibrillation, need for ICU inotropes, need for IABP, duration of intubation, duration of ICU and duration of hospital stay were similar in the early clinical results of patients using del Nido cardioplegia solution and Plegisol® solution. However, the groups were similar in terms of the need for intracardiac defibrillation. In addition, while the groups showed similar results in terms of CRP, which is an indicator of inflammation, we found that Group 1, i.e., del Nido cardioplegia group was lower in terms of CK-MB and CTnT levels, which are indicators of myocardial necrosis.

In the comparison of standard del Nido cardioplegia solution and modified del Nido cardioplegia solution with plain ringer's solution as the base solution, it was reported that the changes between the two groups were similar. It was also reported that ventricular arrhythmias, duration of mechanical ventilation, duration of ICU stay, duration of hospital stay, interleukin-6, tumor necrosis factor-alpha, troponinalpha, and electron microscopy changes after aortic crossclamping were similar between the groups. In addition, other metrics indicating myocardial protection were similar between the groups. In developing countries where standard del Nido cardioplegia solution is unavailable or expensive, modified del Nido cardioplegia solution is an acceptable alternative [13]. In another study, it was reported that modified del Nido cardioplegia solution and Custodiol® cardioplegia provided equivalent protection in minimally invasive mitral valve surgery [14].

Many studies on the use of del Nido cardioplegia solution in cardiac surgery show that this method is safer and superior to conventional methods in terms of aortic crossclamping time, CPB time, amount of cardioplegia solution used, and biochemical values in the heart and other organs [7–9]. A systematic review and meta-analysis examining del Nido cardioplegia for myocardial protection in adult cardiac surgery revealed that del Nido reduced postoperative cardiac enzyme levels (CTnT and CK-MB), CPB time,

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Variables		Group 1 (n = 38)	Group 2 (n = 30)	Test statistics	р
Age (year) (mean $\pm$ SD)		$62.97 \pm 8.41$	$64.36\pm9.12$	-0.653	0.516 <sup>a</sup>
$C_{\rm exp} \log \left( a \cdot \theta_{\rm c} \right)$	Female	18, (47.4)	17, (56.7)	0.590	0.446 <sup>b</sup>
Gender (n, %)	Male	20, (52.6)	13, (43.3)	0.580	
	CABGX1	1, (2.6)	2, (6.7)		
	CABGX2	5, (13.2)	3, (10.0)		0.892 <sup>b</sup>
Type of survival are assure (n. 9/)	CABGX3	12, (31.6)	9, (30.0)	1 677	
Type of surgical procedure (n, %)	CABGX4	10, (26.3)	10, (33.3)	1.077	
	AVR	8, (21.1)	4, (13.3)		
	MVR	2, (5.3)	2, (6.7)		
Cigaratte emplaire $(n, \theta')$	None	27, (71.1)	24, (80.0)	0.716	$0.398^{b}$
Cigarette smoking (n, %)	Yes	11, (28.9)	6, (20.0)	0.710	
University (n. 9/)	None	10, (26.3)	4, (13.3)	1 739	0.189 <sup>b</sup>
Hypertension (II, 76)	Yes	28, (73.7)	26, (86.7)	1.728	
COPD (n %)	None	34, (89.5)	28, (93.3)	0.016	0.899 <sup>c</sup>
COPD (fi, %)	Yes	4, (10.5)	2, (6.7)	0.010	
Dispetes $(n, \theta')$	None	22, (57.9)	19, (63.3)	0.207	$0.649^{b}$
Diabetes (fi, 76)	Yes	16, (42.1)	11, (36.7)	0.207	
Hyperlinideemie (n. %)	None	24, (63.2)	20, (66.7)	0.000	0.764 <sup>b</sup>
Hypernpidaenna (n, 76)	Yes	14, (36.8)	10, (33.3)	0.090	
Height (cm) (mean $\pm$ SD)		$170.71\pm9.47$	$167.13\pm9.83$	1.521	$0.133^{a}$
Weight (kg) (mean $\pm$ SD)		$76.52\pm10.51$	$79.20\pm13.55$	-0.916	$0.363^{a}$
BSA (mean $\pm$ SD)		$1.83\pm0.15$	$1.87\pm0.20$	-0.959	$0.341^{a}$
Flow (L) (mean $\pm$ SD)		$4.44\pm0.36$	$4.50\pm0.46$	-0.586	$0.560^a$
Preoperative % EF (mean $\pm$ SD)		$50.26\pm8.53$	$46.16\pm9.53$	1.866	$0.066^a$
Total Perfusion Time (minutes) (mean $\pm$ SD)		$105.23\pm26.67$	$114.40\pm40.31$	-1.125	$0.265^a$
Aortic cross clamp time (minutes) (mean $\pm$ SD)		$77.28 \pm 29.99$	$88.73 \pm 35.36$	-1.443	$0.154^{a}$

Table 2. Demographic characteristics.

<sup>*a*</sup>, independent sample *t*-test; <sup>*b*</sup>, Chi-square test; <sup>*c*</sup>, Chi-square corrected test; SD, standard deviation; n, frequency; %, percent; COPD, chronic obstructive pulmonary disease; BSA, body surface area; EF, ejection fraction; CABG, coronary artery bypass graft; AVR, aortic valve replacement; MVR, mitral valve replacement.

aortic cross-clamping time and cardioplegia volume compared to conventional cardioplegia. In addition, the need for intraoperative defibrillation was less in the del Nido group. However, no difference was found in mortality rates [15].

Del Nido cardioplegia solution raises some concerns. One of the most important problems is the existence of formula variations with up to 300 different chemical combinations under the same name. In coronary artery disease, homogeneous distribution cannot be guaranteed due to extensive vascular disease and impaired microcirculation. The high potassium content of del Nido may cause residual potassium to lead to coronary vasoconstriction and thus complications of myocardial ischaemia. In addition, the low nutrient content of del Nido (21 kcal/L) may adversely affect energy-depleted myocardium. Infusion of multiple doses of del Nido may increase myocardial lidocaine concentration, causing lidocaine toxicity associated with peripheral vasodilatation, negative inotropy, ventricular arrhythmias and seizures [6,9].

While there are many studies in the literature comparing the results of del Nido cardioplegia with the results of cardioplegia other than Plegisol® solution, the studies comparing the results of these two cardioplegia are very limited. In addition, there are many studies indicating that del Nido cardioplegia is superior or safer than other cardioplegies [16–18]. However, we observe that the study comparing Plegisol® solution is very limited in these comparisons [19]. In our study, we compared the results of these two cardioplegia solutions and although they showed similar results, we found that del Nido cardioplegia was more advantageous at some points.

Reidy MR *et al.* [19] compared the results of del Nido cardioplegia and Plegisol® solution in patients undergoing CABG surgery. They retrospectively analysed 155 consecutive patients. They compared 70 patients who received del Nido cardioplegia with 85 patients who received Plegisol®. As a result of their study, they found that CPB time and aortic cross-clamping time were shorter in the del Nido cardioplegia group. They also reported that the mean operating theatre time was shorter in the del Nido cardioplegia group. However, the number of CABGs, mean extubation time, ICU length of stay, and total postoperative hospital stay were similar in the groups. They also reported that the groups showed similar results in terms of 30- and 180-day

Parameters	Period	Group 1 ( $n = 38$ ) (mean rank)	Group 2 ( $n = 30$ ) (mean rank)	Ζ	р
Carbohydrate reactive protein (CRP) (mg/L)	Preoperative	35.07	33.78	-0.266	$0.791^{d}$
	Postoperative day 1	35.32	33.47	-0.383	$0.702^d$
	Postoperative day 5	32.24	37.37	-1.062	$0.288^d$
Mass creatine kinase-	Preoperative	33.51	35.75	-0.463	$0.643^{d}$
myocardial bound (CK- MB) (µg/L)	Postoperative day 1	29.74	40.53	-2.236	$0.025^d$
	Postoperative day 5	35.92	32.70	-0.669	$0.503^{d}$
Condice transmin T	Preoperative	35.76	32.90	-0.593	$0.553^{d}$
(CTnT) (ng/L)	Postoperative day 1	27.47	43.40	-3.301	$0.001^d$
	Postoperative day 5	27.43	43.45	-3.319	$0.001^{d}$

Table 3. Comparison of markers of inflammation and myocardial necrosis.

<sup>d</sup>, Mann-Whitney U test.

Variables		Group 1 (n = 38)	Group 2 (n = 30)	Test statistics	р
	No Need	35, (92.1)	26, (86.67)	0.110	0.741 <sup>c</sup>
Pacemaker requirement (n, %)	Needed	3, (7.9)	4, (13.33)	0.110	
	No Need	28, (73.7)	21, (70.00)	0.112	0.737 <sup>b</sup>
Intracardiac defibrillation requirement (n, %)	Needed	10, (26.3)	9, (30.00)	0.113	
Destances time in stars a series of (n. 0/)	No Need	14, (36.8)	2, (6.67)	0.404	$0.004^{b}$
Postoperative inotrope requirement (n, %)	Needed	24, (63.2)	28, (93.33)	8.484	
ICI in strong as guing mont $(n, 0/)$	No Need	4, (10.5)	4, (13.33)	0.000	$1.000^{c}$
ICO instrope requirement (n, %)	Needed	34, (89.5)	26, (86.67)		
LADD requirement $(n, \theta)$	No Need	35, (92.1)	28, (93.33)	0.000	1.000 <sup>c</sup>
IABP requirement (n, 76)	Needed	3, (7.9)	2, (6.67)	0.000	
Postoperatif VIS (mean $\pm$ SD)		$9.05 \pm 1.88$	$10.76\pm2.40$	-3.296	$0.002^a$
ICU VIS (mean $\pm$ SD)		$9.18 \pm 1.82$	$9.53 \pm 1.75$	-0.795	$0.429^{a}$
Intubation time (hours) (mean $\pm$ SD)		$6.13 \pm 1.80$	$7.06\pm3.25$	-1.503	$0.138^{a}$
ICU time (days) (mean $\pm$ SD)		$2.97 \pm 1.17$	$3.20\pm1.21$	-0.777	$0.440^a$
Duration of hospitalisation (days) (mean $\pm$ SD)		$8.97 \pm 3.78$	$9.93 \pm 3.88$	-1.026	$0.309^{a}$

Table 4. Early clinical outcomes.

<sup>*a*</sup>, independent sample *t*-test; <sup>*b*</sup>, Chi-square test; n, frequency; <sup>*c*</sup>, Chi-square corrected test; %, percent; ICU, intensive care unit; IABP, Intra Aortic Balloon Pump; VIS, Vasoactive-Inotropic Score.

mortality, stroke, renal failure, ventilation time longer than 48 hours, atrial fibrillation, tracheostomy, re-intubation and mechanical circulatory support [19]. Although we found similar results in our study, we found that the duration of CPB, i.e., total perfusion time and aortic cross-clamp time were similar between the groups in our study. We think that it would not be correct to attribute this difference only to cardioplegia and that factors such as the clinical course of the patient and the surgical team may also be effective.

In the literature, the fact that del Nido cardioplegia can be administered only once, without the need for repeated doses, is emphasized as an important advantage over other cardioplegia solutions. Unlike other solutions that require repeated doses every 20–30 minutes, this single dose approach significantly reduces perfusion volume. This reduction can result in less need for blood transfusion during surgery, more stable hematocrit levels and less hemodilution [20]. Moreover, del Nido cardioplegia helps surgical procedures to proceed more smoothly without the need to interrupt them with repeated administrations. It has also been reported that this may lead to a shortening of total per-

fusion and aortic cross-clamping time and a shortening of ischemia time [15]. Similarly, it has been reported in the literature that del Nido cardioplegia is more advantageous than crystalloid cardioplegia [21]. However, in our study, although the surgical procedures were similar, similar durations were observed in both cardioplegia groups. Based on this, we think that the differences in surgical times cannot always be attributed to cardioplegia solutions and that different surgical factors may affect the times. In our study, the del Nido cardioplegia solution was more advantageous than the Plegisol® solution regarding myocardial damage. Parameters such as CTnT and CK-MB are biological markers of myocardial damage. CTnT can accurately reflect the degree of myocardial damage, which is closely related to the incidence of adverse events and can be used objectively [15,22]. In our study, the fact that two cardioplegia solutions were compared based on CTnT and CK-MB parameters is important in terms of demonstrating strong results.

This study has various limitations. The limitations include the single-center, retrospective nature of the study, the small number of patients, and insufficient patient data. In addition, insufficient data are among the limitations of the study. We think that a multicentre and prospective study with more patient populations and more data would provide more comprehensive results.

# Conclusions

In conclusion, when the findings obtained in our study were evaluated, it was observed that del Nido cardioplegia solution provided better myocardial protection and was more advantageous in terms of patient stabilization than Plegisol® solution in the perioperative period due to faster recovery of cardiac functions. In addition, del Nido cardioplegia solution was more advantageous in terms of myocardial necrosis, although it showed similar results in some points when compared with Plegisol® solution.

# Abbreviations

CPB, cardiopulmonary bypass; CABG, coronary artery bypass graft; BSA, body surface area; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; ICU, intensive care unit; CK-MB, creatine kinase-myocardial bound; CTnT, cardiac troponin T; CRP, carbohydrate reactive protein; AF, atrial fibrillation; PVC, polyvinyl chloride.

# Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

# **Author Contributions**

BA contributed to the conception and design of the of study. BA, EE, MA, and ME contributed to data acquisition. BA and ME participated in measuring and collating the data. BA and ME were involved in the analysis and interpretation of the data, as well as drafting the manuscript. All authors revised the manuscript critically for important intellectual content. All authors read and approved the finalmanuscript. All authors have participated sufficiently in thework and agreed to be accountable for all aspects of thework.

# **Ethics Approval and Consent to Participate**

In this study, approval was obtained from the institution and the local ethics committee before the study (Harran University Clinical Research Ethics Committee) (Date: 27 May 2024 - Approval no: HRÜ/24.07.10). The study was conducted following the principles of the Declaration of Helsinki. Since only anonymized patient data was used and there was no risk or impact on patient care, informed consent was not required. This consent waiver was approved by the Institutional Review Board and Ethics Committee and complies with regulatory and ethical guidelines for retrospective studies.

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# **Conflict of Interest**

The authors declare no conflict of interest.

# References

- [1] Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, *et al.* Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. Journal of the American College of Cardiology. 2020; 76: 2982–3021. https://doi.org/10.1016/j.jacc.2020.11.010
- Sarkar M, Prabhu V. Basics of cardiopulmonary bypass. Indian Journal of Anaesthesia. 2017; 61: 760–767. https://doi.org/10.4103/ija. IJA\_379\_17.
- [3] Misra S, Srinivasan A, Jena SS, Bellapukonda S. Myocardial Protection in Adult Cardiac Surgery With del Nido Versus Blood Cardioplegia: A Systematic Review and Meta-Analysis. Heart Lung Circulation. 2021; 30: 642–655. https://doi.org/10.1016/j.hlc.2020.10.016
- [4] Carvajal C, Goyal A, Tadi P. Cardioplegia. In: StatPearls. StatPearls Publishing: Treasure Island (FL). 2023.
- [5] Nowicki R, Berezowski M, Kulbacka J, Bieżuńska-Kusiak K, Jasiński M, Saczko J. Custodiol HTK versus Plegisol: in-vitro comparison with the use of immature (H9C2) and mature (HCM) cardiomyocytes cultures. BMC Cardiovascular Disorders. 2022; 22: 108. https://doi.org/10.1186/s12872-022-02536-6.
- [6] Lazar HL. Commentary: del Nido cardioplegia-the jury is still out and a new trial is needed. The Journal of Thoracic and Cardiovascular Surgery. 2022; 164: 537–538. https://doi.org/10.1016/j.jtcvs. 2020.09.053.
- [7] Eris C, Engin M, Erdolu B, Kagan As A. Comparison of del Nido Cardioplegia vs. blood cardioplegia in adult aortic surgery: Is the single-dose cardioplegia technique really advantageous? Asian Journal of Surgery. 2022; 45: 1122–1127. https://doi.org/10.1016/j.asjs ur.2021.09.032.
- [8] Sanri US, Özsin KK, Toktaş F, Yavuz Ş. Comparison of Del Nido Cardioplegia and Blood Cardioplegia in Terms of Development of Postoperative Atrial Fibrillation in Patients Undergoing Isolated Coronary Artery Bypass Grafting. Brazilian Journal of Cardiovascular Surgery. 2021; 36: 158–164. https://doi.org/10.21470/ 1678-9741-2020-0047.
- [9] Amaç B, Selçuk M, Bölükbaş S, Kahraman F, As Ak, Savran M, et al. Use of del Nido cardioplegia in adult cardiac surgery. The European Research Journal. 2022; 8: 139–144. https://doi.org/10.18621/eurj .970465.
- [10] Sanetra K, Pawlak I, Cisowski M. Del Nido cardioplegia what is the current evidence? Polish Journal of Cardio-Thoracic Surgery. 2018; 15: 114–118. https://doi.org/10.5114/kitp.2018.76477.
- [11] Orak Y, Kocarslan A, Boran OF, Acıpayam M, Eroglu E, Kirisci M, et al. Comparison of the operative and postoperative effects of del Nido and blood cardioplegia solutions in cardiopulmonary bypass surgery. Brazilian Journal of Cardiovascular Surgery. 2020; 35: 689– 696. https://doi.org/10.21470/1678-9741-2019-0436.
- [12] Demmy TL, Molina JE, Ward HB, Gorton ME, Kouchoukos NT, Schmaltz RA, *et al.* Custodiol versus Plegisol: A phase 3 multicentre myocardial protection study. The International Journal of Angiology. 2008; 17: 149–153. https://doi.org/10.1055/s-0031-1278300.
- [13] Talwar S, Harshavardhan N, Kapoor PM, Makhija N, Rajashekar P, Sreenivas V, et al. Plasmalyte-A Based del Nido Cardioplegia Versus Plain Ringer Based del Nido Cardioplegia: Double-Blind Random-

ized Trial. World Journal for Pediatric & Congenital Heart Surgery. 2022; 13: 187–195. https://doi.org/10.1177/21501351211073610.

- [14] Kang J, Hoyer A, Dieterlen MT, Oetzel H, Otto W, Ginther A, et al. Comparison of modified Del Nido and Custodiol® cardioplegia in minimally invasive mitral valve surgery. European Journal of Cardio-Thoracic Surgery. 2024; 65: ezae161. https://doi.org/10. 1093/ejcts/ezae161.
- [15] Zhai K, Cheng X, Zhang P, Wei S, Huang J, Wu X, *et al.* Del Nido cardioplegia for myocardial protection in adult cardiac surgery: a systematic review and update meta-analysis. Perfusion. 2023; 38: 6–17. https://doi.org/10.1177/02676591211031095.
- [16] Sanetra K, Domaradzki W, Cisowski M, Shrestha R, Białek K, Bochenek A, *et al.* The impact of del Nido cardioplegia solution on blood morphology parameters. Perfusion. 2023; 38: 277–284. https://doi.org/10.1177/02676591211049020.
- [17] Mohammed S, Menon S, Gadhinglajkar SV, Baruah SD, Ramanan SV, Gopalakrishnan KA, *et al.* Clinical outcomes of del nido cardioplegia and st thomas blood cardioplegia in neonatal congenital heart surgery. Annals of Cardiac Anaesthesia. 2022; 25: 54–60. https://doi.org/10.4103/aca.aca\_220\_20.
- [18] Garcia-Suarez J, Garcia Fernandez J, Sanz S, Martinez Lopez D, Reques L, Forteza Gil A. Del Nido Cardioplegia Versus Cold Blood Cardioplegia in Adult Cardiac Surgery: Protocol for a Randomized Controlled Trial. JMIR Research Protocols. 2020; 9: e17826.

https://doi.org/10.2196/17826.

- [19] Reidy MR, Jimenez E, Omer S, Cornwell LD, Runbeck SX, Preventza O, et al. Single-Dose del Nido Cardioplegia Compared With Standard Cardioplegia During Coronary Artery Bypass Grafting at a Veterans Affairs Hospital. Texas Heart Institute Journal. 2021; 48: e196981. https://doi.org/10.14503/THIJ-19-6981.
- [20] Kuserli Y, Turkyilmaz S, Turkyilmaz G, Kavala AA. Comparison of del Nido Cardioplegia and Blood Cardioplegia in Aortic Root Surgery. The Heart Surgery Forum. 2020; 23: E376–E384. https: //doi.org/10.1532/hsf.2861.
- [21] Borulu F, Arslan Ü, Çalik ES, Tayfur K, Erkut B. Comparison of Del Nido (a different application) and crystalloid blood cardioplegia on arrhythmia and early results. Journal of Cardiothoracic Surgery. 2024; 19: 230. https://doi.org/10.1186/s13019-024-02675-1.
- [22] Russell S, Butt S, Vohra HA. In search of optimal cardioplegia for minimally invasive valve surgery. Perfusion. 2022; 37: 668–674. ht tps://doi.org/10.1177/02676591211012554.

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