

#### 43228-Answering Reviewers

- Given intestinal permeability is an important outcome measure, its measurement needs more description. Is the use of Urine  $^{51}\text{Cr}$ -EDTA clearance a gold standard? Why was this measurement chosen? To my knowledge there are other methods of measuring intestinal permeability and the authors must describe clearly why this method was chosen over the others, as well as its pros and cons.

*Many methods for measuring intestinal permeability in the clinical setting have been validated, but none has proven to be superior to others nor has it usually entered everyday clinical practice (see for example Bischoff et al. BMC Gastroenterology 2014, 14: 189). In our study we chose to use the  $^{51}\text{Cr}$ -EDTA test for two reasons:*

*1) it is poorly influenced by bacterial degradation in cases of small intestine bacterial overgrowth, sometimes associated with NAFLD*

*2) it is easily repeatable and less time-consuming for the health workers compared to oligosaccharides-based tests.*

*We have rewritten the paragraph in the methods section to better explain the reason for our choice*

- The authors need to explain the significance of the results of intestinal permeability as well as provide an explanation. There should had been more discussion on the interpretation of the study results in the Discussion section rather than a literature review on intestinal permeability (paragraph 3 and 4 of discussion)

*A possible interpretation of the negative result of the modulation of intestinal permeability, in the opinion of the authors, has been integrated in the discussion section.*

- There should be a description on how many were screened and recruited as well as how many were excluded (with reasons), especially since the authors mentioned the difficulty of recruitment.

*The description of flow-chart of study patients was updated as follows:*

*Fifty-four patients with NAFLD underwent liver biopsy at our centre during the two-year timeframe. Twenty-four patients were not eligible for the study because of one or more exclusion criteria (16 patients for ALT levels  $< 1.5$  time the upper normal limit, 5 patients for diabetes, 3 patients for BMI  $\geq 35 \text{ kg/m}^2$ ). Ten patients refused to participate in the study (5 patients because of lack of motivation*

*to start a diet program and 5 patients because of working reasons). Twenty patients were enrolled.*

- The Methods section should also describe other study outcomes e.g. body weight, liver biochemistry.

*Description of requested outcomes have been included in the methods section.*

- How did the investigators maintain subject compliance to both diet and physical activity during the study period? The ratio of compliance to both issues needs to be described in the Results section.

*Patients were re-evaluated bimonthly for compliance to diet and physical activity. Concerning compliance evaluation, two patients were judged not adherent to Mediterranean diet and other two patients to low fat diet, as described in result section. No patient modified his or her level of physical activity during the study. We have rewritten the paragraphs in the methods section and result section for a better comprehension.*

- Besides Vitamin E, what other health supplements were not allowed during the study?

*None. This was specified in the methods section.*

- First paragraph of discussion, I am uncertain if the conclusion of non-statistically significant reduction in HOMA-IR is due to normal values of blood glucose at baseline, this is an over hypothetical assumption, as those with normal glucose can still have insulin resistance.

*We thank reviewer for this remark. This comment has been deleted from discussion section.*