68247_Auto_Edited.docx

WORD COUNT 4021
TIME SUBMITTED 15-MAR-2022 03:38PM
PAPER ID 83662213

Name of Journal: *World Journal of Hepatology*
Manuscript NO: 68247
Manuscript Type: ORIGINAL ARTICLE

Observational Study

Gut dysbiosis and body composition in cirrhosis

Maslennikov R *et al*. Dysbiosis and body composition in cirrhosis

Abstract

BACKGROUND

Gut dysbiosis and changes in body composition (*i.e.*, a decrease in proportion of muscle mass and an increase in extracellular fluid) are common in cirrhosis.

AIM

To study the relationship between the gut microbiota and body composition in cirrhosis.

METHODS

The observational study included 46 patients with cirrhosis. Stool microbiome was assessed using 16S rRNA gene sequencing. Multifrequency bioelectrical impedance analysis was performed to assess body composition in these patients.

RESULTS

An increase in fat mass and a decrease in body cell mass were noted in 23/46 (50.0%) and 15/46 (32.6%) patients, respectively. Changes in the gut microbiome are not independently associated with the fat mass percentage in cirrhosis. The abundance of *Bacteroidaceae* (P = 0.041) and *Eggerthella* (P = 0.001) increased, whereas that of *Erysipelatoclostridiaceae* (P = 0.006), *Catenibacterium* (P = 0.021), *Coprococcus* (P = 0.033),

Desulfovibrio (P = 0.043), *Intestinimonas* (P = 0.028), and *Senegalimassilia* (P = 0.015) decreased in the gut microbiome of patients with deficiency of body cell mass. The amount of extracellular fluid was increased in 22/46 (47.6%) patients. Proteobacteria abundance (P < 0.001) increased, whereas Firmicutes (P = 0.023), Actinobacteria (P = 0.026), Bacilli (P = 0.008), *Anaerovoraceceae* (P = 0.027), *Christensenellaceae* (P = 0.038), *Eggerthellaceae* (P = 0.047), *Erysipelatoclostridiaceae* (P = 0.015), *Erysipelotrichaceae* (P = 0.003), *Oscillospiraceae* (P = 0.024), *Rikenellaceae* (P = 0.002), *Collinsella* (P = 0.030), *Hungatella* (P = 0.040), *Peptococcaceae* (P = 0.023), *Slackia* (P = 0.008), and *Senegalimassilia* (P = 0.024) abundance decreased in these patients. Patients with clinically significant ascites (n = 9) had a higher abundance of Proteobacteria (P = 0.031) and a lower abundance of Actinobacteria (P = 0.019) and Bacteroidetes (P = 0.046) than patients without clinically significant ascites (n = 37).

CONCLUSION

The changes in amount of body cell mass and extracellular fluid are associated with the changes in the gut microbiome in cirrhosis patients.

Key Words: Dysbiosis; Microbiome; Microbiota; Gut-Liver axis; Sarcopenia; Malnutrition; Cirrhosis

Maslennikov R, Ivashkin V, Alieva A, Poluektova E, Kudryavtseva A, Krasnov G, Zharkova M, Zharikov Y. Gut dysbiosis and body composition in cirrhosis. *World J Hepatol* 2022; In press

Core Tip: The abundance of *Bacteroidaceae* and *Eggerthella* increased, whereas that of *Erysipelatoclostridiaceae*, *Catenibacterium*, *Coprococcus*, *Desulfovibrio*, *Intestinimonas*, and *Senegalimassilia* decreased in the gut microbiome of patients with deficiency of body cell mass. Proteobacteria abundance was increased, whereas Firmicutes, Actinobacteria, Bacilli, *Christensenellaceae*, *Anaerovoraceceae*, *Eggerthellaceae*, *Erysipelatoclostridiaceae*,

Erysipelotrichaceae, *Oscillospiraceae*, *Peptococcaceae*, *Rikenellaceae*, *Collinsella*, *Hungatella*, *Slackia*, and *Senegalimassilia* abundance decreased in cirrhosis patients with excess extracellular fluid.

INTRODUCTION

Cirrhosis is the final stage of chronic liver diseases. However, it is not limited to the lesion of this organ and associated also with a decrease in muscle mass (sarcopenia) and water accumulation in the body. 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 myostatitis, 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].

Bioelectrical impedance analysis is a method for the complex assessment of body composition and is based on measurements of capacitive and active resistance of the human body. These can be used to identify fat and lean (free-fat) mass. The latter is represented by body cell mass, consisting mainly of musculoskeletal mass, and extracellular mass, comprised mainly of extracellular fluid. Although fat is located within cells, it and body cell mass are conditionally considered to be different components of the body in this analysis. Fat is practically non-conductive. Cells are capacitors (*i.e.*, an electrolyte solution surrounded by a dielectric membrane) and give

rise to the capacitive component of resistance, while free extracellular fluid contributes to the active resistance. Therefore, it is possible to assess body composition (amount of fat, body cell mass, and extracellular fluid) by analyzing the capacitive and active components of resistance of the body[10-13].

Although recent publications have reported the associations of some taxa of the gut microbiome with sarcopenia diagnosed with computed tomography[4,5], there are not studies that investigated the relations between the gut microbiome and all three main body components (fat, cells, and extracellular fluid) in cirrhosis.

The aim of the present study was to assess the relationship between the gut microbiota and body composition in cirrhosis.

MATERIALS AND METHODS

Patients

In this observational study, 97 patients with cirrhosis were consecutively admitted to the Department of Hepatology of Clinic for Internal Medicine, Gastroenterology and Hepatology at Sechenov University (Moscow, Russia) and screened for participation. The procedures were explained to potential participants, and written informed consent was obtained before enrollment. The study was approved by the Ethics Committee of Sechenov University in accordance with the Declaration of Helsinki.

The inclusion criteria were diagnosis of cirrhosis verified by histological examination or clinical, biochemical, and ultrasound findings, and age between 18 and 70 years. The exclusion criteria included use of lactulose, lactitol, or other prebiotics, probiotics, antibiotics, or metformin in the past 6 wk, alcohol consumption in the past 6 wk, or diagnosis of inflammatory bowel disease, cancer, or any other serious disease. The exclusion criteria were specifically selected to remove the influence of these factors on the composition of the gut microbiota. Of the original 97 patients screened for inclusion, 46 were enrolled in the study while 51 were excluded (Figure 1).

In addition, 14 healthy persons were examined.

Gut microbiome analysis

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.

A stool sample was taken into a sterile disposable container the morning after admission and immediately frozen at -80 °C[14].

Total DNA was isolated using AmpliPrime DNA-sorb-AM kit (NextBio, Russia) for clinical specimens, according to the manufacturer's protocol. The isolated DNA was stored at -20 °C. For qualitive and quantitative assessment of the isolated DNA we used NanoDrop 1000 equipment (Thermo Fisher Scientific, Waltham, MA, United States). 16S library preparation was carried out according to the protocol of 16S Metagenomic Sequencing Library Preparation (Illumina, San Diego, CA, United States), which is recommended for Illumina MiSeq sample prep. The first round of amplification of V3-V4 16S rDNA variable regions was performed using the following primers: forward (TCGTCGGCAGCGTCAGATGTGTATAAGAGACAG-CCTACGGGNGGCWGCAG) and reverse (GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAG-GACTACHVGGGTATCTAATCC). These primers are aimed at the amplification of bacterial (more than 90%) but not archaeal (less than 5%) rRNA genes. The amplification program (Applied Biosystems 2720 Thermal Cycler, Foster City, CA, United States) was the following: (1) 95 °C for 3 min; (2) 30 cycles: 95 °C for 30 s; 55 °C for 30 s; 72 °C for 30 s; (3) 72 °C for 5 min; and (4) 4 °C.

The derived amplicons were purified using Agencourt AMPure XP (Beckman Coulter, Brea, CA, United States) beads according to the manufacturer's protocol. The second amplification round was used for double-indexing samples with a combination of specific primers. The amplification program was the following: (1) 95 °C for 3 min; (2) 8 cycles: 95 °C for 30 s; 55 °C for 30 s; 72 °C for 30 s; (3) 72 °C for 5 m; and (4) 4° C.

The purification of PCR products was also carried out using Agencourt AMPure XP. Concentration of the derived 16S rDNA libraries was measured using Qubit® 2.0 fluorimeter (Invitrogen, Carlsbad, CA, United States) using QuantiT™ dsDNA High-Sensitivity Assay Kit. The purified amplicons were mixed equimolarly according to the

derived concentration values. Quality of the libraries was evaluated using Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, United States) and Agilent DNA 1000 Kit. Sequencing was carried out on MiSeq machine (Illumina) and MiSeq Reagent Kit v2 (paired-end reads, 2 × 300 nt).

First, forward and reverse reads were merged using MeFiT and CASPER[15]. For the most samples more than 99% reads have been successfully merged. Non-merged reads have been excluded. Next, the merged reads were analyzed by the DADA2 package (a part of the Bioconductor project) for R[16] in order to infer RSV (ribosomal sequence variants). The analysis included the following steps: (1) Primer sequences were removed using cutadapt; (2) Reads were filtered by quality; (3) Error distribution models were derived based on read quality profiles; (4) Sequencing errors were estimated and corrected; (5) RSV sequences were obtained; and (6) Chimeric RSVs were eliminated. Next, taxonomic annotation of the derived RSVs was performed with DADA2 package using Silva (version 138) 16S reference sequence database[17].

Bioelectrical impedance analysis

Bioelectrical impedance analysis was performed on the day after patient admission in the morning, to ensure that the patient was on an empty stomach. The MEDASS device (Russia) was used for this purpose in accordance with the manufacturer's instructions.

The measurement was carried out by passing alternating current with frequencies of 5 and 50 kHz through the patient. Conduction originates almost entirely due to the extracellular fluid in the presence of constant current. With alternating current, the intracellular fluid also contributes to current conduction, depending on its frequency. 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. This software also calculated individual norms for each patient based on his/her anthropometric data, age, sex, and the results of a local population study. Patients with fat mass value above the upper limit of their individual norm were included in the group of patients with excess fat mass, and those with body cell mass

below the lower limit of their individual norm were included in the group of patients with cell mass deficiency. Similarly, patients with extracellular fluid amount higher than the upper limit of their individual norm were included in the group of patients with excess extracellular fluid.

The underlying principle of this analysis and methods used for calculating the indicators have been described in detail in previous publications[10,11].

We used the ratio of body cell mass to free-fat mass to assess body cell mass and the ratio of extracellular fluid to total fluid to quantitate the amount of extracellular fluid. This method ensured minimal influence of values of fat and body cell mass and extracellular fluid on each other.

Statistical analysis

Statistical analysis was performed with STATISTICA 10 (StatSoft Inc., Tulsa, OK, United States). The data are presented as medians (interquartile ranges). The abundance of taxa of the gut microbiome is presented as a percentage. Differences between continuous variables were assessed with the Mann-Whitney test. Fisher's exact test was used to assess the differences between categorical variables. Correlations between variables were computed using Spearman's rank correlation. If the compared groups were differed in age, sex or severity of cirrhosis, multivariate regression analysis was performed. P-values ≤ 0.05 were considered as statistically significant.

RESULTS

The characteristics of the patients enrolled in the study are listed in Table 1.

The amount of extracellular fluid and the fat mass were higher but the body cell mass was lower in patients with cirrhosis than in healthy individuals. The abundance of Bacteroidetes, Proteobacteria, and Bacilli was higher, but the abundance of Firmicutes and Clostridia was lower in the gut microbiome of these patients than in that of healthy individuals (Table 2).

The fat mass was found to increase in 23/46 (50.0%) patients. The abundance of Bacteroidetes, Desulfobacteria, *Barnesiellaceae*, *Coriobacteriaceae*, *Eggerthellaceae*, *Marinifilaceae*, *Bilophila, Senegalimassilia, Slackia*, and *Parasutterella* was higher in the gut microbiome of these patients. On the other hand, the abundance of *Clostridiaceae, Odoribacter*, and *Veillonella* was decreased in the gut microbiome of these patients (Table 3).

The proportion of fat mass in total body mass showed a positive correlation with abundance of Bacteroidetes, Desulfobacteria, *Coriobacteriaceae*, *Barnesiellaceae*, *Bilophila*, *Collinsella*, *Megamonas*, *Parasutterella*, and *Slackia* and a negative correlation with the abundance of *Clostridiaceae*, *Campylobacter*, and *Veillonella* (Table 4).

Since the groups under comparison differed with respect to age, sex, and severity of cirrhosis, we performed a multivariate regression analysis and found that these changes in the gut microbiome are not independent factors affecting the percentage of fat mass in the total body mass of these patients.

The body cell mass was found to decrease in 15/46 (32.6%) patients. The abundance of *Bacteroidaceae* and *Eggerthella* increased in the gut microbiome of these patients, whereas that of *Erysipelatoclostridiaceae, Catenibacterium*, *Coprococcus*, *Desulfovibrio*, *Intestinimonas*, and *Senegalimassilia* decreased (Table 5).

The proportion of body cell mass correlated positively with the abundance of *Barnesiellaceae*, *Erysipelatoclostridiaceae*, *Anaerotruncus*, *Catenibacterium*, *Oscillospira*, and *Senegalimassilia*, whereas a negative correlation with abundance of *Bacteroidaceae* and *Veillonella* was observed (Table 4).

The amount of extracellular fluid increased in 22/46 (47.6%) patients. The abundance of Proteobacteria was increased in the gut microbiome of these patients. However, the abundance of Firmicutes, Bacilli, *Anaerovoraceceae*, *Christensenellaceae*, *Eggerthellaceae*, *Erysipelatoclostridiaceae*, *Erysipelotrichaceae*, *Oscillospiraceae*, *Peptococcaceae*, *Rikenellaceae*, *Actinobacteria*, *Collinsella*, *Hungatella*, *Slackia*, and *Senegalimassilia* was decreased in the gut microbiome of these patients (Table 6).

The proportion of extracellular fluid in total body fluid in these patients was positively correlated to the abundance of Proteobacteria and *Bilophila*, and negatively correlated to that of Firmicutes, Bacilli, and Clostridia in the gut microbiome (Table 4).

There was no significant difference between these groups of patients in terms of the indices of microbiota biodiversity (Shannon, Chao1, ACE—Figure 2)[18], and no significant correlation was found between the latter and indicators of body composition.

Comparison of the gut microbiome at the Phylum level between patient groups is represented in Figure 3.

Patients with clinically significant ascites (stages 2 and 3 according to the classification of the International Club of Ascites; n = 9) had a higher abundance of Proteobacteria [17.3 (7.9-23.2)% *vs* 5.03 (2.26-7.93)%; P = 0.031] and a lower abundance of Actinobacteria [0.11 (0.09-0.66)% *vs* 1.04 (0.36-3.89)%; P = 0.019] and Bacteroidetes [35.2 (12.9-37.6)% *vs* 43.2 (29.4-60.3)%; P = 0.046] in their gut microbiome than patients without clinically significant ascites (n = 37).

The abundance of Firmicutes decreases in patients with excess extracellular fluid regardless of the presence of clinically significant ascites, while a decrease in the abundance of Bacteroidetes occurs only in those patients with excess extracellular fluid who have clinically significant ascites (Figures 4 and 5). The abundance of Proteobacteria is progressively increasing, and the abundance of Actinobacteria is progressively decreasing in the transition from patients without excess of extracellular fluid to patients with excess of extracellular fluid but without clinically significant ascites and further to patients with clinically significant ascites (Figures 4 and 5).

DISCUSSION

Gut dysbiosis is common in cirrhosis and is associated with the development of hepatic encephalopathy, lower serum albumin and cholinesterase levels, systemic inflammation, and poorer short- and long-term prognosis[19-21]. The aim of the present

study was to assess the relationship between the gut microbiota and body composition in patients with cirrhosis.

The changes in the body composition and gut microbiome with cirrhosis in our study were mostly consistent with earlier findings[1,6,19-21].

Although malnutrition is typical for patients with cirrhosis, half of the patients enrolled in the present study had an excess of fat mass. This can be explained by the fact that 30% of included patients had compensated cirrhosis (class A Child-Pugh score), while severe cirrhosis (Child-Pugh class C), for which malnutrition was most characteristic, was observed in less than a quarter of the patients. Inclusion of a small percentage of patients with severe cirrhosis is both a disadvantage and an advantage of our study, since we have included patients with all degrees of severity of cirrhosis, which enables a more generalized analysis.

Cirrhosis was less severe in patients with excess fat mass. In terms of the taxa of gut microbiota, the increased abundance of Bacteroidetes in these patients was the most significant change. However, obesity in patients without cirrhosis is associated with a decrease in the abundance of Bacteroidetes[22,23]. The change in abundance of Bacteroidetes in cirrhosis is controversial: studies have reported its decrease[24-26], increase[27], and non-significant changes[19]. One study reports an increased in Bacteroidetes abundance in compensated cirrhosis, which decreases further to attain normal levels with decompensation[28]. Patients with excess fat mass had less severe cirrhosis and were older than patients without excess fat mass. Multivariate regression analysis established that the age and Child-Pugh score value, but not the gut microbiome status, significantly determine the level of fat mass in patients with cirrhosis, thereby resolving this contradiction.

Patients with deficiency in body cell mass that were considered as persons with sarcopenia accounted for one third of the included patients. They also had another sign of malnutrition (namely, hypoalbuminemia), although they did not show significant difference in values of other biomarkers of liver failure (serum bilirubin and prothrombin) and portal hypertension (clinically significant ascites and spleen length)

compared to patients with normal body cell mass. Patients grouped with respect to body cell mass deficiency did not show significant differences in the gut microbiome at the level of higher taxa (phyla), although the abundance of *Bacteroidaceae* was higher in patients with deficiency in body cell mass. These patients had also increased abundance of *Eggerthella*, which is considered as a biomarker for fragility[29,30]. These findings are consistent with recent studies of the gut microbiome in cirrhosis patients with sarcopenia[4,5]. However, body cell mass deficiency in cirrhosis patients was found to be associated with a decrease in the abundance of *Coprococcus*, *Intestinimonas*, *Catenibacterium*, and *Barnesiellaceae* in our study, which was not reported in these earlier studies[4,5]. A decrease in the abundance of the butyrate-producing *Coprococcus* has been reported in hemodialysis patients with sarcopenia[31]. *Intestinimonas* produces butyrate and vitamin B12, and is involved in the metabolism of bile acids and glucose in hosts[32-34]. *Catenibacterium* is associated with the development of insulin resistance in morbid obesity[35], so it is quite possible that a decrease in its content in the gut microbiome is associated with malnutrition. A decreased abundance of *Barnesiellaceae* and increased abundance of *Veillonella* in the gut microbiome, found in our study in patients with deficiency in body cell mass, have been previously described in the general cohort of sarcopenic patients[36], but not in earlier investigations of sarcopenia in cirrhosis patients[4,5].

The pathophysiology of sarcopenia in cirrhosis has started to attract more attention[37]. The present study is the third publication to describe the changes in the gut microbiome in this condition. The major findings from all three publications partially correspond to each other, but there are also some differences between them, which highlights the need for further studies of these relationships. We did not obtain a significant correlation between the main taxa responsible for bacterial translocation (Proteobacteria and Bacilli) and a decrease in the body cell mass. This diminishes the plausibility of the hypothesis of their relationship. Unfortunately, we were unable to investigate blood levels of myostatin and ammonia and the correlations between them, the body cell mass, and taxa of the gut microbiome. Thus, the exact mechanisms of the

effects of gut microbiota on muscle mass in cirrhosis should be established by further researchers.

An increase in the content of extracellular fluid in the body was accompanied by a more frequent development of clinically significant ascites and splenomegaly. Among the large number of taxa that changes were associated with an increase in the content of extracellular fluid in patients with cirrhosis, the most important changes were an increase in the abundance of Proteobacteria and a decrease in that of Firmicutes.

An increase in the abundance of Proteobacteria and other taxa belonging to this phylum has been earlier described for patients with cirrhosis compared to healthy individuals in most studies[19,24,26-28,38-44]. Proteobacteria have an active endotoxin, which is believed to be associated with the development of systemic inflammation, vasodilation, and subsequent compensatory accumulation of extracellular fluid in cirrhosis[45]. Despite multiple reviews touching upon this aspect, our present study is the first to prove that an increased abundance of Proteobacteria in the gut microbiome is indeed associated with the accumulation of extracellular fluid in patients with cirrhosis.

Firmicutes are mainly represented by the class of autochthonous strict anaerobes Clostridia and the class of facultative anaerobes Bacilli. Among the Bacilli, there are many opportunistic species associated with endogenous infections in cirrhosis[46]. The abundance of Clostridia and Bacilli changes differently with the progression of cirrhosis: while the former decreases, the latter increases[19,28]. Therefore, the net change in the abundance of Firmicutes in cirrhosis has been reported to increase in some studies[25] and decrease in others[41]. The association of increased extracellular fluid content with decreased abundance of beneficial Clostridia was expected, but the observed association with a decreased abundance of harmful Bacilli was surprising. However, Bacilli, unlike Proteobacteria, do not produce endotoxin. Therefore, it seems that it is endotoxin, but not other factors of bacterial pathogenicity, plays a major role in the accumulation of extracellular fluid in patients with cirrhosis.

Our study showed that fluid retention develops before the development of clinically significant ascites. At the same time, there is a further increase in the abundance of Proteobacteria with a decrease in the abundance of Bacteroidetes in patients with clinically significant ascites. We observe a stepwise change in the gut microbiome at the phylum level with an increase in the content of extracellular fluid in the body: first Proteobacteria displace Firmicutes, and then they override Bacteroidetes (Figure 5).

The strength of the present study includes the facts that this represents the first comprehensive report on the relationship of gut microbiota with changes in body composition in cirrhosis and the first confirmation that an increased abundance of Proteobacteria is associated with increased extracellular fluid in patients with cirrhosis. In addition, this study is one of the few works that have investigated the relationship between the gut microbiome and sarcopenia in patients with cirrhosis.

The limitation of our study lies in its small sample size, although this did not prevent us from obtaining significant results.

CONCLUSION

In conclusion, we have shown that the different body components are differently associated with changes in the gut microbiome in cirrhosis. The amount of fat mass unlikely depends on its composition, the amount of body cell mass is associated with the changes in the abundance of its minor taxa, and the amount of extracellular fluid is associated with the changes in the abundance of the main taxa of the gut microbiome (Proteobacteria, Firmicutes, and Bacteroidetes).

ARTICLE HIGHLIGHTS

Research background

Gut dysbiosis and changes in body composition (*i.e.*, a decrease in proportion of muscle mass and an increase in extracellular fluid) are common in cirrhosis.

Research motivation

To study the relationship between the gut microbiota and body composition in cirrhosis.

2

Research objectives

To study the relationship between the gut microbiota and various body components in cirrhosis.

Research methods

The observational study included 46 patients with cirrhosis. Stool microbiome was assessed using 16S rRNA gene sequencing. Multifrequency bioelectrical impedance analysis was performed to assess body composition in these patients.

Research results

The abundance of *Bacteroidaceae* and *Eggerthella* increased, whereas that of *Coprococcus*, *Erysipelatoclostridiaceae*, *Intestinimonas*, *Desulfovibrio*, *Catenibacterium*, and *Senegalimassilia* decreased in the gut microbiome of patients with deficiency of body cell mass. Proteobacteria abundance was increased, whereas Firmicutes, *Oscillospiraceae*, *Rikenellaceae*, *Actinobacteria*, Bacilli, *Christensenellaceae*, *Collinsella*, *Eggerthellaceae*, *Erysipelatoclostridiaceae*, *Erysipelotrichaceae*, *Anaerovoraceceae*, *Hungatella*, *Slackia*, *Peptococcaceae*, and *Senegalimassilia* abundance decreased in cirrhosis patients with excess extracellular fluid.

Research conclusions

The changes in amount of body cell mass and extracellular fluid are associated with changes in the gut microbiome in cirrhosis patients.

Research perspectives

Further studies are required to establish the mechanisms of the influence of the gut microbiota on the value of the body cell mass.

68247_Auto_Edited.docx

ORIGINALITY REPORT

3%
SIMILARITY INDEX

PRIMARY SOURCES

1	Roman Maslennikov, Vladimir Ivashkin, Irina Efremova, Elena Poluektova et al. "Gut Dysbiosis and Hemodynamic Changes as Links of the Pathogenesis of Complications of Cirrhosis", Research Square Platform LLC, 2021 Crossref Posted Content	40 words — 1%
2	Roman Maslennikov, Vladimir Ivashkin, Irina Efremova, Elena Poluektova, Anna Kudryavtseva, George Krasnov. "Gut dysbiosis and small intestinal bacterial overgrowth as independent forms of gut microbiota disorders in cirrhosis", World Journal of Gastroenterology, 2022 Crossref	27 words — 1%
3	www.molvis.org Internet	15 words — < 1%
4	www.wjgnet.com Internet	14 words — < 1%
5	link.springer.com Internet	13 words — < 1%

EXCLUDE QUOTES ON
EXCLUDE BIBLIOGRAPHY ON
EXCLUDE MATCHES < 12 WORDS