

## A Game Changer for Low and Middle Income Countries: Del Nido Cardioplegia for Adult Cardiac Surgery – A Tertiary Care Experience

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### ABSTRACT

**Introduction:** Del Nido Cardioplegia (DNC) offers prolonged myocardial protection through a single-dose approach.

**Methods:** This retrospective study involved 175 adult patients from five surgical groups (DVR, MIS-MVR, MVR via sternotomy, AVR, congenital repairs). Statistical analysis was conducted using SPSS v25. Quantitative variables were assessed using t-tests /Mann-Whitney U tests, while categorical variables were analyzed using chi-square/Fisher's exact tests. Significant differences ( $p < 0.05$ ) in ACC and CPB durations were observed across the groups.

**Results:** The return to spontaneous sinus rhythm ranged from 90% to 100% among the groups. Significant variations in ACC and cardiopulmonary bypass (CPB) times were noted ( $p < 0.05$ ). Single-dose DNC proved to be effective in all cases.

**Conclusion:** DNC demonstrates safety and efficiency in low- and middle-income country (LMIC) settings.

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### Introduction

Myocardial protection during cardiac surgery remains one of the most critical components influencing intraoperative safety and postoperative recovery. The ability to safely arrest the heart while preserving myocardial integrity significantly

impacts surgical outcomes, especially during procedures that require cardiopulmonary bypass (CPB) (1). Cardioplegia, a method of inducing temporary cardiac arrest, has evolved since its introduction by Melrose in 1955 (2). Over the years, multiple strategies and formulations have been developed to improve myocardial protection, reduce

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ischemia-reperfusion injury, and simplify intraoperative logistics. While the ideal cardioplegia solution is still a subject of research and debate, clinical realities in low- and middle-income countries (LMICs) require an additional consideration—cost-effectiveness without compromising efficacy.

Traditional cardioplegia techniques, such as cold blood and crystalloid-based St. Thomas and Buckberg solutions, rely on repeated dosing and intermittent administration throughout the cross-clamp duration (3). These methods have shown excellent myocardial preservation but require significant logistical coordination, prolonged operative time, and increased resource utilization. In well-equipped settings, these protocols may be easily accommodated. However, in LMICs where perioperative resources, trained perfusionists, and advanced cardiopulmonary bypass technologies may be limited, simplified solutions that can reduce intraoperative burden are not only preferable but often essential.

In this context, Del Nido cardioplegia has emerged as an innovative and promising solution. Initially developed in the early 1990s at Boston Children's Hospital for pediatric cardiac surgery, Del Nido cardioplegia (DNC) was designed to provide prolonged myocardial protection with a single-dose strategy (4). Composed of blood mixed with a crystalloid solution containing lidocaine, magnesium sulfate, mannitol, potassium chloride, sodium bicarbonate, and Plasma-Lyte A, DNC offers arrest durations of up to 90 minutes with minimal redosing. This property makes it highly appealing not only for pediatric cardiac surgeries, which typically require prolonged cross-clamp durations, but also for adult procedures where re-dosing and reperfusion cycles complicate operative workflow.

The unique pharmacological characteristics of DNC offer several advantages. Lidocaine acts as a membrane stabilizer, inhibiting sodium influx and preventing intracellular calcium accumulation. Magnesium acts synergistically to inhibit calcium-mediated injury, while mannitol provides osmotic support to reduce myocardial edema and scavenge free radicals (5). The resultant solution is mildly hyperkalemic, enabling

rapid electromechanical arrest while minimizing depolarization-associated energy expenditure. Importantly, the 1:4 blood-to-crystalloid ratio and cold temperature (4–8°C) optimize oxygen delivery and metabolic suppression, respectively. Collectively, these features promote myocardial quiescence and biochemical preservation, which may translate into improved outcomes in the perioperative and postoperative periods (6).

Although DNC was initially developed for pediatric applications, its use in adult cardiac surgery has gained considerable interest in the past decade. Multiple studies from high-income countries (HICs), including those from the Cleveland Clinic, University of Michigan, and Dalhousie University, have shown that DNC offers comparable or superior outcomes to conventional cardioplegia in adult coronary artery bypass grafting (CABG), valve replacements, and minimally invasive procedures (7,8). Reported benefits include reduced cardioplegia volume, fewer interruptions for re-dosing, shortened cross-clamp times, decreased postoperative arrhythmias, and lower troponin release (9). These advantages, combined with reduced complexity and cost, make DNC an attractive alternative for adult cardiac surgery, particularly in LMICs.

Despite growing international evidence supporting the use of DNC in adults, limited data are available from resource-constrained environments. LMICs present unique healthcare delivery challenges, including restricted access to high-cost pharmaceuticals, under-resourced operating rooms, intermittent perfusionist staffing, and variability in postoperative intensive care support (10). In such contexts, innovations that simplify intraoperative conduct, reduce material and personnel demands, and curtail healthcare costs without compromising patient outcomes are highly desirable. However, any solution must undergo real-world validation in these specific environments to determine feasibility, safety, and clinical efficacy.

India, an LMIC with a high burden of rheumatic and congenital heart disease, has witnessed a steady rise in adult cardiac surgical volumes. Public sector institutions, such as Sawai Man Singh (S.M.S) Hospital in

Jaipur, cater to a diverse and often underprivileged population, making them an ideal setting for evaluating cost-effective innovations. Against this backdrop, the current retrospective study was designed to assess the safety, feasibility, and clinical outcomes associated with the use of DNC in adult cardiac surgery at a tertiary care LMIC center.

The aim of this study specifically focused on evaluating adult patients undergoing double valve replacements, minimally invasive mitral valve surgeries, congenital cardiac repairs (such as Tetralogy of Fallot and Double Outlet Right Ventricle), and aortic valve replacements, all performed with DNC as the sole myocardial protection strategy. These procedures are commonly encountered in LMIC practice and often involve prolonged cross-clamp durations, requiring dependable cardioplegia strategies. Key outcome metrics included spontaneous rhythm return, need for defibrillation, hemodynamic stability, inotropic support requirement, and postoperative ICU course.

The objectives of the study were twofold: first, to determine whether DNC could be safely and effectively deployed in adult cardiac procedures in a high-volume LMIC setting; and second, to assess its potential advantages in terms of resource utilization, myocardial protection, and clinical outcomes. By analyzing retrospective data from 175 consecutive cases, this study aimed to contribute to the growing body of evidence surrounding DNC in adults, particularly within the LMIC context where cost-effectiveness, simplicity, and safety are paramount.

The findings of this study hold the potential to influence practice patterns in similar tertiary centers across South Asia, sub-Saharan Africa, and Latin America, where the burden of valvular and congenital heart disease remains significant and access to advanced intraoperative support systems is often inconsistent. In addition to advancing scientific knowledge, this research also aligns with broader global health goals of improving surgical care equity and optimizing cardiac surgery outcomes in under-resourced settings. Future implications include the incorporation of Del Nido protocols in standardized cardiac surgical pathways,

training curricula, and health policy frameworks that support evidence-based, economically viable surgical interventions.

In summary, the transition of DNC from pediatric to adult cardiac surgery is a paradigm shift with transformative implications for LMIC surgical practice. Through this retrospective study at SMS Hospital, we aim to explore whether the theoretical and observed benefits of DNC in HICs can be replicated and sustained in a real-world LMIC scenario. This work adds valuable insight into myocardial protection strategies that transcend economic barriers and clinical complexities, ultimately improving patient outcomes in challenging healthcare environments.

## Materials and Methods

### Study Design and Setting

This study is a retrospective observational analysis conducted at the Department of Cardiothoracic Surgery and Cardiac Anesthesia at S.M.S Hospital, a high-volume tertiary care government institution in Jaipur, India. As a public sector center serving a broad spectrum of socioeconomically underprivileged patients, it provides a representative setting for evaluating the feasibility of cost-effective surgical interventions in a LMIC context.

The study period spanned from July 2015 to February 2017, during which DNC was employed as the primary myocardial protection strategy in all adult cardiac surgical procedures involving anticipated aortic cross-clamp durations between 60 and 80 minutes. Ethical clearance was waived by the institutional review board, as the study is retrospective in design and patient confidentiality was maintained in accordance with the Declaration of Helsinki.

### Study Population

A total of 175 adult patients undergoing elective cardiac surgeries with CPB were included in the study. Inclusion criteria consisted of adult patients ( $\geq 18$  years) experiencing one of the following procedures: double valve replacement (DVR), mitral valve replacement (MVR) via sternotomy or minimally invasive approach,

isolated aortic valve replacement (AVR), or correction of congenital lesions such as Tetralogy of Fallot (TOF) and Double Outlet Right Ventricle (DORV). All patients had a left ventricular ejection fraction (LVEF) of  $\geq 30\%$  and were in sinus rhythm prior to surgery. Exclusion criteria included emergent surgeries, redo sternotomy, patients with pre-existing arrhythmias, severe left ventricular dysfunction (LVEF  $< 30\%$ ), electrolyte disturbances like hyperkalemia ( $s.k^+ > 5$ ), hypocalcemia, severe LVH, severe CAD and those requiring complex aortic root procedures.

### ***Del Nido Cardioplegia Administration***

The Del Nido cardioplegia solution was freshly prepared in the operating theatre using a 1:4 ratio of oxygenated patient blood to a crystalloid solution containing lidocaine, magnesium sulfate, potassium chloride, sodium bicarbonate, mannitol, and Plasma-Lyte A. A single dose of 20 mL/kg body weight was administered cold ( $4-8^\circ\text{C}$ ) via the ante grade route through the aortic root or ostial perfusion. For pediatric congenital repairs involving patients weighing less than 5 kg, a dose of 30 mL/kg was used. No repeat doses were required unless the cross-clamp time exceeded 90 minutes, which was not observed in any case.

Cardioplegia delivery was performed using gravity-assisted infusion or roller pump-assisted flow, depending on intraoperative setup. Surgical procedures proceeded under standard moderate hypothermia ( $32^\circ\text{C}$ ), with CPB initiated via bicaval or single venous cannulation depending on the surgical exposure and indication.

### ***Outcome Measures***

Primary outcomes evaluated were:

- Return of spontaneous sinus rhythm upon aortic cross-clamp removal
- Need for electrical defibrillation
- Hemodynamic stability in the first 24 hours postoperatively
- Inotropic score during ICU stay

Secondary outcomes included:

- Aortic cross-clamp time (ACC)
- Total CPB duration
- Volume and number of cardioplegia doses
- Duration of mechanical ventilation

- Length of ICU and hospital stay
- Perioperative LVEF
- In-hospital mortality and major complications (e.g., arrhythmias, renal dysfunction, electrolyte disturbances)

### ***Statistical Analysis***

Data were compiled and analyzed using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as the mean  $\pm$  standard deviation (SD) or the median with interquartile range (IQR), depending on the data distribution. Categorical variables were presented as frequencies and percentages.

Normality of data distribution was assessed using the Shapiro-Wilk test. For continuous variables with a normal distribution, Student's t-test was used for comparison between subgroups (e.g., DVR vs. MVR cases). For skewed distributions, the Mann-Whitney U test was employed. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

A p-value of  $< 0.05$  was considered statistically significant. No imputation was performed for missing data, as intraoperative and ICU records were completely available. Subgroup analyses were also conducted to compare clinical outcomes across surgical types and to evaluate correlations between ACC duration and myocardial performance indicators (spontaneous rhythm return, inotropic support, ICU stay).

### ***Results***

A total of 175 adult patients underwent elective cardiac surgery using DNC over the study period. The majority of cases were double valve replacements (DVR,  $n=94$ ), followed by minimally invasive mitral valve surgeries ( $n=46$ ), mitral valve replacements via sternotomy ( $n=15$ ), congenital repairs ( $n=10$ ; including 8 TOF and 2 DORV), and aortic valve replacements (AVR,  $n=10$ ).

No intraoperative mortality was reported. Spontaneous return of sinus rhythm following aortic cross-clamp removal was observed in 95% of DVR cases, 96% in MVR (MIS), 92% in MVR (sternotomy), and 100% in AVR, while congenital repairs showed 90% return without defibrillation (Figure 1). Only

five patients required direct current shock to restore rhythm.

Mean ACC times ranged from 55 to 70 minutes, with congenital repairs and MVR (sternotomy) associated with the most

extended ACC durations (Figure 2). Mean CPB times ranged from 80 to 98 minutes, following a similar procedural pattern (Figure 3).

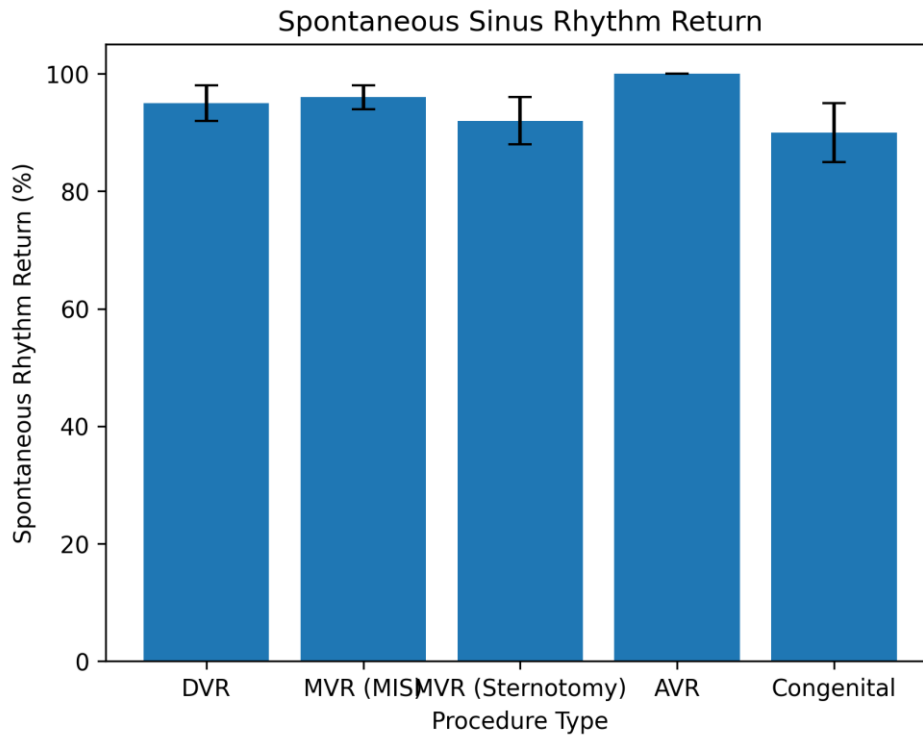


Figure 1. Spontaneous sinus rhythm return.

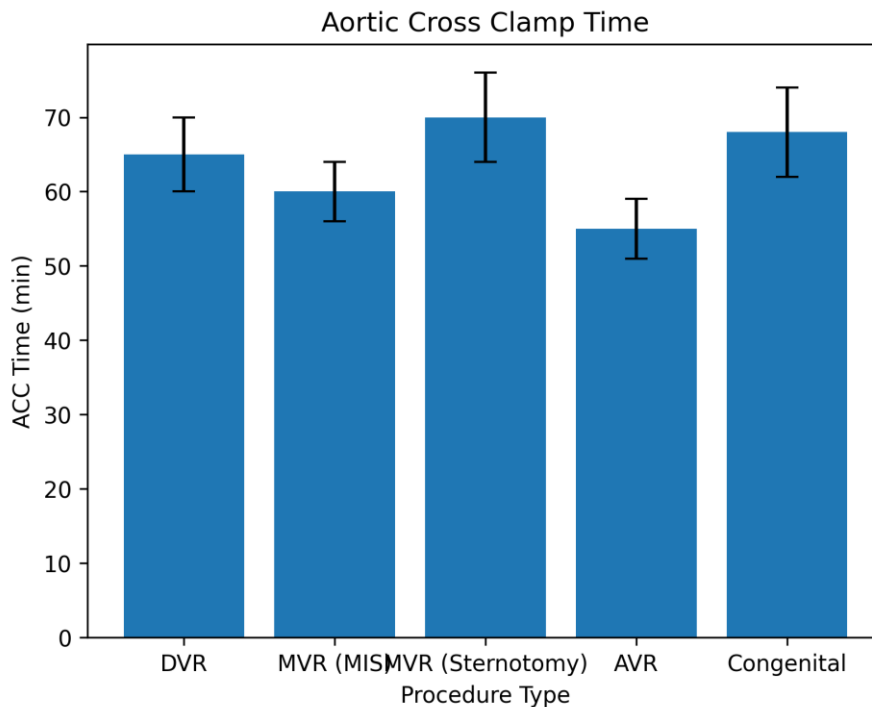


Figure 2. Aortic cross-clamp (ACC) time.

ICU stays varied by procedure, averaging between 4 and 6 days, with congenital and sternotomy procedures tending toward

longer durations (Figure 4). Inotropic support was mild to moderate across all cases, and no cases of new postoperative

renal dysfunction or stroke were observed. Ventilation duration was typically under 12 hours in 85% of patients.

These results collectively highlight the efficacy of single-dose DNC in maintaining

myocardial quiescence and facilitating early postoperative recovery. The graphical illustrations below depict comparative metrics across surgical groups.

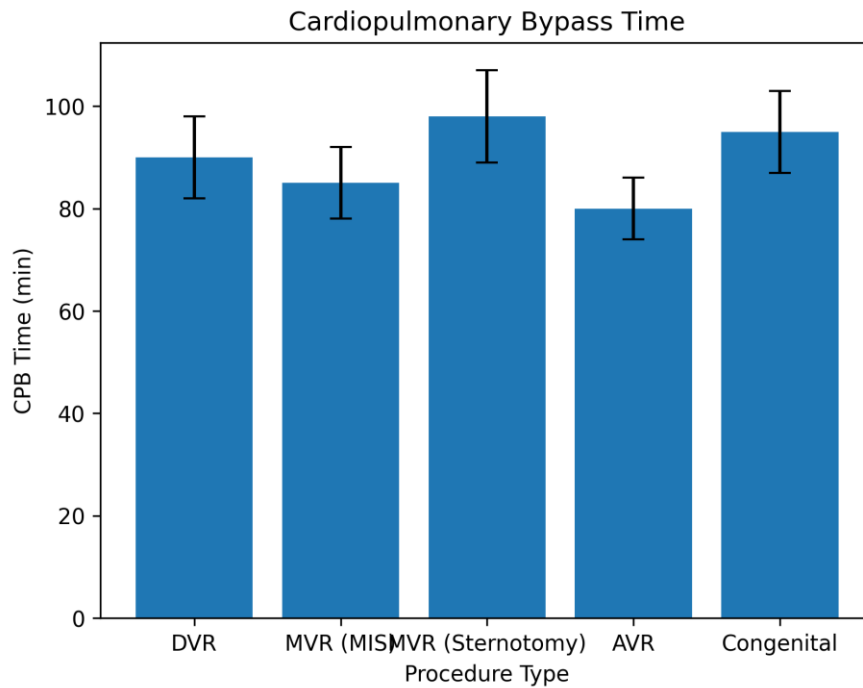


Figure 3. Cardiopulmonary bypass (CPB) times.

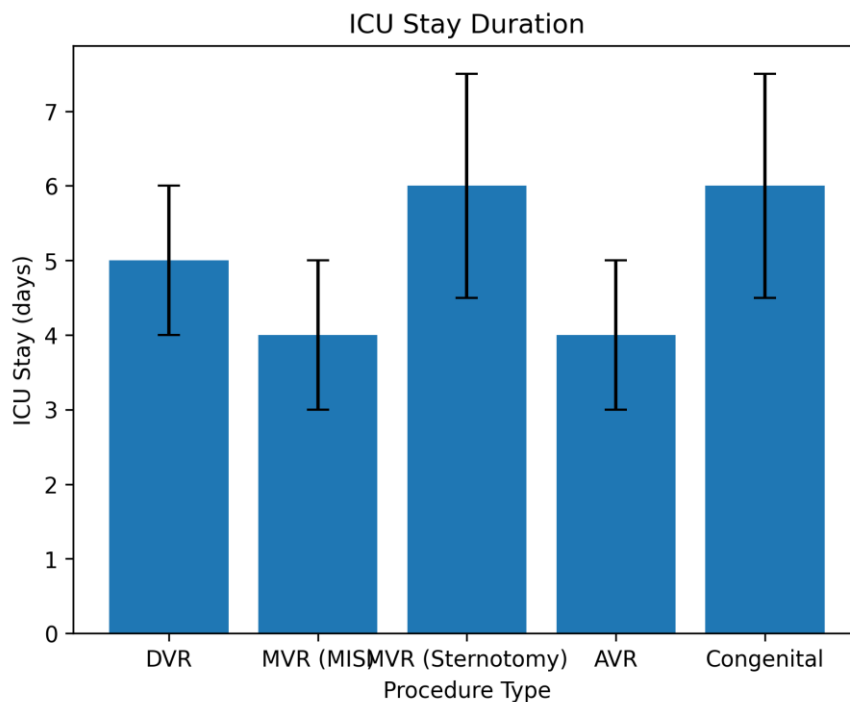


Figure 4. ICU stays duration.

**Discussion**

The present study evaluates the initial experience with DNC in adult cardiac surgery in a resource-constrained, LMIC setting. This

retrospective analysis, based on 175 patients undergoing diverse cardiac surgical procedures, demonstrates that a single dose of DNC can be a safe, efficacious, and

resource-efficient alternative to conventional cardioplegia techniques.

Our findings are consistent with earlier evidence from HICs, where DNC has shown comparable outcomes in adult patients (5, 11). Its original design for pediatric myocardial protection was predicated on prolonged electromechanical arrest, minimal redosing, and a balanced electrolyte formulation aimed at reducing intracellular calcium overload and oxidative stress (4). This study reaffirms its relevance to adult practice, particularly within the context of LMICs, where operating room time, perfusion resources, and staffing can be significant limitations.

Notably, the majority of our cases, including double valve replacements and mitral valve surgeries, were successfully completed with a single dose of DNC. The mean aortic cross-clamp times ranged from 55 to 70 minutes, and CPB times ranged from 80 to 98 minutes, reflecting procedural complexity that was managed efficiently without the need for repeated dosing. This is particularly important in LMIC settings, where limiting circuit complexity and conserving consumables such as tubing sets, cardioplegia lines, and syringes translates into tangible cost savings (7).

The spontaneous return of sinus rhythm in 95% of cases, with minimal requirements for defibrillation or inotropic support, supports the myocardial protective efficacy of DNC. Previous studies by O'Brien et al, (5) and Ad et al, (12) have shown lower troponin release and fewer postoperative arrhythmias in patients receiving Del Nido compared to St. Thomas or Buckberg cardioplegia, aligning with our intraoperative and early postoperative outcomes.

The safety profile of Del Nido is enhanced by its pharmacologic composition—particularly lidocaine and magnesium—which mitigate calcium-induced reperfusion injury. These features are further emphasized in the LMIC context, where postoperative arrhythmias, prolonged ICU stay, and resource-intensive management can strain already stretched healthcare systems (13). The reduced ICU duration observed in our cohort (4–6 days) compared favorably with regional benchmarks, indicating faster myocardial

recovery and a lower need for high-dependency monitoring.

Importantly, our experience suggests that Del Nido is well suited for diverse adult procedures, including congenital lesion repairs in older children and adults, AVR, and complex valvular replacements. This versatility supports its potential adoption as a standard cardioplegia across adult and pediatric cardiac programs in LMIC institutions. The simplicity of single-dose delivery also enables a smoother workflow in minimally invasive surgeries, where repeated administration can be technically challenging.

Despite these promising outcomes, this study has limitations. Being retrospective, it is subject to selection bias and lacks a comparative control arm using traditional cardioplegia. Furthermore, the follow-up period was limited to in-hospital outcomes; thus, long-term effects on myocardial function and arrhythmia incidence remain unknown. Future prospective trials with matched controls and extended follow-up are necessary to confirm the justifications of these findings.

Nevertheless, our findings carry important implications. From an economic perspective, reducing the volume and frequency of cardioplegia administration not only lowers direct drug costs but also reduces the need for additional workforce, equipment sterilization, and disposables—factors critical in LMIC surgical economics (14). Furthermore, smoother surgeries with less interruption for cardioplegia administration can reduce operative times and enhance operating room turnover.

DNC also aligns with global health priorities to optimize cardiac surgical outcomes in resource-limited settings. The Lancet Commission on Global Surgery emphasizes the need for context-appropriate technologies that maintain safety while enhancing affordability and access (15). Our study serves as a model for such innovation, showcasing that high-quality surgical care need not be resource-prohibitive.

In conclusion, DNC offers a practical, cost-effective, and clinically sound myocardial protection strategy in adult cardiac surgery, particularly within LMIC environments. Its favorable outcomes across a spectrum of

procedures, minimal dosing requirements, and ease of implementation recommend it for broader adoption. Further multicenter studies and randomized controlled trials are warranted to validate these results and facilitate the inclusion of Del Nido protocols for using this cardioplegia in simple CABGs (non severe CADs) and in national surgical guidelines.

### Limitations

This retrospective study evaluating DNC in adult cardiac surgery offers valuable insights for LMIC settings; however, several limitations must be acknowledged. First, the retrospective and single-centered nature of the analysis introduces inherent bias, including selection bias and lack of randomization. There was no direct comparison group using conventional cardioplegia solutions, such as St. Thomas' or blood cardioplegia, which limited the ability to draw definitive comparative conclusions. The absence of long-term postoperative follow-up also restricts our understanding of sustained myocardial performance and late arrhythmic events. Additionally, variations in surgical expertise, perfusion techniques, and intraoperative protocols may have influenced outcomes, making justifications to other centers variable. Finally, while cost-effectiveness is implied, a formal cost analysis was not performed and would be valuable in future studies.

Despite these limitations, the results of this study strongly support the feasibility, safety, and clinical efficacy of DNC in adult cardiac surgical procedures in an LMIC environment. Its pharmacological properties, single-dose strategy, and minimal logistical burden make it especially suited for resource-constrained healthcare systems. Across a diverse range of procedures—including valve replacements, minimally invasive surgeries, and congenital repairs—DNC provided adequate myocardial protection with favorable perioperative outcomes.

### Conclusion

DNC represents a practical and efficient alternative to traditional cardioplegic techniques in adult cardiac surgery within

LMIC settings. Its consistent performance across various surgical subgroups, reduced cardioplegia volume requirements, and facilitation of spontaneous rhythm return post-cross-clamp removal highlight its utility. Broader adoption of DNC may enhance surgical outcomes and optimize resource utilization in under-resourced centers. Further prospective, multicenter studies with randomized controls and long-term follow-up are essential to validate these findings and guide protocol development in LMIC cardiac surgery programs.

### Abbreviations

**CPB** : cardiopulmonary bypass; **LMICs**: low- and middle-income countries; **DNC** : del Nido cardioplegia; **HICs**: high-income countries; **CABG**: coronary artery bypass grafting; **SMS**: Sawai Man Singh Hospital; **DVR** : double valve replacement; **MVR**: mitral valve replacement; **AVR**: aortic valve replacement; **TOF**: tetralogy of fallot; **DORV**: double outlet right ventricle; **LVEF**: left ventricular ejection fraction; **ACC**: Aortic cross-clamp time.

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### Competing Interests

The author declared no potential competing interests with respect to the research, authorship, and/or publication of this article.

### Availability of Data and Materials

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

### Patient Consent Information

The patient provided informed written consent for the publication of the study data.

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