Abnormal resistance artery structure in essential hypertension:

a prognostic and correctable supplemental target for therapy

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ABSTRACT

The PhD dissertation is based on three studies being held at the Department of Pharmacology, University of Aarhus, and with the clinical part of the study being carried out at the Department A of Medicine and Cardiology, Aarhus University Hospital. The main purpose was to examine whether changes in resistance artery structure during antihypertensive therapy relate to the vasodilating effect rather than the BP-lowering effect. We also evaluated the prognostic role of structural changes in resistance artery in essential hypertensive (EH) patients.

In study 1, we evaluated the usefulness of forearm venous occlusion plethysmography as a method for monitoring vascular tone and vascular structure in terms of the forearm resting (R_{rest}) and forearm minimum vascular resistance (R_{min}). At rest, vascular resistance is determined by vascular tone level, and changes in R_{rest} thus reflect changes in vascular tone. Measured during post-ischaemic reactive hyperaemia with maximal vascular relaxation, vascular resistance is, in contrast, determined by the architecture of the vascular bed. We found that hyperaemic arterial inflow may be influenced by a gradual recovery of vascular tone, making this an influencing factor on R_{min} assessment. However, the influence from vascular tone was small during the initial phase of flow recordings. R_{min} showed high reproducibility whereas R_{rest} showed a relatively high day-to-day variation.

Study 2 was a prospective treatment study done in two parallel parts. The aim was to examine whether changes in R_{min} during antihypertensive treatment at an individual level would correlate with changes in R_{rest} rather than with changes in BP. A total of 21 untreated EH patients (group A) were allocated to various forms of antihypertensive treatment, and 28 β-blocker-treated EH patients (group B) were switched to a vasodilator, represented by eprosartan, with no intended change in BP. Follow-up was six months. In both studies, changes in R_{min} and R_{rest} correlated, whereas the BP-reduction in group A patients did not correlate with the reduction in R_{min}. BP remained unchanged in group B patients. The study strongly supports the notion that resistance artery structure will improve only to the extent to which vasodilation is achieved. It also demonstrates that EH patients on long-term β-blocker therapy may improve their resistance artery structure if a BP-neutral shift to a more vasodilating regime is provided.

Study 3 was a retrospective outcome evaluation in a cohort of 159 patients with uncomplicated EH, who had previously been referred to our clinic for in vitro assessment of small artery structure during a treatment study. Baseline status with respect to resistance artery structure significantly predicted the cardiovascular outcome even after adjusting for Heart Score, which is a risk-estimate that integrates age, gender, smoking habits, systolic BP and total cholesterol. In perspective our studies support the notion that abnormal resistance artery structure may indeed be a parameter that should be considered in the early management of EH, since it carries BP-independent prognostic information in uncomplicated EH and is correctable in a BP-independent fashion, namely through vasodilation.