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Commentary on Viewpoint: Exercise and cardiovascular risk reduction: Time to update the rationale for exercise?

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TO THE EDITOR: Since the 1990s, endothelial dysfunction has been increasingly recognized as a conditio sine qua non for atherogenesis (5a) and several studies documented its prognostic relevance for cardiovascular morbidity and mortality (6). Hence it is today regarded as an excellent surrogate endpoint in clinical studies.

The viewpoint article by Green et al. (3) in the *Journal of Applied Physiology* is a timely reminder that physical exercise has a direct beneficial effect on preservation of normal endothelial function independent from its effects on classical risk factors. This concept has evolved from a series of studies on the effects of exercise training in patients with coronary artery disease performed over the last decade. Among others, our Leipzig group was able to show that regular endurance exercise in patients with stable coronary artery disease *without classical risk factors* (i.e., diabetes, hyperlipidemia, smoking, hypertension) leads to improved endothelial function (5), higher expression and activity of the endothelial nitric oxide synthase (4), reduced ROS generation via vascular NADPH oxidases (1), and consequently an improved NO bioavailability.

The adequate stimulus by which exercise is able to mediate the endothelium-protective effects is most likely the intermittent increase in laminar shear stress associated with the increase in coronary and peripheral blood flow during endurance exercise—a pleiotropic mechanism that can not yet be activated pharmacologically. Although there certainly is a dose-response relationship between exercise time/day (2) and effects on endothelium-dependent vasodilation, it is the change from sedentary to active that has the greatest effect. It is now time to prescribe exercise to our patients as one of the most potent anti-atherogenic interventions.

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