Microcirculation in hypertension and cardiovascular disease

Axel R. Pries1,2*

1Department of Physiology and Center for Cardiovascular Research, Charité, Charitéplatz 1, Berlin D-10117, Germany
2Deutsches Herzzentrum Berlin, Augustenburger Platz 1, Berlin D-13353, Germany

The microcirculation of terminal vascular beds represents the ‘business end’ of the circulation, which supplies oxygen and nutrients to the tissue, controls inflammation and repair as well as fluid exchange with the tissue.1 The microcirculation comprising vessels ranging from small arteries or arterioles with diameters below 100–300 μm to corresponding venules is also the site of regulation for flow resistance and perfusion.2–4 In relation to hypertension, the establishment and regulation of flow resistance and perfusion is of special importance.

The high flow resistance in the arteriolar part of microvascular networks leads to a strong reduction in intravascular pressure, before the blood enters the capillary section of the network. The maintenance of mean arterial pressure (and low capillary pressures) for different functional conditions and with increasing or decreasing tissue mass requires a fine-tuned set of regulatory controls of microvascular flow resistance. Hypertension can be interpreted as the result of an inadequate regulation of microvascular resistance. Possible underlying pathophysiological mechanisms include changes in the systemic circulation (i.e. an increased cardiac output), in central control mechanisms (e.g. hormonal status), and in cellular reactions in the microvessels (e.g. endothelial function).4–6

Vessels and especially microvessels are capable of continuous adaptation in response to varying conditions and functional demands.7–13 This includes not only acute changes in vascular smooth muscle tone but also more sustained changes in vessel structure and number (‘angioadaptation’14). The respective feedback signals are derived from haemodynamic conditions including blood flow (shear stress), and blood pressure (circumferential wall stress) in addition to those derived from the metabolic state of the tissue.9

Vascular reactions to shear stress have been known since Thoma’s observation in 1893 that vessels carrying a high blood flow exhibit an increase in vessel diameter and vice versa. In a comprehensive treatment, Rodbard15 deduced that changes in vascular diameter in response to blood flow and shear stress would act to maintain the vascular shear stress at a constant level in the presence of changes in blood flow. According to the equation \( \tau = \eta \times 4Q/(\pi r^4) \) (where \( Q \) is the blood flow rate, \( r \) is the vessel diameter and \( \eta \) the blood viscosity16), wall shear stress (\( \tau \)) is proportional to the blood flow but varies inversely with the vessel diameter.

In larger human arteries, shear stress values between about 4 and 15 dyn/cm² (0.4 and 1.5 Pa) are observed, while values in veins range about one order of magnitude lower. Structural vascular responses to pressure are well established and are linked to the development of hypertension.9,17–20 If increases in transmural pressure difference (\( P \)) lead to an increase in the vessel wall thickness and/or a reduction in vessel diameter, these responses can stabilize circumferential wall stress (\( \sigma = PD/2w \), where \( w \) is the vessel wall thickness), similar to the stabilization of shear stress addressed above. Owing to the higher pressure level on the arterial side vascular pressure, this leads to smaller, thicker wall vessels on the arterial side which exhibit higher levels of shear stress and thus contributes to arterio-venous differentiation.

Figure 1 analyses the relations between microvascular angioadaptation and the establishment of hypertension: an increase in cardiac output and thus arterial pressure not only leads to a myogenic increase in tone, but also to inward remodelling19,21 and vascular rarefaction21,22 reducing tissue supply and increasing flow resistance (angiadapptive responses, central grey box). The increase in resistance, in turn, results in a further increase in pressure, establishing a positive feedback (structural autoregulation9,24). It has been stated that microvascular changes in hypertension may be both cause and effect of the pathophysiological development.4

But irrespective of the initial trigger for the increase in flow resistance and arterial blood pressure, the positive

* Corresponding author. Tel.: +49 30 450 528 501, Fax: +49 30 450 528 920, Email: axel.pries@charite.de

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2013.
For permissions please email: journals.permissions@oup.com
feedback or ‘vicious cycle’ by which an increase in pressure leads to increase in tone, inward remodelling and rarefaction thus causing further increase in pressure—and in parallel an undersupply of the tissue which is related to end organ damage. This is also a reason why there are many possible therapeutical targets for the treatment of hypertension. However, different approaches which are equally potent in controlling hypertension have been shown to exhibit different capacities to trigger the reversal of hypertension-associated structural changes in the microcirculation. Future experimental and clinical studies are required to probe the importance of this re-remodelling and to optimize therapeutical strategies accordingly.

Conflict of interest: none declared.

References