Myocardial stunning

DEFINITION

Myocardial stunning is defined as a transient postischemic myocardial dysfunction, occurring during full reperfusion after a short episode of non-lethal ischemia. This phenomenon was first recognized by Heyndrickx et al. and termed "myocardial stunning" by Braunwald and Kloner. The initial description of stunning i.e. a total coronary occlusion of only 5 to 15 minutes that was not associated with detectable myocardial necrosis, resulted in impairment of ventricular systolic function that lasted for several hours following reperfusion. Since then, myocardial stunning has been demonstrated experimentally under a variety of conditions and in many different animal species. Several of these conditions become extremely important for a better understanding of the clinical relevance of myocardial stunning. At first there is the problem of "peri-infarction stunning". It has been well established that during prolonged coronary artery occlusion only a variable fraction of the area at risk will become necrotic. A "border zone" of myocardial tissue, adjacent to necrotic myocardium will survive mainly due to collateral flow, and myocardial stunning can be demonstrated in this border zone after delayed reperfusion of the blocked vessel. Therefore, the akinetic area related to infarction can easy be overestimated in the early reperfusion phase: at this stage differentiation between viable and necrotic tissue cannot be made on the basis of regional function studies alone. Second, not only regional ischemia will result in stunning upon reperfusion but also global ischemia or anoxia. This finding has important implications because it explains why hearts of patients undergoing cardiac surgery are very often dysfunctional in the early period of reperfusion after cross clamping of the aorta despite cardioplegic protection. A third important circumstance under which stunning can be demonstrated is that stunning also occurs in the presence of partial coronary stenosis instead of complete occlusion.

followed by reperfusion. Obviously relative ischemia due to imbalance between oxygen supply and demand can induce stunning as well as a complete occlusion of the coronary vessel. This observation is important because it explains why transient coronary spasm may result in regional myocardial dysfunction.

Stunning and myocardial viability

By detailed assessment of subcellular myocardial structure during progression of ischemia, a clear sequence of morphological changes can be described. After a few minutes of ischemia, the first subtle morphological alterations are found in the mitochondria: the small osmiophilic granules embedded in the mitochondrial matrix disappear. When ischemia proceeds, more pronounced alterations occur in the mitochondria: clearing of the mitochondrial matrix, swollen and disrupted cristae, and rupture of inner and outer mitochondrial membrane. These lesions can be used to create a scoring system for the semi-quantitative grading of ischemic injury. However, when ischemia passes the "point of no return" in terms of cell viability, a clear morphological picture is found: disruption of the sarcolemma, inclusion of typical amorphous dense bodies in the mitochondria, intracellular edema, and chromatin clumping and margination in the nucleus. It is remarkable that under all these conditions, the contractile system (sarcomeres and myofibrils) remain structurally intact as far as can be detected with the electron microscope. Only at a late stage after the onset of irreversible damage, does the contractile system disintegrate. It is obvious that irreversibly damaged myocytes are, and remain, non-functional. There is, however, no direct correlation between the amount of myocardial necrosis and the extent of myocardial dysfunction in a given perfusion area of the blocked and reperfused coronary vessel. Indeed, viable postischemic tissue will be non-contractile as well for hours to days while ultrastructure reveals only very minor abnormalities. In a previous experimental study, we showed that upon reperfusion after 90 minutes of coronary occlusion in dogs, salvage of 68 % of the perfusion area of the occluded artery was obtained. Viability of the myocardium in this area was demonstrated by electron microscopy. However, postischemic regional function was completely lost in the first 24 hours, despite this considerable amount of viable time. Nevertheless, regional function recovered after 1 week of reperfusion, which suggests the presence of stunned myocardium in the early postischemic phase.

These observations imply that indirect noninvasive assessment of viability (i.e. differentiation between ischemia, necrosis and stunning) cannot be based only upon the lack of regional function in the presence of flow i.e. reperfusion. Indeed, in a previous study, we could demonstrate that necrotic tissue is transiently hyperperfused in the initial reperfusion phase before the "no reflow phenomenon" develops while the viable, stunned borderzone transiently looses its maximal dilatory capacity.

Mechanisms of stunning

The basic mechanisms responsible for this transient reduction of postischemic contractility (up to 7 days before complete recovery) are not fully elucidated.