“Propofol cardioplegia” and myocardial protection: What’s in a name!

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Central Message

An interesting clinical study relating to propofol supplementation of blood cardioplegia is discussed.

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Over the past 40 years of cardiac surgery, cardioplegia has been the technique of choice to induce and maintain rapid diastolic arrest. Cardioplegia delays the onset of irreversible ischemic injury and provides the surgeon with an operating window of relatively safe ischemia for correction of the lesion. Most cardioplegic solutions (of which there are many in use throughout the cardiac surgical arena) essentially use a moderate elevation of the potassium concentration (hyperkalemia) to levels that induce rapid depolarization of the resting membrane potential to a new steady state (~ -50 mV), thereby preventing the voltage activation of the fast Na^+ -channel and inducing cardiac arrest. These solutions also usually contain an anti-ischemic agent (eg, magnesium) that enhances protection.¹ Other surgeon-specific characteristics of cardioplegic solutions include vehicle (crystalloid or blood), temperature of infusion (cold, tepid, warm), and mode of infusion (antegrade, retrograde, antegrade combined with retrograde), and these have all been shown, in various experimental or clinical studies, to provide adequate and similar myocardial protection.² During the past 10 to 15 years, however, the patients who are receiving cardiac surgery are older and sicker, and have more severe and diffuse cardiac disease. Therefore, it is likely that these patients would benefit from improved myocardial protection. Accordingly, there have been many, mainly experimental, studies demonstrating the potential improvements that can be achieved by inducing procedures such as preconditioning, postconditioning, or remote preconditioning.³ However, little clinical evidence for their efficacy has been seen when large clinical trials have been conducted (eg, the recent Effect of Remote Ischemic Preconditioning on Clinical Outcomes in Patients Undergoing Coronary Artery Bypass Graft Surgery [ERICCA] trial for remote preconditioning involving 1600 patients that failed to demonstrate improved heart bypass outcomes⁴). Likewise, many experimental cardioplegia studies have demonstrated

the beneficial effects of various pharmacologic additives to conventional cardioplegic solutions⁵; however, it is relatively rare that these experimental studies are followed up with subsequent clinical studies. In addition, when they are conducted, they generally do not show the expected benefits that were observed in the experimental animal studies; this can be explained in a number of ways, but, predominantly, the clinical variety experienced in patient studies is very different than the usually healthy animals and controlled uniform conditions of experimental studies!

In this issue of the *Journal*, Rogers and colleagues⁶ report on the addition of the general anesthetic, propofol, to cardioplegia solutions used in patients undergoing isolated coronary artery bypass grafting or aortic valve replacement surgery. This clinical study comes after the same group has published many careful and relevant experimental animal-based studies that demonstrated the beneficial effects that propofol exerted on cardioplegic protection. The authors are to be commended on completing an interesting and carefully conducted clinical study with relevant outcome measures; the primary outcome measure of cardiac troponin T has been shown to correlate with long-term mortality and morbidity.⁷ There are a number of issues worthy of comment that arise from this study. First, propofol was used as an anesthetic in all study patients, and the systemic concentration of propofol that was present in the blood cardioplegia of the control patients was approximately half that of the supplemented cardioplegia.

One wonders whether this difference is sufficient for the propofol to exert any significant additional clinical effect, despite the measured difference of a 15% reduction in overall troponin T release. Second, the patients selected were all low risk and, as such, probably not in need of any additional cardioprotection! It would have been of interest to use high-risk patients who, by definition, may need enhanced cardioprotection and may have demonstrated a more profound effect. Third, it is curious that different cardioplegic solutions were used for the patients undergoing coronary artery bypass grafting (warm blood Calafiore formulation solution) and the patients undergoing aortic valve replacement (cold blood Harefield Hospital formulation [basically, St Thomas' Hospital solution]), and the rationale for this should be specified. It would be tempting to analyze the 2 surgical groups in terms of troponin T release (as per Figure 2 in the article⁶) to see whether there were any cardioprotective differences between these cardioplegic solutions (although the patient numbers in each group would not be powered to detect differences)! Finally, it seems rather misleading to use "propofol cardioplegia" in the title of this article! This implies that the main protective agent of the cardioplegia is propofol; this is obviously not the case because any effect of the propofol is only a minor aspect of the overall protective efficacy of the cardioplegic solution (as demonstrated

by the results)! Overall, however, this is an extremely interesting, timely, and well-conducted study that exemplifies translational research. Further studies (as suggested by the authors), particularly examining a dose-range of supplemental propofol, would be extremely worthwhile.

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