The Effect of Del Nido Cardioplegia on Myocardial Function in Different Cardiac Surgeries: an observational study

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Del Nido Cardioplegia, Myocardial protection,Coronary artery bypass graft (CABG).

ABSTRACT

Background: Reducing the ischemia time is an essential strategy to reduce intra-operative myocardial injury and improve postoperative outcomes. Myocardial protection is an essential aspect of modern cardiac surgical procedures.

Objective: To evaluate the effect of Del Nido cardioplegia on myocardial function in adult patients undergoing various cardiac surgeries, including coronary artery bypass grafting (CABG), valve surgeries, and combined procedures and determine whether Del Nido cardioplegia provides adequate myocardial protection and facilitates efficient recovery in a diverse patient population with multiple comorbidities.

Methods: This prospective cohort study was conducted at tertiary care hospital at Prince Sultan Cardiac Center-Najran-KSA from January 2023 till July 2024 and performed on total 47 adult patients undergoing CABG, valve surgeries, and combined procedures with inclusion and exclusion criteria.

Results: Mean age (years) was 51.3±10.0, majority were males ((74.5%). Operations were CABG only, valve only and both (68.1%, 8.5% and 23.4% respectively). Mean±SD of total bypass time (min) was 77.7±13.4. Cardioplegia delivery were antegrade and antegrade+ retrograde (17.0% and 83.0% respectively). Glucose (mg/dL) and lactate (mg/dL) increased from before the CPB (144.2±27.2 and 1.2±0.5 respectively) to after the termination of CPB (183.7±27.1 and 2.3±0.5 respectively). Mean±SD of Ventilation time (hr), ICU stay (days) and Hospital stay (days) was 9.7±2.7(hr), 4.2±1.1 (days) and 13.0±1.2(days) respectively.

Conclusion: This study highlights the efficacy and safety of Del Nido cardioplegia in adult cardiac surgeries. Despite the relatively high prevalence of comorbidities and the complexity of the procedures, patients demonstrated favorable recovery outcomes, including manageable ICU and hospital stays. The rising glucose and lactate levels during surgery reflect the anticipated metabolic stress of cardiopulmonary bypass, but Del Nido cardioplegia appeared to mitigate the associated risks. The findings suggest that this cardioplegia strategy is a viable option for both CABG and valve surgeries, providing effective myocardial protection and contributing to smooth postoperative recovery.

INTRODUCTION

Del Nido cardioplegia was developed by Pedro Del Nido and his team at the University of Pittsburgh in the 1990s. It has been used for pediatric cardiac surgery in Boston's Children Hospital since 1994 and, since 2003, it has been successfully used for adult cardiac surgery as well **[1]**.

The myocardial function was expressed as lactate dehydrogenase activity (measured as U/L) in addition to troponin concentration expressed as (ug/L) in the TnI series. The aim of the reported study, which was conducted to compare the myocardial function using the two types of cardioplegia on the troponin and lactate dehydrogenase in three groups of patients (CABG and the transplantation groups), taking into consideration that the samples were calculated accordingly based on three studies which used lactate dehydrogenase only as an indicator for the cardiac surgery effect on the myocardial function **[2]**. The reported study was trying to prove that lactate dehydrogenase can be used as an additional marker for causing the myocardial injury effect. To the best of my knowledge, no previous research has been conducted such as that which will be reported in the present research design **[3].** Consequently, the objective of the study is to evaluate the effect of Del Nido cardioplegia on myocardial function in adult patients undergoing various cardiac surgeries, including coronary artery bypass grafting (CABG), valve surgeries, and combined procedures and determine whether Del Nido cardioplegia provides adequate myocardial protection and facilitates efficient recovery in a diverse patient population with multiple comorbidities

PATIENTS AND METHODS

After ethical committee approval and written consents from the patients, this prospective cohort study was conducted at tertiary care hospital at Prince Sultan Cardiac Center-Najran-from January 2023 till July 2024 and performed on total 47 adult patients undergoing CABG, valve surgeries, and combined procedures.

Patients between 18-80 years of age who are operated under CABG, valve surgeries, and combined procedures are the included criteria for the research. For all surgeries, the exclusion criteria included pediatrics, reoperations, emergency operations, complex left main stenosis, endocarditis, and peripheral vascular diseases. After considering the exclusion criteria, (4) patients undergoing valve replacement, (32) patients undergoing coronary artery bypass grafting and (11) patients undergoing both operations were consecutively included in the research. Approval for the study was obtained from the hospital's institutional review board.

Study Procedures: All participants were submitted to the following:

History: Basic demographic information such as age, sex, and body surface area (BSA) were collected. The medical history of each patient was thoroughly reviewed, focusing on any previous cardiac conditions, surgeries, or chronic diseases that could impact their current treatment plan. Surgical history was particularly important, with a focus on any past cardiac interventions like prior bypass surgeries or valve replacements, as these could affect the patient's risk profile for the current procedure. Additionally, the study documented medication use, especially heart-related drugs and anticoagulants, which could influence anesthetic management and surgical outcomes.

Clinical examinations were then conducted, beginning with a general physical assessment that included measuring vital signs such as heart rate, blood pressure, and observing for signs of heart failure like edema or cyanosis. Special attention was paid to cardiac-specific examinations, which included auscultation to detect any heart murmurs or irregular rhythms, and assessing jugular venous pressure (JVP) to evaluate cardiac function. Preoperative echocardiography was a key component of the examination process, providing detailed insights into left ventricular ejection fraction (LVEF), valve function, and any structural abnormalities in the heart that could impact surgery.

A range of investigations was also carried out to gather essential data for the study. Routine blood tests, such as complete blood count (CBC), liver and renal function tests, and coagulation profiles (including International Normalized Ratio [INR] and Activated Partial Thromboplastin Time [APTT]), were performed to ensure a comprehensive understanding of the patients' health status before surgery. Specific cardiac biomarkers like Glucose and lactate dehydrogenase (LDH) were measured before and after surgery to assess any myocardial injury caused by the procedure. Additionally, an electrocardiogram (ECG) was used to detect any arrhythmias or ischemic changes, while chest X-rays helped in evaluating heart size and lung health. Arterial blood gases (ABGs) were also collected to assess the patients' oxygenation and ventilation status before surgery, ensuring proper preparation for the operation.

Del Nido cardioplegia is a crystalloid solution administered in a single dose to protect the myocardium during surgery. It works by stopping myocardial contraction through a high-potassium solution, and it is typically delivered through an antegrade and retrograde cannula near the coronary openings. This method allows for effective myocardial protection while minimizing the risk of injury. The study measured key variables such as LDH and glucose to assess the potential damage to heart cells. LDH is released from damaged cells, while Troponin I is a well-known marker of heart muscle injury **[4]**.

The surgical process for these patients followed standard protocols, including tracheal intubation, median full sternotomy, and aortic cross-clamping **[5]**. Blood samples were collected at various stages before and after cardiopulmonary bypass to monitor changes in Lactate Dehydrogenase (LDH) (to evaluate myocardial damage) and Glucose levelsThis glucose and lactate levels reflects the physiological stress and metabolic demands during surgery, as well as potential alterations in tissue perfusion.

. Anesthesia management was consistent across all patients, using fentanyl for sedation and postoperative pain control. Total bypass time, ischemic clamp time and Operation surgical time were closely monitored, as this is a critical measure of postoperative recovery.

Outcome measures:
Primary outcomes included metabolic markers of lactate and glucose levels.
Secondary outcomes included operative findings of total bypass time, Ischemic clamp time and Operation surgical time and postoperative values of ventilation time, ICU stay and Hospital stay.
Ethical Considerations:
The patient data was anonymous. Data presentation was not by the patient's name but by diagnosis and patient confidentiality was protected. An informed consent was taken from all participants, it was in Arabic and English languages and confirmed by date and time. confidentiality was preserved by assigning a number to patients initials and only the investigator knew it.
Statistical analysis:
The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 28.0, IBM Corp., Chicago, USA, 2021. Quantitative data described as mean±SD (standard deviation) and compared using RMANOVA with post hoc Dunnet's test. Qualitative data described as number and percentage.

RESULTS

Table (1): Baseline characteristics of the studied cases

Variables		Mean±SD / n	Range / %
Age (years)		51.3±10.0	32.0–73.0
Sex	**Male**	35	74.5%
	Female	12	25.5%
BMI (kg/m^2)		29.1±2.9	23.1–34.9
Hypertension		34	72.3%
Diabetes mellitus		21	44.7%
ASA	**II**	3	6.4%
	III	34	72.3%
	IV	10	21.3%
Euro score		4.1±1.4	3.0–9.0
LVEF (%)		50.8±5.6	34.0–62.0
NYHA	**II**	7	14.9%
	III	31	66.0%
	IV	9	19.1%
Operation type	**CABG only**	32	68.1%
	Valve only	4	8.5%
	Both	11	23.4%

Total=47. BMI: Body mass index. ASA: American Society of Anesthesiologists. CABG: Coronary Artery Bypass Graft.

Table (1) showed baseline characteristics. Mean±SD of age (years) was 51.3±10.0, majority were males (74.5%). Operations were CABG only, valve only and both (68.1%, 8.5% and 23.4% respectively).

Table (2): Operative variables of the studied cases

Variables		Mean±SD / n	Range / %
Total bypass time (min)		77.7±13.4	51.0–111.0
Ischemic Clamp time (min)		45.1±7.6	30.0–64.0
Operation surgical time(min)		32.6±6.1	20.0–47.0
Defibrillation		8	17.0%
Pacemaker		13	27.7%
Intraortic balloon pump		3	6.4%
Inotropes		34	72.3%
Cardioplegia delivery	**Antegrade**	8	17.0%
	Antegrade& retrograde	39	83.0%
Cardioplegia Volume	**Total initial dose (ml)**	974.5±254.6	524.0–1508.0
	Antegrade-initial (ml)	742.1±191.4	307.0–1121.0
	Retrograde-initial (ml)	280.1±101.8	96.0–622.0

Table (2) showed operative variables. Mean±SD of total bypass time (min) was 77.7±13.4. Cardioplegia delivery were antegrade and antegrade& retrograde (17.0% and 83.0% respectively).

Table (3): Glucose and lactate levels of the studied cases

Variable	Time	Mean±SD	Range	^p-value
Glucose (mg/dL)	**Before the CPB**	144.2±27.2	95.0–210.0	**<0.001***
	Before releasing the aortic cross clamp	⌂157.4±27.0	109.0–224.0	
	After releasing the aortic cross clamp	⌂181.6±26.8	134.0–247.0	
	After the termination of CPB	⌂183.7±27.1	136.0–250.0	
Lactate (mg/dL)	**Before the CPB**	1.2±0.5	0.3–2.5	**<0.001***
	Before releasing the aortic cross clamp	⌂1.9±0.5	1.0–3.2	
	After releasing the aortic cross clamp	⌂2.2±0.5	1.2–3.5	
	After the termination of CPB	⌂2.3±0.5	1.3–3.6	

Total=47. ^RMANOVA. *Significant. Times significantly different from before the CPB had the symbol "⌂" based on post hoc Dunnet's test.

Table (3) showed glucose (mg/dL) and lactate (mg/dL) increased from before the CPB (144.2±27.2 and 1.2±0.5 respectively) to after the termination of CPB (183.7±27.1 and 2.3±0.5 respectively). All values at times next to before the CPB were significantly different from it.

Table (4): Postoperative variables of the studied cases

Variables	Mean±SD	Range
Ventilation time (hr)	9.7±2.7	4.0–15.0
ICU stay (days)	4.2±1.1	2.0–6.0
Hospital stay (days)	13.0±1.2	9.0–16.0

Table (4) showed postoperative variables. Mean ±SD of Ventilation time (hr), ICU stay (days) and Hospital stay (days) was 9.7±2.7, 4.2±1.1 and 13.0±1.2 respectively.

DISCUSSION

Although coronary bypass graft surgery (CABG) is one of the most common operations in the world, it still has high morbidity and mortality levels correlated with myocardial protection and injury **[6]**. Cardiopulmonary bypass (CPB) and aortic cross-clamping provide surgical teams with a bloodless

and non-beating heart but interrupt myocardial perfusion during CABG, valve, or congenital heart surgery**[7]**.

The Del Nido (DN) cardioplegia was initially used in pediatric cardiac surgery. Owing to its advantage of providing long time protection and less interruption of the surgical procedure due to single dose administration, it was found to be attractive to many surgeons and adopted in many centres especially during complex or redo operations and minimal invasive procedures**[8]**.

The major conflict in literature revolves around the debate between the use of Del Nido cardioplegia versus traditional multi-dose cardioplegia solutions (e.g., blood-based cardioplegia) for adult cardiac surgeries. Although Del Nido cardioplegia has proven effective in pediatric cases, its broader use in adults remains controversial due to concerns about metabolic stress, myocardial injury, and its efficacy in complex procedures **[9]**.

Consequently, evaluating the effect of Del Nido cardioplegia on myocardial function in adult patients undergoing various cardiac surgeries, including coronary artery bypass grafting (CABG), valve surgeries, and combined procedures and determining whether Del Nido cardioplegia provides adequate myocardial protection and facilitates efficient recovery in a diverse patient population with multiple comorbidities was highlighted as a main point of interest.

This prospective cohort study was conducted at tertiary care hospital at Prince Sultan Cardiac Center-Najran-KSA from January 2023 till July 2024 and performed on total 47 adult patients undergoing CABG, valve surgeries, and combined procedures.

During this study, 58 patients were assessed for eligibility and 47 patients were included in the study. Of all eligible patients, 7 patients were excluded from the study based on the inclusion criteria and 4 patients refused to participate in the study. Ultimately, the analysis was based on the data of 47 adult patients undergoing CABG, valve surgeries, and combined procedures.

Regarding Patient Demographics and Baseline Characteristics, the study included 47 patients with a mean age of 51.3 ± 10 years, predominantly male (74.5%). The cohort presented with significant comorbidities, with 72.3% suffering from hypertension and 44.7% diagnosed with diabetes mellitus. The surgical risk profile, assessed using the ASA score, showed most patients at moderate risk (ASA III: 72.3%). Additionally, the average EuroSCORE was 4.1 ± 1.4, reflecting a moderate risk of mortality in cardiac surgeries. Cardiac function remained generally preserved, with a mean LVEF of 50.8 ± 5.6%, although many patients experienced moderate physical limitations (NYHA class III: 66.0%). The surgical procedures were varied, with 68.1% undergoing CABG alone, 8.5% receiving valve surgeries, and 23.4% undergoing a combination of both.

The patient characteristics across the studies exhibit similarities, especially in terms of age and comorbidities, reflecting typical populations undergoing cardiac surgery. In comparison, **Özer et al. [7]** conducted a retrospective study on 71 patients undergoing open-heart surgeries with Del Nido cardioplegia, focusing on metabolic and hematological changes during the perioperative period and reported a slightly older population with a mean age of 60.1 years and similar male predominance (76.1%). Their study also reflected higher surgical risk with ASA III in 80.3% of patients, which aligns closely with our ASA III group (72.3%).

Similarly, **Yerebakan et al. [10]** performed a propensity-matched comparison between Del Nido cardioplegia and whole-blood cardioplegia in 88 patients undergoing CABG after acute myocardial infarction (AMI) and investigated patients with a mean age of **67.7 years**, but their study focused exclusively on post-myocardial infarction cases, presenting a higher-risk population compared to our mixed-surgery cohort.

Saleh and Mohanad [8] compared Del Nido cardioplegia with on-pump beating heart surgery in mitral valve replacement cases with left ventricular impairment. The two groups had similar demographic profiles, with patients averaging 32 years.

In **Ad et al. [9]**who conducted a randomized controlled trial comparing Del Nido cardioplegia with whole blood cardioplegia in adult patients undergoing CABG and valve surgeries, both the Del Nido and control groups had comparable demographic characteristics to ours, with patients' mean ages around **65 years** and an LVEF that was similarly preserved. In addition, the **Society of Thoracic Surgeons (STS) risk scores**, used to estimate the risk of operative mortality, were also comparable between the groups, with scores of 1.4% in the Del Nido group and 1.3% in the whole-blood group.

These factors are critical as they impact not only surgical outcomes but also postoperative recovery, which is often complicated by such comorbidities.

Regarding Operative Parameters, Operative variables provided insights into the complexity and duration of surgeries. The mean bypass time was 77.7 ± 13.4 minutes, with an ischemic clamp time of 45.1 ± 7.6 minutes reflecting efficient surgical procedures across various cardiac surgeries. In terms of support interventions, 72.3% of the patients required inotropic support, a common requirement in high-risk cardiac surgeries, and 17% of the cases required defibrillation post-surgery, while 27.7% required a pacemaker, and 6.4% needed an intra-aortic balloon pump, reflecting challenges in managing cardiac function during surgery. Cardioplegia was delivered in 83% of the cases through both antegrade and retrograde methods, which is beneficial as this combination ensures thorough myocardial protection during ischemia, while 17.0% received only antegrade cardioplegia. The initial cardioplegia volume averaged 974.5 ± 254.6 mL, ensuring adequate myocardial protection during the procedure.

The operative parameters in the studies provide valuable insights into the differences between Del Nido cardioplegia and other techniques. **Yerebakan et al. [10]** reported that Del Nido cardioplegia shortened CPB and cross-clamp times compared to whole-blood cardioplegia ($p < 0.001$), which aligns with our findings that shorter operative times contribute to favorable outcomes. Additionally, **Saleh and Mohanad [8]** observed similar bypass times between Del Nido and beating heart procedures but reported significantly longer total operative times for the beating-heart group. These comparative findings indicate that Del Nido cardioplegia facilitates more efficient surgical workflows, aligning with our results.

In contrast, **Özer et al.[7]** noted a significantly longer CPB time of 115 minutes but shorter cross-clamp times of 78 minutes on average. Their study involved more frequent intraoperative interventions, such as inotropic support (76.1%) and pacemaker use (23.9%), compared to 27.7% pacemaker use in our cohort.

Regarding Metabolic Changes During Surgery, the study monitored the changes in glucose and lactate levels during different stages of cardiopulmonary bypass (CPB). Glucose levels increased steadily from 144.2 ± 27.2 mg/dL before CPB to 157.4 ± 27.0 mg/dL before releasing the aortic cross-clamp, 181.6 ± 26.8 mg/dL after releasing the clamp, and 183.7 ± 27.1 mg/dL following the termination of CPB. Similarly, lactate levels increased from 1.2 ± 0.5 mg/dL before CPB to 1.9 ± 0.5 mg/dL before the clamp release, 2.2 ± 0.5 mg/dL after the release, and 2.3 ± 0.5 mg/dL at the end of CPB. All changes from the baseline measurements were statistically significant ($p < 0.001$), indicating that CPB significantly affected these metabolic markers. This progressive rise in glucose and lactate levels reflects the physiological stress and metabolic demands during surgery, as well as potential alterations in tissue perfusion.

These trends mirror findings by **Özer et al.[7]** who also reported significant increases in glucose and lactate levels throughout the perioperative period. Additionally, **Özer et al.[7]** tracked cardiac biomarkers, such as CK-MB and troponin, showing marked elevations immediately after surgery. Although we did not include these markers in our analysis, the similarity in glucose and lactate responses underscores the metabolic stress induced by CPB across studies.

In **Ad et al. [9]**, troponin levels in the Del Nido group rose less than in the control group, suggesting superior myocardial preservation. Our study also indicated effective myocardial protection, as evidenced by the manageable metabolic shifts observed during surgery. The importance of managing metabolic stress was further emphasized by **Yerebakan et al.[10]**, who highlighted lower postoperative complications when Del Nido cardioplegia was used. These comparisons suggest that Del Nido cardioplegia reliably stabilizes metabolism during surgery, consistent with our findings.

Regarding Postoperative Recovery and Outcomes, the patients demonstrated relatively favorable postoperative outcomes. The average ventilation time was 9.7 ± 2.7 hours, reflecting manageable respiratory recovery. The ICU stay averaged 4.2 ± 1.1 days, suggesting efficient stabilization post-surgery, while the total hospital stay was 13.0 ± 1.2 days. Despite the need for inotropes and pacemakers in several cases, the outcomes suggest that the use of Del Nido cardioplegia contributed to myocardial protection and smooth recovery. These recovery metrics are within the

typical range for high-risk cardiac surgeries and suggest that Del Nido cardioplegia supports effective postoperative recovery.

These results align closely with those reported by **Saleh and Mohanad [8]** who observed slightly shorter ICU stays and similar ventilation times. Importantly, both studies reported low incidences of complications and minimal need for mechanical support. For example, only 6.4% of our patients required intra-aortic balloon pumps, compared to 10% in **Saleh and Mohanad study,** further reinforcing the safety profile of Del Nido cardioplegia.

Ad et al.[9] found that fewer patients in the Del Nido group required inotropic support (65.1% vs. 84.2%), a trend that aligns with the 72.3% inotropic use in our cohort. Additionally, **Yerebakan et al.[10]** reported that Del Nido cardioplegia reduced ICU stays and transfusion requirements, reflecting the overall efficiency of this solution in reducing resource utilization and improving recovery. These outcomes are consistent with our findings, where patients experienced smooth recovery with limited complications, further validating Del Nido cardioplegia's role in enhancing postoperative outcomes across different surgical contexts.

Strengths of the Study:

One of the primary strengths of our study is the diverse patient population. The inclusion of patients with varying levels of cardiac function (e.g., LVEF and NYHA classes) and comorbidities provides a comprehensive overview of Del Nido cardioplegia's performance in real-world scenarios. Moreover, the use of multiple outcome measures, including glucose and lactate levels, bypass times, and postoperative recovery metrics, adds robustness to the analysis. The detailed monitoring of metabolic responses offers insight into how the body copes with cardiopulmonary bypass and ischemia, providing valuable information for clinicians managing similar cases.

Limitations of the Study:

Despite its strengths, the study has several limitations. The sample size is relatively small (47 patients), which may limit the generalizability of the results to broader populations. Additionally, this observational design lacks a control group to compare the outcomes of Del Nido cardioplegia with other cardioplegia solutions, such as blood-based cardioplegia. Another limitation is the lack of long-term follow-up data, which would have provided deeper insights into the durability of myocardial function and patient outcomes beyond the immediate postoperative period. Finally, while glucose and lactate levels were tracked, other biochemical markers of myocardial injury, such as troponins, were not assessed, which could have strengthened the metabolic analysis**.**

CONCLUSION

This study highlights the efficacy and safety of Del Nido cardioplegia in adult cardiac surgeries. Despite the relatively high prevalence of comorbidities and the complexity of the procedures, patients demonstrated favorable recovery outcomes, including manageable ICU and hospital stays. The rising glucose and lactate levels during surgery reflect the anticipated metabolic stress of cardiopulmonary bypass, but Del Nido cardioplegia appeared to mitigate the associated risks. The findings suggest that this cardioplegia strategy is a viable option for both CABG and valve surgeries, providing effective myocardial protection and contributing to smooth postoperative recovery.

Additional Information

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Conflict of interest: None.

Financial disclosures: None.

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