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Arterial structural modifications in hypertension

Effects of treatment

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Hypertensive changes in the vasculature occur at all levels of the circulation—from the large arteries through to the microcirculation. Detection of these changes may offer useful predictive information in assessing cardiovascular risk and the need for treatment. Recent evidence shows that at least some of these changes are reversible with anti-hypertensive treatment.

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Cardiovascular structural change associated with hypertension confer increased morbidity and mortality risk. Hypertensive left ventricular hypertrophy (LVH) with electrocardiograph strain pattern in the Framingham cohort carried a five-fold increased 5-year mortality — a worse outlook than for many forms of cancer[1]. It is now known that regression of LVH with antihypertensive treatment effectively reduces cardiovascular risk. It is less widely recognised that vascular structural changes also predict increased risk. This is hardly surprising as structural and functional changes in blood vessels are more intimately involved in the process leading to atheroma and thrombosis. Heart muscle damage occurs as a consequence of occlusive events in the coronary arteries.

Hypertensive vascular changes include:

Thickening of the walls of large elastic and muscular arteries.

Remodelling of small muscular arteries resulting in increased wall to lumen ratio.

Reduced number of vessels in the microcirculation.

Lengthening of small arteries.

Large arteries

Amongst the large arteries the carotid has been studied in most detail with the use of two-dimensional ultrasound imaging. The carotid lies superficially and ultrasound allows accurate measurement of the intima–media thickness (IMT) of the arterial wall[2,3]. This wall thickness increases with both age and hypertension[4] and there is a close association between hypertension, carotid-IMT and LVH[4–6]. Smoking, hypercholesterolaemia, and raised fibrinogen are also associated with increased carotid-IMT[5,7]. It is very likely that increased arterial wall thickness is an early stage in the development of atherosclerosis. Subjects with greater carotid-IMT have been shown to have a significantly increased risk of events recognised as the end products of atherosclerosis, both myocardial infarctions and excess cerebral white matter lesions[8,9]. It is also evident that the walls of the epicardial coronary arteries thicken with hypertension[10]. With regard to treatment, hypertension control with an ACE inhibitor plus calcium antagonist based regimen has now been shown to reduce carotid-IMT[11] (Fig. 1). ACE inhibitors and calcium antagonists have been shown to have a greater effect in increasing large artery compliance in hypertensive patients than other drug classes[12–14]. In addition, lipid-lowering therapy is effective not only in stabilising atheromatous plaque, but also in reducing carotid-IMT[15–17].

Wall structure in resistance arteries

In the small resistance arteries there is an increase in wall to lumen ratio which confers a structural component to the hypertensive increment in peripheral vascular resistance[18,19]. This is paralleled by in vivo findings of diminished vasodilator capacity in hypertensive peripheral circulations. These studies have largely measured minimum forearm vascular resistance (FVR) under circumstances of maximum vasodilatation[20,21]. The morphological studies support the view that either

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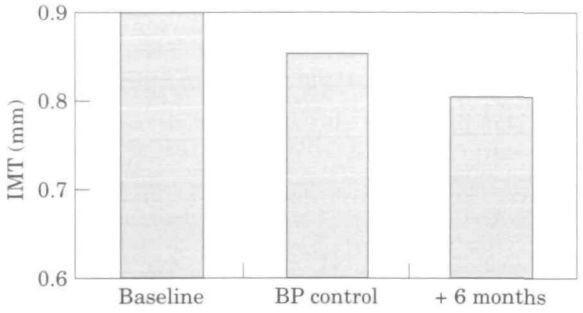

Figure 1 **Regression of carotid-IMT in a group of hypertensive subjects from baseline following treatment with an ACE-inhibitor+calcium antagonist based regime at 8 weeks (time of BP control) and 6 months. (Reproduced with permission[11].)**

hypertrophy or remodelling underlies the hypertensive increase in wall to lumen ratio[22,23]. Folkow proposed that this structural change with a restricted lumen is the mechanism that maintains the elevated blood pressure and is responsible for the amplified responses to vasoactive agents seen in hypertension[24].

There is evidence that 'minimum-FVR' improves following various anti-hypertensive drug treatments[25]. This appears to be the case with most anti-hypertensive regimes other than β-blockers (with the exception of pindolol)[26]. Histological studies of small arteries dissected from buttock fat biopsies of treated hypertensives have shown that effective anti-hypertensive treatment causes a partial improvement in the wall to lumen ratio measured in vitro[27]. Two studies have reported more effective reversal of small vessel structural change following treatment with an ACE inhibitor than with a β-blocker based regimen[28,29] (Fig. 2). It is evident, however, that structural improvement at the resistance level takes a great deal longer than normalization of blood pressure[30].

Small artery geometry

Several groups have described a reduced number of small vessels in the microcirculation of hypertensive subjects. This has been termed 'vascular rarefaction' and is evident in the mesentery[18], the conjunctiva[31,32], the nailfold[31,33], the retina and skeletal muscle[34,35]. Vascular rarefaction may equally confer an increased peripheral vascular resistance. This structural change may be 'cause or consequence' in the process of hypertension; although it is found in borderline hypertension[36], and a greater 'minimum FVR' has been demonstrated in normotensive young men with a family history of hypertension[37]. It is uncertain whether rarefaction represents a real loss of small vessels or a functional vasoconstriction.

The retinal fundus offers direct observation of small arterial architecture. The angles between subsequent branch arteries at bifurcation points are narrower

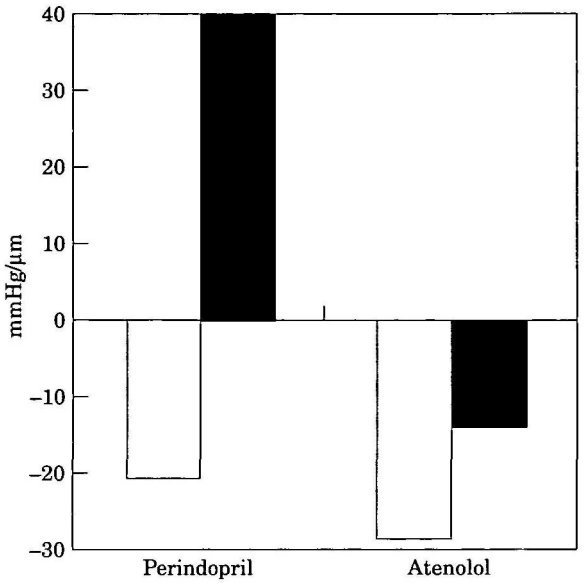

Figure 2 **Effect of treatment of hypertensive subjects on blood pressure (□) and lumen diameter (■) of small resistance arteries after 12 months treatment with either perindopril or atenolol. (After Thybo[28].)**

in the hypertensive retina[38]. The consequence of this change is again a vascular rarefaction. In addition the retinal arteries in hypertensive subjects have a much greater length:diameter (L:D) ratio than in normotensives[39]. If these structural changes are reflected elsewhere in the vasculature they will have important influence on circulatory efficiency and energy costs[40]. Some data suggest that such changes may arise very early in life — possibly in advance of development of high blood pressure[41]. Although the gross features of hypertensive retinopathy are to some extent corrected by treatment, it is not yet known whether these more subtle geometric abnormalities are reversible.

Hypertension impacts on several aspects of vascular structure. Blood pressure reduction per se is effective in improving some of the consequences. There is growing evidence that the drug-specific manner in which blood pressure is lowered can offer particular advantages in terms of greater vascular structural benefits. It is not yet clear whether these structural benefits will translate into survival advantages in the same way as for left ventricular regression[42].

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