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Commentary: Does form follow function or predict recovery?

Juan A. Crestanello, MD

Del Nido cardioplegia has been successfully used in the pediatric population, and its use has recently expanded into adults.¹⁻⁴ Del Nido cardioplegia is a modified depolarizing cardioplegia that limits intracellular calcium accumulation during arrest. The components of the solution are designed to arrest the heart, decreasing myocardial oxygen demands (potassium chloride and hypothermia), hyperpolarize cell membranes, preventing intracellular calcium overload (magnesium, lidocaine), prevent acidosis (sodium bicarbonate), and decrease oxidative stress (mannitol, blood).¹ The prolonged effect of lidocaine on sodium channels allows for increased duration between doses while achieving comparable results with conventional multidose cardioplegia, decreasing ischemic time, cardiopulmonary bypass time, and operative time.³ However, the evidence supporting the timing between the doses of del Nido cardioplegia is limited.⁵

In this issue of the *Journal*, Jung and colleagues⁶ examined time-induced changes to mitochondria and nuclear ultrastructure after a single dose of del Nido cardioplegia using electron microscopy. The experiments were conducted in 7 recipient human hearts explanted during transplantation. The authors found a progressive increase in the proportion of mitochondria with “moderate,” “severe,” and “irreversible” injury after 90 minutes of ischemia.

This study provides an important observation on the time-dependent morphologic changes after the administration of del Nido cardioplegia. While the morphologic changes are important, they are not necessarily associated with irreversible changes in mitochondria or myocardial

Myocardial myofibers and mitochondria in the rat heart (courtesy J. Crestanello).

CENTRAL MESSAGE

Changes in mitochondrial structure are more severe 90 minutes after del Nido cardioplegia administration. Their correlation with myocardial function and recovery is unknown.

function. Mitochondria are dynamic structures not only involved with the regulation of energy metabolism but also with production of oxygen radicals, intracellular signaling, regulation of intracellular calcium, and regulation of cell death.⁷ Dynamic changes occur in mitochondria that allow mitochondria to heal and regenerate themselves through fusion, fission, mitophagy, and biogenesis. These are mechanisms that allow for repair and recovery of damaged mitochondria, generation of new mitochondria from healthy portions of damaged mitochondria, and elimination of dysfunctional mitochondria. When the severity of mitochondrial injury exceeds its repair capacity, it triggers cell death.⁷

The present article demonstrated that there is a linear increase in the severity of mitochondria changes with time, and that more severe changes occur after 90 minutes. While this article nicely demonstrated morphologic changes that may support the redosing of cardioplegia after 90 minutes, there are several limitations to its findings. First, these were not normal hearts. They were hearts with end stages of heart failure in need for heart transplantation that can induce mitochondrial morphologic and functional changes and confound the interpretation of these findings. Second, morphologic changes have not been associated with mitochondrial functional derangements or their ability to recover during reperfusion. Third, the protective effect of an additional dose of cardioplegia

From Cardiovascular Surgery, Mayo Clinic, Rochester, Minn.

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Address for reprints: Juan A. Crestanello, MD, Mayo Clinic, 200 First St SW, JO-5200, Rochester, MN 55905 (E-mail: Crestanello.Juan@mayo.edu).

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and the ability to reverse those morphological changes was not explored.

Certainly, this article does not completely answer the question of the safe timing for redosing del Nido cardioplegia in adult patients, but the authors need to be congratulated on providing a morphologic timeline of the changes of mitochondria ultrastructure. Their observations provide the foundation for additional studies where form, function, and ability to recover after reperfusion are examined.

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Commentary: del Nido cardioplegia—the jury is still out and a new trial is needed

Harold L. Lazar, MD

A major area of concern when using del Nido cardioplegia (DNC) in adult cardiac surgery is when and how much additional cardioplegia should be administered after the initial dose. DNC appears to be safe for low-risk, elective patients with minimal comorbidities when undergoing isolated coronary artery bypass grafting or aortic valve replacement procedures during which the crossclamp time is no longer than 60 minutes. However, in more complex procedures when the crossclamp time exceeds 60 minutes, the margin of safety after a single dose of DNC is unknown.

In this edition of the *Journal*, Jung and colleagues¹ report the results of their study, which sought to determine the safe

Harold L. Lazar, MD

CENTRAL MESSAGE

The margin of safety after a single dose of del Nido cardioplegia in adult cardiac surgery has not been determined.

period of ischemia after a single dose of DNC in 7 hearts extracted from patients undergoing heart transplantation. After an initial 1-liter infusion of DNC, hearts were extracted and placed in a water bath filled with normal saline to maintain a myocardial temperature of 18°C. Serial biopsies of the left ventricle (LV) were obtained every 30 minutes for 180 minutes. Irreversible ischemic injury in the myocardial mitochondria and nuclei were first detected 90 minutes after the initial DNC infusion and increased in a significant linear correlation over the next 90 minutes. The authors concluded that irreversible injury begins to occur 90 minutes following

From the Division of Cardiac Surgery, Boston University School of Medicine, Boston, Mass.

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Address for reprints: Harold L. Lazar, MD, 80 East Concord St, Boston, MA 02118 (E-mail: harold.l.lazar@gmail.com).

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