Reviewer’s report

Title: Plasma disappearance rate of Indocyanine green is a prognostic indicator in acute liver failure

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Reviewer: Daniel Inderbitzin

Reviewer’s report:

Congratulations to the authors for a well written manuscript describing the value of ICG-Plasma-Disappearance-Rate (ICG-PDR) in the setting of acute liver failure.

ICG-PDR was determined daily in 25 patients with acute liver failure and values below 6.3%/min on study day 1 were found to correlate with a fatal course of the liver disease. An ICG-PDR value at any timepoint below 5.3%/min predicted death or the need for urgent liver transplantation.

Major remarks:

Our own early experiences with ICG-PDR coincide with the results presented in the paper (Inderbitzin et al JoGS 2005; 9; 1155-1162, Fig 2). All surgical patients with values greater than 5.0%/min survived, while the others required liver transplantation or deceased.

However, in a second step we expanded ICG measurements on patients after extended liver resections with limited hepatic reserve and expected to be able to predict survival early on in the clinical course. Unfortunately, conflicting results were obtained, and we observed a considerable rate of ICG-measurement failures (due to unstable signal quality) in hemodynamically unsteady patients (i.e. around 10-20%, data not published).

To determine the precision of ICG-PDR we therefore decided to measure ICG-PDR in completely anhepatic patients (n=24) during liver transplantation (Bruegger et al JoGS 2008; 12; 67-72). Unfortunately, ICG-PDR values were clearly different from zero (average: 1.55%/min) and even extreme values of ICG-PDR (i.e. 5.4 and 7.8%/min) were seen in completely anhepatic patients (Table1).

This precision problem is reflected in the overlap of your raw-data in Figure 1 (survivors vs non-survivors). You face the general problem that on one side cohort prediction is quite good, but does on the other side not help in decision-making in the individual case (i.e. you found an ICG-PDR of 0.0%/min on day 4 in a survivor, and on the other hand an ICG-PDR of 10.0%/min in a non-survivor).

From my point of view the mentioned published findings merit discussion in the
manuscript and words of caution about the precision and the (physiologically completely unclear) extrahepatic ICG elimination or decay have to be included in the discussion section.

Minor remarks:

Were 100% of ICG-measurements technically possible? If not please report the failure rate in the results section.
Statistics: Why did you choose to use Mann-Whitney U? Non-normal distribution of data?

Thank you for the opportunity to review your paper. It was a privilege and a pleasure.

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**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests'

Daniel Inderbitzin