Cardioprotection by pre-infarct angina: training the heart to enhance myocardial salvage

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By failing to prepare, you are preparing to fail. (Benjamin Franklin)

Timely reperfusion of the acutely ischaemic myocardium in patients with ST-elevation myocardial infarction (STEMI) is associated with enhanced myocardial salvage and improved survival rates.1,2 Despite the overwhelming evidence in favour of prompt reperfusion with primary percutaneous coronary intervention, other factors, such as the size of the area at risk, collateral circulation, pre-infarction angina (PA) as well as pre and postconditioning, have been also shown to influence the results of infarct size reduction studies.3

The most powerful intervention in experimental studies which augments the benefits of rapid reperfusion following coronary occlusion is ischaemic preconditioning.4,5 The possibility that an innate mechanism of myocardial protection might be inducible in the human heart has generated considerable excitement and enthusiastic research. Data from limited clinical studies are encouraging by demonstrating that brief episodes of ischaemia before a total coronary occlusion in STEMI protect the heart and result in a smaller infarct size.6 It has been speculated that preconditioning may occur naturally in patients with myocardial infarction as angina preceding an acute myocardial infarction. Indeed, the presence of PA has a significant impact on the clinical course of myocardial infarction. PA has been shown to be associated with reduced infarct size, improved left-ventricular function, a decrease in the number of cardiac arrhythmias, and improved clinical outcome.7–9 However, data from clinical studies are scarce and hampered by small sample sizes, selected populations, single-centre and retrospective study designs.

In this issue of the European Heart Journal Cardiovascular Imaging, Masci et al.10 prospectively evaluated the influence of PA on myocardial salvage using the current gold standard for myocardial damage assessment cardiac magnetic resonance (CMR) imaging. The authors could nicely demonstrate in their multicentre study that PA is associated with higher myocardial salvage and reduced reperfusion injury. Consequently, the present study suggests that the previously observed clinical benefits in patients with PA are mediated through cardioprotection resulting in increased myocardial salvage and reduced microvascular damage. However, the exact cardioprotective mechanisms of PA leading to improved myocardial salvage are incompletely understood and unfortunately not addressed by the current paper. The following mechanisms might explain the clinical benefit of PA: (i) ischaemic preconditioning seems to be the most likely explanation.4,11 PA could have prepared the heart and made it resistant to severe ischaemia associated with coronary artery occlusion in acute STEMI; (ii) PA could result in enhanced collateral blood flow, thereby limiting myocardial infarct size;12 (iii) PA may attenuate platelet-mediated thrombosis, thrombus composition, and thrombus burden in STEMI patients.13 Regardless of the exact underlying mechanisms, the important observations of Masci et al.10 help explain the intriguing finding that PA results in less myocardial damage.

Another interesting fact of the study is that a significant portion of patients had to be excluded from myocardial salvage assessment by CMR due to insufficient image quality. CMR has emerged as the gold standard for accurate assessment of myocardial and microvascular damage. However, it is well known that T2-weighted sequences for the detection of myocardial oedema may be hampered by poor image quality and artefacts affecting data analysis and interpretation.14,15 Consequently, CMR protocols for oedema detection still require further optimization. Mapping techniques (T1 and T2 mapping) may be more reliable and robust for the assessment of the myocardium at risk and myocardial salvage.16,17 However, further studies in various clinical settings and larger cohorts are needed before broad utilization of these promising new mapping sequences.17

Despite some limitations of the study by Masci et al. like the fact that the assessment of PA does not take into account silent ischaemia, e.g. in diabetic patients, no clinical nor CMR follow-up data, exclusion of a large number of patients for myocardial salvage assessment and unclear mechanisms of the protective effect of PA, the findings of the study add to the growing evidence that PA leads to cardioprotection. Further studies are required to investigate the underlying mechanisms of this protection. Improving our understanding of the basic mechanisms underlying these phenomena could also lead to further elucidation of cellular signalling pathways and novel...
therapeutic targets. It appears that PA exerts an impressive protective effect by inducing tolerance to severe ischaemia and reperfusion injury. Consequently, PA seems to train and prepare the heart for enhanced myocardial salvage in acute STEMI.

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References