THE ATLANTIC Journal of Medical Science and Research

Atlantic J Med Sci Res 2026;6(2):234-42
DOI: 10.5455/atjmed.2026.03.019

Original Article

The efficacy of single-dose del nido cardioplegia for myocardial protection in patients with chronic total occlusion: The role of well-developed collaterals

Tolga Onur Badak, Hasan Uncu

University of Health Sciences Adana City Training and Research Hospital, Department of Cardiovascular Surgery, Adana, Türkiye

Received: 07 March, 2026
Accepted: 16 May, 2026
Published: 11 June, 2026

Corresponding Author: Tolga Onur Badak, University of Health Sciences Adana City Training and Research Hospital, Department of Cardiovascular Surgery, Adana, Türkiye
Email: drtolgaonurbadak@gmail.com

CITATION
Badak TO, Uncu H. The efficacy of single-dose del nido cardioplegia for myocardial protection in patients with chronic total occlusion: The role of well-developed collaterals. Atlantic J Med Sci Res. 2026;6(2):234-42. DOI:10.5455/atjmed.2026.03.019

Abstract

Aim: Adequate myocardial protection during cardiac surgery poses a particular challenge in patients with chronic total occlusion (CTO). This study evaluates the comparative efficacy of single-dose Del Nido cardioplegia (DNC) versus conventional blood cardioplegia (CBC) in patients undergoing coronary artery bypass grafting (CABG) for CTO, with emphasis on the modulatory role of coronary collateral development.

Materials and Methods: A retrospective, non-randomized analysis was conducted on 250 consecutive patients who underwent isolated CABG for CTO between January 2018 and January 2026. Patients were stratified into two groups according to the cardioplegia method administered in routine clinical practice by the operating surgeon: DNC (n=128) and CBC (n=122). Primary endpoints included postoperative cardiac troponin I (cTnI) and creatine kinase-MB (CK-MB) levels. Collateral circulation was graded according to the Rentrop classification system.

Results: Among patients with well-developed collaterals (Rentrop 2–3), the DNC group demonstrated significantly lower 24-hour cTnI levels compared with the CBC group (1.4 ± 0.6 vs. 3.1 ± 1.3 ng/mL, $p<0.001$), with a large effect size (Cohen's d = 1.65). This cardioprotective advantage was not observed in patients with poorly developed collaterals ($p=0.124$). In the overall cohort, the DNC group exhibited a lower requirement for inotropic support (18.8% vs. 32.0%, $p=0.021$) and a shorter hospital length of stay (6.8 ± 2.4 vs. 8.2 ± 3.1 days, $p=0.035$). Multivariate logistic regression identified CBC use (OR: 2.34, 95% CI: 1.28–4.27) and poor collateral development (OR: 3.12, 95% CI: 1.67–5.83) as independent predictors of postoperative myocardial injury.

Conclusion: Single-dose DNC confers superior myocardial protection compared with CBC in CTO patients undergoing CABG; however, this benefit is contingent upon the presence of well-developed collateral vessels. These findings indicate that preoperative assessment of collateral circulation may serve as a valuable guide for individualized cardioplegia selection.

Keywords: Coronary occlusion, coronary artery bypass, cardioplegic solutions, collateral circulation, myocardial reperfusion injury

INTRODUCTION

Chronic total occlusion (CTO) is defined as complete obstruction of a coronary artery with Thrombolysis in Myocardial Infarction (TIMI) grade 0 flow persisting for a minimum of three months. The condition is encountered in approximately 18–30% of patients referred for coronary angiography and represents an advanced manifestation of coronary artery disease (1,2). Although surgical revascularization may be indicated in a substantial proportion of these patients, achieving adequate myocardial protection during the procedure remains a formidable challenge. Effective delivery of cardioplegia to the myocardial territory subtended by the occluded vessel is critically dependent on the presence and functional adequacy of coronary collateral channels (3).

Coronary collateral circulation constitutes an adaptive vascular

network that develops progressively in response to chronic myocardial ischemia, functioning as an endogenous mechanism to sustain myocardial viability (4). Despite its recognized clinical importance, the influence of collateral vessel quality on cardioplegia distribution and the relative efficacy of different cardioplegia strategies in this patient population has not been systematically investigated.

Del Nido cardioplegia (DNC) was originally formulated for use in pediatric cardiac surgery, offering the distinctive advantage of sustained cardiac arrest for 60–90 minutes following a single administration. Its unique composition—characterized by reduced calcium concentration and supplementation with lidocaine and magnesium—is specifically designed to prevent myocardial contracture during the ischemic interval (5). In recent years, DNC has been increasingly adopted in adult cardiac surgery programs (6,7). It was hypothesized that the lower viscosity of DNC relative to conventional blood cardioplegia may facilitate more effective distribution through the high-resistance collateral channels, thereby enhancing myocardial protection distal to the CTO.

The primary objective of this study was to determine whether single-dose DNC provides superior myocardial protection compared with Conventional Blood Cardioplegia (CBC) in CTO patients, with particular emphasis on those with well-developed collateral vessels. Both cardioplegia strategies were evaluated by analyzing postoperative myocardial injury biomarkers and clinical outcomes in a large cohort of patients undergoing isolated coronary artery bypass graft (CABG).

MATERIALS AND METHODS

Study Design and Patient Population

This retrospective cohort study was conducted at the University of Health Sciences, Adana City Training and Research Hospital, Department of Cardiovascular Surgery. Ethical approval was obtained from the institutional review board (University of Health Sciences, Adana City Training and Research Hospital Clinical Research Ethics Committee, Decision No: 19.02.2026/22-1065). Given the retrospective nature of the study, individual patient consent was waived. A consecutive series of 250 patients who underwent isolated CABG with at least one angiographically confirmed CTO (TIMI 0 flow for ≥3 months) between January 2018 and January 2026 was included. The distribution of occluded vessel territories was recorded for group comparisons. Exclusion criteria comprised concomitant valvular or aortic procedures, emergency operations, preoperative cardiogenic shock, recent myocardial infarction (within 7 days), and significant hepatic or renal dysfunction. No randomization was performed because of the retrospective design. The selection of cardioplegia strategy was determined by the operating surgeon's clinical judgment in routine practice.

Preoperative Assessment and Collateral Classification

Coronary collateral vessels were graded according to the documented preoperative angiographic review using the Rentrop classification system (8): grade 0 denotes the absence of visible collateral filling; grade 1 indicates faint opacification of side branches; grade 2 represents partial filling of the epicardial vessel; and grade 3 corresponds to complete collateral filling. For the purposes of analysis, Rentrop grades 2–3 were designated as "well-developed collaterals" and grades 0–1 as "poorly developed collaterals." Interobserver agreement among the evaluating cardiac surgeons was excellent (κ=0.86, $p<0.001$). Each coronary angiogram was independently reviewed and graded by two of the five cardiac surgeons. In cases of disagreement (n=12, 4.8%), a consensus was reached by a third senior surgeon. The final grade used for analysis was the consensus grade.

Surgical Technique and Cardioplegia Protocols

All procedures were performed under cardiopulmonary bypass with mild systemic hypothermia (32–34°C). Myocardial protection was achieved via antegrade cardioplegia delivery. Retrograde delivery and selective graft cardioplegia were not evaluated in the present study.

Conventional Blood Cardioplegia (CBC) Protocol: CBC was prepared using oxygenated blood and crystalloid at a blood-to-crystalloid ratio of 4:1. The initial dose was 15–20 mL/kg, followed by supplemental doses of 5–10 mL/kg administered at 20–30 minute intervals.

Del Nido Cardioplegia (DNC) Protocol: A single dose of 15–20 mL/kg was administered at a blood-to-crystalloid ratio of 1:4. The Del Nido solution consisted of Plasma-Lyte A containing 1.36 g/L sodium chloride, 0.37 g/L potassium chloride, 0.3 g/L magnesium sulfate, 0.15 g/L sodium acetate, and 0.8 g/L sodium gluconate, supplemented with 13 mL of 1% lidocaine, 4 mEq of sodium bicarbonate, and 10 units of regular insulin per 1000 mL. The final blood-to-crystalloid ratio was 1:4. Conventional blood cardioplegia was prepared by mixing oxygenated blood with a crystalloid solution in a 4:1 ratio. The crystalloid component contained 50 mEq/L of sodium bicarbonate, 40 mEq/L of potassium chloride, and 20 mEq/L of magnesium sulfate, titrated to achieve a final potassium concentration of 20-25 mEq/L for the initial dose and 10-12 mEq/L for maintenance doses. In cases where aortic cross-clamp time exceeded 90 minutes, a half-dose supplement was administered.

Clinical and Laboratory Evaluation

Primary endpoints were serum cardiac troponin I (cTnI) and creatine kinase-MB (CK-MB) concentrations measured at 6 and 24 hours postoperatively. Secondary outcomes included the requirement for inotropic support, development of low cardiac output syndrome, postoperative arrhythmias, intensive care unit (ICU) and hospital length of stay, and 30-day mortality.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria). All tests were two-tailed, with a significance threshold of $p<0.05$.

Continuous variables conforming to a normal distribution are expressed as mean ± standard deviation (SD); non-normally distributed variables are presented as median with interquartile range [IQR]. Categorical variables are reported as frequencies and proportions. Normality was assessed using the Kolmogorov-Smirnov test. Between-group comparisons of normally distributed continuous variables were performed using the independent samples t-test; the Mann-Whitney U test was applied for non-normally distributed data. Categorical variables were compared using the chi-square or Fisher's exact test, as appropriate.

Temporal changes in cardiac biomarkers were analyzed using repeated-measures ANOVA with Greenhouse-Geisser correction, or the Friedman test when parametric assumptions were violated. Effect sizes for continuous variables were quantified using Cohen's d. Pre-specified subgroup analyses were conducted according to collateral status (Rentrop 2–3 vs. Rentrop 0–1).

Multivariate logistic regression was employed to identify independent predictors of postoperative myocardial injury, defined as cTnI exceeding 5.0 ng/mL. Variables with $p<0.10$ on univariate analysis, along with clinically relevant covariates, were entered into the model using forward stepwise selection. Model calibration was assessed with the Hosmer-Lemeshow test, and discriminative ability was evaluated using the area under the receiver operating characteristic curve (AUC). Results are expressed as odds ratios (OR) with 95% confidence intervals (CI). An interaction term between cardioplegia type and collateral status was incorporated to evaluate effect modification. Sample size estimation, based on pilot data from 20 patients, indicated that a minimum of 56 patients per group was required to achieve 80% statistical power at $\alpha=0.05$ for the detection of a clinically meaningful difference in 24-hour cTnI; the final sample size substantially exceeded this threshold.

RESULTS

Patient Characteristics and Operative Data

Of the 250 enrolled patients, 128 (51.2%) received DNC and 122 (48.8%) received CBC. Baseline demographic characteristics, comorbidities, and cardiovascular risk factors were comparable between the two groups (Table 1). The distribution of occluded vessel territories and the proportion of patients with well-developed collaterals were similarly balanced (44.5% in DNC vs. 43.4% in CBC, p=0.864).

Intraoperative parameters are summarized in Table 2. No statistically significant differences were identified in cardiopulmonary bypass time (86.4 ± 22.3 min for DNC vs. 89.7 ± 24.1 min for CBC, p=0.264) or aortic cross-clamp duration (58.2 ± 16.7 min for DNC vs. 61.3 ± 18.2 min for CBC, p=0.158). As anticipated, total cardioplegia volume was significantly lower in the DNC group ($p<0.001$).

Table 1. Preoperative demographic and clinical characteristics

Variable	DNC Group (n=128)	CBC Group (n=122)	p-value
Age (years)	64.7 ± 9.3	65.2 ± 8.9	0.667
Male gender, n (%)	94 (73.4)	87 (71.3)	0.785
BMI (kg/m²)	28.4 ± 4.2	28.9 ± 4.5	0.365
Diabetes mellitus, n (%)	58 (45.3)	54 (44.3)	0.902
Hypertension, n (%)	86 (67.2)	83 (68.0)	0.892
Hyperlipidemia, n (%)	72 (56.3)	68 (55.7)	0.937
Smoking (current/former), n (%)	79 (61.7)	74 (60.7)	0.898
Peripheral artery disease, n (%)	18 (14.1)	16 (13.1)	0.856
Prior MI (>30 days), n (%)	42 (32.8)	39 (32.0)	0.893
Preoperative creatinine (mg/dL)	0.94 ± 0.21	0.96 ± 0.23	0.474
LVEF (%)	48.2 ± 8.6	47.5 ± 9.1	0.532
LVEF < 40%, n (%)	22 (17.2)	24 (19.7)	0.628
EuroSCORE II (%)	2.4 ± 1.8	2.5 ± 1.9	0.670
CTO vessel, n (%)			0.814
LAD	41 (32.0)	40 (32.8)	
CX	30 (23.4)	27 (22.1)	
RCA	57 (44.5)	55 (45.1)	
Collateral grade, n (%)			0.864
Poor (Rentrop 0-1)	71 (55.5)	69 (56.6)	
Good (Rentrop 2-3)	57 (44.5)	53 (43.4)	

Data are presented as mean ± SD or n (%). BMI: Body mass index; MI: Myocardial infarction; LVEF: Left ventricular ejection fraction; LAD: Left anterior descending artery; CX: Circumflex artery; RCA: Right coronary artery.

Table 2. Operative data

Variable	DNC group (n=128)	CBC group (n=122)	p-value
CPB time (min)	86.4 ± 22.3	89.7 ± 24.1	0.264
Cross-clamp time (min)	58.2 ± 16.7	61.3 ± 18.2	0.158
Number of distal anastomoses	3.2 ± 0.9	3.3 ± 1.0	0.405
Total cardioplegia volume (mL)	1120 ± 245	1890 ± 420	<0.001
Need for additional cardioplegia, n (%)	21 (16.4)	84 (68.9)	<0.001
LIMA use, n (%)	120 (93.8)	114 (93.4)	0.920
Radial artery use, n (%)	28 (21.9)	26 (21.3)	0.915

CPB: Cardiopulmonary bypass; LIMA: Left internal mammary artery

Cardiac Biomarkers

Postoperative cardiac enzyme profiles are presented in Table 3 and Figure 1. Across the entire cohort, the DNC group exhibited significantly lower cTnI levels at both 6 hours (2.8 ± 1.2 vs. 4.1 ± 1.8 ng/mL, p=0.008) and 24 hours (1.9 ± 0.9 vs. 3.2 ± 1.4 ng/mL, p=0.003) postoperatively compared with the CBC group.

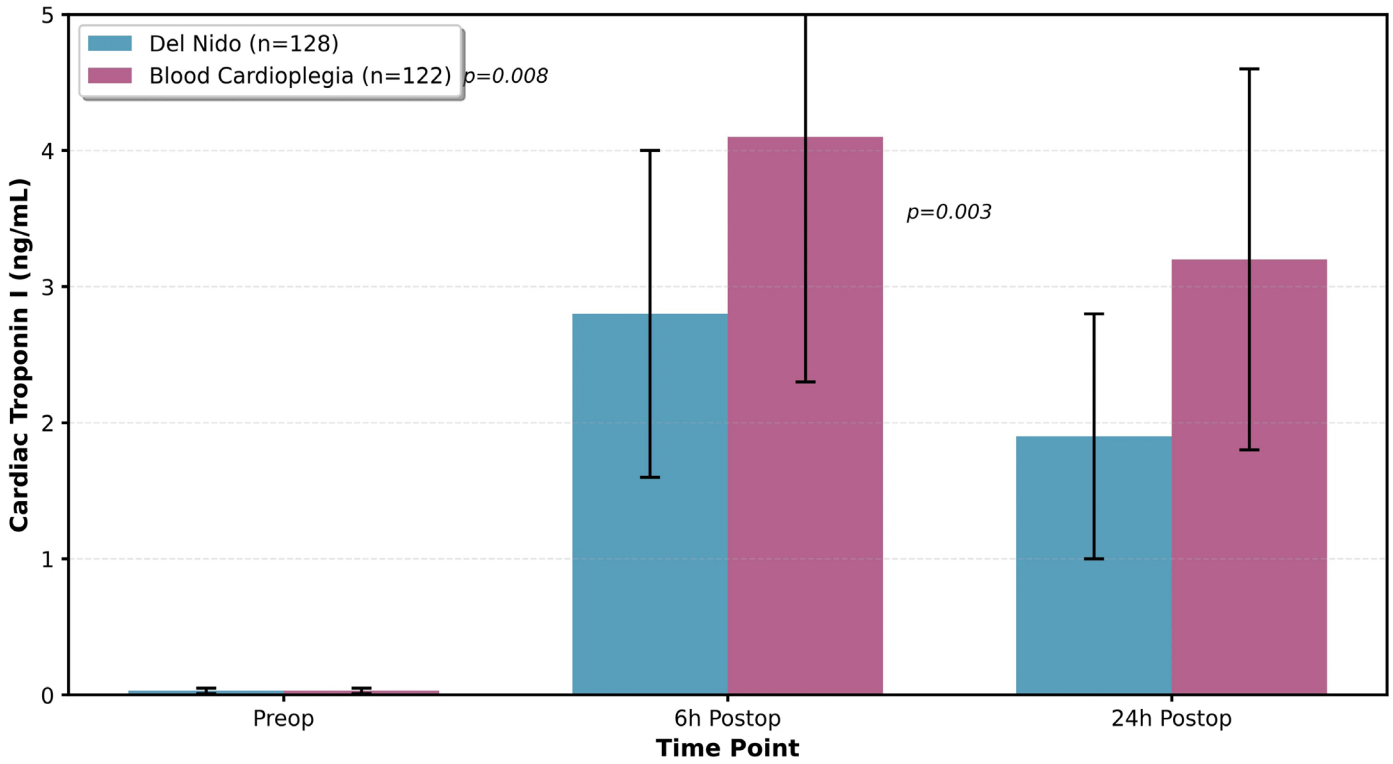

Figure 1. Postoperative Cardiac Troponin I Levels Over Time. A line graph depicting mean cTnI levels for the DNC and CBC groups at baseline, 6 hours, and 24 hours postoperatively. The DNC group demonstrates a consistently lower trajectory across all time points

Subgroup Analysis: Impact of Collateral Status

Stratified analysis according to collateral development status revealed a pronounced differential effect of cardioplegia type (Table 3, Figure 2). In patients with well-developed collaterals (Rentrop 2–3), DNC was associated with markedly superior myocardial protection, with 24-hour cTnI levels less than half those observed in the CBC group (1.4 ± 0.6 vs. 3.1 ± 1.3 ng/mL, p<0.001). In contrast, among patients with poorly developed collaterals (Rentrop 0–1), no statistically significant intergroup difference in cardiac enzyme release was detected (24-hour cTnI: 2.3 ± 1.1 vs. 3.3 ± 1.5 ng/mL, p=0.124). These findings indicate that the cardioprotective advantage of DNC is contingent upon an adequate collateral network.

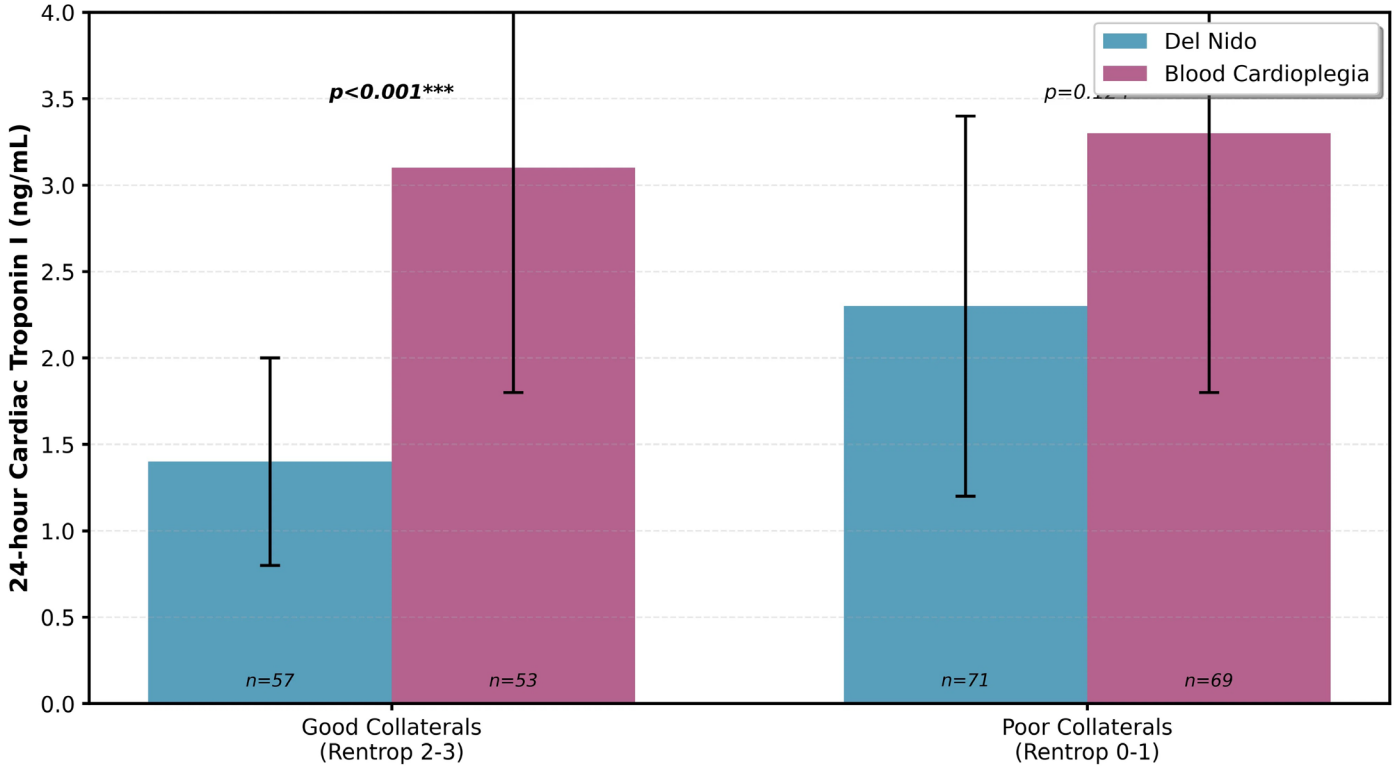

Figure 2. Postoperative 24-hour cTnI Levels Stratified by Collateral Status. A bar chart comparing mean 24-hour cTnI levels for the DNC and CBC groups within the well-developed collateral (Rentrop 2–3) and poorly developed collateral (Rentrop 0–1) subgroups. A statistically significant intergroup difference is evident exclusively within the well-developed collateral subgroup.

Table 3. Postoperative cardiac biomarker levels

Variable	DNC Group (n=128)	CBC Group (n=122)	p-value
All Patients			
Preoperative cTnI (ng/mL)	0.03 ± 0.02	0.03 ± 0.02	0.923
Postoperative 6h cTnI (ng/mL)	2.8 ± 1.2	4.1 ± 1.8	0.008
Postoperative 24h cTnI (ng/mL)	1.9 ± 0.9	3.2 ± 1.4	0.003
Postoperative 24h CK-MB (U/L)	14.2 ± 5.8	22.6 ± 8.4	0.005
Good Collaterals (Rentrop 2-3)	n=57	n=53	
Postoperative 24h cTnI (ng/mL)	1.4 ± 0.6	3.1 ± 1.3	<0.001
Postoperative 24h CK-MB (U/L)	11.8 ± 4.2	24.3 ± 8.9	<0.001
Poor Collaterals (Rentrop 0-1)	n=71	n=69	
Postoperative 24h cTnI (ng/mL)	2.3 ± 1.1	3.3 ± 1.5	0.124
Postoperative 24h CK-MB (U/L)	16.4 ± 6.8	20.8 ± 7.9	0.185

cTnI: Cardiac troponin I; CK-MB: Creatine kinase-MB.

Clinical Outcomes

Clinical outcome data are presented in Table 4. The DNC group demonstrated a significantly lower rate of postoperative inotropic support requirement (18.8% vs. 32.0%, p=0.021) and a reduced incidence of low cardiac output syndrome (7.0% vs. 15.6%, p=0.038). ICU length of stay (2.1 ± 1.2 vs. 2.8 ± 1.8 days, p=0.042) and total hospital length of stay (6.8 ± 2.4 vs. 8.2 ± 3.1 days, p=0.035) were also significantly shorter in the DNC group. Thirty-day mortality did not differ significantly between groups.

Table 4. Postoperative clinical outcomes			
Variable	**DNC Group (n=128)**	**CBC Group (n=122)**	**p-value**
Inotropic support requirement, n (%)	24 (18.8)	39 (32.0)	0.021
Low cardiac output syndrome, n (%)	9 (7.0)	19 (15.6)	0.038
Postoperative AF, n (%)	22 (17.2)	32 (26.2)	0.096
Mechanical ventilation time (hours)	9.2 ± 4.6	12.4 ± 6.8	0.058
ICU stay (days)	2.1 ± 1.2	2.8 ± 1.8	0.042
Hospital stay (days)	6.8 ± 2.4	8.2 ± 3.1	0.035
30-day mortality, n (%)	1 (0.8)	3 (2.5)	0.361

AF: Atrial fibrillation; ICU: Intensive care unit.

Risk Factor Analysis

Multivariate logistic regression analysis identified CBC use (OR: 2.34, 95% CI: 1.28–4.27, p=0.006) and poor collateral development (OR: 3.12, 95% CI: 1.67–5.83, p<0.001) as the strongest independent predictors of postoperative myocardial injury (Table 5). A statistically significant interaction between cardioplegia type and collateral status was demonstrated (p=0.008), confirming that the cardioprotective efficacy of DNC is modulated by the quality of collateral vessels.

Table 5. Multivariate logistic regression analysis for postoperative myocardial injury (cTnI >5.0 ng/mL)			
Variable	**Odds Ratio (OR)**	**95% CI**	**p-value**
LVEF (%)	0.95	0.92-0.98	0.004
Cross-clamp time (min)	1.03	1.01-1.05	0.012
CBC use (vs. DNC)	2.34	1.28-4.27	0.006
Poor collaterals (Rentrop 0-1)	3.12	1.67-5.83	<0.001

CI: Confidence interval; LVEF: Left ventricular ejection fraction; CBC: Conventional blood cardioplegia.

DISCUSSION

This study investigated the myocardial protective efficacy of single-dose DNC during CABG in patients with CTO and yielded three principal findings. First, DNC was associated with attenuated postoperative cardiac enzyme release across the entire study population. Second, this cardioprotective benefit was substantially amplified in patients with well-developed collateral vessels, with 24-hour cTnI levels reduced by more than 50%. Third, in patients with inadequate collateral development, no significant difference in myocardial injury markers was observed between cardioplegia strategies. These laboratory findings were mirrored by clinically meaningful outcomes: a 41% reduction in inotropic support requirement and a 17% decrease in hospital length of stay in the DNC group. To our knowledge, this represents the first study to systematically examine the interaction between cardioplegia type and collateral vessel quality in CTO patients.

The Challenge of Myocardial Protection in Chronic Total Occlusion

The fundamental difficulty in achieving adequate myocardial protection in CTO patients lies in delivering cardioplegia to the ischemic territory, a process that is entirely dependent on the functional capacity of collateral vessels (3). In the setting of complete coronary occlusion, antegrade cardioplegia delivery is precluded, and myocardial protection of the subtended territory relies exclusively on collateral-mediated distribution. The multivariate analysis in the present study identified poor collateral development as the most powerful independent predictor of postoperative myocardial injury (OR: 3.12, 95% CI: 1.67–5.83, p<0.001), underscoring the critical prognostic significance of these vessels in determining surgical outcomes. These data support the systematic preoperative assessment of collateral circulation as an integral component of risk stratification in CTO patients. In patients with poorly developed collaterals (Rentrop 0–1), antegrade cardioplegia delivery to the distal myocardial territory is likely limited regardless of cardioplegia formulation, which may explain why similar results were observed in the two groups within this subgroup.

CTO establishes a pathophysiological milieu in which the myocardium is subjected to sustained hypoperfusion and must develop adaptive responses accordingly. Over a protracted course, chronically ischemic myocardium undergoes metabolic and molecular remodeling, including upregulation of anaerobic metabolic pathways, enhanced expression of heat shock proteins, and increased angiogenic factor production (9,10). These adaptations confer relative resistance to acute ischemic injury

compared with myocardium subjected to abrupt flow cessation. However, the functional integrity of this protective phenotype is contingent upon adequate collateral perfusion. Collateral vessels serve as the sole conduit for substrate delivery to the ischemia-adapted myocardium; failure to achieve effective cardioplegia distribution through these channels negates the inherent cytoprotective mechanisms and exposes the myocardium to severe ischemia-reperfusion injury.

Mechanisms Underlying the Superior Performance of Del Nido Cardioplegia

Several mechanistic explanations may account for the superior cardioprotective efficacy of DNC in patients with well-developed collaterals. The most compelling relates to the rheological properties of the solution. DNC is prepared at a blood-to-crystalloid ratio of 1:4, in contrast to the 4:1 ratio employed for CBC, resulting in substantially lower viscosity. In accordance with the Hagen-Poiseuille equation, fluid flow through a conduit is inversely proportional to viscosity (11). Given that collateral vessels are characterized by small caliber, tortuous morphology, and elevated vascular resistance, they are particularly susceptible to the rheological properties of the perfusate. The reduced viscosity of DNC facilitates more effective penetration of these high-resistance pathways, promoting more homogeneous distribution to the myocardium distal to the CTO. This rheological advantage may be further amplified by impaired vasodilatory capacity in chronically recruited collateral vessels (12).

An additional consideration pertains to the hemodynamic stability afforded by single-dose administration. The CBC protocol necessitates repeated interruptions for supplemental cardioplegia delivery, each of which may compromise collateral perfusion pressure gradients (13). Lidocaine and magnesium may also contribute to myocardial protection by reducing energy expenditure and limiting calcium-mediated injury during ischemia-reperfusion (14-17).

Clinical Significance of Findings

The reduction in postoperative cardiac biomarker release observed with DNC carries direct clinical relevance beyond its biochemical significance. Elevated troponin concentrations following cardiac surgery have been consistently associated with increased morbidity and adverse long-term outcomes (18). A 55% reduction in 24-hour cTnI levels in patients with well-developed collaterals (1.4 vs. 3.1 ng/mL) represents a clinically meaningful improvement in myocardial protection. This laboratory benefit translated into tangible clinical advantages: a 41% reduction in inotropic support requirement and a 17% decrease in hospital length of stay.

Although no statistically significant difference in 30-day mortality was observed (0.8% vs. 2.5%, p=0.361), no inference regarding an early survival advantage of either cardioplegia strategy should be made from the present data. Postoperative inotropic support requirement is recognized as a marker of myocardial dysfunction and is independently associated with prolonged ICU admission, increased susceptibility to nosocomial infection, and inferior long-term prognosis (19). The reduced need for inotropic agents in the DNC group implies more favorable early myocardial functional recovery. A mean reduction in hospital stay of 1.4 days (6.8 vs. 8.2 days) also carries significant health economic implications, encompassing reduced direct hospitalization costs and more efficient utilization of institutional resources.

Comparison with Existing Literature and Alternative Strategies

The present findings extend the existing evidence base, which has generally demonstrated the safety and efficacy of DNC in adult cardiac surgery (6,7). However, the majority of prior investigations evaluated DNC across heterogeneous cardiac surgical populations without specific focus on CTO or the potential modifying effect of collateral vessel quality. A recent meta-analysis by Li et al. demonstrated lower postoperative troponin levels with DNC compared with blood cardioplegia, but did not stratify outcomes according to collateral status (20). The current study is the first to demonstrate a statistically significant interaction between cardioplegia type and collateral quality, establishing that the cardioprotective benefit of DNC is not universal but is specifically realized in patients with adequate collateral networks.

Retrograde cardioplegia has been advocated by some surgical groups for CTO patients on the premise that venous delivery circumvents the dependence on collateral distribution (21). However, this approach is associated with recognized limitations, including the risk of coronary sinus hypertension, heterogeneous myocardial distribution, and suboptimal right ventricular protection (22). In the present study, only antegrade delivery was evaluated. The present data suggest that antegrade DNC achieves effective myocardial protection in patients with well-developed collaterals, whereas retrograde or combined strategies may warrant consideration in patients with poor collateral development. The single-dose administration also simplifies the operative workflow by eliminating the need for repeated cardioplegia cannula manipulations.

Alternative cardioplegia solutions, including Histidine-Tryptophan-Ketoglutarate (HTK) and Celsior, have been employed in cardiac surgery, particularly in the transplantation setting. Comparative data between these agents and DNC in the specific context of CTO patients are currently lacking, and their higher viscosity profiles may limit their efficacy in collateral-dependent myocardial protection. Prospective comparative trials evaluating these solutions against DNC in CTO patients are warranted.

Clinical Implications and Recommendations

The findings of this study have practical implications for the perioperative management of CTO patients undergoing CABG. Systematic preoperative assessment of collateral

vessel development using the Rentrop classification should be incorporated into routine risk stratification protocols for this population. The Rentrop system, despite its inherent subjectivity, provides clinically actionable information that can guide cardioplegia strategy selection. On the basis of the present findings, patients with well-developed collaterals (Rentrop 2–3) appear to be reasonable candidates for antegrade single-dose DNC, while those with poorly developed collaterals (Rentrop 0–1) may benefit from alternative approaches, including retrograde cardioplegia, hybrid delivery strategies, or consideration of percutaneous revascularization.

A proposed decision algorithm for cardioplegia strategy selection in CTO patients should be regarded as a hypothesis-generating clinical framework: (1) preoperative collateral assessment using the Rentrop classification; (2) administration of single-dose DNC for patients with Rentrop grade 2–3; (3) consideration of retrograde cardioplegia or combined antegrade-retrograde approaches for patients with Rentrop grade 0–1; and (4) postoperative monitoring of troponin kinetics to assess the adequacy of myocardial protection. This individualized approach, grounded in patient-specific anatomical and physiological characteristics, may contribute to improved surgical outcomes in this challenging population.

Study Limitations

Several limitations of the present study merit acknowledgment. First, the retrospective design introduces the potential for selection bias. Although baseline characteristics were well balanced between groups and cardioplegia selection was based on surgeon preference rather than patient-specific factors, the influence of unmeasured confounders cannot be excluded. Surgeon-specific technical proficiency and subtle intraoperative variables may have contributed to outcome differences that are not fully captured in the analysis. Second, collateral grading using the Rentrop classification is inherently qualitative and subject to interobserver variability. Despite the high level of agreement achieved in this study (κ=0.86), the system does not provide a quantitative measure of collateral flow capacity. Objective hemodynamic indices such as fractional flow reserve (FFR) or collateral flow index (CFI) would offer more precise characterization but are not routinely obtained in the preoperative setting. Third, the single-center design limits the generalizability of the findings to institutions with different patient demographics, surgical techniques, and anesthetic protocols. Fourth, the 30-day follow-up period precludes assessment of long-term outcomes, including late mortality, ventricular function, and health-related quality of life. The potential long-term prognostic benefits of superior early myocardial protection remain to be established through extended follow-up studies.

Additionally, sex-disaggregated analyses were not performed in the present study. Emerging evidence suggests that collateral vessel development and myocardial ischemic tolerance may differ between male and female patients (23), and future investigations should examine whether the cardioprotective advantages of DNC are consistent across sexes.

CONCLUSION

Single-dose Del Nido cardioplegia provides demonstrably superior myocardial protection compared with conventional blood cardioplegia in patients with CTO undergoing CABG, with this benefit being specifically contingent upon the presence of well-developed collateral vessels. The proposed mechanisms include enhanced cardioplegia distribution through collateral channels attributable to lower solution viscosity, hemodynamic stability afforded by single-dose administration, and the pharmacological properties of the DNC formulation. These findings support the integration of preoperative collateral assessment into cardioplegia strategy planning for CTO patients. Prospective randomized controlled trials are required to validate these observations, elucidate the long-term prognostic implications, and define optimal myocardial protection strategies across the spectrum of collateral development in this complex surgical population.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
Ethical approval was obtained from University of Health Sciences, Adana City Training and Research Hospital Clinical Research Ethics Committee, Decision No: 19.02.2026/22-1065.

Patient Consent
Given the retrospective nature of the study, individual patient consent was waived.

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