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Reducing myocardial infarct size: myth or reality

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This year marks the 30th anniversary of the first report of "ischemic preconditioning," which after reperfusion is the most powerful endogenous intervention for reducing myocardial infarct (MI) size.[1] The last 3 to 4 decades have witnessed the accumulation of a huge amount of published literature in the research field of "cardioprotection"—a term used here to describe mechanical and pharmacological interventions for reducing MI size. Much of the research has focused on targeting "myocardial reperfusion injury," which denotes the myocardial injury and cardiomyocyte death that paradoxically occur on reperfusing acutely ischemic myocardium and which has been demonstrated to contribute up to 50% of the final MI size.[2,3] Despite timely reperfusion by primary percutaneous coronary intervention (PPCI), mortality and morbidity after an acute ST-segment elevation MI (STEMI) remain significant, with 7% death and 22% heart failure at 1-year follow-up.[4] Thus, novel cardioprotective therapies are required to target myocardial reperfusion injury and reduce MI size in order to preserve left ventricular systolic function and prevent the onset of heart failure after STEMI. However, the results of a large number of clinical studies in reperfused STEMI patients have failed to demonstrate reduced MI size and improved clinical outcomes. The reasons for this are multiple and complex and have been discussed extensively in the literature; they can be attributed to problems with the design of both experimental and clinical studies used to test novel cardioprotective therapies.[5-8]

In this issue of *Heart and Metabolism*, leading researchers in the field review some of the recent developments in the topical area of cardioprotection. The issue opens with an introduction by Gerd Heusch highlighting the importance of acute myocardial reperfusion injury as a target for cardioprotection and alluding to myocardial reperfusion as a double-edged sword.[9] The metabolic consequences of acute ischemia and reperfusion on the myocardium are elegantly reviewed by Gary Lopaschuk in the Refresher Corner. These metabolic effects highlight opportunities for cardioprotection using metabolic modulation agents such as trimetazidine, a topic discussed in the article by Petr Widimsky.

Mechanical interventions for targeting myocardial reperfusion injury and reducing MI size, such as ischemic postconditioning (IPost) and remote ischemic conditioning (RIC), are reviewed by Hans Erik Bøtker. Of these, RIC holds the most promise for reducing MI size and improving clinical outcomes in reperfused STEMI patients (highlighted in the Hot Topics article by Luciano Candilio)—and is currently being tested in the ongoing European CONDI2/ERIC-PPCI trial (Effect of Remote Ischemic Conditioning on Clinical Outcomes in STEMI Patients Undergoing PPCI).[10] Investigating the signaling pathways underlying ischemic

preconditioning and postconditioning has unveiled numerous cardioprotective targets, many of which have been tested using pharmacological agents—a topic reviewed here by Michel Ovize. Assessing the efficacy of cardioprotective therapies for reducing MI size requires the quantification both of the area at risk and MI size. For this purpose, cardiac magnetic resonance imaging has emerged as the noninvasive imaging modality of choice, a subject that is summarized by Colin Berry in the current issue. More advanced imaging methods, such as hybrid cardiac positron emission tomography/magnetic resonance imaging (PET-MRI), have been investigated in reperfused STEMI patients to elucidate the in vivo metabolic effects of acute ischemia/reperfusion injury on the myocardium. The article by Heerajnarain Bulluck illustrates the use of PET-MRI in two case reports.

In summary, this issue of *Heart and Metabolism* highlights some of the recent developments in the field of cardioprotection and illustrates the challenges and opportunities faced when investigating therapies to reduce MI size and improve clinical outcomes in STEMI patients treated by PPCI. ■

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