

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The work of Maslennikov et al. interestingly examines for the first time the effects of body composition modification on gut microbiota composition of cirrhotic patients. Major concerns: • In Introduction section authors state "The aim of the present study was to assess the relationship between gut microbiome and body composition in cirrhosis". Please better describe the rationale of the study.

Authors' reply: Introduction section has been edited:

"The pathogenesis of sarcopenia in cirrhosis is complex, and it is assumed that changes in composition of the gut microbiota (gut dysbiosis) and small intestinal bacterial overgrowth (SIBO) play important roles in its development^[1-5]. It is believed that these disorders of the gut microbiota promote bacterial translocation (the penetration of bacteria and their components into body tissues) and hyperammonemia, which increase protein catabolism and levels of myostatin, a protein that inhibits muscle growth^[2].

Water retention in cirrhosis has also been suggested to be associated with disorders of the gut microbiota and occurs in response to bacterial translocation-induced vasodilation^[6]. This leads to hypotension and compensatory fluid retention to maintain normal blood pressure levels. Although these relationships have been established with respect to SIBO^[7,8], there are no studies on such associations with gut dysbiosis.

In addition, the gut microbiota status is known to be associated with disorders of lipid metabolism, leading to an increase in fat content in the body^[9]."

- Authors must reorganize Results section in a more fluent form, for example by grouping the statistically significant taxa by taxonomic ranks and add "ssp." after genus.

Authors' reply: Done.

We have transferred almost all the digital data in the tables. We also changed the order of taxa in the text to hierarchical one. However, with your permission, we will not add "spp." to the genus names, since this is usually not used in articles devoted to the gut microbiota to make text more fluent.

- Authors must discuss the mechanisms by which the gut microbiota and the body components interact each other.

Authors' reply:

We have edited the Discussion section. The mechanism of the influence of Proteobacteria on the increase in the content of extracellular fluid is well described in the literature and is explained in this section, while the mechanisms of the influence of taxa of the gut microbiota on the body cell mass are under study. We have all published data on this issue collected in the Discussion section.

Minor concerns: • Page 5, Line: modify "the state of the gut microbiota" with gut microbiota status.

Authors' reply: Done.

- Please modify extracellular liquid with extracellular fluid

Authors' reply: Done.

- Since the authors conducted a compositional analysis, they should replace "gut microbiome" with "gut microbiota".

Authors' reply: The term "gut microbiota" is used to describe the community of bacteria living in the gut. The term "gut microbiome" is used to describe a cumulative genome of these bacteria. Thus, the analysis of the gut microbiome is a tool for analyzing the composition of the gut microbiota. In this article, we use the term "gut microbiota" when we mean "the community of bacteria living in the gut", and the term "gut microbiome" when we describe the results obtained from the analysis of the cumulative genome of these bacteria.

Added to the Materials and Methods section.

"The gold standard for studying the composition of the gut microbiota is analysis of the gut microbiome that is a cumulative genome of gut bacteria."

- In Materials and Methods section, Page 6, Line 64, authors mean "beads cleaning"?

Authors' reply: Yes. It was replaced.

- Please, rephrase the sentence "Therefore, based on the obtained values of conduction on passing alternating current with different frequencies through patients, their age, sex, and anthropometric parameters (height, weight, etc.), a manufacturer's software provides estimates of fat and body cell mass and total and extracellular fluid.", Pag. 7, Lines 85-88.

Authors' reply: This has been edited:

"The manufacturer's software provides the values of fat and body cell mass and total and extracellular fluid based on these values of conduction and patient's age, sex, height, and weight."

- Please check eventual typos in the text, for example Eggethella, Lines 138 and 232, Proteobacteria at line 184 and serum albumen in tables 1-4.

Authors' reply: Done.

- In figure 2, authors should remove the no statistically significant p-values.

Authors' reply: With your permission, we would like to keep these values to show that there were no significant differences between the patient groups.

- In Figure 3, the stars do not clearly define what are the statistically significant groups, so authors must provide a better representation. In addition, authors should provide a white background to the image.

Authors' reply: Done.

- In Figure 4 authors should add the p-values and the bars above the boxplots.

Authors' reply: Done.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear Editor, In this manuscript by Maslennikov, the authors investigated the relationship between gut microbiota and body composition in liver cirrhosis. In general, in this study, the researchers examined the stool of cirrhotic patients to evaluate gut microbiota using 16s rRNA gene sequencing and compared the results with body composition in these patients. Accordingly, the alternations of the gut microbiota were compared to any change in fat and body cell mass. Although this study aimed to provide some useful insights into the correlation of the gut microbiome and body composition in cirrhosis, there are several major concerns regarding the study.

- Liver cirrhosis is the end stage of a variety of chronic liver diseases with various etiologies. As no single pathomechanism can be implicated exclusively, various must act in concert to induce cirrhosis. Therefore, each etiology of liver cirrhosis could have its specific microbiome alternations and dysbiosis. As the authors concluded that "Changes in amount of body cell mass and extracellular liquid are associated with changes in the gut microbiome in cirrhosis patients", so, how the authors could explain that the obtained results regarding to the dysbiosis in the cohorts could indicate any correlation between body composition and gut dysbiosis?!

Authors' reply:

Most studies have shown that changes in the gut microbiome in cirrhosis are minimally dependent on its etiology, just as the course of cirrhosis itself also minimally depends on its etiology. The authors of those studies also almost never analyze changes in the

gut microbiome for each etiology separately, considering that these changes are practically independent of it.

- The analysis and comparison of a control group without cirrhosis and any other hepatic disorders must be implemented in this study. Of note, this comparison could provide valid information about body composition and gut microbiome regardless of cirrhosis effects on the microbial composition.

Authors' reply: Done.

- The authors should clarify the etiology of cirrhosis in the enrolled patients clearly.

Authors' reply:

The etiology of cirrhosis is presented in Table 1.

- There is no description of the analysis of microbiota in the text, i.e., sequence processing, data quality control, the approach of sequence analysis, etc.

Authors' reply:

This section has been edited.

- Why the authors did not analyze the microbiota composition at the level of family, genus, and species?! Importantly, any analysis at lower taxonomic levels could provide important information about the characterization of gut microbiota in the cohorts.

Authors' reply:

Microbiome analysis is presented at level of phylum, class, family, and genus. The analysis at level of species had not given additional information, but had overloaded the article with redundant data, therefore it was not presented.

- The presentation of the results is confusing. The authors should rewrite the Results section more clearly.

Authors' reply:

The results section has been edited.

- The English language of the text should be revised and corrected carefully.

Authors' reply:

The English language was checked by native speakers from the service www.editage.com.

- The discussion section should be organized better and shortened. For example, the first paragraph of the discussion should describe your main findings in this study. The discussion is about general information, this information should be included in the introduction. Thus, you should omit extra information in the Discussion section.

Authors' reply:

The discussion section has been edited.

Minor concerns: • The title of the manuscript is too short and obscure. I recommend that the title be modified to provide an accurate representation of the content.

Authors' reply:

According to the guideline, the title should be short and fully reflect the essence of the study. Our title does this. The authors were unable to modify the title to better reflect the results of the study and the reviewer did not submit his/her version.

- "Liver cirrhosis" should be added to the Keywords.

Authors' reply: Done.

- In my opinion, the order of the presentation of results should be changed. For instance, the results of microbial diversity should be presented before the results of the microbiota abundances.

Authors' reply: The location of this data corresponds to the logic of the presentation of the results, especially since no significant difference in these parameters was obtained. The authors tried to move this data to the beginning of the results section, but this option turned out to be worse than the current one.

(1) Science editor:

5 Issues raised:

The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy(ies) of any approval document(s);

Authors' reply: Done.

Year of publication is missing in reference n 22. Please provide it;

Authors' reply: Done.

The "article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text (and directly before the References);

Authors' reply: Done.