

## Preconditioning of the heart: The anaesthetist's contribution to protecting the heart

John G. T. Augoustides MD, FASE

Associate Professor Cardiothoracic and Vascular Section, Anesthesiology and Critical Care.  
University of Pennsylvania, Philadelphia, USA.

Preconditioning of the heart occurs when brief exposure to a stimulus protects the heart from subsequent ischemia. This technique is important for the anesthetist, given that myocardial ischemia is a leading cause of perioperative morbidity and mortality.

The preconditioning stimulus may be ischemic or pharmacologic. An ischemic stimulus may be local (that is, ischemia of the myocardium) or remote (that is, ischemia of a tissue other than the heart). A perioperative pharmacologic stimulus may be inhalational or intravenous. This lecture will discuss (1) local ischemic preconditioning; (2) remote ischemic preconditioning; (3) inhalational preconditioning; (4) intravenous preconditioning; and (5) future directions.

In 1986 Murry and colleagues first described ischemic preconditioning in canine myocardium. In clinical trials, ischemic preconditioning decreases myocardial dysfunction and damage after cardiac surgery. Although effective, further adequately powered trials must demonstrate a significant outcome advantage before this therapy can be recommended for routine clinical application.

Remote ischemic preconditioning protects the heart by inducing ischemia in non-cardiac tissue. This has been validated in multiple laboratory models. In pediatric cardiac surgery, brief cycles of lower limb ischemia prior to cardiopulmonary bypass were tested for remote ischemic preconditioning of the heart. This ischemic stimulus was associated with significant reductions in postoperative troponin release and inotropic support. Remote ischemic preconditioning also significantly reduced intensive care unit stay and myocardial infarction after abdominal aortic aneurysm repair. The preconditioning stimulus was lower limb ischemia due to iliac artery clamping. These two trials can be considered as proof-of-concept only. Further trials must dem-

onstrate outcome benefit before conclusive recommendations can be formulated.

Myocardial preconditioning with volatile anesthetics and noble gases has been demonstrated in multiple laboratory and clinical studies. The identified cellular agents include mitochondrial receptors, sarcolemmal receptors, cytosolic kinases, and intracellular reactive oxygen species. Recent meta-analysis of 22 randomized trials in cardiac surgery (N = 1922) demonstrated that volatile anesthetics are associated with significant reductions in myocardial infarction (odds ratio 0.51; 95% CI 0.32-0.84;  $p = 0.008$ ) and mortality (odds ratio 0.31; 95% CI = 0.12-0.80;  $p = 0.02$ ). These data can likely be extrapolated to patients with coronary artery disease undergoing noncardiac surgery. The 2007 AHA/ACC guidelines for noncardiac surgery recommend volatile anesthetics for maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia (class IIa recommendation; level of evidence B).

Intravenous anesthetic preconditioning has been demonstrated for opioids and propofol. Cardiac surgery trials favor preconditioning with inhaled anesthetics. However, in the setting of left ventricular dysfunction, this has not been rigorously tested due to the myocardial suppression from volatile anesthetics.

Levosimendan is an inodilator with anti-ischemic effects. It limits myocyte apoptosis via mitochondrial membrane channels. A recent study demonstrated that levosimendan preconditioning reduced myocardial damage after cardiac surgery. Larger randomized clinical trials are thus indicated.

Future trials will explore genotypic influences such as genetic modulation of preconditioning and gene therapy strategies to induce a permanently preconditioned cardiac phenotype. The perioperative application of myocardial preconditioning has great promise.