THE MICROCIRCULATION AND THE HAEMODYNAMICS OF HYPERTENSION

Harry A.J. Struijker-Boudier, Dept. of Pharmacology and Toxicology, Universiteit Maastricht, Maastricht, the Netherlands; Enrico Agabiti Rosei, Università degli Studi di Brescia, Dipartimento di Medicina, Spedali Civili di Brescia, Brescia, Italy

The haemodynamic characteristic of essential and most forms of secondary hypertension consists of an elevated blood pressure and peripheral vascular resistance. Blood pressure comprises two components: a pulsatile (pulse pressure) and a steady (mean arterial pressure; MAP) component. Pulse pressure is predominantly influenced by the elastic properties of the larger conduit arteries, whereas MAP is determined by the resistance to flow in smaller arteries and arterioles, ranging in diameter from 10 to 300 μm [1, 2]. The small arteries and arterioles are a continuous segment of the vascular system associated with a gradual drop in pressure. Instead of referring to specific components as resistance vessels, the entire arterial microcirculation vessels of between 10 and 300 μm should be regarded as a site of resistance, and thus MAP, control. The exact location of the pressure drop may differ in relation to tissue. In cardiac tissue, for example, the pressure drop occurs distally in the arterial tree, whereas in the mesentery it is located more proximally [2].

Isolated small arteries

Great progress has been made in the last decade in understanding the pathological changes in the small arteries and arterioles in hypertension. This progress is at least partly due to progress in technologies which study microcirculation in humans. One area of advancement has been the use of isolated small arteries mounted using a steel wire or pressure micromyograph. Biopsies of subcutaneous fat from the gluteal region have been used to investigate the function of small arteries 100–300 μm in diameter. Rizzoni et al. showed that small arteries taken from patients with essential hypertension showed an inward eutrophic remodelling, different from the outward hypertrophic remodelling observed in diabetic patients [3]. In addition, these authors showed that microvascular changes in small arteries taken from subcutaneous fat tissue were related to coronary flow reserve [4] and were predictive of cardiovascular morbidity in a heterogeneous cohort of hypertensive patients at high cardiovascular risk, including those with secondary hypertension and diabetes [5]. Increased wall-to-lumen ratios of subcutaneous tissue have also recently been found to predict cardiovascular events in hypertensive patients at mild cardiovascular risk [6, 7].

Interestingly, there was no prognostic role pertaining to endothelial dysfunction in the subcutaneous small arteries of hypertensive patients [8].

Retinal arterioles

Recent studies have expanded the in vitro analyses of subcutaneous small arteries to in vivo retinal arterioles ranging from 100 to 250 μm in diameter. Advances in retinal photography and computing technologies have enabled precise measurements to be made of small artery and arteriolar vessel size from digital retinal images. Several large, population-based studies have applied this approach to quantitatively determine retinal vessel diameters, and these have documented a consistent association between elevated blood pressure and narrowed retinal arterioles [9–11]. Similar studies have also indicated that retinal arteriolar narrowing predicts future blood pressure elevation in previously normotensive persons [12–14].

Schmieder et al. [15, 16] have taken retinal microvascular analysis a step further by applying in vivo scanning laser Doppler flowmetry. This approach has not only allowed them to determine retinal arteriolar diameters, but also their wall-to-lumen ratio. They found that subjects with essential hypertension had a higher wall-to-lumen ratio of retinal arterioles than normotensive subjects [16]. Multiple regression analysis including a variety of known cardiovascular risk factors revealed that blood pressure is independently associated with an increased wall-to-lumen ratio of retinal arterioles. In a similar study Harazny et al. [15] showed that the wall-to-lumen ratio was significantly increased in patients with overt cerebrovascular disease as well as in hypertensive patients with poor blood pressure control, when compared to patients with good blood pressure control.

Coronary microcirculation

Currently, no technique allows the direct in vivo visualisation of coronary microcirculation in humans [17]. Several measurements that rely on the quantification of blood flow through the coronary circulation are commonly used to describe the function of coronary microvasculature. These include intracoronary thermodilution, an intracoronary Doppler wire, and transthoracic Doppler echocardiography [17]. Cardiovascular magnetic resonance imaging and positron-emission tomography are some of the technically more demanding methods to assess coronary microvascular function. A parameter often used to express coronary microvascular function is the coronary flow reserve. Coronary flow reserve is the magnitude of the increase in coronary flow that can be achieved in going from basal coronary perfusion to maximal coronary vasodilatation. Coronary flow reserve is determined by measuring coronary or myocardial blood flow and taking measurements both at rest and with maximal hyperaemia. Abnormal coronary flow reserve has been demonstrated in patients with essential hypertension, despite the presence of angiographically normal coronary arteries and the absence of left ventricular hypertrophy [17, 18]. The cause of the reduced coronary flow reserve in hypertension has been related to remodelling of the coronary small arteries and arterioles as well as the interstitial fibrosis. The remodelling of the arterioles leads to a decreased density of vessels in the coronary microvasculature, whereas the inter-
Capillary rarefaction reinforces their effects by compressive forces, increased myocardial wall stress and impaired relaxation. Abnormalities of coronary flow reserve are regionally heterogeneous in some patients, whereas in others the entire myocardium is affected [19]. Regional abnormal myocardial function may predispose patients to abnormal patterns of electrical activity or to regional myocardial ischaemia during conditions in which a high flow is necessary.

**Capillary densities in hypertension**

One of the most consistently observed microcirculatory changes in hypertension is rarefaction of the capillaries. In humans capillary rarefaction is usually assessed using in vivo capillaroscopy of the nailfold microvasculature. Capillary rarefaction is not only a consequence of hypertension, but can also precede elevation of blood pressure. Evidence for an early role of capillary rarefaction was obtained in borderline hypertensives [20] as well as in offspring from hypertensive parents [21]. In animal models of hypertension both capillary and arteriolar rarefaction were observed in a range of tissues. This raised the question of whether an impaired angiogenic response to tissue ischaemia might be at the basis of early microvascular abnormalities in hypertension. Evidence for such a role in experimental animal models was recently reviewed by Feihl et al. [22]. However, it remains to be established whether similar evidence exists for human essential hypertension.

**References**


