EDITORIAL COMMENT
Moving Preconditioning From Bench to Bedside*

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Ischemic preconditioning is the one maneuver that has consistently been shown to reduce myocardial necrosis due to ischemia/reperfusion injury in experimental models (1). Brief coronary occlusions of a few minutes to 10 min followed by brief reperfusion periods markedly reduce the size of a subsequent myocardial infarction (MI) induced by a longer coronary artery occlusion followed by reperfusion. The ability of ischemic preconditioning to reduce myocardial infarct size has been observed in every species in which the phenomenon has been tested. Ischemic preconditioning also confers other benefits, including a reduction in lethal ventricular arrhythmias (2). There is now ample evidence that ischemic preconditioning can occur in the human heart (3). Studies of isolated cardiac myocytes and human cardiac muscle have shown that, in vitro models that simulate ischemia/reperfusion, preconditioning protocols can protect the compromised heart tissue. During sequential percutaneous coronary artery angioplasty balloon inflations and deflations, the evidence for ischemia in humans (chest pain, ST-segment elevation, lactate production, and regional left ventricular dysfunction) are reduced during repeat inflation/deflation sequences compared with a first balloon inflation. Induction of an ischemic preconditioning protocol by intermittent aortic cross clamping preserves myocardial adenosine triphosphate levels during coronary artery bypass graft surgery. Patients that experience pre-infarct angina pectoris, especially during the first 24 h before acute MI, demonstrate smaller myocardial infarcts, lower mortality, better left ventricular function, and less congestive heart failure (3–5). Second messenger pathways have been described to explain ischemic preconditioning, and release of adenosine with ischemia/reperfusion, preconditioning protocols can protect the compromised heart tissue. During sequential percutaneous coronary artery angioplasty balloon inflations and deflations, the evidence for ischemia in humans (chest pain, ST-segment elevation, lactate production, and regional left ventricular dysfunction) are reduced during repeat inflation/deflation sequences compared with a first balloon inflation. Induction of an ischemic preconditioning protocol by intermittent aortic cross clamping preserves myocardial adenosine triphosphate levels during coronary artery bypass graft surgery. Patients that experience pre-infarct angina pectoris, especially during the first 24 h before acute MI, demonstrate smaller myocardial infarcts, lower mortality, better left ventricular function, and less congestive heart failure (3–5). Second messenger pathways have been described to explain ischemic preconditioning, and release of adenosine with ischemia/reperfusion, preconditioning protocols can protect the compromised heart tissue. During sequential percutaneous coronary artery angioplasty balloon inflations and deflations, the evidence for ischemia in humans (chest pain, ST-segment elevation, lactate production, and regional left ventricular dysfunction) are reduced during repeat inflation/deflation sequences compared with a first balloon inflation. Induction of an ischemic preconditioning protocol by intermittent aortic cross clamping preserves myocardial adenosine triphosphate levels during coronary artery bypass graft surgery. Patients that experience pre-infarct angina pectoris, especially during the first 24 h before acute MI, demonstrate smaller myocardial infarcts, lower mortality, better left ventricular function, and less congestive heart failure (3–5). Second messenger pathways have been described to explain ischemic preconditioning, and release of adenosine with ischemia/reperfusion, preconditioning protocols can protect the compromised heart tissue. During sequential percutaneous coronary artery angioplasty balloon inflations and deflations, the evidence for ischemia in humans (chest pain, ST-segment elevation, lactate production, and regional left ventricular dysfunction) are reduced during repeat inflation/deflation sequences compared with a first balloon inflation. Induction of an ischemic preconditioning protocol by intermittent aortic cross clamping preserves myocardial adenosine triphosphate levels during coronary artery bypass graft surgery. Patients that experience pre-infarct angina pectoris, especially during the first 24 h before acute MI, demonstrate smaller myocardial infarcts, lower mortality, better left ventricular function, and less congestive heart failure (3–5). Second messenger pathways have been described to explain ischemic preconditioning, and release of adenosine with ischemia/reperfusion, preconditioning protocols can protect the compromised heart tissue.

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for acadesine to reduce the incidence of perioperative MI suggests that it might have an anti-necrosis effect possibly by stimulating preconditioning pathways via adenosine. Whether myocardial infarct size was truly reduced by acadesine remains to be determined from this study. Other issues that remain to be resolved is whether acadesine imparted some anti-arrhythmic effect in these patients or whether it improved long-term global and regional left ventricular function.

In summary, the present study by Mangano et al. (15) provides original data that suggest that a preconditioning mimetic agent can be used to improve survival of patients who develop a perioperative MI associated with a coronary artery bypass surgery. The adenosine-regulating agent acadesine reduced mortality by 4.3-fold in these patients, and the benefit was long-lasting. This study successfully moves forward the concept of preconditioning as a therapy from bench to bedside.

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