Coronary Endothelial Dysfunction and Cerebrovascular Events

To the Editor:

Targonski et al reported that coronary endothelial dysfunction (ED) in individuals without obstructive coronary artery disease (CAD) quadrupled the risk of cerebrovascular events, and these findings might offer insight into mechanisms of stroke and ischemic heart disease (IHD).

ED fosters atherosclerosis, and Targonski et al focused on this effect of ED to explain ischemic stroke—a position consistent with the standard view that ischemic stroke and IHD are due directly to occlusions of conduit arteries by atherosclerotic complications as stenoses and thromboses. However, significant carotid atherosclerosis was probably absent in these middle-aged patients; carotid atherosclerosis is associated with CAD, and these cases lacked obstructive CAD.

ED has other effects that appear to explain the association of ED with stroke in these cases; ED is vasoconstrictive, is associated with multiple cardiovascular risk factors, and is a systemic disorder affecting conduit and resistance vessels in various vascular beds. In keeping with these effects, I earlier proposed that spasm of resistance vessels (S-RV) induces symptoms in stroke (Targonski et al did not include S-RV in hemorrhagic stroke). This S-RV concept asserts that risk factors (which are vasoconstrictive) operate basically through S-RV; severe atherosclerosis favors symptoms through ischemia-induced S-RV and spasm-inducing platelet aggregation. ED no doubt also operates to induce stroke through atherosclerosis; but atherosclerosis may be mild, favors S-RV, and is only one of multiple risk factors.

The S-RV concept is regarded as a challenging paradigm; these models are tested by verification/falsification, a method recently used to evaluate plaque rupture/thromboses. Verification/falsification is designed to test the ability of paradigms to explain events without inconsistencies, and evidence presented here will focus on verifications for S-RV as the mechanism of stroke.

The concept includes migraine and Raynaud’s disease, disorders attributed to S-RV, and their interrelationships with stroke and IHD are used as evidence; also, evidence that IHD is caused by S-RV is relevant. Migraine, Raynaud’s disease, ischemic stroke, and IHD, as well as (vasoconstrictive) hypertension, share multiple vasoconstrictive risk factors. Each of these 5 disorders occur more frequently with each of the other 4, and migraine merges into stroke. Ischemic stroke is related to hemorrhagic stroke by findings as transformation of ischemic to hemorrhagic infarct, and association of migraine with both ischemic and hemorrhagic stroke. Also, risk factors as hypertension, circadian rhythms, smoking, dyslipidemia, and cocaine use operate in both ischemic and hemorrhagic stroke. Additionally, the altered homeostatic theory offers a common pathophysiological basis for ischemic and other related disorders.

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