Are There Any Associations Among Coagulation Factor VII Gene Polymorphism, Plasma Activated Factor VII Levels, and Cerebrovascular Disease?

To the Editor:

We read with interest the article by Ghaddar et al. showing no association of subclinical atherosclerosis with plasma coagulation factor VII (FVII) level or with FVII gene polymorphism (FVII R353Q), both of which were reported to be associated with myocardial infarction in whites. There are marked racial differences in cardiovascular disease between whites and Japanese. Compared with whites, Japanese show a much lower incidence of coronary artery disease but a higher incidence of stroke. Recently, a direct assay for plasma activated FVII (FVIIa) levels has been developed, and FVIIa levels were found to be more associated with cardiovascular disease than FVIIc or FVII antigen (FVIIag) levels. However, the relationships of FVIIa and FVIIag levels with ischemic stroke, including the subclinical silent stage, in relation to R353Q polymorphism have not been investigated.

We studied 328 Japanese subjects consisting of an asymptomatic hypertensive group (n = 149), a clinically overt ischemic stroke group (n = 83), and a normotensive healthy control group (n = 96). To assess silent cerebral infarction, MRI was performed in the hypertensive patients, who were classified as the positive group with ≥1 lacunes (n = 61) and the negative group without lacunes (n = 88). The subjects studied all resided in the same district, and they did not include any first-degree relatives. Genomic DNA was extracted from citrated whole blood, and FVII R353Q polymorphism was identified by the previously described method using polymerase chain reaction.

The 353Q allele was reported to be present in 22% of whites, whereas it was detected in 38 (12%) of the 328 Japanese studied. We found no differences in the FVII 353Q allele frequency among the normotensive control group, the hypertensive group, and the stroke group (0.057, 0.067, and 0.042, respectively). There were also no significant differences in the levels of FVIIa, FVIIc, and FVIIag among these groups, and there were no significant differences in either the frequency of FVII 353Q allele or the levels of FVIIa, FVIIc, and FVIIag between those with silent lacunes and those without any lacunes. On the other hand, those having the 353Q allele had lower plasma levels of FVIIa (~43%), FVIIc (~24%), and FVIIag (~28%) than the homozygotes of normal 353R in each group. Thus, in Japanese, FVII R353Q polymorphism, which is more closely related to FVIIa levels than FVIIc or FVIIag levels, seems to have a less important influence on both silent and clinically overt cerebrovascular diseases.

Kazuomi Kario, MD, PhD
Hypertension Center
Cornell University Medical College/The New York Hospital
New York, NY
Department of Cardiology
Jichi Medical School
Tochigi, Japan
Masafumi Matsuo, MD, PhD
Division of Genetics
International Center for Medical Research
Kobe University School of Medicine
Kobe, Japan
Toshiyuki Miyata, PhD
Research Institute
National Cardiovascular Center
Osaka, Japan

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Kazuomi Kario, Masafumi Matsuo and Toshiyuki Miyata

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