



The del Nido cardioplegia in adult cardiac surgery: reinventing myocardial protection?

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Provenance: This is an invited Editorial commissioned by Executive Editor-in-Chief Jianxing He (Director of the Thoracic Surgery Department, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China).

Comment on: Ad N, Holmes SD, Massimiano PS, *et al.* The use of del Nido cardioplegia in adult cardiac surgery: A prospective randomized trial. *J Thorac Cardiovasc Surg* 2018;155:1011-8.

Submitted Oct 31, 2018. Accepted for publication Nov 05, 2018.

doi: 10.21037/jtd.2018.12.65

View this article at: <http://dx.doi.org/10.21037/jtd.2018.12.65>

Myocardial protection is essential in performing successful open heart surgery. Indeed, hypothermia, potassium induced arrest and ventricular offloading are major concepts that have improved surgical results in the last decades. The cold potassium-based cardioplegia given in a single induction dose followed by intervals doses have been adopted by many in their daily practice with good results. However, the ideal myocardial strategy remains elusive. The del Nido cardioplegia (DNC) was conceived and introduced for pediatric cardiac surgery at the University of Pittsburgh in the early 1990s (1). The solution is based on Plasma-Lyte A, which has an electrolyte milieu similar to extracellular fluid, with the addition of mannitol, magnesium sulfate, sodium bicarbonate, potassium chloride (26 mEq), and lidocaine (2). This solution is calcium free. Therefore, the potential advantages of the DNC are: a better myocardial protection by preventing calcium overload-mediated injury (3) and a reduction of cross clamp times as a single dose is effective for up to 90 min. Although DNC has been studied in pediatric patients, its effectiveness in adult cardiac surgery remains to be determined as adult myocardium is more sensitive to ischemia. Nevertheless, several studies have reported favourable results with the use of DNC in adult cardiac surgery when performing single or multiple valve surgery, coronary artery bypass grafting (CABG) and reoperative procedures (4-9).

We enjoyed reading the study “*The use of del Nido cardioplegia in adult cardiac surgery: a prospective randomized trial*” by Ad *et al.* (10) published in *The Journal of thoracic and cardiovascular surgery*. This study is the first randomized trial on the use of DNC in adult cardiac surgery. The authors randomized 89 adult patients undergoing a first-time CABG, valve or CABG and valve surgery to the DNC (n=48) or whole blood cardioplegia (n=41). Patients >80 years, with preoperative inotropic or mechanical support were excluded. The primary endpoint was myocardial protection assessed by return to spontaneous rhythm, defibrillation requirements, inotropes, and troponin levels. Secondary outcomes were perioperative complications, CBP and cross clamp times. The study was initially designed to assess non-inferiority of the DNC with a calculated sample size of 250 patients per group. However, with interim results showing the superiority of the DNC on primary endpoints, there was no justification to continue the study with a non-inferiority design. The adjusted P value for superiority was $P < 0.001$.

In terms of findings, the authors reported a higher proportion of return to spontaneous rhythm with the DNC when compared to the control group (97.7% *vs.* 81.6%, $P = 0.023$). In addition, fewer patients required inotropic support in the DNC group (65.1% *vs.* 84.2%, $P = 0.05$). There was no difference in terms of defibrillation (DNC

4.7% *vs.* control 13.2%, $P=0.244$). In the DNC group, the troponin did not increase as much as for the control group ($P=0.040$). At 24 hours, the troponin level was 2.3 in the DNC group and 7 in the control group ($P=0.053$). Nevertheless, there was no postoperative ejection fraction and electrocardiographic changes. The CPB times were similar among both groups while cross clamp time was shorter in the DNC arm (80 *vs.* 83 minutes, $P=0.018$). The composite endpoint of STS defined postoperative morbidity was lower in the DNC group (11.6% *vs.* 26.3%) whereas this result did not achieve statistical significance ($P=0.089$). While the volume of administered plegia was lower in the DNC group, the rate of postoperative transfusions and discharge hematocrit was similar between both groups. Interestingly, 28% of DNC patients received a second dose of cardioplegia. Based on these findings, the authors concluded that the DNC use in routine adult cardiac surgery is safe and could improve streamline surgical workflow with comparable clinical outcomes.

This study has some limitations. First, this an interim analysis of a projected larger trial. Therefore, statistical power (calculated at 56%) was not sufficient to draw definitive conclusions. In addition, this study is a non-blinded randomized trials and postoperative inotropes use was not standardized postoperatively, potentially introducing some bias in the author's conclusions. Lastly, this trial did not include patients older than 80 years, those requiring inotropic or mechanical support preoperatively and reoperations. Indeed, the mean cross clamp was short (<85 minutes) making any extrapolation of these results to sicker patients and more complex procedures impossible.

Is DNC reinventing myocardial protection in adult cardiac surgery? Based on this trial and the available literature, DNC reduce cross clamp times and is at least comparable to standard myocardial protection strategies in terms of mortality, cardiac enzyme release, or the need for inotropic support in low-risk and first-time adult cardiac surgery (11). While some studies have compared DNC to other plegia solutions in more complex procedures (12), this remains a matter of debate and should be clarified in further studies. Nevertheless, Ad and colleagues (10) should be commended for conducting such a timely relevant randomized trial, marking the unrelenting pursuit of a simple and efficient myocardial protection solutions that can be used in various settings in adult cardiac surgery.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Luo W, Bouhout I, Demers P. The del Nido cardioplegia in adult cardiac surgery: reinventing myocardial protection? *J Thorac Dis* 2019;11(Suppl 3):S367-S369. doi: 10.21037/jtd.2018.12.65