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MEETING REPORT

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Stunning – great paradigmatic, but little clinical importance

In this author's personal view, stunning is of eminent importance as a paradigm of early and, therefore, both reversible and therapeutically modifiable ischemia/reperfusion injury. Stunning has emerged as an important paradigm of early ischemia/reperfusion injury because its end-point, i.e., contractile function, is easily accessible and continuously quantifiable. Experimental studies on stunning have contributed a lot to the understanding of the underlying mechanisms of early, reversible ischemia/reperfusion injury (3). On a side note, the author of the present article has made a good living by using stunning to study the mechanisms of early/reversible ischemia/reperfusion injury and strategies of its therapeutic modification (8–16, 27–30, 32, 44) and he will continue to do so.

Interestingly, however, although the phenomenon of stunning became popular with the advent of clinical reperfusion interventions (5), its clinical importance appears minimal:

1) The best defined and "purest" clinical scenario of stunning is most probably that of PTCA. With routine clinical PTCA, stunning is rarely seen (4). If stunning occurs, it is only mild, mostly diastolic, and quickly reversible (20, 36, 46). Only with prolonged inflation times (4–7 min) does PTCA cause stunning, which then resolves during the following 24 h (38). Although in this study there were reduced ejection fraction and diastolic function abnormalities for 24 hours, their severity was so moderate that no clinical problems were reported.

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2) Unstable angina is another clinical scenario, where stunning may occur (18, 22). However, there are no more than 11, i.e., 5 in the study by Nixon et al. (22) and 6 in the study by Jeroudi et al. (18), cases where stunning has been made likely in the setting of unstable angina, and even there the confounding influences of multiple medical treatment were present and persistent microcirculatory disturbances were not excluded by adequate measurements.

3) Stunning can indeed be documented following exercise-induced ischemia in patients with chronic stable angina (1, 19, 34, 43). Again, however, the contractile abnormalities are mild and rapidly reversible within 2 h at the latest. In this particular setting of regional dysfunction following exercise-induced ischemia, the presence of stunning may be more of a diagnostic value than of any clinical importance. Also, relevant regional hypoperfusion may be present beyond the protocol of exercise-induced ischemia and cause contractile dysfunction, and this was only excluded in one of the above studies (1) by scintigraphy at 30 min reperfusion (7, 35).

4) Stunning is probably also present in the recovery process following non-transmural myocardial infarction (2, 17, 24, 31, 33, 37, 39, 42). However, there is no single study where persistent perturbations of microcirculatory perfusion were excluded. Also, the recovery of neuroendocrine activation and morphological remodeling processes have not been adequately distinguished from stunning.

5) Stunning is also likely to be present after cardioplegic cardiac arrest (6, 26). However, there are major confounding influences, i.e., hypothermia, altered ionic concentrations, altered loading conditions, persistent microcirculatory perfusion abnormalities, etc., which have not been adequately distinguished from stunning per se.

6) Stunning, in a repetitive form, has been proposed to be the underlying mechanism of hibernation (4). While this is an

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attractive hypothesis, supportive data in patients are exclusively derived from PET measurements of myocardial blood flow (21, 45) which are all limited by the lack of PET's transmural resolution and its inability to exclude persistent subendocardial ischemia (25). Furthermore, experimental studies reporting normal resting flow in chronically dysfunctional myocardium, but single episodes of stunning (41) – surprisingly after such short periods of stress-induced ischemia which were traditionally thought not to induce stunning (23) – did not reproduce the morphological phenotype of hibernating myocardium, but only a small rim of myocytes with myofibrillar lysis and increased glycogen content surrounding multifocal microinfarcts (40).

In summary, stunning probably occurs in the clinical setting of various ischemic syndromes, but in most instances it is difficult to distinguish from other potential causes of contractile dysfunction, in particular persistent microcirculatory flow disturbances. When stunning is identified as the cause of contractile dysfunction, it will not need treatment in most instances. When stunning requires treatment because the dysfunction is severe and involves large parts of the left ventricle, inotropic support will improve contractile function without jeopardizing the recovery. Thus, stunning per se does not appear to be an important clinical problem which impacts on a patient's prognosis. In part, the apparent lack of importance of stunning in the clinical setting may be due to pretreatment of patients with drugs known to attenuate stunning, e.g., calcium antagonists and ACE inhibitors.

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