α-Adrenergic Blockade in Myocardial Infarction

To the Editor:

I read with interest the article by Gregorini et al1 that showed that α-adrenergic blockade improves recovery of myocardial perfusion and function after stenting in acute myocardial infarction (AMI), and I suggest that this finding can be explained by a basic principle of the spasm of resistance vessel (S-RV) concept of ischemic heart disease (IHD), a theory that asserts that S-RV induces symptoms in IHD.2

A basic premise of the concept is that severe ischemic injury is a major cause of S-RV, and it is known that injury incites S-RV.3 It seems reasonable that stenotic coronary artery disease (CAD) can cause sufficient ischemic injury to induce ischemic injury–induced (II-I) S-RV, and the concept attributes effort angina to II-I S-RV; however, other vasoconstrictive forces, such as emotional stress, can also be operative. The severe necrotic injury of AMI is considered to cause continuing II-I S-RV and no-reflow (reduced myocardial perfusion),2 and the reduced perfusion studied by Gregorini et al1 is regarded as no-reflow. In keeping with these positions, there is evidence for both ischemic- and injury-induced coronary S-RV,2 and no-reflow has recently been attributed to S-RV by others.4

II-I S-RV is regarded as an expression of the hemostatic response, which is a basic defensive or homeostatic mechanism designed to prevent exsanguination after injury.1 Hemostasis includes initial vasoconstriction and subsequent thrombosis, but local thromboses would not be expected with ischemic injury because, unlike the usual injury, vascular disruption does not occur; however, no-reflow secondary to S-RV is assumed to favor secondary thromboses upstream in epicardial arteries.2 While hemostatic S-RV ordinarily is short-lived,3 hemostatic S-RV due to ischemic injury could be prolonged by a vicious circle of ischemic injury, II-I S-RV, more ischemia and injury, and more II-I S-RV; consistent with this, Heusch et al5 described feedback aggravation of myocardial ischemia due to cardiac sympathetic nerve activity and progressive vasoconstriction.

The finding by Gregorini et al1 that α-adrenergic blockade improves myocardial perfusion during AMI seems highly consistent with the position that reduced perfusion during AMI (no-reflow) is due to activation of hemostatic II-I S-RV. Consistent with this, the sympathetic nervous system plays an important role in mediating hemostatic spasm.3

The principle of hemostatic II-I S-RV to explain reduced perfusion during AMI relates this reduced perfusion to a basic homeostatic mechanism, ie, the ancient and important injury-spasm response. Also, the principle of hemostatic II-I S-RV provides a mechanism by which stenotic CAD favors clinical IHD.

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Response

Dr Hellstrom proposes a hemostasis-related spasm rather than α-adrenergic coronary vasoconstriction to explain the decreased myocardial perfusion and function that we observed after coronary stenting and that we resolved by either phenolamine or urapidil. We discussed the involvement of hemostasis-related factors (page 488, right column, 2nd paragraph)1 but found it played a minor role. In particular, in the experimental study by Heusch et al,2 ischemia increased the activity of the cardiac sympathetic nerves. Aspirin pretreatment did not influence the traffic along the cardiac sympathetic nerves. Only the segmental anesthesia of cardiac innervation prevented the nerve firing. In addition, our patients were treated with full doses of aspirin and ticlopidine, with such treatment beginning 24 hours after thrombolysis. Also in our patients, heparin (100 U/kg) was injected during coronary stenting.

Activated platelets release vasoactive substances, but the combined antiplatelet and anticoagulant treatment attenuates both intrinsic and extrinsic coagulation pathways.3,4 Hemostasis activation did not increase during the procedure, irrespective of the magnitude of endothelial or plaque abrasion (rotational ablation or coronary stenting). Moreover, vasoconstriction did not correlate with thrombin generation.3 Patients were never in a condition of no-reflow but in a condition of left ventricular function changes that correlated with macrocirculatory and microcirculatory perfusion changes.5 The impairment of left ventricular function that was observed both in the infarct-related artery and the non–infarct-related artery–dependent myocardium does not exclude the influence of locally released factors but strongly suggests the involvement of cardio-cardiac and cardio-sympathetic reflexes2 and the electrical syncytium demonstrated among the cardiac cells.6

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