Reviewer's report

Title: SERUM BTP CONCENTRATIONS ARE NOT AFFECTED BY HEPATIC DYSFUNCTION

Version: 1 Date: 10 Jun 2017

Reviewer: Amy Karger

Reviewer's report:

While I appreciate the author's response to my initial comments, the response did not adequately address the issues with this manuscript and did not adequately frame its conclusion in light of the Mindikoglu paper. If you read the Mindikoglu paper carefully, you will note that they did in fact perform urinary iothalamate clearance measurements, which the author suggested was a weakness of their analysis. In fact they performed urinary clearance simultaneously with plasma clearance and found no significant difference in a subset of subjects, leading to the following statement taken directly from the supplementary material in their manuscript:

"There were no significant differences between the mean GFRs measured by plasma (57.1 mL/min/1.73 m²) and urinary iothalamate (61.5 mL/min/1.73 m²) clearances (P = .407). The similar plasma and urinary clearances provide evidence against significant "third-spacing" of this marker."

Secondly, in the author's response they state that the Mindikoglu study does not "detract from the importance of the current study findings." I would disagree; one of the primary conclusions from the author's manuscript is that "BTP might serve as a particularly useful marker of GFR." The Mindikoglu paper on the contrary specifically concludes from their data that BTP was NOT helpful for predicting mGFR in patients with cirrhosis. The advantage of their paper is that they did measure GFR, whereas this current manuscript did not.

While I think the data from this manuscript is interesting to know given the interest in incorporating BTP into GFR estimation and the challenges with GFR estimation in cirrhotic patients, the discussion of the manuscript needs to be written in such a way to more significantly acknowledge the Mindikoglu paper and argue as to why we should "care" about BTP given the Mindikoglu paper's conclusions about BTP, and/or more accurately critique the Mindikoglu study design (the current critique on p. 7 in this revision is not accurate, since they did in fact look at urinary clearance to vet their plasma clearance results).
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?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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I have been involved with research studies that have received free testing supplies from Siemens Healthcare Diagnostics for BTP testing. I have also served as principal investigator on assay validation studies with Siemens Healthcare Diagnostics with no direct compensation, only funds paid to our testing laboratory (fee for service). However none of these studies would be financially impacted by this publication.

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