Author’s response to reviews

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

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Dear Prof. Dr. Franz,

Thank you very much for your reply and the possibility to publish our manuscript entitled ‘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’ in BMC Cardiovascular Disorders.

We would like to thank the reviewers for the critical reading of our manuscript.

Please find below the digest of our manuscripts’ revision.

Reviewers’ comments:

Christian Jung (Reviewer 1):

There are no further points that should be addressed.

Alexander Lauten (Reviewer 2):

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 suitable to generate a Hypotheses needing further confirmation to transfer these findings into biological insights.

We added a paragraph comprising “strength and limitations of this study” after the conclusions (p.19, line 463 - p.20, line 471).

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.

We apologize for the confusing declaration of the number of patients. First, we corrected the wrong number of patients in the manuscript from 1,224 to 1,204 (p.8, line 155). Secondly, we added detailed information about the number of analyzed patients in accordance with the flowchart (p.7, line 152 – p. 8, line 157).

“1,430 patients underwent elective cardiac surgery requiring cardiopulmonary bypass (e.g. coronary
artery bypass graft, valve surgery, ascending aorta replacement) between January 2011 and May 2014. DNA samples were taken from 1,385 patients. After exclusion due to protocol violation or insufficient DNA quality or quantity, DNA was analysed from 1,204 patients. 1,170 (871 males, 299 females) patients met eligibility criteria after applying quality control and excluding patients with missing genotypes or phenotypic information.”

Many thanks in advance

Sincerely,

Patrick Meybohm