Peripheral endothelial dysfunction after subarachnoid haemorrhage: what the fingertips can tell us

N. Scherbakov1 and W. Doehner1,2*
1 Center for Stroke Research Berlin, Charité-Universitätsmedizin, Berlin, Germany
2 Department of Cardiology, Charité Medical School, Campus Virchow-Klinikum, Berlin, Germany
* Corresponding author. E-mail: wolfram.doehner@charite.de

Endothelial dysfunction is a widely used term to describe an inability of endothelial cells for participating in vasodilation but also haemostasis, immune, and inflammatory reaction.1 Over past decades, an interdisciplinary switch in research on endothelial function could be observed. Primarily, its role was recognized in the variety of cardiovascular/metabolic disorders such as atherosclerosis, hypertension, heart failure, and diabetes mellitus.2 – 4 Recently, an association of endothelial dysfunction and cerebrovascular diseases has been reported.5 – 7

In clinical research, there are a number of techniques used for determination of endothelial dysfunction.8 A widely used method in the clinical trials for determination of peripheral endothelial dysfunction is a non-invasive ultrasonographic imaging of endothelial-dependent flow-mediated dilatation of the brachial artery.9 10 Endothelial dysfunction therefore is expressed as a percentage of post-stimulus artery dilatation diameter to baseline diameter. Still, there are some technical and interpretive limitations of this method and also a strong expertise is required for precise implementation.11 12

Recently, a new method of peripheral arterial tonometry (PAT) in the fingertip, EndoPAT, was introduced.13 This method is based on changes in artery digital pulse volume during reactive hyperaemia termed ‘reactive hyperaemia index’ (RHI) which is used as a surrogate for endothelial dysfunction.14 The advantage of EndoPAT technology is that it could be easily applied to the patients; it has high reproducibility and is non-invasive. Recent studies revealed a reduced RHI in patients with coronary endothelial dysfunction, hypertension, smoking, hypercholesterolaemia, and ischaemic stroke suggesting decreased peripheral hyperaemic response and therefore provided an evidence of endothelial dysfunction.7 14 15

In this issue, Bergström and colleagues16 revealed evidence of peripheral endothelial dysfunction in the acute phase after aneurysmal subarachnoid haemorrhage (SAH). A vasospasm is a common complication after SAH that may occur up to several days later and is associated with poor clinical outcome. The authors aimed to identify a peripheral endothelial dysfunction in the early stage after SAH by EndoPAT in order to predict the development of cerebral vasospasm. This study revealed a decrease in RHI in patients in the first days after SAH and also an association with L-arginine/asymmetric dimethylarginine ratio, a marker of endothelial function.17 Interestingly, in patients who died within 30 days after SAH, RHI was decreased compared with survivors. However, the authors did not find an association between RHI and established outcome predictors after SAH such as transcranial Doppler measurements of V_MCA, plasma nitrite/nitrate level, or S-100B. They concluded that regulation of large cerebral blood vessels may occur by the nitrite/nitrate pathway and on the microvascular level via L-arginine/nitric oxide pathway what is in line with their previous findings.18 However, further studies of pathophysiological mechanisms of central cerebral and peripheral endothelial activation are required.

The number of clinical trials applying EndoPAT technology for functional vascular assessment is growing and its interdisciplinary applicability as well as easy-to-use technique suggest that EndoPAT might have a good perspective as a clinical diagnostic tool. To this end, EndoPAT as a diagnostic method needs to be better established with standard reference values from large clinical cohorts and strong background for data interpretation. We also need to learn how far we can transfer the data obtained from the peripheral vascular bed to
the global endothelial function. However, a development of new (alternative) strategies for the diagnostics and treatment of endothelial dysfunction in various diseases is required.

Declaration of interest
None declared.

References
16 Bergström A, Staalsa JM, Romner B, Olsen NV. Impaired endothelial function after aneurysmal subarachnoid haemorrhage correlates to the arginine:asymmetrical dimethylarginine ratio. Br J Anaesth 2014; 112: 311 – 18


EDITORIAL II

β-Blockers and cardiac protection: 5 yr on from POISE

P. Foex and J. W. Sear*
Nuffield Department of Anaesthetics, University of Oxford, John Radcliffe Hospital, Oxford OX3 9DU, UK
* E-mail: john.sear@gtc.ox.ac.uk

For many years, β-blockers have been regarded as the best drugs to protect patients with, or at risk for, coronary heart disease, from perioperative major adverse cardiac events (MACE). This was based on observational studies, randomized controlled trials (RCTs), experts’ opinions, and guidelines. The strongest support was expressed in the 1997 guidelines of the American College of Physicians,1 after very encouraging results after administration of atenolol before non-cardiac surgery by Mangano and colleagues.2 The guideline advocated the administration of atenolol to all patients with, or at risk for, coronary disease undergoing surgery. In the USA, initiation of perioperative β-blockade was regarded as having the greatest strength of evidence in its favour.3 However, a less supportive view was expressed in the American College of