Time Course of Sympathetic Neural Hyperactivity After Uncomplicated Acute Myocardial Infarction

To the Editor:

The article by Graham et al.1 reported an increase in muscle sympathetic nerve activity (MSNA) in patients studied 2 to 4 days, 3 months, and 6 months after uncomplicated acute myocardial infarction (AMI). This protracted sympathetic overactivity did not appear to correlate with arterial blood pressure, ie, with baroreceptor mechanisms, leading the authors to hypothesize that cardiac reflexes might be involved.

An excitatory sympathetic cardio-cardiac reflex elicited by transient coronary occlusion in anesthetized cats was described a long time ago.2 Subsequently, the functional properties of the ventricular sympathetic sensory endings responsive to myocardial ischemia and/or to chemical substances like bradykinin were also detailed.3 Hence, a neural substratum seems to exist that is capable of generating excitatory sympathetic reflexes arising from the heart.

Conversely, the use of power spectrum analysis of heart rate variability (HRV) has made it possible to obtain a noninvasive assessment of the state of sympathovagal balance, a widely used tool. With this approach, it was found4 that a shift of the balance toward sympathetic predominance was present in patients after myocardial infarction, and that change lasted for at least 6 months. This finding is crucial, because it refers to cardiac neural modulation, whereas MSNA recordings pertain to a different sympathetic district. Although sympathetic excitation is sometimes rather generalized, this may not always be the case.

We fully agree with the authors that sympathetic excitation “may provide an explanation for the delayed cardiovascular morbidity and mortality after AMI.” We have recently published a general hypothesis5 centered on the role of cardiovascular sympathetic afferent fibers in mediating a state of sympathetic reflex overactivity, with positive feedback characteristics, in numerous pathophysiological conditions such as ischemic heart disease, arterial hypertension, and the initial phases of congestive heart failure. In all of these cases, the sympathetic excitation would not subserve a homeostatic function, ie, would be independent of baroreceptor mechanisms, and is likely to be detrimental.5

A more adequate clinical appreciation of these excitatory neural mechanisms and their appropriate therapeutic correction may provide quite beneficial results in the near future.5

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Response

The letter by Malliani and Montano raises important issues regarding the mechanisms and implications of our finding of protracted sympathetic hyperactivity after uncomplicated acute myocardial infarction (AMI).1 Regarding mechanisms, our data indicated that the hyperactivity was not solely attributable to changes in arterial pressure. As it is not always possible to unequivocally define and quantify reflex mechanisms in humans, we speculated that the sympathetic hyperactivity was related to cardiac receptor function in view of its inverse relation to left ventricular ejection fraction. In terms of their reflex effects, these receptors may be classified into groups that lead either to reflex inhibition or excitation of sympathetic neural output.2 We speculated1 that the sympathetic hyperactivity resulted from impairment of the tonic action of the inhibitory receptor group, as the hyperactivity was sustained for 6 months after AMI. Malliani and Montano speculated further that the sympatho-excitatory group was involved, which would imply that this group was subject to excessive stimulation for this period of time. We cannot rule out the argument that both mechanisms might have been involved, at least over different times after AMI. We agree with the authors that reflex sympathetic control is heterogeneous, and that the hyperactivity may involve peripheral and cardiac regions. We discussed the latter,1 using published evidence on the use of cardiac norepinephrine spillover rate in unstable angina.

Finally, we hope to clarify some of these mechanistic issues, and the possible clinical use of the new findings as mentioned in the letter, through an ongoing study of sympathetic changes in patients with a range of acute coronary syndromes who are followed up until the sympathetic activity has returned to normal levels.

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