Reviewer’s report

Title: Multilevel analysis of systolic blood pressure and ACE gene I/D polymorphism in 438 Swedish families - a public health perspective

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Reviewer: MICHEL SAFAR

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This study tries to establish the relationships between SBP and ACE gene polymorphism in Swedish families. The conceptual approach is that the ACE gene I/D polymorphism is a well established genotype (this fact is true) and that BP is a clear cut phenotype, enabling to establish itself a clear-cut and sophisticated classification of patients as well as their response to ACE inhibitors. Most of the research workers so believe that, if a clear cut relationship cannot be established between genotypes and phenotypes, it is mainly because there is a failure in basic research, particularly related to the research relating associations of gene polymorphisms and environmental factors. Another possibility to discuss extensively is that hypertension is not a clear cut phenotype and even constitutes a misleading approach, enabling an inappropriate classification of subjects (in contrast with the gene polymorphisms with give a clear classification in terms of yes/no). Initially, hypertension was defined according to a single point of the BP curve, DBP, which has little meaning in term of cardiovascular (CV) risk. More recently the definition was based on brachial SBP, which is, not only a single point of the brachial BP curve, but also does not reflect at all central SBP. There is a lot of other inadequacy in such definitions so that the primary factor to classify in a large population is mainly the gene polymorphism, not the BP. Another important point to consider is that the study of a CV risk factor as BP cannot be done without the study of other common CV risk factor (diabetes, dyslipidemia…). Apparently this is not possible in the present investigation. Finally, the use of ACE inhibitors as a classifying variable may also be a misleading approach in the studied population. The effectiveness of drug treatment is constantly a subject of discussion for any open study. Furthermore the use of ACE inhibitors is limited to the period during which the drug has been commercialized and thus does not allow any conclusion for a long term follow-up. The present population is interesting and a more available classification of subjects should be interesting to determine and to study.

What next?: Reject because scientifically unsound

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests