Relationship of PON1 192 and 55 gene polymorphisms to calcific valvular aortic stenosis

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Abstract

Introduction and Objectives

Paraoxonases may exert anti-atherogenic action by reducing lipid peroxidation. Previous studies examined associations between polymorphisms in the paraoxonase 1 (PON1) gene and development of coronary artery disease (CAD), with inconsistent results. Given the similarities in clinical and pathophysiological risk factors of CAD and calcific aortic valve stenosis (CAVS), we postulated a link between PON1 alleles and CAVS progression.

Methods

We investigated the association between PON1 55 and 192 single nucleotide polymorphisms (SNPs), their enzyme activity, and CAVS progression assessed by aortic valve area and transvalvular peak velocity in 67 consecutive patients with moderate CAVS and 251 healthy controls.

Results

PON1 paraoxonase activity was higher in CAVS patients (P<0.001). The PON1 genotype Q192R SNP (P=0.03) and variant allele (R192) (P=0.01) frequencies differed between CAVS patients and controls. Significant association existed between PON1 enzyme activity, phenotypic effects of PON1 192 genotype polymorphisms, and CAVS progression, but not between PON1 55 and high-density lipoprotein (P=0.44) or low-density lipoprotein cholesterol (P=0.12), between 192 genotype and high-density lipoprotein (P=0.24) or low-density lipoprotein cholesterol (P=0.52).

Conclusion

The PON1 genotype Q192R SNP has an important effect on CAVS disease progression. This study helps outline a genotype-phenotype relationship for PON1 in this unique population.

Keywords
Calcific aortic stenosis, polymorphism, paraoxonase, atherosclerosis, genetics, association