# Commentary: One and done: The case for single-dose del Nido cardioplegia



Mark R. Helmers, MD, and Pavan Atluri, MD

From the Division of Cardiovascular Surgery, Department of Surgery, University of Pennsylvania, Philadelphia, Pa.

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Address for reprints: Pavan Atluri, MD, Division of Cardiovascular Surgery, Hospital of the University of Pennsylvania, 3400 Spruce St, 6 Silverstein Pavilion, Philadelphia, PA (E-mail: Pavan.Atluri@uphs.upenn.edu).

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Mark Helmers, MD (*left*), and Pavan Atluri, MD (*right*)

**Central Message**

In a meta-analysis of over more than patients, single administration of del Nido cardioplegia reduced operative times, reperfusion ventricular fibrillation, and postoperative cardiac enzyme leak.

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Since Melrose's initial description of hyperkalemic arrest in 1955,[1] there has been considerable study and debate to determine the optimum cardioplegia strategy.[2-4] The perfect cardioplegia solution must rapidly induce diastolic arrest and protect against injury from global ischemia and reperfusion while being easily reversible and nontoxic.[5] Histidine–tryptophan–ketoglutarate (HTK) cardioplegia and del Nido (DN) cardioplegia are 2 solutions that have garnered a great deal of interest and use due to their ability to provide myocardial protection for 90 to 120 minutes without redosing.[6,7] Several randomized controlled trials have compared these solutions with traditional multidose cardioplegia[2-4,8-11]; however, they have been limited by small sample sizes.

In this issue of the *Journal*, Gambardella and colleagues[12] report their results of a meta-analysis of 10 randomized controlled trials and 13 propensity-score matched cohort trials comparing single-dose HTK and DN with traditional multidose blood or crystalloid cardioplegia. When compared with multidose cardioplegia, DN reduced both ischemic time (mean difference –7.18 minutes [–12.52 to –1.84], $P < .01$) and bypass time (mean difference –10.44 minutes [–18.99 to –1.88], $P < .01$), as well as incidence of reperfusion fibrillation (odds ratio 0.16 [0.05-0.54], $P < .01$] and postoperative cardiac enzyme leak (standard mean difference –0.17 [–0.29 to 0.05], $P < .01$). Interestingly, HTK did not offer these benefits but rather increased bypass time and reperfusion fibrillation.

Furthermore, there was no difference in mortality and myocardial infarction between groups. Concern exists among some surgeons regarding the ability to achieve a complete and uniform distribution of cardioplegia with a single dose in patients with severe coronary artery disease.[13] Multivariable meta-regression performed by the authors demonstrated that this similarity in mortality rates was not only independent of type of surgery (coronary vs valve) but also of surgical approach (minimally invasive vs full sternotomy) and left ventricular ejection fraction.

While the authors performed an excellent analysis, there are important limitations of the original studies that deserve consideration when applying these findings to clinical practice. Patients with low ejection fraction, previous cardiac surgery, preoperative inotropic or mechanic support, urgent or emergent operative status, and severe coronary artery disease or preoperative myocardial infarction were often excluded. As a result, operative times were often relatively short. Furthermore, as the authors astutely point out, even despite the large sample size gained by the meta-analysis, the study is likely still underpowered to detect differences in mortality.

Nevertheless, the results are exciting and suggest that DN cardioplegia is here to stay. Certainly single-dose cardioplegia streamlines surgical workflow. The surgeon can dedicate more attention to the operation itself instead of repeated interruptions for myocardial protection. In our practice, we use DN routinely for minimally invasive mitral cases and selectively for full sternotomy cases.

These results are particularly interesting, as they imply that DN may even offer better myocardial protection than traditional multidose cardioplegia. Surgeons may therefore get "more for less" with DN. While DN did not increase survival, decreased bypass and ischemic times have been shown to be independent risk factors for operative mortality.[14-16] Further study with larger clinical registries is

needed to determine the effect of DN on patient survival. Moreover, the effectiveness and safety of DN remains to be clearly demonstrated in high-risk patients and those requiring long, complex cases. Optimal redosing strategies must also be determined. Additional laboratory and clinical investigation is therefore warranted.

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