
Letters to the Editor

Comment on: Kretowski et al. (2007) Polymorphisms of the Renin-Angiotensin System Genes Predict Progression of Subclinical Coronary Atherosclerosis: *Diabetes* 56:863–871

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In their recently published study, Kretowski et al. (1) explored the role of some genetic variants of proteins involved in the renin-angiotensin system, in subjects with type 1 diabetes, as predictors of progression of coronary artery calcification (CAC), a marker of subclinical coronary artery disease. Three polymorphisms were studied: variants of angiotensinogen (AGT) (M235T), ACE (I/D), and angiotensin type 1 receptor (ATR1) (A1166C). The authors show that patients without albuminuria and/or hypertension with the AGT TT genotype had more CAC progression than patients with the AGT MT or the AGT MM genotype (percentages with progression: 28.2, 7.1, and 6.7%, respectively; $P = 0.001$). Other polymorphisms were not discriminative in any subgroup. In logistic regression analysis, the authors identified combinations of polymorphisms with an even more

increased risk of progression. The AGT TT–ACE ID–ATR1 AA/AC genotype combination had an odds ratio (OR) of 11.6 (95% CI 4.5–29.6, $P < 0.0001$) versus remaining genotypes. Based on this observation, the authors concluded that certain genotype combinations seem to have an additive effect on CAC progression. However, we feel that this conclusion is not valid, since it was not tested whether certain combinations predict CAC progression better than the AGT TT genotype alone. Furthermore, the data suggest that this might not be the case. The OR of CAC progression with the AGT TT genotype versus other genotypes was 5.1 (see Table 5 in ref. 1), which is well in range of the 95% CI of the OR (4.5–29.6) for the AGT TT–ACE ID–ATR1 AA/AC genotype. Therefore, we believe that this study does support a relation of AGT M235T polymorphism with CAC in patients with type 1 diabetes but does not support the suggestion that certain genetic variants of proteins involved in the renin-angiotensin system pathway have an additive effect on progression of CAC.

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