Reviewer’s report

Title: Early atherosclerosis and cardiac autonomic responses to mental stress: a longitudinal population-based study of the moderating influence of impaired endothelial function

Version: 1 Date: 30 October 2009

Reviewer: Raymond Yan

Reviewer’s report:

In this study by Chumaeva et al. of a young subgroup of 61 men and women enrolled in the Cardiovascular Risk in Young Finns Study, the interactions between acute mental stress-induced cardiac reactivity/recovery surrogated by changes in each of RSA and PEP, and endothelial function surrogated by FMD, on subclinical atherosclerosis as measured by carotid IMT was examined. While there was no significant cross-sectional relationship between each of the baseline measure of RSA and PEP as well their reactivity with IMT, there was significant interaction between each of RSA recovery and PEP recovery with FMD in predicting IMT. Specifically, among the supra-median FMD subgroup, enhanced RSA recovery was predictive of lower IMT, whereas among the intra-median FMD subgroup, better PEP was associated with lower IMT. The results are interesting and of academic relevance to better understand the role of stress on the development of subclinical atherosclerosis.

major Comments:

(1) In examining interactions, the variables of interest together with their interaction term should often be entered simultaneously into the multivariable regression model. The robustness of the interaction is more assured when significance was demonstrated for both the variables as well as their interaction term. Apparently, only the interaction term was entered in the linear regression model. Was this the case? What are the results when the variables of interest, together with their interaction term are simultaneously entered? Are the interaction terms still significant?

(2) The author should explain or hypothesize in more detail on the reasons underlying the observed discrepant FMD-median stratified subgroup association between RSA recovery and PEP recovery respectively with IMT.

(3) Given blood pressure is a known correlate with each of FMD and IMT, it should be adjusted for in the multivariable models. While as the author stated that BP responses were not measured, however, is there any other BP measurement available, such as pre-examination baseline BP, or any other BP measurement taken around the time of examination? Are the results modified by introduction of BP measurement?
Minor comments:

(4) Given the relatively limited sample size and as such the limited number of permissible covariate adjusted, the author should acknowledge that residual confounding as a potentially important limitation.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests