Left Ventricular Hypertrophy and Sudden Death

Haider et al. (1) and the editorial by Frohlich (2) remind us of the poor prognosis conferred by left ventricular hypertrophy (LVH) in hypertensive subjects. They accurately point out that much work still remains to be done to elucidate the mechanisms by which LVH leads to sudden cardiac death and other adverse consequences.

Although considerable research has been directed at cardiac ultrastructure, electrophysiology and the coronary microcirculation in LVH, the relationship between hemorheology and hypercoagulability in hypertension, especially if LVH is present, has been relatively neglected. Although the blood vessels are exposed to high pressures in hypertension, the main complications of hyper-tension and LVH (that is, stroke and myocardial infarction) are paradoxically thrombotic rather than hemorrhagic (3). Indeed, the hypothesis that hypertension and LVH may confer a hypercoagulable state can be examined by careful reference to Virchow’s triad (3).

In a high proportion of patients suffering sudden death, post-mortem examination demonstrates the immediate cause to be thrombotic occlusion of a major epicardial coronary artery (4). Indeed, a number of hemorheologic and thrombotic markers have been shown to be significantly related to, and predictive of, (thrombotic) cardiovascular events in hypertension (3,5). In keeping with Virchow’s triad for thrombus formation (thrombogenesis), patients with hypertension demonstrate abnormalities of vessel wall (endothelial dysfunction or damage), blood constituents (abnormal levels of hemostatic factors, platelet activation and fibrinolysis) and blood flow (rheology and flow reserve), suggesting that hypertension does confer a prothrombotic or hypercoagulable state (3). These components appear to be related to target organ damage and long-term prognosis, and are altered by treatment.

In the Leigh general practice study, for example, hypertensive subjects with plasma fibrinogen levels >3.5 g/l had a 12-fold higher cardiovascular risk than those with plasma fibrinogen levels <2.9 g/l (5). We recently reported that hypertensive patients with LVH had higher plasma fibrinogen levels compared with those without LVH; fibrinogen levels were also significantly correlated with left ventricular mass, left ventricular mass index and left atrial size (6). Hemorheologic abnormalities, such as increases in whole blood viscosity or fibrinogen, may account for the reduced coronary flow noted in LVH.

We believe that further study of hemorheology and hypercoagulability in hypertension and of the relationship to LVH would increase our understanding of the mechanisms by which LVH leads to sudden death. The main mechanisms for sudden death in LVH are unlikely to be simply electrophysiologic or arrhythmogenic, as suggested by Frohlich (2), but are also very likely to be thrombotic in origin.

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REFERENCES


To Trust or Not To Trust

I am writing in response to two articles recently published by Watanabe et al. (1,2) in the Journal. The accompanying editorial (3) highlights the fact that there is debate within the scientific community concerning the results published by this group of investigators.

These articles are the latest in a series examining pharmacologic interventions aimed at preventing nitrate tolerance. The interventions range from angiotensin-converting-enzyme inhibition to vitamin C, vitamin E and now, carvedilol (1,2,4–9). Measures of nitrate effects include platelet cyclic GMP responses along with vascular effects documented by blood pressure and forearm plethysmography. The results in each case have been striking, with definitive prevention of tolerance across experimental groups that include normal volunteers, patients with coronary disease and those with congestive heart failure. The experimental results are enviable, with closely matched treatment groups (despite small sample sizes) and highly consistent results in response to the