Consequences of Reocclusion After Successful Reperfusion Therapy in Acute Myocardial Infarction

Ohman et al. recently reported in an issue of Circulation that patients with reocclusion after successful thrombolytic therapy had a higher in-hospital mortality (11% versus 4.5%; p = 0.01); therefore, reocclusion has a significant consequence, considering that reocclusion rates range from about 12.4% to 20% or 30%.1

Reocclusion usually is ascribed to atherosclerotic plaques, as thrombi usually develop over complicated plaques,2 and some studies (but not Ohman’s) report more reocclusions with severe stenoses.1,2 However, the occurrence of 75% of reocclusions by 3 days1 suggests that an additional and time limited factor favors rethromboses; if reocclusions are due only to complicated atherosclerotic lesions, it seems reasonable that they would be spaced out and not limited to the immediate postinfarct period. I propose that no-reflow after infarction encourages reocclusion; the stasis of no-reflow would foster rethromboses, especially in areas of stenotic atherosclerosis, and there is evidence that no-reflow is severe after myocardial infarction3,4 and that it persists for about 1 week.3

That no-reflow favors reocclusions is a variant of the proposal made by the TIMI study group. In 1971 that no-reflow favors thromboses and that thromboses are secondary to infarction.3 No-reflow was attributed to spasm of resistance vessels (S-RV) which occurred as an injury reaction to infarction, and evidence for the spastic cause of no-reflow recently was reviewed.5 Also, the idea of injury-induced S-RV led to the development of a separate paradigm for ischemic heart disease which proposed that primary S-RV induced symptoms in this disorder.6 The theory includes a mechanism for plaque rupture; severe S-RV causes reflex spasm in epicardial arteries which in turn ruptures plaques.

There has been disinterest in myocardial no-reflow, in part because this phenomenon was generally not accepted for a number of years; in spite of earlier demonstrations of this change,3,4,7,8 some studies failed to show significant no-reflow.9 However, these latter studies used chronic instrumentation of coronary arteries, and there is evidence that such instrumentation inhibits S-RV.3,5 As experimental models are rather similar, the recent interest in reperfusion injury should help clarify the involvement of no-reflow with infarction, but reperfusion flows have been measured in only a minority of such studies. Some studies of reperfusion injury with appropriate flow measurements showed significant no-reflow, but others did not; the failure to demonstrate appreciable no-reflow is attributed to suppressing S-RV by coronary artery instrumentation and to measuring flows too soon after reperfusion.10 Reactive hyperemia immediately after reperfusion is prominent and is considered to oppose S-RV and to prevent the expression of spasm and no-reflow; flows measured within 90 minutes after reperfusion were 101% of control flows but were 51% after 3 hours when reactive hyperemia had mainly abated and even lower at later times.3

No-reflow after infarction might have serious consequences. It might favor reocclusion and might play a significant role in reperfusion injury; severe ischemia secondary to no-reflow reasonably would worsen tissue injury from mechanisms as free oxygen radicals.5 Thrombolytic therapy might advantageously be combined with appropriate agents to reduce no-reflow, reocclusion, and reperfusion injury.

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References

Reply
The hypothesis raised by Hellstrom, suggesting that coronary flow after reperfusion in acute myocardial infarction is due to spasm of resistance vessels and causing reocclusion is indeed interesting. Unfortunately, our observations1 cannot explore this hypothesis any further. Our data suggest that impaired coronary flow may be a critical predictor of reocclusion after successful reperfusion.2 Patients with reduced Thrombolysis in Myocardial Infarction (TIMI) flow (TIMI flow 1 or 2) at the 90 minute angiography, had a 29% incidence of reocclusion during hospitalization. These data support Hellstrom’s hypothesis as the TIMI classification of coronary flow is based on the run-off in the distal coronary bed, which may be affected by spasm in the distal resistance vessels. In addition, recent observations have shown an absence of reocclusion after successful thrombolysis in patients who have been treated with intra-aortic balloon pumping during the acute phase.3,4 The presumed mechanism is enhancement in coronary flow due to improved diastolic perfusion.5 These findings, in aggregate, suggest that coronary flow is a critical variable leading to reocclusion. The severity of a lesion in the infarct-related artery may not be important, unless it impairs coronary flow.

We have presumed that the major mechanism of reocclusion is recurrent thrombosis; and the tendency for thrombosis should be profoundly affected by the coronary flow. If the mechanism of spasm of the resistance vessels is operating after reperfusion, it is potentially resistant to conventional pharmacological strategies as all the patients in our series were treated with aspirin, calcium antagonists, and intravenous nitroglycerin. Reperfusion after thrombolysis may be intermittent during the early phase as documented by continuous 12-lead electrocardiographic recording.6 Newer pharmacological approaches that prevent platelet aggregation7 and subsequent release of vasoactive substances8 may enhance thrombolysis to achieve normal coronary flow rapidly after thrombolysis.

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