Author’s response to reviews

Title: The COMT-polymorphism is not associated with the incidence of acute kidney injury after cardiac surgery - a prospective cohort study

Authors:

Mehmet Oezkur (mehmet.oezkur@uk-halle.de)
Attila Magyar (Magyar_A@ukw.de)
Phillip Thomas (E_Thomas_P@ukw.de)
Stefan Störk (Stoerk_S@ukw.de)
Peter U. Heuschmann (E_Heuschma_P@ukw.de)
Rainer G. Leyh (Leyh_r@ukw.de)
Martin Wagner (Wagner_M@ukw.de)

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Author’s response to reviews:

Dear Prof. Dr. De Caestecker,

Thank you for the revision and the positive evaluation of our manuscript. We are glad to hear we could address the main concerns. Furthermore, we addressed the remaining concerns in the re-revised version. We hope that the manuscript is now suitable for publication.

1) While you now include clear language stating differences in AKI criteria used between the two other studies and this one, the discussion does not attempt to explain how and why these differences in AKI criteria so profoundly affect the results in the way they have, in particular as it now appears one of the papers showed the opposite results. You need to spend some time thinking about this and clearly explaining your thoughts;

This is a very interesting point in the discussion. We spent some time thinking about this problem and concluded:

Page 14 lines: 18-25:

“While all papers used the RIFLE classification for AKI definition, we used the latest definition by the Kidney Disease Improving Global Outcome (KDIGO) published in 2012 [4-7]. The authors stated that the RIFLE classification might be more robust for AKI diagnosis after cardiac surgery, but most recent evidence suggests that the KDIGO definition with its strict increase of
SCr of 0.3ml/dl within 48hrs definition has an impact on short- and longterm outcome [20, 21, 28-32]. Even slight rises in SCr levels are associated with a significant increase of early postoperative mortality [29]. Mild AKI are associated with enhanced mortality and rehospitalisation rates after cardiac surgery also [20, 28].”

2) You should include the cardiac data in the paper, including methods, and then discuss why these data are important;

Thank you for this important comment. We added the following to the manuscript:

Page 9, lines 13-14:

“The prevalence of cardiac dysfunction was lowest in the Val/Met group (31.5%), while in the Val/Val group the prevalence was 71.9%.”

Page 10, lines: 5-11:

“To further understand the role of cardiac dysfunction, we performed additional analyses but did not find any meaningful and significant association of the COMT genotype, cardiac dysfunction and the occurrence of postoperative AKI. Also in logistic regression analyses, cardiac dysfunction was not associated with the incidence of AKI neither in univariate (OR 0.7, 95% CI 0.33 – 1.51, p=0.4), nor in multivariate modelling (OR 0.70, 95% CI 0.31- 1.57, p=0.4) controlling for COMT genotype and also including the interaction of COMT genotype and cardiac dysfunction.”

Page 13 lines 10-15:

“In our analyses, we found an association between cardiac dysfunction and the COMT polymorphism, which has not been described in the literature. We found a higher prevalence of cardiac dysfunction in the Val/Val genotype group, while the Val/Met genotype was associated with a low prevalence of impaired LV function. Further analyses did not reveal any association between cardiac dysfunction and the incidence of AKI. Our findings of a potentially existing clinical relation of cardiac dysfunction and the underlying COMT genotype, admittedly being based on limited statistical power, need to be confirmed by future studies.”

3) Your use of English is not very good; there are numerous errors throughout the text.

We did an overall revision and substantially changed the used language. Thank you for pointing out the errors.

Best Regards

Mehmet Oezkur