COMMENTS AND RESPONSES

PPARγ Variant Influences Angiographic Outcome and 10-Year Cardiovascular Risk in Male Symptomatic Coronary Artery Disease Patients

Response to Regieli et al.

Peroxisome proliferator–activated receptor (PPAR)γ is a nuclear transcription factor modulating the transcriptional regulation of many genes involved in metabolism and energy homeostasis. Although several studies have addressed the metabolic profile of carriers of a common polymorphism in *PPARγ2* (Pro12Ala), there is no clear consensus on whether the metabolic benefits that accompany 12Ala carriers would translate into a protection from cardiovascular disorders. The study of a potential association between the Pro12Ala polymorphism and angiographic and cardiovascular outcome in the REGRESS (Regression Growth Evaluation Statin Study) cohort by Regieli et al. (1) has concluded that carriers of the 12Ala allele in *PPARγ2* have less widespread coronary artery disease (CAD) and a lower 10-year cardiovascular morbidity and mortality. We believe that the authors have overgeneralized their finding in terms of study cohort population, methods, and results regarding the conclusion made.

It is of note that, in their study, the carriers of the 12Ala allele did not have such a favorable metabolic profile as reported many times previously (2), except that the 12Ala allele carriers had lower systolic and diastolic blood pressure (that did not account for the decrease in CAD in the study). Also, the number of smokers was almost significantly lower among the carriers of the 12Ala allele in the REGRESS study cohort, yet neither smoking nor age as a major cardiovascular risk factor seemed to be entered as a confounding variable in the multivariate analysis. The authors admit that they could not identify what factor(s) accounts for the reduced cardiovascular risk for 12Ala allele carriers in their study cohort. In addition, in this study, the unique male patient cohort was investigated employing a distinct means of CAD assessment. Another angiographic study did not find an association between the 12Ala allele carriers and atherosclerosis (3). Our own data, though obtained from a smaller sample size, show that the 12Ala allele confers an even higher CAD risk in men (4). We additionally found that the 12Ala allele was even positively correlated with quintiles of the extent score of coronary disease ($r = 0.23$; $P = 0.01$) when age, BMI, LDL and HDL cholesterol, homeostasis model assessment, and smoking status were controlled for.

The present study confirms results from a number of previous studies mainly demonstrating fewer myocardial events in carriers of the 12Ala allele (5), and the authors demonstrate for the first time an association between the Pro12Ala polymorphism and cardiovascular disease mortality. However, we wanted to point out that there are questions remaining with regard to the effect of the 12Ala allele in *PPARγ2* on CAD that warrant further studies. Therefore, it may be too early for a generalized conclusion on the association between the Pro12Ala polymorphism in *PPARγ2* and vascular disease.

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DOI: 10.2337/dc09-0393

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

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