Author's response to reviews

Title: Sensitivity and specificity of plasma disappearance rate of indocyanine green as a prognostic indicator in acute liver failure

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Author's response to reviews:

Dear Dr. Edmunds,

Thanks for considering our paper for publication and for the excellent reviews of the two reviewers. We revised our manuscript thoroughly and addressed each concern the reviewers had raised.

Point-to-point-response

Ad Reviewer 1:
Ad Major Remark:
As suggested by reviewer 1 words of caution about precision and the potential extrahepatic ICG elimination or decay are included in the discussion section (page 9).

Ad Minor Remarks:
Ad ‘Were 100% of ICG-measurements technically possible? If not please report failure rate in results section.’
Indeed, luckily 100% of ICG-measurements in our study were technically possible.

Ad ‘Statistics: Why did you choose to use Mann-Whitney U? Non-normal distribution of data?’
As – compared to the t test - the non-parametric Mann-Whitney U test is valid for both non-normally distributed data and normally distributed data and is much less likely to give a spuriously significant result because of one or two outliers, we decided to use this more robust test.

Ad Reviewer 2
Ad Major Compulsory Revisions
As suggested by reviewer 2 the limitations of the study are now discussed more thoroughly and the 95% confidence intervals are stated (pages 8 – 10).

Because of the very valuable comment of reviewer 2, the manuscript is now formalised according to the STARD initiative (please find attached the STARD checklist).

As noted by reviewer 2 reference 16 was wrong and is changed to the correct reference.

The second reviewer comments that assessment of the performance of King’s College criteria is not possible in our cohort because these criteria were, in the reviewer’s understanding, used to select transplant candidates. However, as in all likelihood not stated clearly enough in the first manuscript version, in our cohort the decision to transplant a patient was not only based on fulfilment of King’s College criteria but on the attending physician’s overall assessment of the patient’s likely prognosis. Nevertheless, we agree with the reviewer that the results have to be interpreted with caution as fulfilment of the King’s College criteria influenced the selection of transplant candidates in our study at least in part. Therefore, in the revised manuscript a more clear statement regarding the decision making has been introduced to the methods section and the issue is discussed in the discussion section (pages 4, 5, 9, and 10).

Ad Minor essential revisions

Ad Introduction

‘It does not represent liver blood flow.’ is changed to ‘It does not represent the liver blood flow alone.’ (page 3).

Ad Results

Correlational data are now presented in detail:

‘When analyzing correlation of ICG-PDR measured at day 1 with INR, bilirubin, creatinine, AST, ALT, Apache II score, and MELD score, significant correlations were obtained for INR (r=-0.41; P=0.043), bilirubin (r=-0.53, P=0.006), and MELD score (r=-0.67; P<0.001).’ (page 8).

Unfortunately correlation with blood lactate can not be performed as blood lactate was not obtained after inclusion into the study.

Please find attached the revised manuscript in a marked and in an unmarked version.

Yours sincerely,
Uta Merle