to achieve polarized arrest that reduces (1) Na^+ and Ca^{2+} loading, (2) vasoconstriction, (3) endothelial dysfunction, (4) reperfusion arrhythmias, and (5) contractile stunning.² In the 1990s, adenosine triphosphate-sensitive K^+ channel openers provided initial hope for a method to induce polarized arrest³; however, severe post-arrest arrhythmias thwarted clinical adoption.

The clinical study by Jakobsen and colleagues¹ tested the hypothesis that cold 1.2 mmol/L adenosine crystalloid cardioplegia can achieve polarized arrest and provide superior cardioprotection compared with a 20 mmol/L hyperkalemic solution in low-risk patients. Their study found that adenosine cardioplegia arrested the heart faster, reduced the incidence of atrial fibrillation by more than 50%, and was associated with lower postoperative plasma K^+ levels. There were no differences in postoperative troponin T, creatine kinase-MB, creatinine, hemodynamics, cardiac index, or endothelial activation.¹

Adenosine has been investigated as a potential cardioprotective agent in cardiac surgery during the past several decades. In 1989, Schubert and colleagues⁴ were the first to show that 10 mmol/L of adenosine rapidly arrested the heart. However, persistent atrioventricular block⁴ precluded its further development as a polarizing arresting agent, and it became an adjunct to supranormal potassium.⁵ During the past 20 years, the benefits of adjunctive adenosine (<2 mmol/L) in cardioplegia have been mixed, ranging from modest effects⁵ to no benefits at all.⁶ The protocol reported by Jakobsen and colleagues¹ used 1.2 mmol/L adenosine to achieve polarized arrest. However, this concentration is approximately one tenth that used in earlier studies in which adenosine was the primary arresting agent.⁴ This discrepancy raises an important question of whether adenosine is really the sole arresting agent in Jakobsen's study.

In 2004, Dobson and Jones⁷ reported that adenosine (0.2 mmol/L) and lidocaine (0.5 mmol/L) (AL) in

a modified Krebs–Henseleit solution arrested the heart in a polarized state, with significantly improved functional recoveries compared with St Thomas' solution. Although both lidocaine and procaine are Na^+ fast-channel blockers, lidocaine was chosen in AL cardioplegia because as a class 1B antiarrhythmic, it shortens repolarization time, whereas procaine (class 1A) prolongs repolarization time, which may cause postoperative reanimation irritability. The AL concept of polarized arrest was subsequently confirmed in the canine model of cardiopulmonary bypass.⁸

Therefore, the efficacy of adenosine cardioplegia in the study by Jakobsen and colleagues¹ could be due to its combination with procaine. Whether adenosine acted alone or not is important because future studies testing adenosine as the primary arresting agent will derive their impetus from studies such as the one by Jakobsen and colleagues.¹ Precedence has been set for a polarized alternative using adenosine and local anesthetic (eg, lidocaine), which is the proprietary composition of Hibernation Therapeutics Global, Inc (Wicklow, Ireland) and is trademarked and available as Adenocaine in the United States from Central Admixture Pharmacy Services (Kent, Wash). A recent prospective randomized trial in Verona, Italy, showed superiority of an AL cardioplegic formulation in high-risk patients compared with a 4:1 Buckberg solution⁹; further clinical confirmation for use of AL as a primary arresting formulation that extends the data of Corvera and colleagues⁸ is forthcoming. The good news is that these studies collectively give hope that an alternative to supranormal potassium cardioplegia is on the horizon for the good of low- and high-risk pediatric and adult patients alike.

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<http://dx.doi.org/10.1016/j.jtcvs.2013.02.049>

Reply to the Editor:

We greatly appreciate the interest by Drs Vinten Johansen and Dobson in our article showing the efficacy and beneficial impact of adenosine instead of hyperkalemia in cold crystalloid cardioplegia. Their comments raise interesting and relevant questions regarding adenosine in cardioplegia

as an arresting and cardioprotective agent, and the concomitant use of a local anesthetic.

A major object of our study was to investigate whether this combination was efficient in normokalemic cardioplegia, because possible negative effects of hyperkalemia have been debated for decades and normokalemic adenosine/local anesthetic cardioplegia has been shown to be superior in animal studies, compared with both high and moderate potassium concentrations.¹ Despite some clinical studies with the use of adenosine in the cardioplegic solution, to our knowledge, this is the first study on the use of normokalemia.

As for the choice of local anesthetic, we used procaine because our standard hyperkalemic cardioplegia derived from St Thomas' Hospital solution contains 1 mmol/L of procaine to reduce the group differences. Both procaine and lidocaine reduce the action potential amplitude and the maximum rate of increase of the upstroke of the action potential, but they differ in the influence of the action potential duration (APD), where procaine increases and lidocaine shortens the APD. They both have rhythm-stabilizing effects after cardiac surgery. Cardioprotective properties, although dose-dependent, have been demonstrated for both drugs in isolated heart studies.² Although larger clinical studies exclusively comparing these 2 local anesthetics in cardioplegia are missing, we agree that adenosine-procaine and adenosine-lidocaine cardioplegia are probably 2 sides of the same coin.

What is most important in achieving cardioplegic arrest: adenosine, magnesium, or Na⁺ channel blockers, such as lidocaine or procaine? Hypothermia is the largest contributor to the arrest, and infusing 750 mL of cold crystalloid solution is going to arrest the heart almost regardless of composition. Whether this solution will protect the heart while in its

resting state or not is another matter. It is not a given that cardiac arrest and cardiac protection are equivalent. Biochemical processes are highly temperature-dependent, and little research has been done to assess the behavior of drugs in hypothermic conditions like the heart is in cardiac surgery. We have previously shown that hypothermia actually reversed the APD shortening of adenosine triphosphate-sensitive K⁺ (K_{ATP}) channel openers, thus theoretically making the K_{ATP} channel openers less effective in achieving cardiac arrest under hypothermic conditions. Nevertheless, the K_{ATP} openers provided cardioprotective properties even in hypothermic conditions.³ We also previously showed that adenosine has no effect on ventricular contractility at normothermia, whereas 1.2 mmol/L of adenosine significantly reduces contractile force at moderate (24°C) hypothermia.⁴

There are now several promising studies from the use of adenosine in cardioplegia, so alternatives to potassium arrest may be in the making. However, several issues still should be addressed regarding the composition, optimal doses, type of delivery, and vehicle. For instance, what are the optimal dose, temperature, and administration of adenosine in crystalloid and blood cardioplegia? What is the role of adenosine in preconditioning? Steensrud and colleagues⁵ have shown that adenosine can induce remote preconditioning when given intra-arterially, but not intravenously, and that this effect is dependent on an intact nerve system but inhibited by nitric oxide. Thus, concomitant medications, such as nitric oxide donors or sulfonylureas and even anesthesia, may play a role in the search of improving the current cardioprotective solution. In the future, we may be able to individualize our cardioplegic strategy according to the patient's needs, that is, if alternatives exist.

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<http://dx.doi.org/10.1016/j.jtcvs.2013.02.049>

FOLDING OR PLICATION TECHNIQUE IN MITRAL VALVE REPAIR: NEW OR RENAMED?

To the Editor:

It was with great interest that we read the article by Tsukui and colleagues¹ on early outcome of the folding mitral valve repair technique without resection for mitral valve prolapse in 60 patients. This folding mitral valve repair technique—or FMVR, as the authors call it—is described as a non-resectional technique with inversion of the prolapsed segment into the left ventricle and ring annuloplasty, also applied for prolapse secondary to ruptured chordae. The authors apply a pilot stitch vertically to the edge of the prolapsed segment of the posterior leaflet, and additional