Texas Heart Institute Journal

Clinical Investigation

Single-Dose del Nido Cardioplegia Compared With Standard Cardioplegia During Coronary Artery Bypass Grafting at a Veterans Affairs Hospital

Michael R. Reidy, MD[1,2]; Ernesto Jimenez, MD[1,2]; Shuab Omer, MD[1,2]; Lorraine D. Cornwell, MD[1,2]; Sabrina X. Runbeck, MPH, PA-C[2]; Ourania Preventza, MD[1,3]; Gabriel Loor, MD[1,3]; Todd K. Rosengart, MD[1,3]; Joseph S. Coselli, MD[1,3]

[1]Division of Cardiothoracic Surgery, Baylor College of Medicine, Houston, Texas
[2]Operative Care Line, Michael E. DeBakey VA Medical Center, Houston, Texas
[3]Cardiovascular Surgery Research, Texas Heart Institute, Houston, Texas

Del Nido cardioplegic solution (DNC), used chiefly in pediatric patients, rapidly induces prolonged cardiac arrest during cardiac surgery. To determine whether surgical outcomes after coronary artery bypass grafting in a United States military veteran population differed when DNC was used instead of our standard Plegisol cardioplegia, we retrospectively reviewed 155 consecutive operations performed from July 2016 through June 2017. Del Nido cardioplegia was used to induce cardiac arrest in 70 patients, and Plegisol in 85.

Compared with the Plegisol group, the DNC group had a shorter mean cardiopulmonary bypass time (96.8 vs 117 min; P <0.01) and aortic cross-clamp time (63.9 vs 71.7 min; P=0.02). On multiple linear regression, DNC use and number of bypasses performed were predictors of cardiopulmonary bypass time. The groups were similar in median number of bypasses performed, median time to extubation, intensive care unit stay, and total postoperative stay; however, the DNC group had a shorter mean operating room time (285.8 vs 364.5 min; P <0.01). Del Nido cardioplegia, number of bypasses, cardiopulmonary bypass time, and red blood cell transfusion were predictors of operating room time. Outcomes in the groups were similar for 30- and 180-day death, stroke, renal failure, ventilation time >48 hours, atrial fibrillation, tracheostomy, reintubation, and mechanical circulatory support. We conclude that single-dose DNC is safe, effective, and cost-effective for achieving cardiac arrest in U.S. veteran populations. ***(Tex Heart Inst J 2021;48(1):e196981)***

Citation:
Reidy MR, Jimenez E, Omer S, Cornwell LD, Runbeck SX, Preventza O, Loor G, Rosengart TK, Coselli JS. Single-dose del Nido cardioplegia compared with standard cardioplegia during coronary artery bypass grafting at a Veterans Affairs hospital. Tex Heart Inst J 2021;48(1):e196981. doi: 10.14503/THIJ-19-6981

Key words: Adult; cardioplegic solutions/administration & dosage; coronary artery bypass; heart arrest, induced/methods; length of stay; operative time; recovery of function; retrospective studies; treatment outcome

Corresponding author:
Ernesto Jimenez, MD, Michael E. DeBakey VA Medical Center, OCL 112, 2002 Holcombe Blvd., Houston, TX 77030

E-mail:
Ernesto.Jimenez3@va.gov

Del Nido cardioplegic solution (DNC), a blood-and-crystalloid solution, is used as a single-dose antegrade infusion to induce rapid cardiac arrest and provide at least 90 minutes of myocardial protection in neonatal heart surgery.[1] Pediatric cardiac surgeons have used it since the early 1990s because of its ability to shorten aortic cross-clamp (ACC) time and reduce the risk of reperfusion injury.

The base solution for DNC, Plasma-Lyte A (Baxter International Inc.), an isotonic electrolyte solution, has a pH of 7.4. One liter has an ionic concentration of 140 mEq sodium, 5 mEq potassium, 3 mEq magnesium, 98 mEq chloride, 27 mEq acetate, and 23 mEq gluconate. It causes rapid arrest by depolarizing the cellular membrane with potassium. Two of its components, magnesium (a natural calcium channel blocker) and lidocaine (a sodium channel blocker), negate intracellular sodium and calcium accumulation during the arrest period.[2-4] Therefore, DNC can be classified as a modified depolarizing agent that promotes a polarized membrane during ischemic arrest and reduces myocardial metabolic energy consumption. The solution is relatively depleted of calcium and is administered at a 1:4 blood-to-DNC ratio.[5-8] Because hypothermia improves protection of the ischemic myocardium by decreasing oxygen and high-energy phosphate consumption, the DNC delivery temperature is usually below 10 °C.

The use of DNC in adult cardiac surgery has been increasing.[9-14] Because of health behaviors and stress, military veterans are a higher-risk population for cardiac surgery than are civilians.[15] We found that the use of DNC during coronary artery bypass grafting (CABG) has not been studied in an adult United States veteran population. Accordingly, we retrospectively compared clinical results in patients in whom DNC or Plegisol cardioplegic solution (Pfizer Inc.) was used. In addition, we evaluated whether the prolonged period of diastolic arrest provided by DNC would enable more time-efficient operations with shorter cardiopulmonary bypass (CPB) and ACC times.

Patients and Methods

We reviewed the records of the 155 patients who underwent isolated CABG at MEDVAMC from July 2016 through June 2017 (Table I). Patients who had concomitant procedures were excluded. Before July 2016, Plegisol was the standard cardioplegic formula used at our institution. When DNC was introduced, 2 surgeons started to use it for CABG operations, and a third continued to use Plegisol. Plegisol is a cold-blood, depolarizing cardioplegic solution that is mixed with sodium bicarbonate and administered at a 4:1 blood-to-Plegisol ratio to induce cardiac arrest. Subsequent maintenance doses of Plegisol were administered at an 8:1 ratio every 15 to 20 minutes. In contrast, DNC was administered at a 1:4 blood-to-DNC ratio for an approximate volume of 20 mL/kg, not to exceed 1 L for the initial cardiac arrest. Plegisol costs $30 per liter; our pharmacy makes DNC for $7 per liter.

Both solutions were delivered antegrade through the aortic root and retrograde through the coronary sinus to induce initial cardiac arrest. The surgeon determined the dose for each patient. Patients were systemically cooled to a temperature of 32 to 34 °C. The surgical resident always participated and performed at least 50% of each operation.

A standard cardiac intensive care unit (ICU) "fast-track" protocol, consisting of early postoperative extubation (<8 hr) and early mobilization, was available to all the CABG patients. On the surgeon's recommendation, this protocol was followed by the cardiac ICU nurse and ICU respiratory therapist.

Preoperative patient characteristics that we evaluated were age, weight, height, preoperative lung function, hematocrit level, need for emergency surgery, and morbidity and mortality risk estimates. The estimates of 30-day morbidity and mortality risks calculated by the VA National Surgery Office were used in the analysis. Intraoperative variables included CPB time, ACC time, need for transfusion, and number of bypasses performed. Outcomes included time to extubation; ICU and total postoperative lengths of stay (LOS); postoperative stroke, renal failure, myocardial infarction, mediastinitis, cardiac arrest, atrial fibrillation, reoperation for bleeding, surgical site infection, tracheostomy, and reintubation; necessary mechanical circulatory support, such as an intra-aortic balloon pump (IABP) or ventricular assist device; prolonged ventilation (>48 hr),

TABLE I. Demographic and Preoperative Characteristics of the Patients

Variable	DNC Group (n=70)	Plegisol Group (n=85)	*P* Value
Female	0	1 (1.2)	0.9999
Age (yr)	67 (63–71)	66 (62–70)	0.61
Weight (kg)	93 (83–104)	93 (79–106)	0.9999
Height (cm)	177 (170.2–180)	177.8 (172.7–182.9)	0.44
Body surface area (m^2)	2.08 (1.9–2.3)	2.1 (1.9–2.3)	0.77
FEV1	2.5 (2.1–2.9)	2.6 (2.2–3)	0.38
Preoperative hematocrit (%)	39.7 (36–43.7)	40.5 (37.2–43)	0.63
Year of surgery	—	—	<0.01
2016	21 (30)	52 (61.2)	—
2017	49 (70)	33 (38.8)	—
Emergency surgery	2 (2.9)	1 (1.2)	0.59
LVEF <35%	12 (17.1)	10 (11.8)	0.34
Mortality risk estimate (%)	1.8 (0.8–2.9)	1.3 (0.8–2.3)	0.15
Morbidity risk estimate (%)	13.4 (10–17.1)	12 (9.3–18)	0.49

DNC = del Nido cardioplegia; FEV1 = forced expiratory volume in 1 second; LVEF = left ventricular ejection fraction

Data are shown as number and percentage or as median and interquartile range. *P* <0.05 was considered statistically significant.

and 30- and 180-day mortality rates. Clinical outcomes were abstracted in a blinded fashion.

This study was approved by the institutional review boards of the Michael E. DeBakey VA Medical Center (MEDVAMC) and Baylor College of Medicine, and by the U.S. Department of Veterans Affairs' Surgical Quality Data Group. The MEDVAMC is a teaching hospital for the thoracic surgery residents of Baylor College of Medicine. As part of the VA Quality Improvement Project, prospective collection of all patient-related data is not voluntary, so informed consent was waived.

Statistical Analysis

Statistical analyses were performed with use of SAS version 9.4 and JMP 13 (SAS Institute Inc.). A P value <0.05 was considered statistically significant, and all tests were 2-sided; P values were not adjusted for multiplicity. Group differences in the preoperative characteristics, intraoperative characteristics, and outcomes were tested with use of the χ^2 or Fisher exact test for categorical variables. Normally distributed continuous variables were compared by using a t test (for means), and nonnormally distributed continuous variables were compared by using the Wilcoxon 2-sample test (for medians). Multiple linear regression models included natural log transformation for time to extubation and ICU length of stay, and inverse transformation for postoperative LOS, to determine significant predictors of CPB, ACC, and operating room times, as well as time to extubation, ICU length of stay, and total postoperative LOS. The candidate list of variables used in the models was based on the data available, as well as variables that are typically important. The preoperative variables used in the multivariable analysis were age, sex, DNC or Plegisol use, left ventricular ejection fraction (LVEF) <35%, forced expiratory volume in 1 second (FEV1), the month during which the operation was performed (month 1, month 2, and so on), mortality risk estimate, and morbidity risk estimate. The intraoperative variables used (where appropriate) were emergency status, number of bypasses, CPB time, ACC time, fresh frozen plasma transfusion, and red blood cell transfusion. When we modeled the time to extubation, we added operating room time; when we modeled ICU and postoperative LOS, we added operating room time, mediastinitis, cardiac arrest, postoperative atrial fibrillation, reoperation for bleeding, prolonged ventilation, surgical site infection, tracheostomy, and reintubation. Insignificant variables were eliminated one by one until all remaining variables had a P value <0.05. Inspection of the variance inflation factors showed that multicollinearity was not an issue.

Results

In total, 155 isolated CABG operations were performed during the study period, in 154 men and 1 woman. Del Nido cardioplegic solution was used to induce cardiac arrest in 70 patients (45.2%), and Plegisol in 85 patients (54.8%). The mean age was 67 years in the DNC group and 66 in the Plegisol group. The only significant difference in demographic or preoperative characteristics

TABLE II. Intraoperative Characteristics

Variable	DNC Group (n=70)	Plegisol Group (n=85)	*P* Value
Operating room time (min)	285.8 ± 60	364.5 ± 84.5	<0.01
No. of bypasses	3 (2–3)	3 (3–3)	0.16
Aortic cross-clamp time (min)	63.9 ± 21.8	71.7 ± 18.6	0.02
Bypasses performed (n)			
1	36.5 (26.5–59.5) (n=4)	48 (34–62) (n=2)	0.82
2	49.5 (38.5–65.5) (n=16)	51.5 (46–57) (n=18)	0.7
3	65 (55–77) (n=43)	74 (67–80) (n=49)	0.01
4	79 (58–85) (n=7)	84 (76–94) (n=16)	0.18
CPB time (min)	96.8 ± 32.1	117 ± 27.3	<0.01
Red blood cell transfusion	18 (25.7)	15 (17.6)	0.41
Fresh frozen plasma transfusion	2 (2.9)	0	0.23

CPB = cardiopulmonary bypass; DNC = del Nido cardioplegia

Data are shown as mean ± SD, as median and interquartile range, or as number and percentage. $P<0.05$ was considered statistically significant.

was that more DNC patients than Plegisol patients underwent operations in 2017, and vice versa in 2016. The number of emergency operations performed was similar between groups. The VA National Surgery Office's preoperative evaluation of cardiac surgery risk showed that the median morbidity and mortality risk estimates did not differ between groups.

Intraoperative Results. The DNC group had shorter mean CPB (96.8 vs 117 min; P <0.01) and ACC times (63.9 vs 71.7 min; P=0.02) than did the Plegisol group (Table II), even though the distribution and median number of bypasses performed in each group were the same. Multiple linear regression analysis revealed that the surgery period (defined as 1–12, corresponding to the month of the study during which a patient underwent CABG) and the number of bypasses predicted ACC time, and that DNC use, surgery period, and number of bypasses predicted CPB time (Table III). The mean total operating room time was also shorter in the DNC group (285.8 min) than in the Plegisol group (364.5 min) (P <0.01) (Table II). Less than 2% of patients needed a subsequent maintenance dose of DNC. Multiple linear regression analysis revealed that DNC use, number of bypasses, CPB time, and the need for packed red blood cells were predictors of operating room time (Table III); however, the need for intraoperative packed red blood cells did not differ significantly between groups.

Postoperative Results. The median ICU and total postoperative LOS results were similar in both groups (Table IV), and multiple linear regression revealed that DNC use predicted neither outcome. The median time to extubation was slightly but not significantly shorter in the DNC group (Table IV), but the regression analysis revealed DNC to be a significant predictor of time to extubation, in addition to age, surgery period, transfusion of packed red blood cells, FEV1, and operating room time (Table V).

Of the total 155 patients studied, 41 (26%) were included in the fast-track ICU protocol. A greater number of patients in the DNC group (32; 45.7%) than in the Plegisol group (9; 10.6%) were fast-tracked to early extubation (P <0.01). Overall, the fast-tracked group had a significantly shorter median time to extubation than did the non–fast-tracked group (5.2 vs 17.7 hr; P <0.0001); however, the median ICU and total postoperative LOS were similar (Table VI). Among the DNC patients, the median LOS in the ICU was significantly shorter in those who were fast-tracked than in those who were not (3 vs 4.9 d; P=0.02).

No differences were found between the DNC and Plegisol groups in terms of postoperative complications (Table VII). Three patients needed postoperative IABP support: 2 in the DNC group because of preoperative ischemia from severe left main stenosis, and a patient in the Plegisol group after weaning from CPB because of

TABLE III. Predictors of Intraoperative Results after Multiple Linear Regression Analysis

	Operating Room Time		Aortic Cross-Clamp Time		CPB Time	
Parameter	***P* Value**	**Estimate** (SE)	***P* Value**	**Estimate** (SE)	***P* Value**	**Estimate** (SE)
Del Nido cardioplegia	<0.01	–47.25 (9.51)	—	—	<0.01	–15.04 (3.8)
Surgery period*	—	—	<0.01	–0.92 (0.31)	0.05	–1.05 (0.52)
No. of bypasses	0.03	–17.14 (7.71)	<0.01	14.17 (1.6)	<0.01	24.34 (2.42)
CPB	<0.01	1.24 (0.2)	—	—	—	—
Red blood cell transfusion	0.02	13.69 (5.57)	—	—	—	—

CPB = cardiopulmonary bypass

*Defined as the month of the study (for example, 1 = first month).

P <0.05 was considered statistically significant.

TABLE IV. Postoperative Characteristics

Variable	**DNC Group** (n=70)	**Plegisol Group** (n=85)	***P* Value**
Time to extubation after surgery (hr)	14.9 (5.9–18.8)	16.9 (15.2–18.2)	0.07
Intensive care unit LOS (d)	3.9 (2.9–5.9)	3.5 (2.1–5)	0.16
Total postoperative LOS (d)	7.4 (6.1–13.2)	7.2 (6–11.1)	0.28

DNC = del Nido cardioplegia; LOS = length of stay

Data are shown as median and interquartile range. P <0.05 was considered statistically significant.

ischemic cardiomyopathy and an LVEF of 20%. Before discharge from the hospital, LVEF was normal in the first 2 patients and markedly improved in the third. We do not think that the need for IABP support resulted from a failure in myocardial protection.

All coronary anastomoses were completed. Postoperatively, we noted no myocardial infarctions, clinically important electrocardiographic changes, or superficial wound infections.

Discussion

Our findings suggest that single-dose DNC is safe for inducing cardiac arrest during CABG in military veterans. Postoperative complication and mortality rates were similar to those in the multidose Plegisol group, as was the postoperative need for transfusions or mechanical support because of low cardiac output. We also confirmed that a single DNC dose shortened CPB, ACC, and total operating room times.

We think that the shorter total operating room time in the DNC group was chiefly related to substantially shorter CBP time. Because shorter pump times are associated with less coagulopathy and platelet dysfunction, earlier hemostasis before sternal closure may have also shortened total operating room time.

Analysis identified DNC as an independent predictor of CPB time, operating room time, and time to extubation. Finally, because of shorter total operating room time, more DNC patients qualified for fast-track status in the ICU, and their median extubation times were shorter than for non–fast-tracked patients. A patient's arrival at the ICU earlier rather than later appeared to be associated with the medical staff's decision to proceed with early extubation.

In a retrospective study of 380 nonveteran, low-risk CABG patients,[16] the results of DNC use did not differ from those of blood cardioplegia use in regard to effects on short-term survival, LVEF, or perioperative morbidity. However, DNC use was associated with significant reductions in CPB time, ACC time, and postoperative troponin T levels. The 180-day mortality rates were not determined. Similar results were reported in a retrospective study of isolated valve surgery in adults.[17]

A prospective randomized trial[18] to compare the use of DNC and St. Thomas cardioplegia in pediatric patients undergoing elective repair of ventricular septal defects or tetralogy of Fallot showed higher levels of interleukin-6 and tumor necrosis factor in the St. Thomas group 24 hours after CPB. Increases in those inflammatory markers were associated with low cardiac output syndrome. Myofibrillar disarray, an ultrastructural marker for myocyte dysfunction, was more extensive in the St. Thomas group.

Questions remain about the best practices for using DNC, and its potential effects. No investigators have reported an optimal dosing interval or blood-to-DNC ratio in adult cardiac surgery. In addition, findings that DNC is superior to cold blood cardioplegia in upregulating genes that reduce apoptosis and in reducing the myocyte contractile state need to be elucidated.[19] Randomized clinical trials comparing single-dose DNC and

TABLE V. Predictors of Postoperative Results after Multiple Linear Regression Analysis

	Time to Extubation After Surgery		ICU Length of Stay		Total Postoperative Length of Stay	
Parameter	***P* Value**	**Estimate** (SE)	***P* Value**	**Estimate** (SE)	***P* Value**	**Estimate** (SE)
Del Nido cardioplegia	<0.01	–0.43 (0.16)	—	—	—	—
Age	0.02	0.02 (0.009)	—	—	—	—
Surgery period*	<0.01	0.05 (0.02)	—	—	—	—
Red blood cell transfusion	<0.01	0.27 (0.08)	—	—	—	—
FEV1	0.01	–0.28 (0.11)	—	—	<0.01	0.02 (0.007)
Operating room time	0.04	0.002 (0.0009)	—	—	—	—
Morbidity risk estimate	—	—	<0.01	1.99 (0.51)	<0.01	–0.24 (0.07)
Mortality risk estimate	—	—	—	—	0.04	0.63 (0.3)
Reintubation	—	—	—	—	<0.01	–0.08 (0.02)
CPB	—	—	—	—	0.01	–0.0003 (0.0001)
Prolonged ventilation (>48 hr)	—	—	<0.01	1.1 (0.22)	—	—

CPB = cardiopulmonary bypass; FEV1 = forced respiratory volume in 1 second; ICU = intensive care unit

*Defined as the month of the study (for example, 1 = first month).

P <0.05 was considered statistically significant.

TABLE VI. Postoperative Results Based on Fast-Tracked Status

Variable	Fast-Tracked* (n=41)	Non–Fast-Tracked (n=114)	*P* Value
Time to extubation after surgery (hr)	5.2 (3.6–6.3)	17.7 (16.3–19.4)	<0.0001
Del Nido	5.2 (3.6–6.9)	18.5 (17.4–26.3)	<0.0001
Plegisol	5.4 (4.2–6.1)	17 (15.8–18.6)	<0.0001
Intensive care unit LOS (d)	3 (2.1–3.9)	3.9 (2.4–5.9)	0.08
Del Nido	3 (2.9–3.9)	4.9 (2.9–6.1)	0.02
Plegisol	2.5 (2–4)	3.7 (2.1–5.4)	0.34
Total postoperative LOS (d)	7.1 (5.9–8.9)	7.8 (6–13)	0.14
Del Nido	7.1 (5.9–9.9)	8 (6.8–15.1)	0.07
Plegisol	7.2 (5.1–8)	7.5 (6–12.3)	0.38

LOS = length of stay

*Extubation <8 hours after operation and early mobilization. The analysis included all 155 patients based on their fast-track status. The fast-tracked group included 32 of 70 patients from the del Nido group and 9 of 85 patients from the Plegisol group.

Data are shown as median and interquartile range. $P < 0.05$ was considered statistically significant.

TABLE VII. Postoperative Complications

Variable	DNC Group (n=70)	Plegisol Group (n=85)	*P* Value
Stroke	1 (1.4)	3 (3.5)	0.62
Renal failure	2 (2.9)	3 (3.5)	0.9999
Death			
30-d	0	2 (2.4)	0.5
180-d	0	5 (5.9)	0.06
IABP support	2 (2.9)	1 (1.2)	0.59
Mediastinitis	0	1 (1.2)	0.9999
Cardiac arrest	1 (1.4)	1 (1.2)	0.9999
Atrial fibrillation	21 (30)	21 (24.7)	0.46
Reoperation for bleeding	1 (1.4)	0	0.45
Prolonged ventilation (>48 hr)	5 (7.3)	4 (4.8)	0.73
Tracheostomy	3 (4.3)	1 (1.2)	0.33
Reintubation	4 (5.7)	2 (2.4)	0.41

DNC = del Nido cardioplegia; IABP = intra-aortic balloon pump

Data are shown as number and percentage. $P < 0.05$ was considered statistically significant.

multidose cold-blood cardioplegia may determine how best to maximize DNC's protective effects on myocytes. Collaborative studies may help to determine the molecular-level effects of CPB and cardiac arrest on human endothelial cells and cardiomyocytes, knowledge that should improve our understanding of the myocardial dysfunction that often occurs after open heart surgery.

Limitations. Our study had several limitations. This single-institution analysis was not a randomized controlled trial, so residual confounding variables may explain observed differences. Postoperative cardiac enzyme levels are not routinely collected at our institution, and the need for defibrillation after cross-clamp release was not recorded. Surgeon- and perfusion-specific details regarding myocardial protection, such as hemoconcentration, were not available. Our study may not have been sufficiently powered to detect differences in our postoperative clinical endpoints; therefore, we cannot state definitively whether DNC is safer than Plegisol cardioplegia. With only one woman included, the study did not reflect a general population. Finally, use of the fast-track ICU protocol depended on the attending surgeon's recommendations, which may have biased our early-extubation data.

Conclusion

In our population of U.S. military veterans who underwent CABG, single-dose DNC use appeared to be safe and effective, and patients given DNC had clinical outcomes similar to or better than those who were given Plegisol cardioplegia. Shorter total operating room times associated with DNC, as well as its lower comparative cost, may produce substantial cost savings within academic VA medical centers.

Acknowledgment

We thank Sanjay Patel, CCP, for helping to obtain intraoperative data.

Published: 4 May 2021

Meeting presentation: Presented at the 2018 Association of Veterans Affairs Surgeons (AVAS) Annual Meeting; Miami Beach, Florida, 5 May 2018.

References

1. Charette K, Gerrah R, Quaegebeur J, Chen J, Riley D, Mongero L, et al. Single dose myocardial protection technique utilizing del Nido cardioplegia solution during congenital heart surgery procedures. Perfusion 2012;27(2):98-103.
2. Chambers DJ. Mechanisms and alternative methods of achieving cardiac arrest. Ann Thorac Surg 2003;75(2): S661-6.
3. Snabaitis AK, Shattock MJ, Chambers DJ. Comparison of polarized and depolarized arrest in the isolated rat heart for long-term preservation. Circulation 1997;96(9):3148-56.
4. Sternbergh WC, Brunsting LA, Abd-Elfattah AS, Wechsler AS. Basal metabolic energy requirements of polarized and depolarized arrest in rat heart. Am J Physiol 1989;256 (3 Pt 2):H846-51.
5. Jimenez E, del Nido P, Feinberg H, Levitsky S. Redistribution of myocardial calcium during ischemia. Relationship to onset of contracture. J Thorac Cardiovasc Surg 1993;105(6):988-94.
6. Jimenez E, del Nido P, Sarin M, Nakamura H, Feinberg H, Levitsky S. Effects of low extracellular calcium on cytosolic calcium and ischemic contracture. J Surg Res 1990;49(3):252-5.
7. Matte GS, del Nido PJ. History and use of del Nido cardioplegia solution at Boston Children's Hospital [published erratum appears in J Extra Corpor Technol 2013;45(4):262]. J Extra Corpor Technol 2012;44(3):98-103.
8. Oliveira MA, Brandi AC, Santos CA, Botelho PH, Cortez JL, Braile DM. Modes of induced cardiac arrest: hyperkalemia and hypocalcemia--literature review [in Portuguese]. Rev Bras Cir Cardiovasc 2014;29(3):432-6.
9. Ad N, Holmes SD, Massimiano PS, Rongione AJ, Fornaresio LM, Fitzgerald D. The use of del Nido cardioplegia in adult cardiac surgery: a prospective randomized trial. J Thorac Cardiovasc Surg 2018;155(3):1011-8.
10. Kim K, Ball C, Grady P, Mick S. Use of del Nido cardioplegia for adult cardiac surgery at the Cleveland Clinic: perfusion implications. J Extra Corpor Technol 2014;46(4):317-23.
11. Koeckert MS, Smith DE 3rd, Vining PF, Ranganath NK, Beaulieu T, Loulmet DF, et al. Del Nido cardioplegia for minimally invasive aortic valve replacement. J Card Surg 2018;33(2):64-8.
12. O'Blenes SB, Friesen CH, Ali A, Howlett S. Protecting the aged heart during cardiac surgery: the potential benefits of del Nido cardioplegia. J Thorac Cardiovasc Surg 2011;141(3):762-70.
13. Yerebakan H, Sorabella RA, Najjar M, Castillero E, Mongero L, Beck J, et al. Del Nido cardioplegia can be safely administered in high-risk coronary artery bypass grafting surgery after acute myocardial infarction: a propensity matched comparison. J Cardiothorac Surg 2014;9:141.
14. Timek T, Willekes C, Hulme O, Himelhoch B, Nadeau D, Borgman A, et al. Propensity matched analysis of del Nido cardioplegia in adult coronary artery bypass grafting: initial experience with 100 consecutive patients. Ann Thorac Surg 2016;101(6):2237-41.
15. Bergman BP, Mackay DF, Pell JP. Acute myocardial infarction in Scottish military veterans: a retrospective cohort study of 57,000 veterans and 173,000 matched nonveterans. Am J Epidemiol 2014;179(12):1434-41.
16. Timek T, Willekes CL, Beutte TA, Ziazadeh DR, Matar RN, Parker JL, et al. Del Nido cardioplegia in adult coronary artery bypass grafting surgery [abstract]. Society of Thoracic Surgeons 54th annual meeting, 2018. Available from p. 154-5: https://www.sts.org/sites/default/files/documents/54AM_AbstractBook_Final2.pdf
17. Mick SL, Robich MP, Houghtaling PL, Gillinov AM, Soltesz EG, Johnston DR, et al. del Nido versus Buckberg cardioplegia in adult isolated valve surgery. J Thorac Cardiovasc Surg 2015;149(2):626-36.
18. Talwar S, Bhoje A, Sreenivas V, Makhija N, Aarav S, Choudhary SK, Airan B. Comparison of del Nido and St Thomas cardioplegia solutions in pediatric patients: a prospective randomized clinical trial. Semin Thorac Cardiovasc Surg 2017;29(3):366-74.
19. Heydarpour M, Ejiofor JI, Gilfeather MS, Body SC, Aranki SF, Muehlschlegel JD. Abstract 19320: Whole genome RNA sequencing analysis of modified Delnido versus whole blood cardioplegia in the human left ventricle [abstract]. Available from: https://www.ahajournals.org/doi/10.1161/circ.134.suppl_1.19320