Small Artery Structure: Time to Take Note?

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Abnormal vascular structure is a hallmark of hypertension, but whether this has clinical significance has not been clear. In a landmark study from 2003, Rizzoni and colleagues1 in Brescia demonstrated in a population of 151 hypertensive and normotensive patients that abnormal small artery structure is a predictor of later cardiovascular events, as it is for left ventricular hypertrophy2 and large artery structure.3 Structure was measured as the ratio of media thickness to lumen diameter ex vivo by myography, the patients being followed up an average of 5.4 years. The events recorded included not only hard end points but also a range of possibly questionable soft end points. The Brescia group has now extended that study4 by including an additional 152 subjects, with an average follow-up time of 6.9 years for the entire population of 303 subjects. With this larger population, the Brescia group has not only confirmed the previous result, but has also been able to show that abnormal small artery structure was a predictor of the predefined hard end points (death, stroke, or infarction)—a significant advance. It is remarkable that the predictive value of the abnormal structure was observable despite the treatments that were given during the follow-up period.

A caveat with the present report, as with the previous report,1 is that the study included a substantial number of diabetic patients. Because such patients are known to have pressure-independent abnormal small artery structure,5 as well as increased cardiovascular risk, this may have confounded the issue. Also, the population included patients with secondary hypertension. A recent report from our laboratory6 has, however, countered those concerns, and shown in a population of 159 subjects with uncomplicated essential hypertension and a follow-up time of 10.4 years, that also here abnormal small artery structure is a predictor of later cardiovascular events.

Taken together these results provide important support for the view that abnormal small artery structure is a risk factor, and not just an adaptive response to increased blood pressure (BP). Therefore this raises the question of whether correction of abnormal artery structure should be an aim of antihypertensive therapy. Numerous studies have now shown that the ability of antihypertensive drugs to reduce BP is not necessarily related to their ability to correct small artery structure (see eg, Mathiassen et al7). Thus, traditional β-blocker (and to some extent diuretic) treatment has little effect on the structure, whereas vasodilator drugs, such as inhibitors of the renin-angiotensin system, are effective. Should these findings provide a basis for recommending vasodilator antihypertensive therapy rather than use of the traditional therapy?

Clearly, this question can only be definitively resolved by a long-term prospective study in which the occurrence of cardiovascular events is related to the effect of treatment on vascular structure. Such a study could, in principle, be performed perhaps using forearm plethysmography to measure vascular structure,7 but would be extremely difficult in practice. In the meantime, we have the situation that we know (1) that small artery structure is abnormal in hypertension, (2) that small artery structure can be corrected by vasodilator therapy, and (3) with the new findings, that small artery structure is a predictor of later cardiovascular events. The findings of the Brescia group1,4 together with those of our group,6 are therefore important links in the argument that correction of small artery structure with vasodilator therapy is the logical treatment for hypertension, although naturally clinical considerations will point to the use of traditional therapy in individual cases.

References


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