Prothrombotic Genetic Risk Factors and Myocardial Infarction at Young Age

To the Editor:

We have read with interest the report by Ardissino et al,1 which concludes that the presence of the PlA2 polymorphic allele is the only prothrombotic genetic factor associated with the risk of myocardial infarction at a young age. These authors find a significant interaction between the presence of the PlA2 allele and smoking.

We studied 178 men younger than 50 years old who were diagnosed with coronary disease.2 The prevalence of PlA2 allele was 24% in case subjects compared with 26% in 200 age- and sex-matched control subjects. We also investigated whether the PlA2 allele was associated with other risk factors. No differences were found in patients between smokers (40 of 167) and nonsmokers (3 of 11) (24% v 27%), hypertensives (18 of 66) and normotensives (25 of 112) (27% v 22%), diabetics (4 of 15) and nondiabetics (39 of 163) (27% v 24%), and neither when the total cholesterol/high-density lipoprotein [HDL] cholesterol ratio greater than (37 of 150) or less than 5 (5 of 28) was used (25% v 18%).

In reference to the biochemical parameters,3 the only significant difference was found for LDL-cholesterol values. Thus, average low-density lipoprotein (LDL)-cholesterol values were 167 ± 75 mg/dL among PlA2-carrier patients and 146 ± 36 mg/dL among PlA1/PlA1 patients (P < .02).

Weiss et al4 described a high frequency of family members homozygous for Pro at codon 33 (the PlA2 allele) in kindreds with a high prevalence of acute coronary events at a young age (<60 years). This observation led them to postulate that carriers of the PlA2 allele could be more susceptible to develop symptomatic coronary heart disease. In a case-control study,5 the same authors found a higher prevalence of the PlA2 allele among patients than among controls, and the association was strongest in patients who had coronary events before the age of 60 years.

At least 2 case-control studies6,7 failed to find the same association between the PlA2 allele of the glycoprotein IIIa gene and acute coronary thrombosis. In agreement with these, we didn’t find a significant difference between genotypic frequencies of patients and controls.

The discrepancies may reflect differences in the definition of the phenotype in the patients or in the selection and size of both cases and controls. We analyzed patients and controls from a homogeneous Caucasian population. Our study was based on a number of patients (178 cases) and controls (200 individuals) high enough to define any statistically significant association.

In addition, we did not find a significantly increased frequency of the PlA2 allele among patients younger than 50 years. Finally, A2A2 homozygous patients were not more frequent among patients than among controls, and did not develop coronary disease at a younger age. Taken together, these data suggest a true lack of association between the PlA2-allele and the development of acute coronary artery disease in our population.

Coronary artery disease is a polygenic trait in which inherited and environmental factors interact to drive the disease process. Some gene polymorphisms could be associated to the disease in some populations and not in others. Thus, it is possible that in those populations showing an association between PlA2 and coronary disease, this allele is in linkage disequilibrium with some other mutation at the Pl gene, this mutation being responsible for the association. We are currently searching for mutations at the glycoprotein IIIa gene (single-strand conformation polymorphism analysis) in our patients.

We investigated whether the PlA2 allele is associated with other risk factors. We found no evidence of association between the PlA2 allele and smoking status, hypertension, or diabetes. These data are in agreement with the work of Ridker et al.8 In addition, the association between PlA2 and dyslipemia was also investigated. We found that patients with the PlA2 allele showed a significantly higher concentration of LDL cholesterol.

Finally, we agree with the authors that prospective studies are needed to evaluate the clinical value of the interaction between environmental and genetic factors.

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REFERENCES

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