Racial Differences in Coronary Vasomotor Response or Selection Bias?

To the Editor:

Pristipino et al found that, compared with white patients in Italy, Japanese patients with myocardial infarction had a 3-fold-greater incidence of coronary spasm and a vasoconstrictive response to acetylcholine. The authors conclude that these “major racial differences in the coronary constrictor response...warrant further investigations because they may have relevant pathophysiological and therapeutic implications.” In my opinion, interpreting these differences as “racial” can be problematic, particularly in view of the possibility of selection bias stemming from the different risk profile of the study groups. Japanese patients in this study were much older than the white patients (mean age, 68.8 versus 54.8 years) and had much lower mean serum cholesterol levels (183 versus 247 mg/dL), serum triglyceride levels (87 versus 209 mg/dL), and body mass indexes (22.1 versus 26.5 kg/m²). These dramatic differences cast serious doubts on the comparability of the underlying disease process in the 2 groups. Atherosclerotic disease is an extremely complex multifactorial process in which metabolic and physical factors come into play. Furthermore, the old Virchowian hypothesis of the role of inflammation in this process has been recently resurrected.

Compared with Western countries, coronary heart disease (CHD) is very uncommon in Japan. According to 1998 World Health Organization data, CHD mortality rates among men 35–74 years old are 5.7% in Japan, 15% in Italy, and 21.4% in the United States. This low CHD risk is consistent with the low cholesterol and low body weight of the Japanese population, and the Japanese patients in Pristipino et al’s study fit this general profile. Why then did these patients have a myocardial infarction? Why do they have angiographic features similar to their white counterparts despite their much lower lipid levels? Could it be that, among all the constellation of risk factors involved, the predominant players that caused the underlying atherosclerosis disease in these Japanese patients are different than those in the white patients? For example, hyperlipidemia may play a secondary role, and inflammation, endothelial dysfunction, or other factors (eg, infection?) may be the predominant players. In other words, these 2 groups of patients may suffer from a different form of atherosclerosis, even if it looks similar in the angiogram.

Before concluding that the observed differences are racial, patients who have similar profiles with regard to the major CHD risk factors will need to be compared. For example, how will the vasomotor response of Japanese patients compare with that among lean whites with low cholesterol levels who experience a myocardial infarction?

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Response

We appreciate the stimulating points raised by Dr Nieto. Because our study was performed by the same team using the same protocol, it provides conclusive evidence of a much higher incidence of coronary vasospastic response in Japanese patients than in white patients after a myocardial infarction (MI). The differences we found between Japa-
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