https://doi.org/10.22416/1382-4376-2024-34-3-53-61
UDC 616.36-004-06:616.381-003.217]-07:572.087

Parameters of the Component Composition of the Body and Their Relationship with the Development of Ascites in Liver Cirrhosis

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Aim: to evaluate the relationship of body composition components with the development of ascites in patients with liver cirrhosis.
Materials and methods. One hundred and ten patients (44 men and 66 women) with the established diagnosis of liver cirrhosis were treated at the University Clinical Hospital No 2 of the Sechenov University. The assessment of the component composition of the patients' body was carried out using the ABC-01 "MEDASS" device ("MEDASS", Russia). Ascites diagnosis was performed using ultrasound examination of the abdominal cavity and retroperitoneal space.
Results. The values of body mass index ($p < 0.001$), fat mass ($p = 0.002$), active cell mass ($p < 0.001$), and phase angle ($p < 0.001$) were lower in patients with ascites than without it. Patients with a lower percentage of body fat mass had a more severe ascites severity and vice versa, and the proportion of fat mass was generally higher in women than in men ($r = –0.290$; $p = 0.002$). Patients with lower active cell mass had higher ascites severity ($r = –0.380$; $p < 0.001$). However, this indicator was lower in women than in men. Significant negative correlations were revealed between fat mass, active cell mass, phase angle ($r = –0.395$; $p < 0.001$) and the severity of ascites.
Conclusion. Our study confirms the importance of body composition parameters in the development of ascites in patients with cirrhosis of the liver. Insufficient amount of fat and muscle mass, as well as low values of the phase angle according to the results of bioimpedance can become predictors of the development of ascites. Evaluation of these components can be used in prognostic models to identify patients with an increased risk of ascites. Further research in this area will help to better understand the mechanisms of ascites development and develop effective methods of prevention and treatment of this complication in patients with liver cirrhosis.
Keywords: bioimpedance analysis, fat mass, muscle mass, ascites, liver cirrhosis
Conflict of interest: the authors declare no conflict of interest.

For citation: Kruchinina M.V., Osipenko M.F., Parulikova M.V., Gromov A.A. Electrical and Viscoelastic Parameters of Erythrocytes as a Part of Diagnostic Models for Differentiating Fatty Liver Disease of Mixed Genesis from Non-Alcoholic and Alcohol-Related Fatty Liver Disease. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2024;34(3):53–61. https://doi. org/10.22416/1382-4376-2024-34-3-53-61

Параметры компонентного состава тела и их взаимосвязь с развитием асцита при циррозе печени

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Цель: оценить взаимосвязь компонентов состава тела с развитием асцита у пациентов с циррозом печени.
Материалы и методы. Обследованы 110 пациентов (44 мужчины и 66 женщин) с установленным диагнозом «цирроз печени», проходивших лечение в Университетской клинической больнице № 2 Сеченовского Университета. Оценку компонентного состава тела пациентов проводили при помощи прибора АВС-01 «МЕДАСС» (НТЦ «МЕДАСС», Россия). Диагностику асцита выполняли при помощи ультразвукового исследования органов брюшной полости и забрюшинного пространства.
Результаты. Значения индекса массы тела ($p < 0,001$), жировой массы ($p = 0,002$), активной клеточной массы ($p < 0,001$), фазового угла ($p < 0,001$) были ниже у пациентов с асцитом по сравнению с показателями пациентов без него. Пациенты с более низким процентом жировой массы в компонентном составе тела имели более тяжелую степень тяжести асцита и наоборот. Причем показатель доли жировой массы в целом был

выше у женщин, чем у мужчин (r = –0,290; p = 0,002). У пациентов с более низкой активной клеточной массой степень тяжести асцита была выше (r = –0,380; p < 0,001). При этом у женщин данный показатель был ниже, чем у мужчин. Выявлены достоверные отрицательные корреляции между жировой массой, активной клеточной массой, фазовым углом (r = –0,395; p < 0,001) и степенью тяжести асцита.

Заключение. Наше исследование подтверждает важность изучения параметров состава тела в развитии асцита у пациентов с циррозом печени. Недостаточное количество жировой и мышечной масс, а также низкие значения фазового угла по результатам биоимпедансометрии могут стать предикторами развития асцита у пациентов с циррозом печени. Оценка этих компонентов может быть использована в прогностических моделях для идентификации пациентов с повышенным риском развития асцита. Дальнейшие исследования в этой области помогут лучше понять механизмы развития асцита и разработать эффективные методы профилактики и лечения данного осложнения у пациентов с циррозом печени.

Ключевые слова: биоимпедансный анализ, жировая масса, мышечная масса, асцит, цирроз печени

Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Жариков Ю.О., Жаркова М.С., Гаджиахмедова А.Н., Алиева А.М., Николенко В.Н., Ивашкин В.Т. Параметры компонентного состава тела и их взаимосвязь с развитием асцита при циррозе печени. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2024;34(3):53–61. https://doi.org/10.22416/1382-4376-2024-34-3-53-61

Introduction

Liver cirrhosis (LC) is a chronic progressive disease characterized by damage to the liver parenchyma and changes in its architectonics [1]. One of the main complications of LC is ascites — the accumulation of free fluid in the abdominal cavity [2]. However, the mechanisms underlying the development of ascites in LC are not fully understood. Changes in the structure of the lymphatic system may play an important role in the pathogenesis of this complication. In the early stages of LC, the lymphatic system helps prevent the development of ascites by reabsorbing excess fluid in the abdominal cavity [3]. As a result, lymph flow intensifies, stimulating hepatic lymphangiogenesis. However, in patients with progressive LC, this compensatory mechanism is insufficient [4]. In recent years, more attention has been paid to the role of body composition in the course of LC. It is known that changes in body composition, such as sarcopenia (loss of muscle mass), have a negative impact on many organ systems [5, 6]. However, data on the relationship between sarcopenia and obesity with ascites are limited.

One of the indicators obtained as a result of bioimpedance analysis is the phase angle, which is the arctangent of the ratio of reactive and active resistances for some current frequency. It characterizes the capacitive properties of cell membranes and the viability of biological tissues: it is believed that the higher the phase angle, the better the condition of tissues [7].

Thus, it is required to study the prognostic significance of the component body composition in the development of complications in patients with LC. Early detection and prediction of ascites development are of great practical importance for effective treatment of patients.

Aim: to evaluate the relationship of body composition components with the development of ascites in patients with LC.

Materials and methods

An observational cross-sectional single-center study was conducted, which included analysis of data for the period from February 2020 to December 2022. At the initial stage of the study, which included initial diagnosis of liver disease, analysis of medical records and determination of disease severity according to the Child — Pugh scale, we selected 150 patients. The patients were treated in the Department of Hepatology of the V.Kh. Vasilenko Clinic of Propaedeutics of Internal Diseases, Gastroenterology and Hepatology of the Sechenov University.

Criteria for inclusion of patients in the study: confirmed diagnosis of LC; age from 18 to 70 years. Criteria for exclusion: refusal of further participation in the study; presence of conditions or exacerbations of concomitant diseases diagnosed during the study. According to the above criteria, 110 patients (44 men and 66 women) were examined.

The etiology of liver cirrhosis in the included patients: alcoholic genesis (32.6 %), viral hepatitis C (10.9 %), primary biliary cholangitis (8.7 %), primary sclerosing cholangitis (4.3 %), autoimmune hepatitis (10.9 %), metabolic-associated liver diseases (8.7 %), Wilson's disease (6.5 %), mixed and cryptogenic genesis (17.4 %).

Anthropometric examination was carried out according to the methodological requirements with the assessment of the component body

Table 1. Comparative characteristics of patients with liver cirrhosis with and without ascites
Таблица 1. Сравнительная характеристика больных циррозом печени с асцитом и без асцита

Parameter ***Показатель***	**Patients with ascites** ***Пациенты с асцитом*** **(*n* = 53)**	**Patients without ascites** ***Пациенты без асцита*** **(*n* = 57)**	***p***
Gender / *Пол, n* (%) males / *мужчины* females / *женщины*	 21 (39.6) 32 (60.4)	 23 (40.4) 34 (59.6)	0.124
Age / *Возраст, Me* (IQR)	48.5 (41–55)	43.5 (39–51)	0.343
Anthropometric indicators ***Антропометрические показатели*** ***Me* (IQR)**			
Height, cm / *Рост, см*	170 (166.9–177.3)	174.8 (169.8–182)	0.422
Weight, kg / *Вес, кг*	70 (61.5–81.9)	77.15 (68.5–85.7)	0.651
Waist/hip index / *Индекс талия/бедра*	1.02 (0.91–1.09)	0.96 (0.86–1.03)	0.053
BMI, kg/m^2 / *ИМТ, кг/м^2*	25 (22.5–28.7)	28.5 (24.2–31.6)	0.001*
Body composition ***Компонентный состав тела*** ***Me* (IQR)**			
Fat mass, % / *Жировая масса, %*	29.9 (24.5–37.4)	35.5 (27.7–41.3)	0.002*
Skeletal muscles, % / *Скелетная мускулатура, %*	46.5 (42.8–49.4)	43.5 (40.5–47)	0.063
Active cell mass, % / *Активная клеточная масса, %*	48.6 (44.8–52.8)	53.55 (49.7–56.2)	0.001*
Phase angle, degrees / *Фазовый угол, градусы*	5.2 (4.5–5.83)	5.9 (5.3–6.5)	0.001*
Ultrasound data of the abdominal organs ***Данные УЗИ органов брюшной полости*** ***Me* (IQR)**			
Spleen length, mm / *Длина селезенки, мм*	160 (141.75–173.5)	145 (119–168)	0.258
Spleen width, mm / *Ширина селезенки, мм*	58 (48–67)	55 (43–63)	0.067
Diameter of the splenic vein, mm *Диаметр селезеночной вены, мм*	11 (8.83–12)	9.4 (8–11)	0.043*
Diameter of the portal vein, mm *Диаметр воротной вены, мм*	12.8 (11–14.2)	12.5 (11–14)	0.019*

Note: *Me* — median, IQR — interquartile range, BMI — body mass index; * — statistically significant differences.
Примечание: *Me* — медиана, IQR — межквартильный интервал, ИМТ — индекс массы тела; * — статистически значимые различия.

composition of the patients using the device AVS-01 "MEDASS" ("MEDASS", Russia) [6].

Diagnosis of ascites was performed taking into account the objective examination of patients, as well as according to the results of ultrasound examination of the abdominal cavity and retroperitoneum. When assessing ascites, the classification proposed by the International Ascites Club (IAC) was used.

Statistical analysis was performed in Statistica 10 (StatSoft Inc., USA). Data are presented as medians (*Me*) and interquartile ranges (IQR). The association between variables was evaluated by Spearman rank correlation method. Differences between continuous variables were determined using the Mann — Whitney test. P-value less than 0.05 was considered statistically significant.

A favorable opinion of the local ethics committee of the I.M. Sechenov First Moscow State Medical University (Sechenov University) was obtained (Protocol No. 04-21, February 18, 2020).

Results

Presence of ascites of 2–3 degree was diagnosed in 19.6 % of observations, esophageal varices of 2–3 degree — in 36.9 % of cases, presence of hepatic encephalopathy — 32.5 % of patients, body mass index (BMI) — 27.0 (23.6–30.1) kg/m^2. Child — Pugh scale scores in men and women were 9 (7.3–11.8) and 7 (6–9) points, respectively. The duration of the disease ranged from 4 months to 12 years, with a median of 4.3 years.

During statistical analysis the patients were divided into groups: groups of patients with LC who were diagnosed with ascites of different severity (n = 53) and a group of patients with LC without ascites (n = 57). When comparing the above groups, the following differences were found: body mass index ($p < 0.001$), fat mass ($p = 0.002$), active cell mass ($p < 0.001$), phase angle ($p < 0.001$) were significantly lower in patients with ascites (Table 1) than without it.

Table 2. Ascites severity and body composition components in men and women
Таблица 2. Степень тяжести асцита и компоненты состава тела у мужчин и женщин

Parameter / *Показатель*	Males / *Мужчины* (n = 44)	Females / *Женщины* (n = 66)	p
No ascites / *Нет асцита, n* (%)	23 (52.27)	34 (51.52)	0.699
Ascites severity / *Степень тяжести асцита, n* (%)			
I	8 (18.18)	18 (27.27)	
II	10 (22.73)	12 (18.18)	
III	3 (6.82)	2 (3.03)	
Fat mass, % *Жировая масса, % Me* (IQR)	27.15 (22.83–31.83)	36.65 (30.83–43.08)	< 0.001*
Musculoskeletal mass, % *Скелетно-мышечная масса, % Me* (IQR)	49.60 (46.90–51.38)	42.50 (40.33–45.08)	< 0.001*
Active cell mass, % *Активная клеточная масса, % Me* (IQR)	53.35 (50.08–56.35)	49.50 (46.18–53.75)	0.002*
Phase angle, degrees *Фазовый угол, градусы Me* (IQR)	6.0 (5.40–6.53)	5.20 (4.73–5.98)	< 0.001*

Note: *Me* — median, IQR — interquartile range; * — statistically significant differences.
Примечание: *Me* — медиана, IQR — межквартильный интервал; * — статистически значимые различия.

The diameters of splenic (p = 0.043) and portal (p = 0.019) veins were significantly larger in patients with ascites, indicating the role of portal hypertension in the development of ascites.

The prevalence of ascites with regard to severity and sex differences of patients is demonstrated in Table 2.

The data presented in Figure 1 show that patients with a lower percentage of fat mass had more severe ascites severity and vice versa. It should be noted that the percentage of fat mass was generally higher in women than in men.

To quantify the metabolically active tissue content in the body, active cell mass was determined using bioimpedance analysis (Fig. 2). It was found that the severity of ascites was higher in patients with lower active cell mass. At the same time, this indicator was lower in women than in men.

The same pattern was found in the phase angle study: patients with low values of this index had, as a rule, a more severe degree of ascites severity (Fig. 3).

Significant negative correlations of weak to moderate strength of association of fat mass,

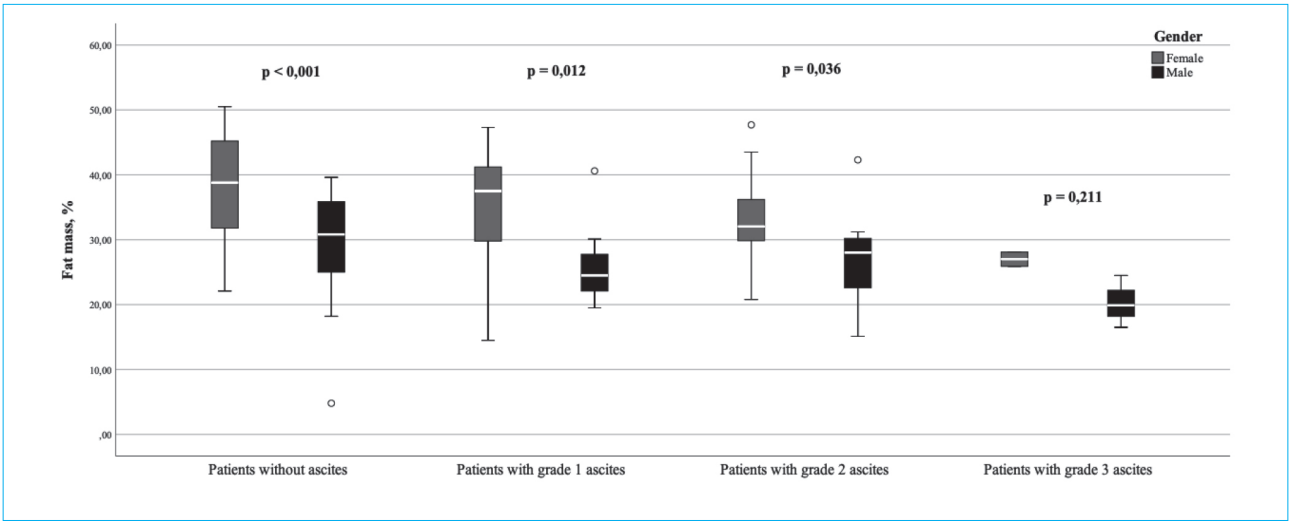

Figure 1. Fat mass of patients with cirrhosis (boxplot plot shows the distribution of data: median, quartiles and outliers among different patient groups)

Рисунок 1. Жировая масса пациентов с циррозом печени (на диаграмме боксплот показано распределение данных: медиана, квартили и выбросы среди разных групп пациентов)

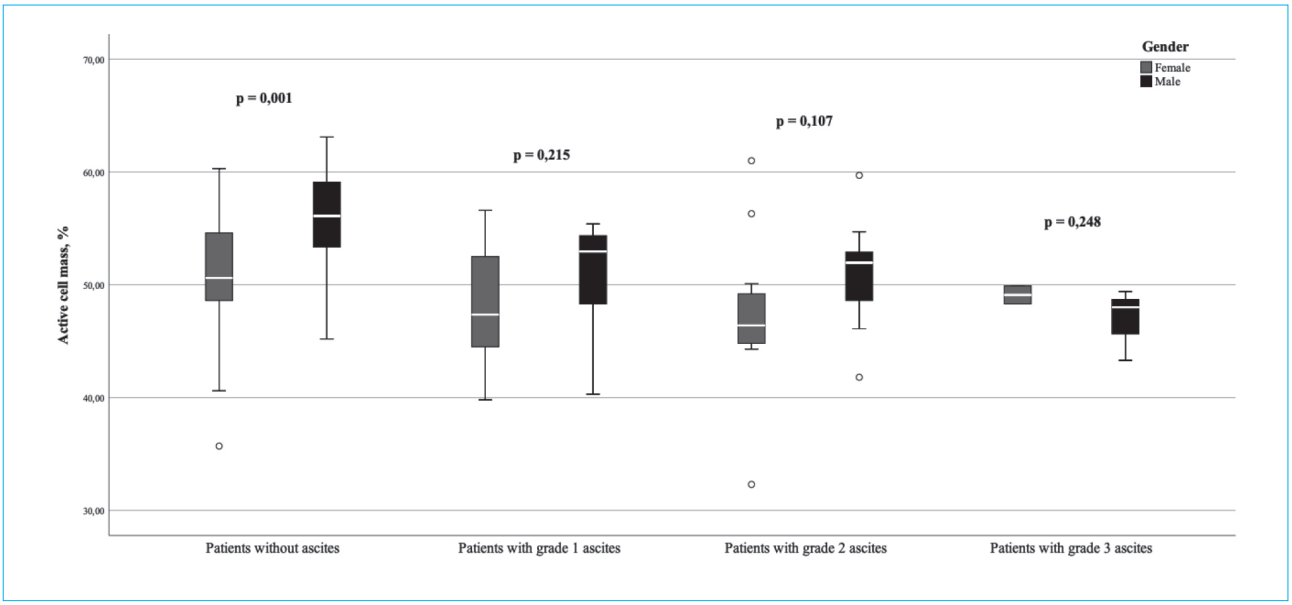

Figure 2. Active cell mass of patients with liver cirrhosis

Рисунок 2. Активная клеточная масса пациентов с циррозом печени

active cell mass, and phase angle with ascites severity were found (Fig. 4–6).

Discussion

Liver cirrhosis is one of the most common liver diseases and a major cause of ascites development [1]. Ascites is an accumulation of fluid in the abdominal cavity that can cause serious consequences in patients with LC [2]. Despite extensive research on this condition, the exact mechanisms of ascites development are not yet fully understood. In advanced cirrhosis, activation of compensatory vasoconstrictor pathways impairs tubular filtration, causing greater sodium and water retention in the kidneys. This mechanism increases lymphatic production, burdening the already inefficient lymphatic system [4]. The inability of the lymphatic system to recycle extravasated albumin may exacerbate pre-existing hypoalbuminemia, leading to changes in the transcapillary oncotic pressure gradient and exacerbating fluid imbalance. Therefore, changes associated with the lymphatic system (such as increased lymph flow with impaired functional ability of lymphatic vessels to absorb interstitial fluid, increased number and density of lymphatic vessels) leads to the development of refractory edema and ascites in cirrhotic patients [3, 4].

In addition, obesity leads to a number of structural and physiological changes in the lymphatic system, including increased lymphatic leakage, decreased contractility of collecting vessels, and changes in the architectonics of lymph nodes, which significantly affect lymphatic transport functions [8]. Based on our previous studies and taking into account the role of the lymphatic system in a wide range of physiological processes, we hypothesize that lymphatic dysfunction may be caused by changes in the component body composition and metabolic disorders, including obesity [9, 10].

The results of our study confirmed the hypothesis about the relationship between body component composition and ascites development in patients with LC. It was found that the distribution of fat and active cell masses in the patients' body, as well as phase angle may be significant factors in the development of this complication. Low values of the above factors are associated with an increased risk of developing ascites. This may be explained by the fact that patients with LC are often malnourished. Malnutrition is also a predictor of other complications of LC. A. Ruiz-Margáin et al. evaluated bioimpedance phase angle as a nutritional marker in their study and concluded that low phase angle values are associated with an increased incidence of hepatic encephalopathy (hazard ratio — 1.80 (1.07–3.03)) [11]. The problem of the influence of the body component composition on complications in LC was also studied by C. Lindqvist et al. The researchers determined that malnutrition is an independent predictor of early posttransplantation complications [12].

The active cell mass consists of muscle, internal organs and nerve cells. Therefore, it is worth

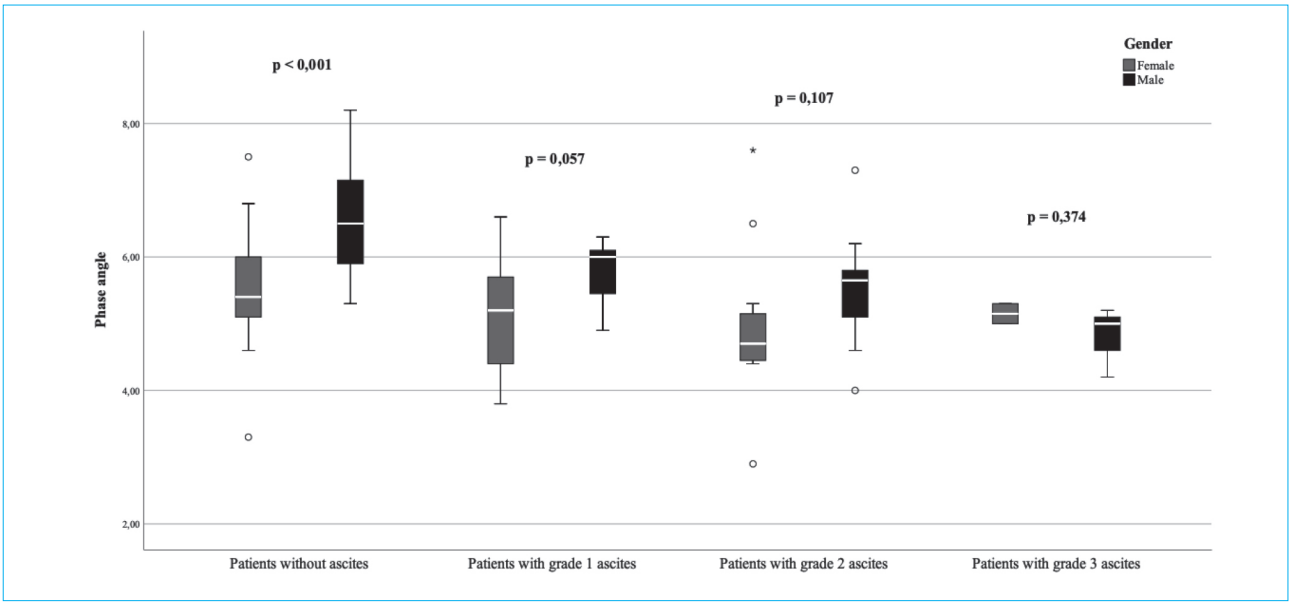

Figure 3. Phase angle of patients with liver cirrhosis

Рисунок 3. Фазовый угол у пациентов с циррозом печени

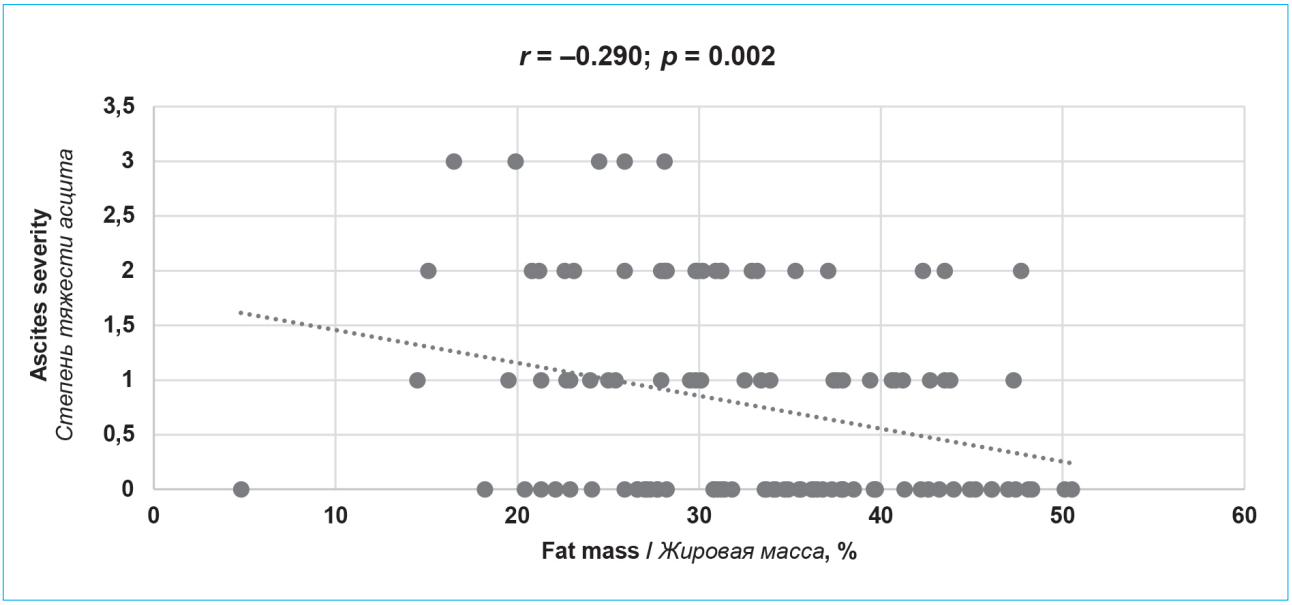

Figure 4. Correlation of the patient's fat mass percentage with the severity of ascites (the dots indicate the fat mass of patients depending on the severity of ascites; the line connecting the dots is a regression line and reflects the degree of dependence between two variables)

Рисунок 4. Корреляция доли жировой массы пациента со степенью тяжести асцита (в виде точек обозначены значения жировой массы пациентов в зависимости от степени тяжести асцита; линия, соединяющая точки, является линией регрессии и отражает степень зависимости между двумя переменными)

noting that our findings are consistent with the work of E. Dajti et al. who demonstrated the prognostic role of sarcopenia (loss of muscle mass) in the development of ascites (SHR — 2.083; 95 % CI: 1.091–3.978) [6]. X. Zeng et al. obtained similar results: patients with sarcopenia, compared with non-sarcopenic individuals, had a higher prevalence of LC-related complications (81.82 % vs. 62.24 %, $p < 0.001$), including ascites (RR = 1.827; 95 % CI: 1.259–2.651; $p = 0.002$) [13].

Thus, indicators of fat and active cell mass, as well as low phase angle values according to bioimpedansometry results may be predictors of ascites development in patients with LC. The

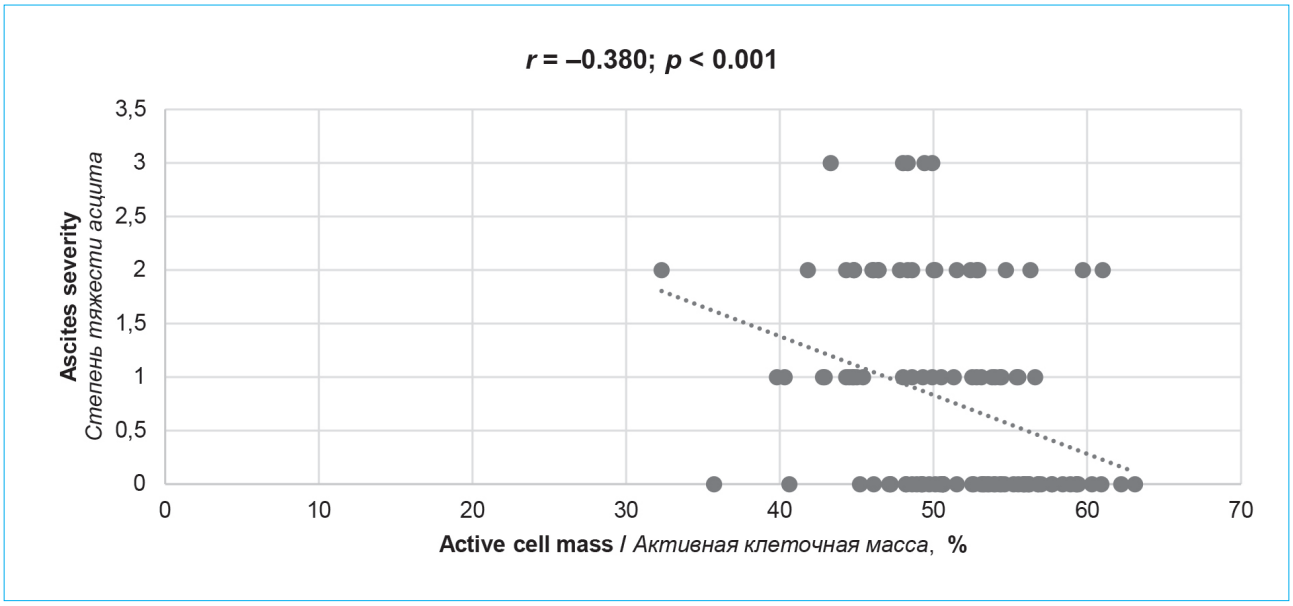

Figure 5. Correlation of active cell mass with the severity of ascites

Рисунок 5. Корреляция активной клеточной массы со степенью тяжести асцита

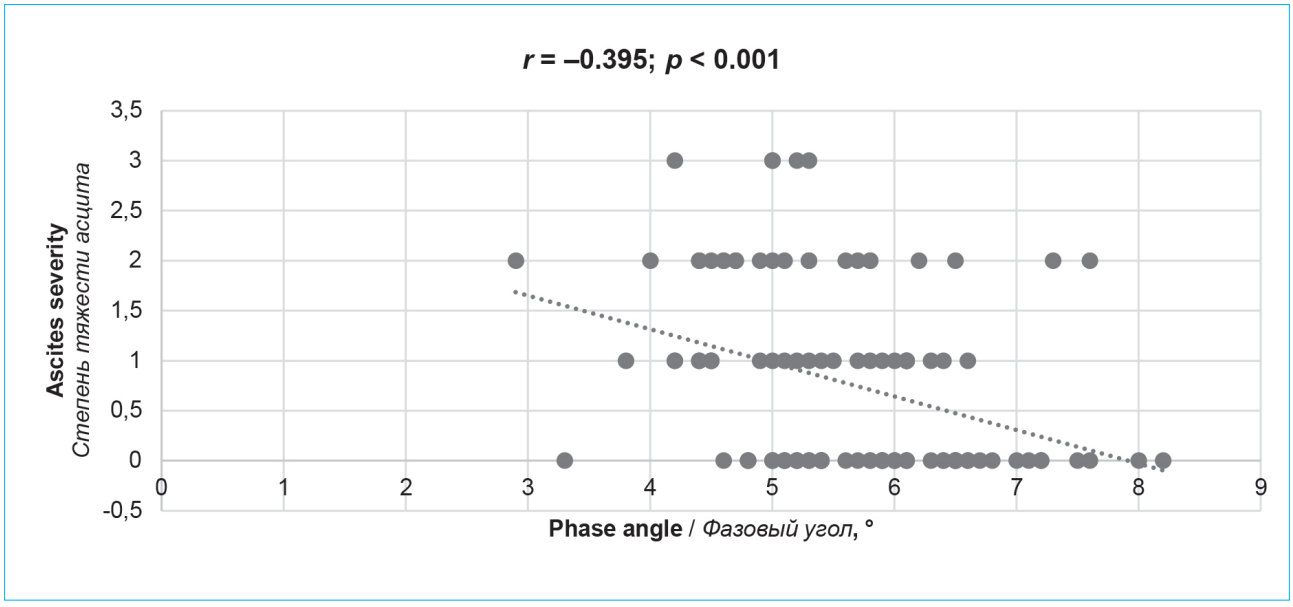

Figure 6. Correlation of the phase angle with the severity of ascites

Рисунок 6. Корреляция фазового угла со степенью тяжести асцита

mechanisms of these relationships require further studies.

Study limitations

We observed patients only from one clinical center, and a limited number of patients were included into the study.

Conclusion

Our study confirms the importance of body composition parameters in the development of ascites in patients with liver cirrhosis. Fat and active mass distribution and phase angle values play a significant role in the pathogenesis of ascites. Evaluation of these components can be used in prognostic models to identify patients at increased risk of developing ascites. Further research in this area will help to better understand the mechanisms of ascites development and develop effective methods of prevention and treatment of this complication in patients with liver cirrhosis.

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Submitted: 25.09.2023 Accepted: 01.02.2024 Published: 30.06.2024
Поступила: 25.09.2023 Принята: 01.02.2024 Опубликована: 30.06.2024