Assessment of reperfusion-induced myocardial injury by echocardiography

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This editorial refers to "The sequential changes in myocardial thickness and thickening which occur during acute transmural infarction, infarct reperfusion and the resultant expression of reperfusion injury" by O. Turschner et al. on page 794.

In the early phase of acute myocardial infarction, timely reperfusion is a prerequisite to contain the extent of cellular and vascular injury. In the absence of reperfusion, severe ischaemia inevitably leads to myocardial necrosis involving all of the area at risk. Early reperfusion may prevent the death of ischaemic cardiomyocytes and is the therapeutic strategy of choice in patients with acute myocardial infarction. However, even after early and adequate reopening of the infarct-related artery, the full benefits of reperfusion may be attenuated by a decrease in microvascular reflow and lethal injury to potentially viable endothelial and myocardial cells during the restoration of flow.

In this issue of European Heart Journal, Turschner and colleagues1 revisit the sequential changes in regional myocardial thickness and function after reperfusion of transmural infarct in an experimental closed-chest pig model by analysing M-mode radio-frequency (RF) data. The most striking results of this study are: (1) the ability of cardiac ultrasound to identify reperfusion-induced oedema as an acute and immediate increase in regional wall thickness in the reperfused infarct area and (2) the description of post-systolic thickening occurring in both transmural infarct and reperfused myocardium, indicating that this parameter is not a consistent marker of myocardial viability.

Reperfusion induces prolonged, but ultimately reversible, myocardial contractile dysfunction ("stunned myocardium"). However, there is controversy over whether reperfusion results in further necrosis of ischaemically injured myocytes. Experimental studies suggest that reperfusion of ischaemic myocardium causes major structural changes in injured myocytes, whereas non-reperfused infarcts are characterised by relatively well-preserved myofibrils.2-4 In most patients, reperfusion salvages only some of the ischaemic myocytes, thus limiting, but not preventing, myocardial infarction. The main mechanism of myocyte death in reperfused infarcts is myocyte hypercontracture, which occurs during the first minutes after flow restoration. During ischaemia, ATP free energy falls in myocytes and cytosolic H⁺, Na⁺, and Ca²⁺ concentrations rise, inducing cytoskeletal and sarcolemmal fragility. Reperfusion and the subsequent oxygen supply immediately restore ATP synthesis, whereas normalisation of cytosolic Ca²⁺ concentration, mainly by sequestration in the sarcoplasmic reticulum, requires some time. During this time, the availability of energy in the presence of elevated Ca²⁺ concentration results in the generation of excessive contractile force, which, in the presence of cytoskeletal fragility, may lead to hypercontracture.5 The mechanical stress imposed by hypercontracture is aggravated by swelling and interaction with surrounding tissue and results in immediate sarcolemmal disruption.5

Myocardial oedema is a characteristic feature of the pathophysiology of reperfusion following prolonged coronary occlusion. There is evidence suggesting that reperfusion oedema may contribute to the death of cardiomyocytes that otherwise would have survived reperfusion. Reperfusion-induced oedema has been explained as the consequence of a large osmotic gradient between the extracellular and intracellular space. During coronary occlusion, accumulation of diffusible catabolites increases the osmolarity on both sides of the sarcolemma. The rapid wash-out of hyperosmotic extracellular fluid during subsequent reperfusion creates an osmotic gradient that has been considered the cause of reperfusion-induced cell swelling.6 Therefore, the primary mechanism of ischaemia-induced oedema formation involves an increase in intracellular Na⁺ attributable to the breakdown of energy-dependent sodium...
extrusion. A secondary mechanism includes the anaerobic conversion of glycogen to lactate and the hydrolysis of high-energy phosphates, increasing intracellular oncotic pressure relative to the interstitium. Cell membrane damage is a third mechanism.

Identifying reperfusion-induced injury may be crucial in the clinical setting of acute myocardial infarction because of prognostic implications and additional therapeutic interventions given at the time of reperfusion to reduce infarct size. Among the various available imaging techniques, magnetic resonance imaging has been proven to accurately identify reperfusion injury and to help in understanding its complex pathophysiology. However, it is not a bedside technique like echocardiography.

After acute myocardial infarction, the prognosis is mainly related to the extent of dyssynergy and the existence of viability. In transmurally infarcted myocardium, detrimental effects of reperfusion-induced oedema will be observed in both systolic and diastolic regional function parameters. Active systolic deformation is impaired and associated with passive post-systolic deformation and increased stiffness. These regional abnormalities may therefore contribute to impair global function and lead to unstable hemodynamic conditions. In addition, interstitial and myocardial cellular oedema might compress the capillaries, leading to microvascular obstruction and contributing to the no-reflow phenomenon.

As reperfusion itself has now been proven to exacerbate the damage sustained during the ischaemic period, numerous studies have attempted to reduce infarct size by a therapeutic intervention administered shortly before, or at the time of reperfusion. In particular, interventions directed against neutrophils have been successful since reperfusion leads to an inflammatory response that includes leukocyte adhesion to the coronary microvasculature. Administration of oxygen free radical scavengers, adenosine, nitric oxide donors, perfluorochemicals, and Na+/H+ exchange inhibitors have been shown to afford cardioprotective benefit in a variety of animal models of ischaemia and reperfusion.

Reperfusion injury after acute myocardial infarction has functional and clinical relevance. Thus, therapeutic interventions at the time of reperfusion are desirable to protect the post-ischaemic myocardium from reperfusion injury and to limit the extent of necrosis. The challenge is now to better identify, in the clinical setting of acute myocardial infarction, patients who exhibit these reperfusion abnormalities and might benefit from adjunctive treatment at the time of reperfusion. This study by Turschner proves that echocardiography is a valuable tool to both identify successful reperfusion and to assess the presence and extent of myocardial oedema associated with reperfusion injury.

References