Forum Minireview

New Methods to Evaluate Endothelial Function: Preface

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Received September 1, 2003; Accepted October 15, 2003

Keywords: endothelial function, nitric oxide, atherosclerosis

Since Furuchgott and Zawadzki reported that endothelium produced endothelium-derived relaxing factor in 1980 and subsequent studies revealed that nitric oxide (NO) was generated by the endothelium, many researchers have investigated endothelial function. Now, most researchers believe that the vascular endothelium is not a simple wall separating the vascular smooth muscle wall and the blood, but is one of the biggest endocrine organs that secretes various vasoactive substances. NO produced by endothelial cells is not only a primary determinant of resting vascular tone but also a potent inhibitor of leukocyte adhesion to the vascular endothelium and platelet aggregation and adhesion. Thus impaired endothelial function is believed to contribute to the pathogenesis of atherosclerosis and to precede overt cardiovascular disease by years. Risk factors for atherosclerosis, including hypertension and diabetes are characterized by impaired endothelium-derived NO bioactivity that may contribute to clinical cardiovascular events. The role of the endothelium in cardiovascular disease recently has become the focus of intense scientific investigation. Although no gold standard for the measurement of endothelial function exists, several methods for evaluating endothelial function have been used experimentally and clinically. In this symposium, we would like to discuss the merit, the limitations, and clinical application of each method.

Higashi and Yoshizumi explain in detail the methods of assessing endothelial function in humans using strain-gauge plethysmography. They show that the measurement of the forearm blood flow response to vasoactive agents using a strain-gauge plethysmograph is a excellent method to assess endothelial function in resistance arteries, and the vasodilatory response to reactive hyperemia is a non-invasive, useful method to assess endothelial function.

Hashimoto et al. show the procedures for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery. They report that the accumulation of coronary risk factors is significantly related to the impairment of endothelial function, and hormone replacement therapy even at half dose of estrogen improves endothelial function in postmenopausal women.

Ishibashi et al. show that the problems arising from the use of blood NOx (NO₂⁻ and NO₃⁻) concentration as an index of NO formation in vivo under many circumstances and that NOx concentration in plasma can not be used as an index of NO formation. They also discuss that the detection of high- and low-molecular weight nitrosothiols as an alternative indices of NO in vivo.

Tsuchiya et al. report a new method for measuring the hemoglobin-nitric oxide complex (HbNO) using electron paramagnetic resonance (EPR). They succeeded in measuring the blood HbNO level as an index of NO by the EPR HbNO signal subtraction method and they suggest that this method is useful for evaluating endothelial function. They show that the administration of an angiotensin-converting enzyme inhibitor dose-dependently improved the HbNO concentration and systolic blood pressure in a L-NAME (N⁶-nitro-L-arginine-methylester)-induced rat endothelial dysfunction.

This forum minireview is based on the symposium at the 76th Annual Meeting of The Japanese Pharmacological Society held on March 25, 2003.

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