Caspase recruitment domain-containing protein 8 rs2043211 polymorphism and cardiovascular disease susceptibility

To the Editor,

We read the publication on "Association between caspase recruitment domain-containing protein 8 rs2043211 polymorphism (CARD8) and cardiovascular disease susceptibility: A systematic review and meta-analysis" with great interest (1). Huang et al. (1) concluded that "CARD8 rs2043211 polymorphism is associated with cardiovascular diseases". There are some concerns with respect to this report. Firstly, the additional effect of ethnic differences should be studied. Secondly, a subgroup analysis should be performed for each cardiovascular disease. Different cardiovascular diseases have different underlying pathophysiological processes, and the effects of underlying genetic polymorphisms may be different. Also, the effect of other concurrent genetic polymorphisms should be mentioned. Along with CARD8 polymorphism, other polymorphisms can affect cardiovascular disease susceptibility. Finally, we tried to analyze and calculate for the difference of molecular weight, using the same technique described in previous publications (2, 3), in cases of different polymorphisms of CARD8. Comparing AT genotypes to AA genotypes, the molecular difference at the corresponding site is 141.1/mol (393.3/mol versus 534.4/mol). This implies that more amount of CARD8 genetic content is required for the processing of the final protein in the AA genotype. This may imply less involvement of CARD8 in the inflammation process, which is further related to the pathogenesis of cardiovascular diseases, in case of the CARD8 AT genotype. This is an additional explanation to the findings of the meta-analysis by Huang et al. (1).

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DOI:10.14744/AnatolJCardiol.2018.24892

Author`s Reply

To the Editor,

We would like to thank the authors of the letter for the comments on our recently published study (1) and for showing interest in our study and putting forward some important points. Genetic polymorphism may be attributed to different ethnic populations or etiology (2, 3). Therefore, the subgroups were analyzed by ethnicity and etiology in our study (Fig. 3) (1). The limitations of our article mentioned "different disease statuses may have influenced the data explanation of the included studies". However, only two subgroups (myocardial infarction and others) were present based on the etiology because the relationship between caspase recruitment domain-containing protein 8 (CARD8) and cardiovascular disease is not fully investigated and understood. Additionally, because Asian and Caucasian populations comprised the ethnicity group in our study, the ethnicity subgroups of these two populations were analyzed. Therefore, further studies with diverse populations and etiologies are needed to explore the association between CARD8 and cardiovascular disease susceptibility. Potential gene polymorphisms for cardivascular disease have been reported rampantly. Indeed, focus on the interaction between the CARD8 rs2043211 polymorphism and the NLR pyrin domain containing 3 (NLRP3) gene polymorphism has been increasing (4); however, the interactions between the CARD8 rs2043211 polymorphism and other gene polymorphisms have not been completely analyzed although the the NLR pyrin domain containing 1 (NLRP1) rs2670660 single-nucleotide polymorphism SNP and the NLRP1 rs12150220–rs2670660 A-G haplotype are associated (4, 5). Because the article concluded that "the exact mechanism by which the CARD8 rs2043211 gene polymorphism influences cardiovascular diseases susceptibility remains to be elucidated," further research is necessary. Finally, the results of the molecular weight and genetic content analyses are concordant with our study and provide another explanation.

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