Reviewer's report

Title: Association of soluble endothelial protein C receptor plasma levels and PROCR rs867186 with cardiovascular risk factors and cardiovascular events in coronary artery disease patients: The AtheroGene Study

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Reviewer: Yohan Bosse

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The authors investigated the relationship of soluble endothelial protein C receptor (sEPCR) plasma levels with cardiovascular risk factors and cardiovascular events in a prospective study (AtheroGene Study, n=1673). They have also studied the impact of one polymorphism (Ser219Gly) known to have an important effect on the plasmatic concentration of sEPCR.

Briefly sEPCR plasma levels are not associated with the risk of cardiovascular events. sEPCR levels were associated with some cardiovascular risk factors including gender, diabetes and variables related to kidney functions (creatinine and cystatin c). As expected the Ser219Gly was strongly associated with sEPCR levels, but not with cardiovascular events.

The manuscript is straight to the point and nicely written. The patients in the AtheroGene Study underwent a comprehensive measurement of cardiovascular related variables. The results are mostly negative, but still important to report. The following points should be considered.

Major points

1) It would be of great interest to know whether other polymorphisms are associated with sEPCR plasma levels. Genotyping was performed on the Affy 6.0 array. The authors must have the genotypes for other SNPs within and near the PROCR gene. Are there any other polymorphisms in this gene that influence the sEPCR plasma levels? A LD plot of this locus would be useful.

Minor points

1) P values testing differences between the two groups in Table 1 should be presented.

2) The median follow-up time is 3.7 years. The number of events during that time is 136. The authors should provide power calculation and indicate whether larger sample size or longer follow-up period is needed.

3) Limitations should be discussed.

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

**Quality of written English**: Acceptable

**Statistical review**: No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests**: I declare that I have no competing interests