Chronic Myocardial Hibernation

The study of Vanoverschelde et al. demonstrated significant abnormalities on morphological analysis of myocardial biopsies from patients with chronic myocardial hibernation. These morphological changes are very similar to those described previously and do not occur in stunning; thus, the investigators correctly state that their patients with left ventricular dysfunction had chronic myocardial hibernation.

The authors proposed that in their patients, myocardial hibernation was the result of, or followed, repeated episodes of myocardial stunning. Their rationale for invoking stunning was based on "no reduction" of resting myocardial blood flow (MBF) to areas of resting left ventricular (LV) wall motion abnormalities. This conclusion was based on the demonstration of similar blood flow measured by positron emission tomography (PET) to collateral-dependent myocardium in a group of 26 patients, 17 of whom had reduced function (group 2) and 9 who had normal function (group 1). Thus, the question that arises is whether MBF in group 2 patients would be expected to be the same as in group 1 patients.

MBF is importantly determined by myocardial oxygen demand: The group 2 patients had 5.6% higher rate-pressure product and 21.7% larger LV volume than group 1 patients; thus, MBF in group 2 patients would be expected to be higher than in group 1 patients. Indeed, MBF in normally functioning LV segments in group 2 patients was higher than in group 1 patients (95.5±26.7 versus 82.7±18.0 mL/min per 100 g, P<.05). MBF in the dysfunctional LV segments in group 2 patients was significantly lower than in normally functioning LV segments in the group 2 patients (77.1±24.6 versus 95.5±26.7 mL/min per 100 g, P<.001). These data demonstrate that MBF to the dysfunctional LV segments was reduced (and not "not reduced," which the authors repeatedly assert). Conversano et al. also have demonstrated using PET that MBF in hibernating myocardium was lower than in normal subjects (40±5 versus 113±33 mL/min per 100 g).

It is possible that MBF to normally functioning LV segments in at least some of their patients, all of whom had coronary artery disease, may have been somewhat reduced, because small reductions of MBF may not necessarily be associated with LV dysfunction. The values for MBF in their group 1 patients (82.7±18.0 mL/min per 100 g) are lower than those previously reported in normal subjects using PET (117±33 mL/min per 100 g). Thus, MBF to the dysfunctional LV segments in group 2 patients (hibernating myocardial segments) may be reduced to a greater extent when compared with normal subjects than would be apparent by comparing it with group 1 patients or even those in group 2.

Data of Conversano et al. support this hypothesis (vide supra). It also would have been very useful to know whether the patients in groups 1 and 2 had disease of coronary arteries (and the percent stenosis in the diseased arteries) other than the totally occluded ones.

The "absolute" MBF during dipyridamole infusion was determined in 11 patients; all experienced angina and significant ST depression. In the three patients in group 1, MBF to the collateral-dependent segments increased by 205%, whereas in the eight patients in group 2, MBF to the collateral-dependent segments increased by only 27% (P<.001). The maximal MBF to normally functioning segments in the patients in groups 1 and 2 was similar. These findings are compatible with the hypothesis of a relatively delicately balanced MBF and LV function in hibernating myocardium. However, LV function before, during, and after the dipyridamole stress test was not reported.

Finally, data were not presented documenting that these myocardial segments exhibited even a single episode of stunning ("prolonged" postischemic dysfunction with recovery of function), let alone repeated episodes of stunning. The mere occurrence of angina does not prove or document the occurrence of stunning; angina also occurs in patients with myocardial hibernation and obviously also in those without either stunning and/or hibernation.

In summary, Vanoverschelde et al. have documented metabolic and morphological correlates of chronic myocardial hibernation in humans, which is a useful contribution. Contrary to the assertion of the authors, the data presented are compatible with the hypothesis that blood flow to the hibernating myocardium was reduced. Therefore, it is not necessary to postulate the occurrence of stunning; moreover, the authors have not documented even a single episode of stunning, let alone repeated episodes of stunning, in their patients.

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References

Reply
Dr Rahimtoo is questioning the interpretation of the flow measurements obtained in dysfunctional hibernating left ventricular segments, which he considers to show reduced flow. If this were the case, the pathogenetic mechanisms responsible for chronic hibernation, which he has brilliantly postulated 5 years ago, would be verified. We still think that it is not the case, at least in this particular model.

With 13N-ammonia as a flow tracer, the normal values for resting myocardial blood flow in volunteers vary from 76±17 to 92±25 mL/min per 100 g, depending on rate-pressure product. These values are not significantly different from those obtained in dysfunctional segments. Taking into account a marginal (5.6%) increase in rate-pressure product and the larger left ventricular volumes, Dr Rahimtoo would have expected a greater-than-normal flow value; therefore, the measured data would be decreased relative to demand. Although as mentioned above, myocardial blood flow is strongly dependent on the rate-pressure product, this appears to be true only in contracting but not in dysfunctional segments. As a matter of fact, in animal studies, flow by microspheres was not shown to be increased in viable dysfunctional segments. In addition, the measurements of oxygen consumption by 13C-acetate kinetics confirm the results of the flow measurements.

Dr Rahimtoo is quoting the study by Conversano et al. In this study, dysfunctional but viable segments were deemed stunned (n=15) or hibernating (n=7) on the basis of the flow values measured with H215O. These measurements are subject to >20% variability and are poorly accurate in regions with low-count recovery. Therefore, we have elected to use 15N-ammonia in our study. Still, in the study by Conversano et al, two thirds of the dysfunctional segments show flow values within their normal limits. Finally, in an animal model of chronic hibernation recently described by Shen et al, normal microsphere flow values were measured.
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