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Commentary: Continuous steady development is made by taking 2 steps forward, 1 step back

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In cardiac surgery, myocardial protection by using a sufficient dose of cardioplegia is essential when performing a cardiac procedure. Subsequently a cardioplegia infusion every 20 to 30 minutes during surgery is standard practice, which interrupts the important procedure. del Nido cardioplegia (DNC) was developed in the early 1990s and it has been widely used because it has several advantages. Although the original protocol stated that subsequent doses were not required within 180 minutes after the initial infusion,¹ subsequent doses of DNC have been administered after 90 minutes of the aortic cross-clamp based on expert opinions—not based on any experimental evidence.² Therefore, Jung and colleagues³ decided to perform this study on extracted human hearts at heart transplantation. There are more patients who require cardiac surgery with an aortic crossclamp than those receiving a heart transplantation, which means a relatively small number of patients would help to establish specific evidence regarding the safe ischemic time for sufficient myocardial protection, to the benefit of the broader sector of cardiac surgery. In this sense, Jung and colleagues³ should be highly lauded for performing this research.

There are several weak points in this study. Firstly, the authors showed how the human heart is damaged over time after a single-dose DNC infusion. However, they

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del Nido cardioplegia has an advantage in that frequent doses are not required, which was proven by histologic evaluation. However, further research focusing on functional outcome is needed.

did not clearly prove that 90 minutes is a real critical point. The authors are therefore encouraged to perform an additional study, which includes a second-dose DNC infusion after more than 90 minutes of ischemia. In addition, the studied hearts were diseased in end-stage heart failure, and therefore any findings should be interpreted with caution. These hearts might not recover after only 1 dose of DNC, and the current dose of DNC also seemed insufficient. Further, the maintenance of myocardial temperature at 18°C with a normal saline bath creates uniform hypothermia, which is very different from the local epicardial and endocardial rewarming seen in clinical settings between cardioplegia doses caused by operating room lights, viscera, and venous return. This warm ischemia reduces the amount of safe time between cardioplegia doses. The conclusions should therefore be carefully framed throughout to ensure casual readers are not given the impression that these data support a 90-minute cardioplegia redosing schedule.

Furthermore, the authors can neither correlate the extent of myocardial ischemic injury with likely functional outcome, nor quantify what extent of irreversible mitochondrial or nucleic injury would indicate irreversible myocardial dysfunction because there has been no previous study evaluating the correlation between ultrastructural changes and global function of the myocardium in a human heart. We should wait for research focusing on

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the functional outcome in addition to mere histologic injuries.

Jung and colleagues³ show preliminary observational data that indicate that myocardial ischemic injury progresses gradually, and that irreversible ischemic injury of the heart with severe reduced cardiac function begins to occur 90 minutes after initial DNC infusion.

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Commentary: How long can you go with del Nido?

Dominick Megna, MD, Pedro Catarino, MD, FRCS, and Joanna Chikwe, MD, FRCS

“Another 5 minutes...” Most cardiac surgeons have uttered something to this effect while our perfusionist is hinting that we should redose del Nido cardioplegia. Although clinical experience tends to dictate much of what we do, this holds especially true with our use of del Nido. A multitude of studies have demonstrated equivalent myocardial protection compared with conventional cold blood cardioplegia in adult cardiac surgery, with the advantage of a single dosing regimen. Expert opinion suggests redosing if the ischemic time is likely to extend much beyond 90 minutes.^{1,2} Are we just settling, or are we truly providing optimal myocardial protection? Answering this question in a clinical study is impractical and would require a prohibitive number of patients.

In an attempt to better understand the progression of myocardial ischemic injury and a safe ischemic time after single dose del Nido, Jung and colleagues conducted an ingenious experiment, reported in this issue of the

Dominick Megna, MD, Pedro Catarino, MD, FRCS, and Joanna Chikwe, MD, FRCS

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Pathoanatomic data suggest that a single dose of del Nido cardioplegia with myocardial hypothermia provides 90 minutes of safe ischemia.

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Journal.³ The authors obtained myocardial tissue from the explanted hearts of transplant recipients, which were arrested before explantation with 1000 mL of del Nido cardioplegia, and then placed in a cold saline bath with the myocardial temperature maintained at 18°C. Using electron microscopy, they evaluated mitochondrial and nuclear changes that can distinguish between reversible and lethal myocyte damage over the first several hours after the cardioplegia dose. The mitochondrial data are most compelling. Injury scores worsened with longer ischemic time, but even at 90 minutes, only 1 in 100 mitochondria had a lethal injury. The proportion increased 5-fold over the next 90 minutes.

These data provide compelling pathoanatomic support for a single-dose strategy providing up to 90 minutes of safe ischemia. Whether redosing at the 90-minute mark attenuates further lethal injury remains to be established. Of