Letter to the Editor

T−786C and G894T Variants of the Endothelial Nitric Oxide Synthase Gene and Training-Induced Correction of Endothelial Dysfunction in Coronary Artery Disease Patient

To the Editor:

The T−786C allele in the promoter, but not the Asp298 (894T) variant in exon 7, of the endothelial nitric oxide synthase (NOS3) gene has been recently associated with a blunted increase in blood flow average peak velocity induced by acetylcholine in coronary or mammary artery after a 4-week exercise training program. By providing a potential explanation for the remarkable individual heterogeneity of responses achieved with exercise in coronary artery disease (CAD) patients, these results extend previous landmark findings from this group. The authors carefully excluded patients with arterial hypertension, insulin-dependent diabetes mellitus, smoking, and hypercholesterolemia, eg, conditions that notoriously induce endothelial dysfunction. However, the study sample size was small; therefore, one wonders if its statistical power, of which no calculation was provided, was adequate and if a selection bias occurred. The latter is suggested by the lack of T−786C homoyzogous, which occurred in 18% to 22% of patients in larger studies, and lack of a frequency of −786C allele (31.6%) and 894T allele (43.1%), which differed from those observed in larger studies.

The average peak velocity increase induced by acetylcholine baseline was blunted in patients with the 894T polymorphism; furthermore, the 3 patients homozygous for this allele exhibited vasoconstriction at baseline with acetylcholine and an impaired average peak velocity increase after exercise training. Therefore, Erbs et al suggested that the presence of either the promoter or the exon 7 polymorphism attenuates endothelium-dependent vasodilatation in CAD patients. To explain the effect of the 894T variant, the authors quoted a study claiming this variant to be more vulnerable to intracellular cleavage, thus implying a decreased in vivo NO generation in CAD patients. To explain the effect of the 894T variant, the authors quoted a study claiming this variant to be more vulnerable to intracellular cleavage, thus implying a decreased in vivo NO generation. Consequently, caution should be used regarding attributing a blunted NO generation to these polymorphisms tested, because of the small number of observations that are prone to serendipity.

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