Reviewer’s report

Title: The Impact of Coronary Artery Disease Risk Loci on Ischemic Heart Failure Severity and Prognosis: Data from the COntrolled ROsuvastatin multiNAtional trial in heart failure (CORONA)

Version: 1
Date: 18 July 2014
Reviewer: Inke König

Reviewer’s report:

In their manuscript, the authors describe an association study on known loci associated with coronary artery disease and the outcome after heart failure. There is a clear rationale for the study, but some issues need to be addressed.

Major compulsory revisions

1. Methods: It is unclear why the authors only consider the seven loci identified in one of the first GWA studies performed. Since 2007, many more loci have been reliably identified, and there is no a priori reason why these should not be part of this study.

2. Methods: The description of when covariates were included needs clarification: Was the mentioned linear model used for the primary outcome? If this is time to event, this is not adequate. Were covariates only considered in the model if they were significant themselves, or if the genotype was significant on the outcome? Why were these covariates chosen in the first place? For a prognostic model, it would be important to include all prognostic variables that have reliably been reported previously.

3. Methods and Results (also in Abstract): The authors need to be more precise on their use of the term significance. For instance, “suggestive evidence for association” should be avoided, since the result from a statistical test can only be significant or not. Similarly, the authors use the term “convincingly associated”, for which there is no definition. Also, “P<0.05” is given in results, which is not sufficient.

4. Results: In describing the associations, it should be stated whether the effects were in the direction expected from the literature.

5. Discussion: The authors state that their sample is exceptionally large. Still, the power of their study to detect meaningful effects should be estimated. Alternatively, there should be a thorough discussion based on the confidence intervals to describe which effects can safely be excluded.

6. Tables: In addition to giving the effect estimates, please show effects for all the genotype groups, for instance, in terms of mean values with variation measures.

Minor essential revisions:

1. Abstract – Methods: Please state the outcome variables here.
2. Background and Abstract: It is not correct to state that the genetic loci affect the risk of CAD or cause CAD, since merely associations have been described.

3. Methods: A distinction is made between normally and non-normally distributed variables, but it is not stated where this information comes from.

4. Methods: The genotypes were coded for an additive model. Is this the model that seemed to be most plausible for all SNPs in the original publication?

5. Results: Please state whether the MAFs were similar as in the original publication.

6. Results: Please state how conformation to Hardy-Weinberg equilibrium was established.

7. Results: In table 3, please highlight the primary outcome.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.