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COMMENTARY

Remote ischemic preconditioning for renal protection in children undergoing surgery for complex congenital heart disease: What do we know now and where do we go next?

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In 1986, Murry, Jennings, and Reimer¹ found in a canine model that brief periods of occlusion of the circumflex coronary artery preceding a 40-minute period of ischemia followed by reperfusion could reduce the size of the resultant infarct. This phenomenon was termed “preconditioning.” Subsequent work found that this protective effect could be elicited by creating brief ischemic episodes in tissue beds remote from the organ to be rendered ischemic. The protective effect of these remote ischemic events could even occur simultaneous to (perconditioning) or after (postconditioning) the ischemic insult.²

Remote ischemic preconditioning (RIPC) has been shown in 2 randomized controlled trials to improve cardiac and pulmonary function in children undergoing cardiac surgery.^{3,4} Other investigators have shown that RIPC has

a favorable impact on renal function.⁵ RIPC is an attractive and exciting area of study. The technique unmasks an innate ability to ameliorate ischemia–reperfusion (I-R) injury. No drugs are required and the technique of RIPC appears to have little or no potential for morbidity.

In the current study, the group from Aarhus University Hospital, Skejby, Denmark, performed an extremely well-structured randomized double-blind placebo-controlled trial of RIPC to assess the potential for protection of renal function among children undergoing cardiac surgery.⁶ On the basis of their initial hypothesis, they found that RIPC provided no protection of renal function in children operated on for complex congenital heart disease. Despite the ultimate clinical study design, perhaps the optimal technique of RIPC for renal protection in this patient population has not been identified. Do we know enough about the proper timing, duration, type, and quantity of vascular bed to be rendered temporarily ischemic to merit a randomized trial? A subanalysis did identify a benefit among patients greater than 6 months of age, suggesting that there is an age-dependent response to RIPC. Clearly, younger patients are at increased risk of I-R injury and multiorgan dysfunction after operations using cardiopulmonary bypass. Any protective impact of RIPC may have been overwhelmed by increased I-R injury seen in young infants.

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The authors of this study readily acknowledge its shortcomings. They had postulated an ambitious 30% reduction in incidence of acute renal injury, whereas they observed a more modest reduction of 10%. Using this 10% difference, they would have needed a much larger ($n = 480$) sample size. What next? Further study might look at organ-specific preconditioning with age-specific “dose-response curves” among the most susceptible groups. A 10% reduction in the incidence of acute renal injury could be of clinical benefit, and a multicenter trial might accrue enough patients within a realistic time frame to see whether this reduction in acute renal injury would be realized. Like all well-designed studies, this one by Pedersen and colleagues identifies areas of future study and adds significantly to our understanding of RIPC.

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