

Hibernation or repetitive stunning – does it matter?

The basic perspective

Gerd Heusch^a and Rainer Schulz^b

^aInstitut für Pathophysiologie, Westdeutsches Herzzentrum Essen, Essen, Germany, and

^bUniversitätsklinikum Essen, Essen, Germany

Correspondence: Gerd Heusch, Institut für Pathophysiologie,
Westdeutsches Herzzentrum Essen, Essen, Germany.
Tel: +492017234480; e-mail: gerd.heusch@uk-essen.de

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Abstract

The long-lasting controversy on whether the contractile dysfunction observed in patients with coronary artery disease reflects hibernation – that is, a regulatory adaptation to persistent ischemia – or stunning – that is, an accumulation of reversible damage due to repeated periods of ischemia/reperfusion – is resolved. The perfect adaptation to persistent ischemia as seen experimentally can not be maintained for more than several hours (arguing against pure hibernation), but dysfunctional myocardium does not only display signs of damage but also an up-regulation of cardioprotective genes (arguing against pure stunning). Thus, as is often the case, both sides were wrong and right.

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The question in the title refers to a historic controversy. Stunning was originally characterized in studies in dogs with coronary artery occlusions of too short a duration to cause irreversible damage but which were nevertheless followed by prolonged, yet spontaneously and fully reversible, contractile dysfunction during reperfusion [1]; the term “stunning” for such prolonged yet reversible postischemic contractile dysfunction was proposed later [2]. The concept of “hibernating myocardium” was first introduced by Rahimtoola in 1985, when he reviewed the results of the first coronary revascularization trials and identified patients with coronary artery disease and chronic left ventricular dysfunction that recovered on revascularization [3]. He proposed the idea that the reduction in contractile function served to match the reduced supply, restore an energetic equilibrium, and

preserve viability. Rahimtoola’s more clinically based idea of hibernating myocardium quickly received support from a number of experimental studies that demonstrated matching of reduced regional myocardial blood flow to reduced regional contractile function [4,5], recovery of energy and substrate metabolism [6,7], persistence of inotropic reserve at the expense of such metabolic recovery, and preservation of viability over several hours of continuing ischemia [8] – that is, evidence for downregulation of contractile function in short-term myocardial hibernation.

Although it became increasingly clear that chronic contractile ventricular dysfunction in patients with coronary artery disease did not necessarily reflect irreversible damage and scar, but was in fact amenable to revascularization, a heated debate developed

as to whether the observed contractile dysfunction reflected hibernation – that is, it was regulatory in nature and an adaptation to continuing ischemia – or stunning – that is, it was an accumulated consequence of repeated bouts of ischemia-reperfusion that left the myocardium in a continuous, yet spontaneously fully reversible contractile deficit even while fully reperfused. The controversy focused on the question whether the clinically observed hibernating myocardium had reduced or normal baseline flow at rest [9,10]. Much of this debate appears to be obsolete today, but it is worthwhile remembering that the essential question was: does chronic contractile dysfunction distal to a coronary stenosis reflect adaptation or damage?

Today, the historic controversy is largely resolved, and – as is often the case – both sides were both wrong and right. The perfect adaptation as observed in short-term hibernating myocardium could not be maintained over more than several hours [11]. Stunning as such is almost entirely a laboratory phenomenon, and of little clinical significance other than in its cumulative manifestation as hibernating myocardium [12]. The contractile dysfunction in stunned myocardium can be attenuated by a variety of interventions, including selective heart rate reduction [13]. Resting blood flow is reduced in hibernating myocardium [14]; however, this is not the result of continuing ischemia, but rather the consequence of repetitive episodes of ischemia-reperfusion in which blood flow is reduced in adaptation to contractile dysfunction [14–16]. Most importantly, in our view, the observed chronically dysfunctional myocardium has features both of damage and replacement fibrosis, and of the upregulation of a cardioprotective gene program [17,18], which puts it into the context of ischemic pre- and postconditioning [14].

To answer the initial question. No, it does not matter whether chronic contractile dysfunction distal to a coronary stenosis is viewed as hibernation or repetitive stunning. Yes, it does matter that we realize that such chronic contractile dysfunction is associated with both destructive **and** protective features, and is amenable to revascularization. ■

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