Reviewer’s report

Title: Genome-wide association study of myocardial infarction, atrial fibrillation, acute stroke, acute kidney injury and delirium after cardiac surgery – a sub-analysis of the RIPHeart-Study

Version: 0 Date: 06 Dec 2018

Reviewer: Alexander Lauten

Reviewer's report:

The authors aimed to identify genetic variants associated with postoperative complications including atrial fibrillation, delirium, non-fatal myocardial infarction, acute renal failure and/or any new stroke after cardiac surgery. The report represents a subanalysis of the RIPHeart-Study, which did not observe outcome differences between the treatment and the sham Group. The cohort comprised 1,224 patients who underwent an elective cardiac surgery, genomic DNA was isolated from whole blood of patients using standard procedures in a total of 1,170 pts. Findings of the study include the observation of concurrence of HSPA8 and RyR2 for atrial fibrillation and myocardial infarction, the involvement of DUSP4 in I/R injury, the role of PHLPP2 in developing complications after cardiac surgery and the involvement of BBS9 in renal dysfunction. The strength of the study is the large number of patients and gen loci investigated, which however also includes the risk of statistical noise due to the mere number of tests performed. As weakness, the association to of the identified polymorphisms with these complications is also purely observational. In most cases, loci are noncoding, and many loci are far from discovered genes in non-coding regions, the effects of SNPs on genes are completely unknown or the functions of the influenced genes are unknown. Nevertheless a study suidable to generate a Hypotheses needing further confirmation to transfer these findings into biological insights.

Minor: the numbers of the samples investigated seem confusing and need to be brought in line between the text and the flowchart. E.g. according to the Flowchart, 1,403 underwent randomization for RIPHeart Trial, however according to the text 1224 pts were analysed. The numbers in the Flowchart Need to be mentioned in the same manner the text. Otherwise it is impossible to understand what was analysed in how many patients and samples.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes
Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English  
Please indicate the quality of language in the manuscript:

Acceptable

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