No-Reflow Phenomenon

To the Editor:

In reviewing no-reflow, Rezkalla and Kloner1 indicted injury-induced microvascular changes, but did not mention spasm of resistance vessels, which might be the basic mechanism of no-reflow. I proposed in 1971 that no-reflow (“stasis”) is due to ischemic injury-induced spasm, and the evidence seemed convincing.2 Short coronary occlusions reversed no-reflow, and this was interpreted as reversal of spasm; occlusion-induced ischemia caused reactive hyperemia, which reversed spasm. The ability to alternate repeatedly between normal and low flows seemed to rule out mechanisms as cell swelling, microvascular obstruction by white cells and platelets, and vascular damage directly causing no-reflow.

Reduced flow (ie, no-reflow) has been attributed by Gregorini et al3 to vasoconstriction in individuals treated with percutaneous transluminal coronary angioplasty (PTCA), cases which support the spastic cause of no-reflow. In cases reported in 1999,3 no-reflow was due to infarction (no-reflow present before PTCA); in cases reported in 1998 and discussed in the 1999 paper,3 no-reflow followed the ischemic insult of PTCA in individuals without infarction. I attribute no-reflow in these cases to spasm from the acute ischemic injury of infarction or PTCA, plus chronic ischemic injury from coronary stenoses. The often sudden and dramatic onset of no-reflow in infarction after short-term interventions1 is consistent with a spastic response to fresh ischemic injury; no-reflow soon after brief ischemic episodes seems poorly explained by microvascular obstruction by cell swelling or cellular elements.

The study by Gregorini et al3 support reversal of no-reflow by short coronary occlusions. Post-infarct mild no-reflow was reversed by PTCA for 15 minutes, after which no-reflow returned, and this is explained by reactive hyperemia generated by PTCA-induced ischemia; reactive hyperemia reversed spasm until vasodilation dissipated, allowing spasm to recur. Also, in cases without infarction, no-reflow occurred 15 minutes after PTCA; delay in developing no-reflow is explained by reactive hyperemia, which reversed spasm until vasodilation dissipated.

Occurrence of systolic flow reversal with no-reflow4 is highly consistent with the spastic cause of no-reflow; this phenomenon was demonstrated during spontaneous angina in microvascular angina,5 which has been attributed to spasm.5 One tracing of the 1971 study2 showed reversed systolic flow, and its limited demonstration is attributed to insensitivity of earlier flow measurement techniques.

Consistent with the mechanism of spasm, verapamil and adenosine improve no-reflow.1 Also, α-adrenergic blockade, which operates against ischemia-induced spasm, reversed no-reflow in cases associated and unassociated with infarction.3 Because α-adrenergic blockade reversed no-reflow,3 this modality might be useful in preventing and treating no-reflow.

H. Richard Hellstrom, MD
Anatomical Pathology
SUNY Upstate Medical University
Syracuse, NY
E-mail hellstrr@mail.upstate.edu


Response

We thank Dr Hellstrom for his interest in our article1 and agree that small vessel spasm may be yet another mechanism that could contribute to no-reflow. However, the experiments that Dr Hellstrom describes2 did not measure anatomic no-reflow as we have.3 No assessment of anatomic perfusion defect by either thioflavin S, carbon black, or other standard marker was used. Thus, it is not known whether short coronary occlusions could reverse the anatomic no-reflow phenomenon observed within a myocardial infarction. Areas of no-reflow in our infarct/reperfusion models are well-delineated subendocardial to midmyocardial, and this is explained by reactive hyperemia generated by PTCA-induced ischemia; reactive hyperemia reversed spasm until vasodilation dissipates.

We thank Dr Hellstrom for his interest in our article1 and agree that small vessel spasm may be yet another mechanism that could contribute to no-reflow. However, the experiments that Dr Hellstrom describes2 did not measure anatomic no-reflow as we have.3 No assessment of anatomic perfusion defect by either thioflavin S, carbon black, or other standard marker was used. Thus, it is not known whether short coronary occlusions could reverse the anatomic no-reflow phenomenon observed within a myocardial infarction. Areas of no-reflow in our infarct/reperfusion models are well-delineated subendocardial to midmyocardial, and this is explained by reactive hyperemia generated by PTCA-induced ischemia; reactive hyperemia reversed spasm until vasodilation dissipates.

Shereif H. Rezkalla, MD
Marshfield Clinic
Marshfield, Wis

Robert A. Kloner, MD, PhD
The Heart Institute
Good Samaritan Hospital
Los Angeles, Calif

No-Reflow Phenomenon
H. Richard Hellstrom

Circulation. 2002;106:e143
doi: 10.1161/01.CIR.0000037128.03240.41
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/106/20/e143

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/