

**Original  
Article**

# Comparison of Del Nido and Intermittent Warm Blood Cardioplegia in Coronary Artery Bypass Grafting Surgery

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**Purpose:** In this study, we aim to investigate the efficacy and clinical results of using Del Nido solution (DNS) in coronary artery bypass grafting (CABG) surgery by comparing with intermittent warm blood cardioplegia (IWBC).

**Methods:** Between March 2017 and February 2018, 297 adult patients who underwent primary isolated CABG surgery with cardiopulmonary bypass (CPB) were included in the study. We used DNS in 112 patients and IWBC was used in 185 patients. We compared both the clinical and the laboratory results.

**Results:** Aortic cross-clamp time, CPB time, and peak glucose level are lower with DNS. But we did not observe any meaningful difference of clinical results between two methods including postoperative myocardial enzyme release.

**Conclusion:** Del Nido cardioplegia was developed for immature heart and pediatric surgery. But in our opinion, it is a good and useful alternative to CABG surgery with similar results to IWBC.

**Keywords:** coronary artery bypass grafting, cardioplegia, myocardial protection, cardiopulmonary bypass

## Introduction

Cardioplegia was developed as a method for protecting the myocardium, maintain an arrested heart, and clear site for surgery during all kinds of cardiac surgeries with cardiopulmonary bypass (CPB). In the efforts of searching for optimal myocardial protection, blood and crystalloid-based solutions, warm and cold solutions, the

way to deliver and timing (intermittent or continuous delivery), modifications in the chemical composition of the cardioplegia have been evolved. Currently, a large variety of cardioplegia solutions for myocardial protection is available in cardiac surgery. There are two main types of cardioplegia solutions based on simple classifications, based on the basic solutions that constitute the contents of blood and crystalloid cardioplegia. The similarity of blood-based cardioplegia solutions to normal physiological oxygen transport capacity seems to be quite advantageous and less risky in terms of myocardial protection. Besides this, hemodilution and related difficulties are less frequently observed in the use of blood cardioplegia when compared with crystalloid cardioplegia. The intermittent warm blood cardioplegia (IWBC) solution is our preferred cardioplegic solution in coronary artery bypass grafting (CABG) surgery. IWBC should be delivered multiple times for optimum results and minimum complications.

Del Nido solution (DNS) was developed for use in pediatric cardiac surgery as an alternative.<sup>1,2)</sup> Del Nido

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**Table 1** Ingredients of solutions

	IWBC	DNS
Basic solution	Whole blood + Ringer lactate	Plasma-Lyte A
KCL	22.5 mEq/L for induction 7 mEq/L to remain	26 mEq/L
NaHCO <sub>3</sub>	none	13 mEq/L
Mannitol 20%	none	16 mL
Magnesium sulfate	6 mEq/L	16 mEq/L
Lidocaine 2%	none	6.5 mL
Blood/crystalloid rate	4/1	1/4
Calcium	1.35 mEq/L	0.8 mEq/L

IWBC: intermittent warm blood cardioplegia; DNS: Del Nido solution;  
KCL: potassium chloride; NaHCO<sub>3</sub>: Sodium bicarbonate

cardioplegia has been in common use in pediatric cardiac surgery for almost two decades. This liquid of cardioplegia is a crystalloid-based solution, mixed with four parts DNS and one part whole blood. The ingredients of DNS and IWBC are presented in **Table 1**. In the congenital heart surgery of pediatric population, safety and efficacy of DNS have been reported.<sup>3)</sup> There is a limited number of studies reporting the use of DNS routinely in coronary artery bypass surgery.<sup>4)</sup> Recently, it has been reported that DNS is safe and effective to use in adult patients for isolated aortic and mitral valve surgery.<sup>5)</sup> DNS can be preferred as an alternative to blood cardioplegia in adult concomitant aortic valve replacement + CABG surgery, provides comparable myocardial protection and may be associated with shorter operative times.<sup>6)</sup> Therefore, we designed this study to investigate the efficacy and safety of DNS when compared to IWBC in CABG surgery.

## Materials and Methods

The current study was approved by the local ethical committee and all participants signed their written informed consent form. From March 2017 to February 2018, 297 patients who underwent elective CABG surgery were randomly assigned to two groups (DNS was used in 112 patients and IWBC was used in 185 patients). The randomization list was generated using the nQuery advisor Version 7.0 with a variable block size. This randomization sequence was transferred to sealed envelopes which were opened by cardiovascular perfusionist at operation room. Patients who needed emergent surgery or any combine operations were not included in the study. Patients who underwent reoperation for bleeding were excluded also because to assess cardiac enzyme values and damage of the myocardium could not be

evaluated objectively in this situation. All operations were performed with CPB and under general anesthesia.

According to our routine anesthesia, practice operation management was conducted. 5–10 µg/kg fentanyl, 0.08–0.10 mg/kg vecuronium, and 0.1–0.2 mg/kg intravenous midazolam were administered to each patient for induction of anesthesia. Sevoflurane inhalation was preferred to maintain the depth of anesthesia. 320–400 IU/kg unfractionated heparin was administered to maintain an activated clotting time (ACT) greater than 480 seconds. Ascending aorta was cannulated and then a single two-stage atrial cannula or bicaval cannulation used for venous drainage. 1350 mL prime volume (1 L isolate S, %20 mannitol 200 cc, %3 NaCl 150 cc, 5000 IU heparin) was admitted. 2.0–2.5 L/min/m<sup>2</sup> flow rate, 180–200 mm Hg Pao<sub>2</sub>, and 35–45 mmHg PCO<sub>2</sub> was maintained. The retrograde cardioplegia cannula was inserted according to the surgeon's preference. Only antegrade fashion was applied for DNS. In our myocardial protection routine, an additional dose should be administered after 60 minutes from the first dose according to our clinical experience. We added a second dose of cardioplegia in only 7 of the 112 patients using DNS. In the other group™BC was delivered via retrograde and antegrade cardioplegia cannulas in 39 patients with many occluded coronary arteries. Following aortic clamping, 1000 mL dose of DNS at +4°C was delivered once. If the patient received IWBC, 1000 mL of blood cardioplegia at 33–34°C was administered and an additional dose was applied every 15–20 minutes during the ischemic period. Topical hypothermia was conducted in all cases. A membrane oxygenator and an arterial line filter used for CPB, during CPB for all patients, aimed at level of hematocrit (Hct) >22%, mean arterial pressure was preserved at 60–80 mmHg, serum glucose was kept between 110 and 180 mg/dL with an infusion of insulin if necessary, cooled

33–34°C (nasopharyngeal core body temperature) and a-stat pH management as considered.

Cardiac troponin-I and creatine kinase-MB isotype (CK-MB) levels were measured immediately before induction of anesthesia and at 6, 12, and 24 hours postoperative in both two groups. Preoperative and postoperative left ventricular ejection fraction was measured and recorded. CPB and cross-clamp times, mechanical ventilation time, intensive care unit, and in hospital length of stay were recorded. A need for inotropic support more than 4 hours or insertion of intra-aortic balloon pump device (for weaning the CPB or within the first 24 hours after surgery) were defined as postoperative low cardiac output syndrome (LCOS). Mortality within 30 days after surgery defined as early mortality. Other clinical records included such as postoperative acute renal failure (defined when urine output <0.5 mL/kg/min for more than 6 hours), electrocardiography (ECG) modifications (new ST segment alterations or new Q wave), new echocardiography wall motion abnormalities defined as myocardial infarction, newly emerging arrhythmias, new onset neurologic events (stroke or transient ischemic attack), need for a permanent pacemaker.

### Statistical analysis

SPSS 25.0 for Windows (SPSS Inc. Chicago, IL, USA) was utilized for statistical analysis. Continuous variables data were presented as mean  $\pm$  SD. Dichotomous data were presented as n (%). Nominal variables are presented as frequency (%). Demographic and preoperative factors were evaluated to make certain about the comparability of the groups. For continuous variables whose distributions approximate normality (Shapiro–Wilk test), a t-test was used for comparisons. When normality assumptions are not as good as satisfactory, the nonparametric Mann–Whitney U-test was utilized. Pearson’s chi-squared test was used to analyze qualitative variables and Fisher’s exact test was utilized when it is necessary. The analysis of variance (ANOVA) test or its nonparametric equipollent, Kruskal–Wallis test were used to determine the distinction between the values of a variable among several independent (statistical) populations. Multiple logistic regression models were utilized to evaluate the variables at the same time.

### Results

The demographic data of the patients are similar and presented in **Table 2**. Aortic cross-clamp time and CPB

time were shorter in the DNS group ( $43.7 \pm 8.6$  minutes,  $54.3 \pm 9.7$  minutes,  $p = 0.0254$  and  $67.9 \pm 11.5$  minutes,  $77.2 \pm 14.1$ ,  $p = 0.0368$ ) than in the IWBC group. Total cardioplegia volume was  $985 \pm 60$  mL in DNS group and  $1540 \pm 230.4$  mL in IWBC group ( $p < 0.001$ ). The number of the grafts were similar in both DNS and IWBC groups  $3.3 \pm 1.3$  versus  $3.5 \pm 1.6$ , respectively ( $p = 0.685$ ). The peak level of glucose was lower in DNS group ( $163 \pm 24$  vs.  $193 \pm 44$  mg/dL,  $p < 0.0001$ ) intraoperative. In this respect, insulin requirements were lower in DNS group comparing to IWBC group (35% vs. 51%, respectively,  $p < 0.001$ ). LCOS was observed in two (1.7%) patients in DNS group and in five (2.7%) in IWBC group ( $p = 0.098$ ). No intra-aortic balloon pump was required for any patients in the postoperative period. Transient ischemic attack or stroke was observed in three (2.67%) patient in DNS group and in seven (3.78%) patients in IWBC group ( $p = 0.076$ ). Postoperative atrial fibrillation developed in 21 (18.75%) patients in DNS group and in 29 (15.6%) patients in IWBC group, there was no significant difference. Postoperative renal insufficiency was developed in one (0.54%) patient in IWBC group and there was no renal failure in DNS group with no statistically significant difference ( $p = 0.770$ ). Two patients died due to LCOS in DNS group. In IWBC group, one patient with postoperative pneumonia, one patient who had a stroke, and one patient died due to LCOS in postoperative 30 days. Mechanical ventilation time, length of intensive care unit stay, length of in-hospital stay, and mortality rate in 30 days values were compared and there was a significant difference between DNS and IWBC groups. All intraoperative data and postoperative clinical results are presented in **Table 3**. Preoperative and postoperative (at 6, 12, and 24 hours) CK-MB and troponin-I levels measured and results are presented in **Table 4**. No statistically significant difference was found between CK-MB and troponin-I level in any of the measurements at different times when the compared the two groups.

### Discussion

In terms of content, there are basically two types of cardioplegia solution (crystalloid and blood cardioplegia). All cardioplegia methods, whether crystalloid-based or blood-based, work to establish hyperkalaemic electromechanical diastolic arrest. The goal is to provide a clear vision and surgical field without motion and to protect the myocardium from ischemic damage as much as possible.

**Table 2 Baseline characteristics of patients**

	DNS group (n = 112)	IWBC group (n = 185)	p value
Male	69	103	0.941
Age, years	62.4 ± 8.7	63.7 ± 9.1	0.874
BMI, kg/m <sup>2</sup>	32.1 ± 6.1	31.8 ± 5.7	0.852
Number of grafts	3.2 ± 1.1	3.3 ± 1.5	0.239
LVEF, %	58.4 ± 10.9	57.8 ± 11.2	0.542
Syntax Score	17.3 ± 9.2	16.7 ± 10.5	0.746
Diabetes	53 (47.3%)	86 (46.5%)	0.147
Hypertension	57 (50.9%)	91 (49.2%)	0.530
COPD	42 (37.5%)	76 (41.1%)	0.078
Dyslipidaemia	49 (43.7%)	61 (32.9%)	0.053
Chronic kidney failure	5 (4.4%)	9 (4.9%)	0.256
Peripheral arterial disease	23 (20.5%)	38 (20.5%)	0.842
Preoperative stroke or TIA	5 (4.4%)	9 (4.9%)	0.662
Smoking	67 (59.8%)	94 (50.9%)	0.241
Euroscore II (%)	4.1 ± 3.9	4.6 ± 3.2	0.094

IWBC: intermittent warm blood cardioplegia; DNS: Del Nido solution; BMI: body mass index; LVEF: left ventricle ejection fraction; COPD: chronic obstructive pulmonary disease; TIA: transient ischemic attack

**Table 3 Intraoperative data and postoperative outcomes**

	DNS group	IWBC group	p value
Cross-clamp time, min (mean ± SD)	43.7 ± 8.6	54.3 ± 9.7	0.0254
CPB time, min (mean ± SD)	67.9 ± 11.5	77.2 ± 14.1	0.0368
Total cardioplegia volume, mL (mean ± SD)	985 ± 60	1540 ± 230.4	<0.001
Peak level of glucose during CPB (mean ± SD)	163 ± 24	193 ± 44	
Peak level of potassium during CPB (mean ± SD)	5.9 ± 1.3	5.7 ± 1.5	
Number of grafts (mean ± SD)	3.3 ± 1.3	3.5 ± 1.6	0.685
Temporary pace maker (n, %)	0 (%0)	1 (%0.54)	0.845
Defibrillation (n, %)	3 (%2.67)	7 (%3.78)	0.186
Low cardiac output syndrome (n, %)	2 (%1.7)	5 (%2.7)	0.098
TIA/stroke (n, %)	3 (%2.67)	7 (%3.78)	0.076
Postoperative myocardial infarction (n, %)	0 (%0)	1 (%0.54)	0.768
Postoperative atrial fibrillation (n, %)	21 (%18.75)	29 (%15.6)	0.078
Postoperative renal insufficiency (n, %)	0 (%0)	1 (%0.54)	0.770
Mechanical ventilation time (mean ± SD, hours)	6.5 ± 3.8	5.9 ± 4.1	0.105
ICU stay (mean ± SD, days)	2.3 ± 1.9	2.7 ± 2.1	0.562
In-hospital stay (mean ± SD, days)	7.6 ± 7.1	6.9 ± 7.8	0.603
Mortality in 30 days (n, %)	2 (%1.7)	3 (%1.62)	0.751

IWBC: intermittent warm blood cardioplegia; DNS: Del Nido solution; CPB: cardiopulmonary bypass; ICU: intensive care unit; TIA: transient ischemic attack; SD: standard deviation

**Table 4 Preoperative cardiac enzymes**

Timing	CK-MB (ng/mL)			Troponin-I (ng/mL)		
	DNS	IWBC	p	DNS	IWBC	p
Preoperative	0.32 ± 0.041	0.24 ± 0.31	0.102	0.04 ± 0.025	0.03 ± 0.029	0.124
6 hours	25.77 ± 8.3	24.82 ± 7.9	0.098	4.73 ± 2.52	5.21 ± 2.45	0.086
12 hours	32.51 ± 11.6	30.81 ± 13.4	0.160	5.45 ± 3.25	6.02 ± 3.18	0.135
24 hours	16.34 ± 9.5	17.03 ± 10.2	0.115	3.54 ± 3.12	3.49 ± 3.51	0.094

IWBC: intermittent warm blood cardioplegia; DNS: Del Nido solution; CK-MB: creatine kinase-MB isotype

In a study conducted by M de Jonge et al., it was reported that there was no difference in the clinical results of crystalloid and blood cardioplegia. According to this study, blood cardioplegia is related to high levels of postoperative CK-MB ( $21.6 \pm 28.9$  and  $24.4 \pm 40.4$  ( $p = 0.004$ ) crystalloid and blood cardioplegia, respectively).<sup>7)</sup> In a meta-analysis of 269 randomized controlled trials comparing blood and crystalloid cardioplegia, Guru et al. reported a reduction in LCOS and decrease in CKMB levels with blood cardioplegia.<sup>8)</sup> In another meta-analysis published by Sa et al., it was reported that there was no difference between the two cardioplegia methods in terms of LCOS.<sup>9)</sup> In a recent randomized controlled trial, Ovrum et al. reported that crystalloid cardioplegia is more advantageous in terms of cost but there is no clinical difference, similar to our results.<sup>10)</sup> Although all these results have been noted as positive references to crystalloid cardioplegia, we believe that there has not been enough study to compare Del Nido cardioplegia which has become increasingly widespread in adult patients in recent years and blood cardioplegia.

Our hypothesis in this study is that Del Nido cardioplegia is not inferior to conventional blood-based methods in the adult patient group. The results of our study support that Del Nido cardioplegia can be safely used in CABG surgery similar to findings of the limited number of observational studies previously published. DNS was developed for immature heart and is frequently used in North America for pediatric heart surgeries.<sup>11)</sup> On the other hand, in recent years using DNS for myocardial protection has become much popular in adult patients.<sup>4-12)</sup>

Ischemic period and CPB times may be shorter with DNS because it is used in a single dose and does not need additional doses for 90 minutes according to some authors.<sup>13,14)</sup> This investigation is not satisfactory to make a definite comment on the best timing strategies for additional doses of DNS in CABG surgery. As a matter of fact, there is no consensus in the provision of timing for repetition of DNS. In patients undergo CABG, a single dose of DNS is usually sufficient and there is no interrupt during surgery. Whereas the mean cross-clamp time in the other group was  $54.3 \pm 9.7$  minutes, which means that on average, cardioplegia is administered twice in each patient. We applied topical hypothermia in all operations according to our clinical myocardial protection routine. Topical cooling may be beneficial, but there are also opinions indicating no benefit.<sup>15,16)</sup> But this study does not include data comparing the effects of topical hypothermia. We did not find a significant difference

when comparing two cardioplegia strategies in terms of myocardial injury. LCOS, postoperative LVEF, troponin-I, and CK-MB levels were similar between the groups. In a meta-analysis performed by Yongnan Li and his colleagues, it was shown that there was no statistically significant difference between the troponin-I, troponin-T, and CK-MB levels in 836 patients with cardiac enzymes, similar to the results of our study.<sup>17)</sup> Lower glucose content is another advantage of DNS in that it requires less insulin use. Neither the Plasma Lyte-A nor the ringer lactate solution contains glucose. The glucose levels in both cardioplegia solutions are related to the amount of blood in the cardioplegia formula. This amount is four times higher than DNS in the IWBC. Glucose-insulin-potassium therapy (GIK) might improve myocardial perfusion and left the ventricular function in a situation of myocardial ischemia (such as aortic cross-clamping). However, the mechanism of GIK in protecting cardiac functions still unclear.<sup>18)</sup> In a study of Vistarini and his colleagues, regarding the use of DNS in minimally invasive aortic valve surgery, the mean duration time of mechanical ventilation was significantly lower when compared to patients receiving blood cardioplegia.<sup>19)</sup>

Elderly patients undergoing heart surgery are at higher risk than younger patients for the development of myocardial dysfunction related to higher levels of intracellular calcium.<sup>20,21)</sup> DNS contains less calcium than standard blood cardioplegia. The results of a recent investigation on rats demonstrated that the intracellular calcium levels in the ischemic period are lower in DNS when it is compared to blood cardioplegia.<sup>22)</sup>

As discussed in previous studies, DNS may be an ideal alternative for conventional methods in adult cardiac surgery, whether it is low-risk patients or high-risk patients.<sup>23)</sup> There was no difference in clinical outcomes such as short-term mortality, length of stay, LCOS, etc., significantly between the two groups in our study. There was no difference in cardiac enzymes and ejection fractions as in the clinical outcome when both groups were evaluated. Another strong indicator of the myocardial protective effect of DNS is that sinus rhythm was restored in a rapid fashion after the cross-clamp is removed according to our observations and the defibrillation requirement is similar to IWBC. It is also beneficial in terms of topical coldness that the crystalloid in the DNS has a ratio of 4:1 and the content are at a temperature of  $4^{\circ}\text{C}$  when compared to IWBC at  $34-35^{\circ}\text{C}$  which is prepared with warm blood taken from the CPB circulation. Almost all of the cases using DNS were completed with a single

dose of cardioplegia. The single dose of cardioplegia results in less cardioplegia volume and in less hemodilution. It is related to the decreased need for red blood cell transfusion. We did not conduct any analysis of the economic efficiency of using DNS but some studies suggest that the use of this crystalloid-based solution is cost-effective due to the content.<sup>14–24)</sup> However, cost evaluation of each institute is unique and it is inevitable that there will be differences among the policy of healthcare systems in different countries.

## Conclusion

In conclusion, our clinical and laboratory outcomes in patients undergoing CABG surgery using DNS are quite satisfactory. The results of our study showed that DNS is as effective and usable as IWBC, which we have routinely used in our clinics for many years. In many respects, both methods are close to each other and yield no obvious superiority. This is a single-center study which focused on the clinical outcomes of the practice and its use in adult coronary surgery, with the limited number of surgical cases. It is not possible to form a general conclusion based solely on these results. Further studies on myocardial cells, especially at the molecular level, will provide more informative data on the future use of cardioplegic methods and the importance of heart surgeon. Our results are encouraging for further studies.

## Disclosure Statement

The authors declare that they have no disclosure and there is no conflict of interest.

## References

- 1) O'Brien JD, Howlett SE, Burton HJ, et al. Pediatric cardioplegia strategy results in enhanced calcium metabolism and lower serum troponin T. *Ann Thorac Surg* 2009; **87**: 1517-23.
- 2) Charette K, Gerrah R, Quaegebeur J, et al. Single dose myocardial protection technique utilizing del Nido cardioplegia solution during congenital heart surgery procedures. *Perfusion* 2012; **27**: 98-103.
- 3) Charette K. Commentary on: Ninety minutes and longer: single dose myocardial protection technique utilizing the del Nido cardioplegia solution for myocardial protection during congenital heart surgery procedures. *Perfusion* 2012; **27**: 104.
- 4) Yerebakan H, Sorabella RA, Najjar M, 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.
- 5) Mick SL, Robich MP, Houghtaling PL, et al. Del Nido versus buckberg cardioplegia in adult isolated valve surgery. *J Thorac Cardiovasc Surg* 2015; **149**: 626-34; discussion 634-6.
- 6) Hamad R, Nguyen A, Laliberté É, et al. Comparison of del Nido cardioplegia with blood cardioplegia in adult combined surgery. *Innovations (Phila)* 2017; **12**: 356-62.
- 7) de Jonge M, van Boxtel AG, Soliman Hamad MA, et al. Intermittent warm blood versus cold crystalloid cardioplegia for myocardial protection: a propensity score-matched analysis of 12-year single-center experience. *Perfusion* 2015; **30**: 243-9.
- 8) Guru V, Omura J, Alghamdi AA, et al. Is blood superior to crystalloid cardioplegia? A meta-analysis of randomized clinical trials. *Circulation* 2006; **114**: I331-8.
- 9) Sá MP, Rueda FG, Ferraz PE, et al. Is there any difference between blood and crystalloid cardioplegia for myocardial protection during cardiac surgery? A meta-analysis of 5576 patients from 36 randomized trials. *Perfusion* 2012; **27**: 535-46.
- 10) Øvrum E, Tangen G, Tølløfsrud S, et al. Cold blood cardioplegia versus cold crystalloid cardioplegia: a prospective randomized study of 1440 patients undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2004; **128**: 860-5.
- 11) Shah S, Gilliland H, Benson G. Agglutinins and cardiac surgery: a web based survey of cardiac anaesthetic practice; questions raised and possible solutions. *Heart Lung Vessel* 2014; **6**: 187-96.
- 12) Kim K, Ball C, Grady P, et al. Use of del nido cardioplegia for adult cardiac surgery at the cleveland clinic: Perfusion Implications. *J Extra Corpor Technol* 2014; **46**: 317-23.
- 13) Kim JS, Jeong JH, Moon SJ, et al. Sufficient myocardial protection of del Nido cardioplegia regardless of ventricular mass and myocardial ischemic time in adult cardiac surgical patients. *J Thorac Dis* 2016; **8**: 2004-10.
- 14) Timek T, Willekes C, Hulme O, 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**: 2237-41.
- 15) Braathen B, Vengen OA, Tønnessen T. Myocardial cooling with ice-slush provides no cardioprotective effects in aortic valve replacement. *Scand Cardiovasc J* 2006; **40**: 368-73.
- 16) Baur HR, Peterson TA, Yasmineh WG, et al. Cold potassium cardioplegia versus topical hypothermia and intermittent aortic occlusion for myocardial protection during coronary artery surgery: a randomized clinical study. *Ann Thorac Surg* 1986; **41**: 511-4.

- 17) Li Y, Lin H, Zhao Y, et al. Del Nido cardioplegia for myocardial protection in adult cardiac surgery: a systematic review and meta-analysis. *ASAIO J* 2018; **64**: 360-7.
- 18) Malmberg K, Rydén L, Efendic S, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 1995; **26**: 57-65.
- 19) Vistarini N, Laliberté E, Beauchamp P, et al. Del Nido cardioplegia in the setting of minimally invasive aortic valve surgery. *Perfusion* 2017; **32**: 112-7.
- 20) Shahian DM, O'Brien SM, Filardo G, et al. The society of thoracic surgeons 2008 cardiac surgery risk models: part 1—coronary artery bypass grafting surgery. *Ann Thorac Surg* 2009; **88**: S2-22.
- 21) Tsukube T, McCully JD, Metz KR, et al. Amelioration of ischemic calcium overload correlates with high-energy phosphates in senescent myocardium. *Am J Physiol* 1997; **273**: H418-25.
- 22) O'Blenes SB, Friesen CH, Ali A, et al. Protecting the aged heart during cardiac surgery: the potential benefits of del Nido cardioplegia. *J Thorac Cardiovasc Surg* 2011; **141**: 762-70.
- 23) Guajardo Salinas GE, Nutt R, Rodriguez-Araujo G. Del Nido cardioplegia in low risk adults undergoing first time coronary artery bypass surgery. *Perfusion* 2017; **32**: 68-73.
- 24) Mick SL, Robich MP, Houghtaling PL, et al. Del Nido versus Buckberg cardioplegia in adult isolated valve surgery. *J Thorac Cardiovasc Surg* 2015; **149**: 626-34; discussion 634-6.