Cardioplegia in minimally invasive cardiac surgery: time to go

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Received: 05 September 2018; Accepted: 14 December 2018; Published: 16 January 2019.

doi: 10.21037/jovs.2018.12.11

View this article at: http://dx.doi.org/10.21037/jovs.2018.12.11

In an interest to accelerate postoperative recovery in cardiac surgery, "minimal invasive cardiac surgery (MICS)" has been introduced to reduce surgical stress for the patients (1). Right thoracotomy and upper hemi-sternotomy are common approaches for MICS, and clinical outcomes of MICS have been reported acceptable compared with conventional median full sternotomy (2,3). The MICS may provide less surgical wound pain compared with full sternotomy and has been reported to confer shorter lengths of hospital stay (4,5). On the other hand, the MICS requires longer cardiac procedural times than the conventional approach (6,7). The longer time requirement is largely attributed to the restriction in movements along with limited exposure of surgical field. In aortic valve replacement through right mini-thoracotomy approach, for instance, the exposure of right coronary cusp of the aortic valve is often limited to ensure straightforward procedures.

In order to minimize systematic inflammatory responses and myocardial damages in cardiac surgery, restricting times of cardiopulmonary bypass and cardiac ischemia has been regarded as the paramount importance. For this reason, multiple or complex cardiac procedures have not been regarded reasonable candidates for MICS approach in the past (8,9). To overcome this time-limitation in MICS, there have been effort to utilize ideal cardioplegic solutions, which may allow sufficient time of cardio-protection long enough to complete the procedures by a less-interruptive single shot of infusion. In this sense, there have been several prerequisites for ideal cardioplegia raised by the experts in MICS as follows: (I) long duration of cardio-protection; (II) availability to infuse in antegrade fashion; and (III) comparable efficacy and safety to conventional blood cardioplegia.

In these regards, Custodiol Histidine-tryptophan-ketoglutarate (HTK) and del Nido (DN) solutions have emerged as most popularized cardioplegia solutions for MICS. HTK is known as an intracellular crystalloid cardioplegic solution providing up to three hours of myocardial protection by a single shot (10,11). This solution was first introduced by Bretschneider 50 years ago (12). Low sodium contents in HTK derive hyperpolarization of the myocyte plasma membrane, thus it induces diastolic cardiac arrest. This solution contains several additions such as histidine, ketoglutarate and tryptophan as a buffer, improving energy source during reperfusion and membrane stabilizer, respectively.

To form the DN solution, blood is combined in a 1:4 ratio with Plasma-Lyte A (Baxter Healthcare Corporation, Deerfield, IL, USA; the solution is composed of KCl, $NaHCO_3$, mannitol, $MgSO_4$, and lidocaine). This combination is to avoid an accruing high level of potassium ion which can induce sequential calcium ion inflow (13). The DN cardioplegia contains substrates (blood), buffers ($NaHCO_3$) and membrane stabilizers (lidocaine) (14). Those additives are considered to maintain similar stability in the recovery of myocardial contraction to that of blood cardioplegia. Even though the development of DN solution was intended to be used in pediatric cardiac surgery, its uses have been expanded into the adult cardiac surgery based on the expectation that the myocardial susceptibility of adult may be similar with the pediatric hearts (15-17). Recently, excellent clinical outcomes have been reported by the use of DN solution in single-valve surgeries, coronary artery bypassing (18,19) and even in complex cardiac procedures (20).

Nevertheless, there are several limitations in these solutions. For example, hyponatremia-related issues driven by the rapid administration HTK solution have been reported (21). In addition, some studies demonstrated that

the HTK solution may trigger the ventricular fibrillation during myocardial reperfusion (22). Meanwhile, the safety issue on the use of DN for adult cardiac surgery, especially for the patients requiring long myocardial ischemic time, have been remained unclear. Consequently, the use of DN in adult cardiac surgery has not been further expanded perhaps due to limited supporting evidences of its safety in long procedures. In our own review, only one randomized trial of the use of DN for adult cardiac surgery has been published (23).

Despite the rising interests on the use of HTK and DN solutions in the MICS, scientific evidences based on the randomized trial have been limited. It is challenging executively, logistically and ethically to conduct randomized controlled trials on patients undergoing cardiac surgery. In addition, observational studies have limitations in controlling confounders such as baseline risk variables, variations in surgical skills and approaches of the MICS. However, given the current rapid growing interests on the MICS, the need for more detailed information on these cardioplegia is increasing. To address these issues, continuous efforts to investigate the advantage and drawbacks of these cardioplegic solutions should be followed. We believe it is time to conduct multi-center, randomized controlled trials to determine optimal cardioplegia in various MICS surgery by international collaborative works.

It is time to conduct multi-center, randomized controlled trials to determine optimal cardioplegia in minimal invasive approach cardiac surgery by international collaborative works.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Peyman Sardari Nia) for the series "Minimally Invasive Mitral Valve Surgery" published in *Journal of Visualized Surgery*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jovs.2018.12.11). The series "Minimally Invasive Mitral Valve Surgery" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/jovs.2018.12.11
Cite this article as: Kim WK, Kim JB, Lee JW. Cardioplegia in minimally invasive cardiac surgery: time to go. J Vis Surg 2019;5:9.

