Reviewer's report

Title: NOX2-generated oxidative stress is associated with severity of ultrasound liver steatosis in patients with non-alcoholic fatty liver disease

Version: 3  Date: 20 December 2013

Reviewer: Sven Francque

Reviewer's report:

Major Compulsory Revisions

The authors report on the parameters of oxidative stress in patients with NAFLD. The question is relevant. The paper is well written and nice to read. Methodology is overall well-elaborated and adequate.

Some issues need to be addressed:

According to the correlation table, the urinary PGF2alpha strongly correlates with BMI and inversely with adiponectin, but to a lesser extent with the US Hamaguchi score. In the regression analysis looking at the dichotomous question NAFLD vs. no NAFLD, BMI appears not to be an independent variable.

This asks for some comments:

First NAFLD is not always NASH, and in terms of inflammation and disease, NASH is considered more dangerous than simple steatosis. The question is whether we expect oxidative stress to be increased in a patient with mild steatosis and without steatohepatitis. So the question remains whether we want to oppose NAFLD vs. no NAFLD (which means that mild degrees of steatosis are also included) or whether the relationship with the severity of the steatosis is more relevant. So I would like to see a regression analysis assessing factors independently related to the severity of the NAFLD, and a regression analysis assessing factors independently related to the degree of oxidative stress as based on the parameters used in this paper.

Furthermore non-invasive scores for the diagnosis and severity of NASH and fibrosis. Most of these scores can be calculated with the parameters that were recorded in these patients. I would therefore like to see an analysis in relation to these scores, and a comparison nash vs. no nash (it can be argued that, as there is no biopsy as golden standard, these scores can be used (with all their inherent limitations)).

It would also be nice to include waist in the analyses, as visceral obesity seems to be more relevant than just the BMI.

The question remains unanswered, as this is a cross-sectional analysis (this should clearly be discussed by the authors) whether oxidative stress, caused by obesity, contributes to the pathophysiology of NAFLD (or perhaps more NASH).
or whether the inflamed liver contributes to the oxidative stress (and hence long term complications).

Discretionary Revisions

A minor remark: overall the paper is very well written, but some of the tables need some correction (cytocheratin 18 e.g.).

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests