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Functional implications of polymorphisms of endothelial nitric oxide synthase gene: Reply

We appreciate the interest of Nagassaki and colleagues in our study.1 The main finding of this study was that the 894 G/T polymorphism of the endothelial nitric oxide synthase (eNOS) gene correlates with the risk for death and myocardial infarction after coronary artery stenting.2 We underscored in the Discussion section that it is presently not possible to outline a causal relationship between the 894 G/T polymorphism and the outcome after stenting.3 We discussed the possible functional role of the 894 G/T polymorphism in the light of previously reported findings relative to the susceptibility to proteolytic cleavage of eNOS with asp298 (expressed in T allele carriers).2 Nagassaki and colleagues refer to another study which findings did not support increased cleavage in T allele carriers and propose another explanation for the association found in our study.4 We hypothesize that behind the association between the 894 G/T polymorphism and the clinical outcome after stenting stays another polymorphism, the −786 T/C polymorphism in the promoter region of the eNOS gene. The authors argue that it is presently not possible to outline a causal relationship between the 894 G/T polymorphism and the outcome after stenting.5 We genotyped the same population included in our previous study1 for the −786 T/C polymorphism: 37.4% were of the −786 TT genotype, 47.5% of the −786 TC genotype, and 15.2% of the −786 CC genotype. The estimated linkage disequilibrium D’ between the 894 T and −786 C alleles was 0.49. In our population, the combined 1-year incidence of death and myocardial infarction was 5.7% among −786 CC patients as compared to 3.8% among the −786 T allele carriers (P=0.15). Taken together, all these findings show that we are still unable to offer a definite mechanism underlying the association between the 894 G/T polymorphism and the outcome of patients undergoing coronary artery stenting.

References
4. Nakayama M, Yasue H, Yoshimura M et al. β-Asp variant of hu-

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