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Ю.Г. Самойлова, М.В. Матвеева*, Е.А. Хорошунова, Д.В. Подчиненова, Я.Л. Якимова

ФГБОУ ВО «Сибирский государственный медицинский университет» Минздрава России, Томск, Россия

ПРЕДИКТИВНАЯ ДИАГНОСТИКА ФАКТОРОВ РИСКА РАЗВИТИЯ САРКОПЕНИИ У ПОЖИЛЫХ ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

Y.G. Samoilova, M.V. Matveeva*, E.A. Khoroshunova, D.V. Podchinenova, Ya.L. Yakimova

Federal State Budgetary Educational Institution of Higher Education «Siberian State Medical University» of the Ministry of Health of Russia, Tomsk, Russia

Predictive Diagnostics of Risk Factors for the Development of Sarcopenia in Early Patients with Type 2 Diabetes

Резюме

Обоснование. Своевременная диагностика саркопении у пациентов с нарушениями углеводного обмена позволит повысить качество и продолжительность жизни. **Цель:** проанализировать наличие основных факторов риска развития саркопении у пациентов с пресаркопенией и СД 2 типа. **Материалы и методы.** Участвовало 82 пациента с СД 2 типа, которые были разделены на 2 группы: с пресаркопенией и группу сравнения. Проведены: анкетирование с помощью опросников (краткая форма оценки здоровья (Health Status Survey (SF-36)), оценка саркопении и качества жизни (Sarcopenia and Quality of Life — SarQoL), сила, помощь при ходьбе, подъем со стула, подъем по лестнице и падения — Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls — SARC-F), определения физической активности (International questionnaire on physical activity — IPAQ), оценка скорости ходьбы, динамометрия, биоимпедансометрия, анализ лабораторных показателей. Статистическая обработка проводилась с помощью программного обеспечения Statistica IBM (русская версия). Достоверными различия считались при p <0,05. **Результаты.** Чаще пациентов с пресаркопенией беспокоят онемение нижних конечностей, головокружение, снижение памяти, лабильность артериального давления, одышка при физической нагрузке. В обеих группах регистрировалось ожирение I ст. В основной группе снижена скорость ходьбы — 1,63 м/сек, по сравнению с группой сравнения — 1,25. Показатели гликемии у лиц с пресаркопенией выше -7,6 ммоль/л, чем в группе сравнения — 7,2. Уровень физической активности в основной группе ниже и составил 40 мин/ в сутки, а также снижен общий показатель качества жизни до 34,99. Пациенты с пресаркопенией чаще принимают: бигуаниды — 46 %, иНГЛТ-2 — 27 %, препараты сульфанилмочевины — 26 %, 46 % получают инсулинотерапию (p<0,05). В группе с пресаркопенией снижена жировая масса, площадь и процентное содержание висцерального жира по сравнению с группой сравнения. Индекс аппендикулярной мускулатуры в 1-ой группе составил 7,0 кг/м², во второй 7,5 кг/м². В 1-ой группе снижено содержание протеинов, минералов и общего количества воды. В лабораторных показателях в группе с пресаркопенией зарегистрированы дислипидемия, гипокальциемия, более высокие значения HbA1c, по сравнению с группой сравнения. **Заключение.** Для первичного скрининга саркопении у больных с СД 2 типа можно использовать динамометрию и биоимпедансометрию. Поддержание целевых параметров гликемии, коррекция дислипидемии, компенсация недостатка витамина Д и гипокальциемии способствует сохранению мышечной массы и силы.

Ключевые слова: *пресаркопения, биоимпедансометрия, сахарный диабет 2 типа, кистевая динамометрия*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

*Контакты: Мария Владимировна Матвеева, e-mail: matveeva.mariia@yandex.ru
*Contacts: Maria V. Matveeva, e-mail: matveeva.mariia@yandex.ru
ORCID ID: https://orcid.org/0000-0001-9966-6686

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Abstract

Objective. **Materials and methods:** 82 patients with type 2 diabetes mellitus participated, which were divided into 2 groups: probable sarcopenia and comparison groups. Conducted: questionnaire surveys (Health Status Survey (SF-36)), Sarcopenia quality and life assessment (SarQoL)), strength, assistance with walking, getting up from a chair, climbing stairs and falling — Strength, Assisted walking, getting up from a chair, Climbing stairs and Falls (SARC-F)), assessment of walking speed and physical activity, carpal dynamometry, bioimpedancemetry, analysis of laboratory parameters. **Results**: the difference between the conducted questionnaires is statistically insignificant. According to bioimpedansometry, obesity of the 1st degree was recorded in the lesions. In the group with presarcopenia, the main decrease in body composition parameters decreases. In addition, in the main group, the rate of intake is reduced, and decompensation of carbohydrate and lipid metabolism occurs. Differences were considered significant at $p < 0.05$. **Conclusion.** Dynamometry and bioimpedance can be used for primary screening of sarcopenia in patients with type 2 diabetes. Maintaining the main indicators of glycemia, correction of dyslipidemia, compensation for obesity D and hypocalcemia of obesity in muscle mass and mass.

Key words: *presarcopenia, bioimpedancemetry, type 2 diabetes mellitus, hand dynamometry*

Conflict of interests

The authors declare no conflict of interests

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DM — diabetes mellitus, EWGSOP- European Working Group on Sarcopenia in Older People, SarQoL– Sarcopenia and Quality of Life, SARC-F — Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls, SF-36 — Health Status Survey

Introduction

Type 2 diabetes mellitus (DM) is one of the most common chronic non-infectious diseases. Over the past decade, the number of patients with DM globally grew 2-fold; by the end of 2021, the number of patients with this condition exceeded 537 million people. According to forecasts by the International Diabetes Federation, by 2030, the number of patients with DM will reach 643 million people, by 2045 — 784 million people [1]. A majority of patients with type 2 DM have obesity or overweight [2]. In the results of the study titled NATION (2013–2015), the highest incidence of type 2 DM was recorded at the age of 65–69 years old [3]. Also, type 2 DM is associated with a high risk of cardiovascular disease and sarcopenia. With age, elderly people have less muscle bulk and strength. This condition is called sarcopenia and is more common in patients with type 2 DM [4]. Insulin resistance, dyslipidemia, hyperglycemia, oxidative stress contribute to faster reduction in muscle bulk, causing reduction and worsening of the quality of life of elderly people [4]. Diabetic polyneuropathy can also cause reduced muscle bulk and functions as a result of a reduced number of functional motor neurons and impaired coordination of muscle contraction. It has been found out that patients with type 2 DM and diabetic polyneuropathy have progressing reduction in muscle strength of lower limbs, whereas patients without diabetic polyneuropathy had their muscle strength preserved [5]. Nevertheless, currently available information whether diabetic polyneuropathy or age-associated reduction in the number of motor neurons have higher impact on reduced muscle strength is controversial.

Development and progression of sarcopenia in type 2 DM can cause vitamin B_{12} deficiency. Vitamin a B_{12} deficiency results in neurogenic disorders including muscle weakness, which increases the risk of falls. Approximately 25 % of cases of reduced vitamin B_{12} levels are accounted for metformin therapy [6]. However, metformin has a reliable evidence base and is a drug of choice in patients with type 2 DM for insulin resistance reduction [7].

Data on the incidence of sarcopenia are controversial, since there are no uniform diagnostic criteria. The results of a study conducted in the Moscow Region during examination of patients with type 2 DM of middle and elderly age (n = 42, mean age: 64 [60;70] years old) with the use of X-ray densitometry showed that 97.6 % of patients met

the criteria for sarcopenia [8]. In another clinical trial conducted at the Federal Bureau for Medical and Social Assessment of the Ministry of Labour of Russia in and for Moscow, among 66 subjects over 50 years of age, 17 % were patients with sarcopenia, the screening of which used handgrip test, Short Physical Performance Battery (SPPB) and bioimpedansometry [9]. Based on the results of several large studies in a large population, Korean and Japanese researches found out that the incidence of sarcopenia in patients with DM is 15.7 % [4]. According to the latest guidelines of the European Working Group on Sarcopenia in Older People (EWGSOP, 2019), handgrip test, Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls (SARC-F) questionnaire, 4 m walking test, appendicular mass calculations used X-ray densitometry or bioimpedansometry are optimal for initial sarcopenia screening [10].

In the revised guidelines (EWGSOP2, 2019), low muscle bulk is the primary parameter of sarcopenia. Potential sarcopenia (pre-sarcopenia) is diagnosed when muscle strength is reduced. Sarcopenia is confirmed if muscle bulk is inadequate. Sarcopenia is considered severe in the presence of low muscle bulk, strength and poor function [10].

There are a number of instrumental methods to diagnose reduced muscle bulk, such as magnetic resonance imaging (MRI), computer tomography (CT), ultrasound, X-ray densitometry, bioimpedansometry. Each method has its advantages and disadvantages. In clinical practice, X-ray densitometry and bioimpedansometry are more common. The main parameters included in X-ray densitometry are assessment of bone mineral density, mineral ratio and lean muscle bulk [11]. It has been established that, unlike total muscle bulk, the results of appendicular mass measurements using densitometry significantly correlate with skeletal muscle CT and MRI results [11]. However, densitometry has its drawbacks: mean values used as control values can differ from mean values in the general population, depending on the region and ethnicity. Besides, it is impossible to identify adipose infiltration inside and around muscle fibres, hence the diagnostic value of densitometry in diagnostics of sarcopenia is reduced drastically [11]. The use of bioimpedansometry to verify reduced muscle bulk has been studied for over 10 years. It has been demonstrated that under standard conditions, bioimpedansometry results have positive correlation with MRI forecasts. Thus, bioimpedansometry can be used instead of densitometry for screening of reduced muscle bulk [11]. According to available information, bioimpedansometry is one of the most accessible methods in clinical medicine for the assessment of the compositional body analysis in elderly patients with type 2 DM [12].

A combination of reduced muscle bulk and strength in patients with DM reduces life expectancy [13]. Sarcopenia in patients with DM is associated with a higher frequency of hospitalisations and cardiovascular accidents [14]. Insulin resistance and oxidative stress are components of the pathophysiological foundation of sarcopenia [15]; on the other hand, they are associated with development of endothelial dysfunction [16], chronic inflammation [17] and lipid infiltration in muscles in DM patients.

The objective of the study is to analyse the presence of the primary risk factors of sarcopenia in patients with pre-sarcopenia and type 2 DM.

Materials and Methods

Study designs: cross-sectional observational comparative study. The study was conducted in accordance with the clinical practice standards and Declaration of Helsinki. The study protocol was approved by the Ethics Committee at the Federal State Budgetary Educational Institution of Higher Education Siberian State Medical University of the Ministry of Health of the Russian Federation No. 8888 dated November 29, 2021. All in all, the study included 82 patients with type 2 DM aged 50 to 85 years old (41 men, 41 women, mean age: 69 [67.5;72] years old), who signed an informed consent form and did not meet any exclusion criteria. DM was diagnosed on the basis of criteria set forth in the Algorithm of Specialised Care for Patients with Diabetes Mellitus (2021) [1]. Exclusion criteria were: decompensated cardiovascular, respiratory, musculoskeletal, GIT diseases, stage 4–5 chronic kidney disease (CKD), a history of limb amputation, vitamin B12 deficiency, alcohol abuse, cardiac pacemaker, large metal prosthetic devices or structures, marked lymphostasis of lower limbs.

Potential sarcopenia (pre-sarcopenia) was diagnosed in accordance with the algorithm recommended by the European Working Group on Sarcopenia in Older People (EWGSOP2, 2019), with muscle bulk reduction of less than 27 kg in men and less than 16 kg in women [10]. Unlike the EWGSOP2 2019 algorithm, handgrip test and not SARC-F [18] was used for group differentiation during initial screening.

Patients were divided into two groups: the main group (reduced muscle bulk) — 55 patients (27 men, 28 women, mean age: 71 [67–71] years old) and control group (no reduction in muscle bulk and strength) — 27 patients (14 men, 13 women, mean age: 67 [68–73] years old). The protocol stipulated measurement of hand strength using handgrip test: recording of the three highest values obtained with both hands in isometric contraction (the standard position was sitting, with elbow extended at 90°). The quality of life was assessed using SF-36 (Health Status Survey, 2006) and SarQol (Sarcopenia and Quality of Life, 2019); for sarcopenia severity, SARC-F (Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls, 2018) was used. The

degree of physical activity was assessed with the help of questionnaires (Physical Activity Questionnaire (PAQ 23), 2013) [19], recording the time of physical activity (min/day) and 4 m walking test (severe sarcopenia was diagnosed if the speed reduced by ≤ 0.8 m/s) [10]. All subjects underwent bioimpedansometry at Inbody 770 (Korea) with the body mass index assessment, analysis of extracellular and intracellular fluid, total body water, body fat, fat mass percent, visceral fat area, and muscle bulk. The obtained data were used to calculate the appendicular index of the skeletal mass as the ratio between lean muscle mass and height in square meters. According to EWGSOP (2019), low muscle bulk was skeletal mass index of < 7.0 kg/m^2 for men and < 5.5 kg/m^2 for women [10]. Carbohydrate metabolism compensation was assessed on the basis of glycaemia (blood biochemistry). Laboratory blood parameters (total protein, albumin, AST (aspartate aminotransferase), ALT (alanine aminotransferase), total bilirubin, urea, uric acid, creatinine, AP (alkaline phosphatase), fats (cholesterol, triglycerides, high-density lipoproteins (HDLP), low-density lipoproteins (LDLP)) were assessed.

Statistical data processing was performed using IBM SPSS Statistics 23 (Russian version 23.0). Parameters were assessed for correspondence to normal distribution; and Shapiro-Wilk's test was used. Data are presented as the median value with interquartile range Me [Q25; Q75] for parameters with distribution other than normal. Categorical variables are presented as absolute values and percent. Qualitative parameters of groups were compared using chi square (χ^2); for quantitative comparison of samples, one-way analysis of variance was used. Correlation analysis was performed using Spearman's or Pearson's test, depending on the distribution of parameters. Results with $p < 0.05$ were statistically significant.

Results:

When medical records of patients were evaluated, patients from the group of potential sarcopenia (n = 55) significantly more often complained of numbness in their lower limbs — 39 (70 %), dizziness — 18 (33 %), difficulty remembering — 13 (24 %), unstable blood pressure — 18 (33 %), dyspnoea during physical activities — 17 (31 %) vs. controls (p = 0.0001).

The characteristics of subjects are presented in Table 1.

When evaluated, BMI of patients in the groups differed: stage I obesity was recorded in 30 (65.2 %) patients, stage II — in 6 (13 %) patients in the main group; in the control group, stage I obesity was observed in 18 (72 %) of subjects and stage II obesity was recorded in 7 (28 %) patients. Also, patients in the main group had weaker muscle function and fewer points in the physical activity test.

Patients in the main group demonstrated reduced walking speed vs. controls. The main group had statistically significant signs of reduced daily physical activity (PAQ 23).

There were no statistically significant differences in SARC-F (Figure 1) and SF-36 (Figure 2) between groups (Figure 1). The low sensitivity of these questionnaires is likely to be related to the small number of patients in the study, elderly age, chronic comorbidities in both groups (Table 2).

When comorbidities in patients with sarcopenia were assessed, thyroid pathologies, a history of cancer, chronic anaemia and DM complication — polyneuropathy ($p \le 0.05$) were significantly more common (see Table 2).

Analysis of SarQol results (Table 3) did not show any statistical significance.

According to medical records, subjects of the study were taking the following medications (Table 4). Patients with pre-sarcopenia took insulins, as well as incretin tablets (dipeptidyl peptidase inhibitors) more often than controls. The frequency of the use of sulfonylureas was similar in both groups. Sodium-glucose linked cotransporter 2 inhibitors (SGLC-2), biguanides were used more often in patients with type 2 DM from the control group.

Table 5 presents the information on the patients' body composition based on bioimpedansometry results. Analysis of data shows reduced fat mass in the main group vs. controls. Also, in the group of pre-sarcopenia, skeletal muscle mass and appendicular muscle index are below the normal value.

Laboratory data (Table 6) show that the patients in the main group had lower total protein, ALT and calcium levels ($p \le 0.05$).

Of note, in a majority of cases, patients with pre-sarcopenia had antihypertensives, whereas in the control group, menopausal hormone therapy, multivitamins, including vitamin D (Table 7), were more common.

The correlation analysis demonstrated that potential sarcopenia is associated with higher fat mass ($r = 0.526$, $p = 0.001$) and BMI ($r = 0.587$, $p = 0.001$), reduced skeletal muscle mass ($r = -0.296$, $p = 0.007$).

Discussion

Improved medical care resulted in a higher number of diagnostic methods to screen pre-sarcopenia and risk factors in patients with impaired carbohydrate metabolism; however, currently, there is no unified model for verification of reduction in muscle bulk and strength [20]. In this paper, SARC-F did not show any statistical significance of results, which can cause inability to identify reduced muscle bulk. SF-36 score in the groups did not have any statistical significance. Since there is no consensus on its interpretation among researchers, very often results are controversial and can require its use together with physical examination results [21, 22].

Table 1. Characteristics of the main and comparison groups

Parameters	Main group (n=55)	Control group (n=27)	p
Age, years	71 [67-71]	67 [68-73]	0,771
Hight, centimeters	161 [159- 163]	168[164,3- 171]	0,384
Weights, kilograms	81 [76-86]	93 [87-99]	0,198
Waist circumference, cm	104 [98-114]	110 [104-115]	0,490
Hip circumference, cm	110 [105-120]	112 [107-120]	0,329
Body mass index, kg/m^2	31,1 [29,4-32,9]	33,2 [31,2-35,1]	0,011
Waist circumference to hip circumference ratio	0,93[0,93- 0,94]	0,97[0,96-0,97]	0,231
Right arm dynamometry, kg	13 [11-15]	23 [19-27]	0,003
Left arm dynamometry, kg	12 [10-14]	22 [19-25]	0,002
Walking speed, m/s	1,63 [1,47-1,79]	1,25 [1,13 — 1,37]	0,090
Glycemia, mmol/L	7,6 [7,0- 8,1]	7,2 [6,6-7,7]	0,573
Physical activity, points	40 [34- 45]	61 [45-77]	0,040

Note: Data are presented as median with interquartile range.

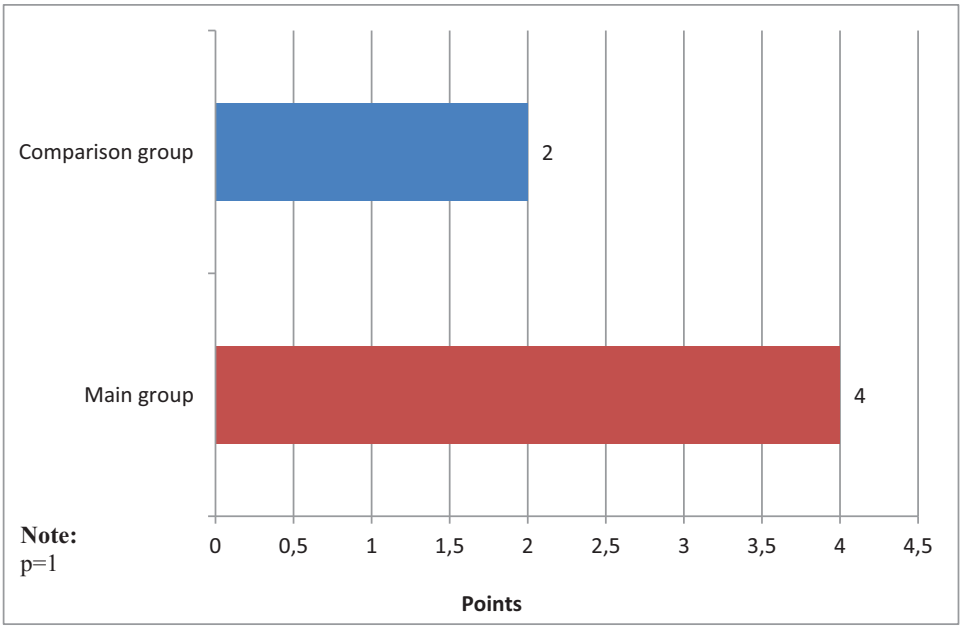

Figure 1. *Results of the SARC-F questionnaire*

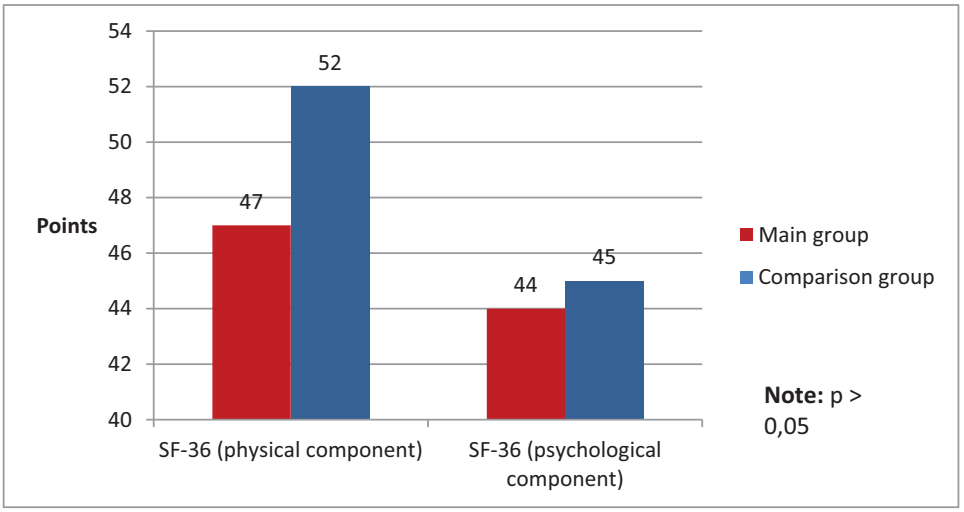

Figure 2. *Results of the SF-36 questionnaire*

Table 2. *Frequency of occurrence of concomitant diseases in the main group and comparison group*

Diseases	Main group (n=55)	Control group (n=27)	p
Cholelithiasis	15 (33 %)	2 (8,%)	0,858
Pathology of the thyroid gland	10 (22 %)	2 (%)	0,046
Arterial hypertension	44 (96 %)	23(92 %)	0,668
Cardiac ischemia	24 (52 %)	12 (48 %)	0,592
History of stroke/heart attack	8 (17 %)	9 (36 %)	0,099
Atrophic gastritis	8 (17 %)	2 (8 %)	0,747
Non-alcoholic fatty liver disease	26 (57 %)	15 (60 %)	0,382
History of cancer	6 (13 %)	1 (4 %)	0,007
Chronic anemia	4 (9 %)	2 (8 %)	0,01
History of coronavirus infection	19 (41 %)	7 (28 %)	0,296
Complications of diabetes			
Diabetic polyneuropathy	40 (73 %)	51,8 (56 %)	0,039
Diabetic nephropathy	25 (45,4 %)	14 (51,8)	0,142
Diabetic retinopathy	29 (52,7 %)	16 (59,2)	0,428
Macroangiopathy of the lower limbs	17 (30 %)	5 (18 %)	0,227

Note: Data are presented as median with interquartile range; GSD — cholelithiasis, IHD — coronary heart disease, CKD — chronic kidney disease

Table 3. *Assessment of parameters of the SarQol questionnaire*

Parameters, points	Main group (n=55)	Control group (n=27)	r	p
SarQoL general (/100)	34,99 [34,95-45,17]	43,87 [43,9-55,0]	-,184	0,970
Physical and mental health (/100)	31,77 [31,1-41]	47,77 [47,77-52,2]	,703	0,055
Ability to move (/100)	25 [25-31,25]	30 [30-38,89]	,445	0,790
Body composition (/100)	30 [29,17-33,33]	45,83 [45,83-50]	-,008	0,069
Functionality (/100)	32,14 [32,14-36,54]	42,31[42,31-71,15]	-,194	0,768
Daily activities (/100)	18,34 [16,67-35]	50 [50-52,78]	-1,072	0,757
Leisure (/100)	3, 33[0 -16,62]	0 [0 -33,25]	0,739	0,529
Fears (/100)	0 [10-75]	75 [75-87,5]	-,454	0,511

Note: Data are presented as median with interquartile range

Table 4. *Antihyperglycemic therapy used in patients with presarcopenia and in the comparison group*

Parameters, drugs	Main group (n=55)	Control group (n=27)	p
Insulin therapy	18 (32 %)	6 (22 %)	0,242
Insulin therapy, basal therapy	40 (72,7%)	13 (48,1)	0,004
Metformin	25 (45,5 %)	20 (74 %)	0,002
and DPP-4 inhibitors	44 (80 %)	6 (22,2 %)	0,001
and GLP-1 — агонист	0	1 (4 %)	0,164
and iNGLT-2 type	8 (14,5 %)	23 (85,1 %)	0,001
Sulfonylureas	36 (65,4 %)	12 (33 %)	0,008

Note: i DPP-4 — dipeptidyl peptidase 4 inhibitors (Gliptins), a GLP-1 — glucagon-like peptide-1 receptor agonists, i SGLT-2 — inhibitor of sodium-glucose cotransporter type 2 (Gliflozins)

Table 5. *Bioimpedancemetry parameters in the main group and in the comparison group*

Parameters	Main group (n=55)	Control group (n=27)	p
Fat mass, kg	33,5 [30- 37]	39,3 [34,5- 44]	0,036
Fat mass, %	40 [38- 43]	42 [38- 45]	0,679
Visceral fat area, cm^2	176 [158- 194]	200 [177- 223]	0,177
Skeletal muscle mass, kg	25,6 [24,4- 27]	29,4 [27,3-31,5]	0,045
Index of appendicular skeletal muscle, kg/m^2	7,0 [6,7-7.3]	7,5 [7,1-7.9]	0,011
Protein, kg	9,2 [8,8- 9,6]	10,4 [9,7-11]	0,869
Minerals, kg	3,2 [3,1- 3,4]	3,7 [3,5-3,9]	0,998
Total amount of water in the body, l	35 [33-37]	40 [37-42]	0,862
Intracellular fluid, l	21[20-22]	24[23-26]	0,951
Extracellular fluid, l	14[13-14]	16[14,5-17]	0,672
Cell mass, kg	30[29-32]	34,5[32-37]	0,941

Note: Data are presented as median with interquartile range

Table 6. *Biochemical parameters in the main group and the comparison group*

Parameters	Main group (n=55)	Control group (n=27)	p
Total cholesterol, mmol/L	5,1 [4,6- 5,6]	4,9 [4,4- 5,4]	0,567
HDL, mmol/L	1,3 [1,2- 1,4]	1,2 [1,1- 1,3]	0,762
LDL, mmol/L	3,8 [2,1- 5,5]	2,8 [2,4- 3,2]	0,628
Triglycerides, mmol/L	3,7 [0,8- 6,3]	2,5 [1,9- 3,1]	0,496
Total bilirubin, mmol/L	13,9 [11,5-16,3]	11,4 [9,7-13.1]	0,238
Total protein, mmol/l	68 [67- 70]	70 [68-72]	0,005
AST, U/L	23 [20- 27]	27 [19-36]	0,057
ALT, U/L	24 [19-29]	37 [21-52]	0,001
Alkaline phosphorus, U/L	64 [54-73]	66 [50-82]	0,523
Creatinine, μmol/L	90 [82-97]	87 [78-95]	0,090
Sodium, mmol/L	135 [128-143]	141 [140-141]	0,331
Potassium, mmol/L	3,8 [3,5-4,0]	4 [3,8-4,0]	0,849
Calcium, mmol/L	1,1 [1,0-1,2]	1,2 [1,1-1,3]	0,001
Uric acid, μmol/L	318 [290-346]	310 [263-357]	0,719
Albumin, g/l	38 [35-41]	33 [26-40]	0,607
Glycated hemoglobin, %	8,2 [7,4-9]	7,6 [6,3-9]	0,200

Note: Data are presented as median with interquartile range; ALT — alanine aminotransferase, AST — aspartate aminotransferase, HDL — high density lipoproteins, LDL — low density lipoproteins, ALP — alkaline phosphatase

Table 7. *Additional drug therapy in patients with presarcopenia and in the comparison group*

Parameters, drugs	Main group (n=55)	Группа сравнения/ Control group (n=27)	p
Antihypertensive therapy	54 (98%)	16 (59,2%)	0,001
Antiarrhythmics	54 (98%)	25 (92,5%)	0,198
Disaggregants	39 (85%)	20 (80%)	0,080
Statins	33 (71,74%)	18 (72,00%)	0,259
Thyroxine	3(5,4%)	1 (3,7%)	0,966
Menopausal hormone therapy	1 (1,8%)	6 (22,2%)	0,001
Vitamin D	3(5,4%)	8 (29,6%)	0,006
Hepatoprotectors	9 (16,3%)	5 (18,5%)	0,747
Bronchodilators	5 (9%)	2 (7,4%)	0,198
Glucocorticosteroids	2 (3,6%)	1 (3,7%)	0,122
Multivitamins	0	5 (18,5%)	0,014

An Iranian study (2012) of the quality of life of elderly and old patients with type 2 diabetes mellitus using SF-36 and WHOQoL–BREF (World Health Organization's Quality of Life) demonstrate that SF-36 and WHOQoL–BREF are reliable clinical questionnaires; however, WHOQoL–BREF results were more specific than SF-36 [23]. According to the study results, it can be suggested that SF-36 can have moderate screening capability to assess the quality of life of patients with type 2 DM and reduced muscle strength. The efficiency of this questionnaire in middle-aged subjects without carbohydrate metabolism disorders requires verification in other clinical trials [24].

Handgrip test results were worse in the main group; it is caused by reduced secretion of anabolic hormones, mitochondrial dysfunction induced by chronic hyperglycemia and inflammatory reaction under the influence of cytokines and free radical [25].

According to some authors, reduced walking speed in patients with potential sarcopenia can be associated with diabetic polyneuropathy and atherosclerosis of lower limb arteries, as well as high glycaemia values. Long-lasting hyperglycemia is known to cause glycosilation of myelin sheath of nerves and neuron death, resulting in reduced muscle fibre innervation and reduced walking speed [26]. Reduced walking speed in patients with type 2 DM can be caused by long-term use of metformin, resulting in cyanocobalamine deficiency and reduced myelin synthesis [27]. Although this study did not find any difference between the use of biguanides in the groups, the fact of the use of this medication was associated with reduced muscle bulk. Timely prevention of complications at early stages of type 2 DM (alpha-lipoic acid and cyanocobalamine) will improve neural trophism and facilitate slower reduction in mass bulk in patients with type 2 DM due to better endoneurial blood flow and higher glutathione values [28].

According to the data obtained during the study, there were no significant differences in glycaemia and HbA1c. However, it is well-known that chronic hyperglycaemia is caused by an increase in the number of glycation end-products, which accumulate in cartilages and skeletal muscles and lead to reduced muscle strength and joint elasticity [29]. Earlier studies revealed that high levels of glycation end-products are associated with low values of handgrip tests and walking speed in elderly people [29]. Based on the results, maintenance of the target glycaemia levels in patients with type 2 DM will help to prevent reduction in muscle bulk and strength [30].

Assessment of the body composition using bioimpedansometry demonstrated that the fat mass percentage was high in both groups; however, in the pre-sarcopenia group, fat mass and BMI were higher. The results are comparable with the study conducted by the Federal Bureau for Medical and Social Assessment of the Ministry of Labour of Russia (2017) [9]. Allegedly, this variant of fat mass distribution can correspond to sarcopenic obesity, which contributes to reduced muscle bulk [9].

In serum of patients with potential sarcopenia, protein levels were reduced as compared to controls, which causes reduction in skeletal muscle mass [9]. This trend is a result of physical inactivity as one of the leading causes of reduced muscle bulk and strength [31] and is confirmed with the results of reduced physical activity in the main group. These results can be associated with the unbalanced diet in the modern population: high levels of simple carbohydrates, saturated fats and trans fats, low intake of protein-rich products. Diet should further be evaluated with the use of bioimpedansometry. In order to prevent sarcopenia, controlled physical aerobic activities for at least 20 minutes and daily intake of 1–1.2 g/kg of protein (depending on pathology) are recommended; it can facilitate better synthesis of muscle protein, reduce fat mass and preserve normal bone mineralisation [31].

Later reduced mineral density will increase the risk of osteosarcopenia and spontaneous fractures in patients with type 2 DM [32, 33]. Therefore, intake of an adequate amount of protein will improve calcium reabsorption and reduced production of parathyroid hormone [34], thus reducing the risk of osteoporosis. Among chronic diseases, severe chronic kidney disease (CKD) should be mentioned, where daily protein intake is reduced to 0.2–0.5 g/kg (at GFR of < 30 mL/min/1.73 m^2) in order to prevent metabolic acidosis [35]. Inadequate mineral density can be a result of vitamin D deficiency and diabetic kidney disease [36]. Preventive doses of vitamin D will likely facilitate bone mass preservation [37]. In this paper, patients with pre-sarcopenia presented took lower amounts of multivitamins and vitamin D; however, there were no differences in the incidence of chronic complications of DM between groups.

Various effects of antidiabetic medications on the quality of muscles flag that selection of medications should account for the risk of sarcopenia, in addition to comprehensive monitoring of glycaemic status and cardiovascular complications. It has been demonstrated that sulfonylureas, insulin and metformin can promote skeletal muscles loss, unlike SGLC-2 inhibitors and DPP-4 [38]. In this study, patients with pre-sarcopenia were more often treated with insulin, DPP-4, while SGLC-2 inhibitors and biguanides were used less often, and it needs further investigation. Also, development of sarcopenia in elderly people is affected by arterial hypertension, e.g. in some studies, angiotensin-converting-enzyme inhibitors show positive protective effect [39]. Another preventive approach can be menopausal hormone therapy, which was prescribed more often to women in the control group; according to some researchers, if combined with physical activities, it may result in muscle building [40].

The limitations of this study were non-assessment of efficacy and lack of a healthy population, who would not have glucose metabolism disorders, with a similar BMI (30 and 35 kg/m^2), in order to compare groups with similar body composition; small sample size, absence of multivariative analysis and evaluation of the nutritional status of patients. These factors will be taken into account and applied in our future study in a larger population.

Conclusion

Thus, an initial screening of reduced muscle bulk and strength in patients with type 2 DM can be performed with the use of handgrip test and bioimpedansometry. Handgrip test is used to diagnose reduced muscle strength, while body composition assessment (bioimpedansometry) can identify reduced muscle and appendicular mass as long as the disease evolves. Despite numerous studies and relevance of the problem, there are no marketed medications to preserve muscle bulk. Prevention measures in patients with type 2 DM aimed at preservation of muscle bulk and strength are: stable target glycaemia levels, prevention of physical inactivity, adequate intake of proteins and preventive doses of vitamin D. The identified risk factors can be red flags of sarcopenia; but their statistical value should be verified in a larger population.

Вклад авторов:

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Самойлова Ю.Г. (ORCID ID: https://orcid.org/0000-0002-2667-4842): разработка концепции, редакция и окончательное утверждение рукописи

Матвеева М.В. (ORCID ID: https://orcid.org/0000-001-9966-6686): разработка концепции и дизайна, анализ материала, редакция и окончательное утверждение рукописи

Хорошунова Е.А. (ORCID ID: https://orcid.org/0000-0002-3596-6732): разработка концепции и дизайна исследования, анализ и интерпретации данных, написание рукописи

Подчиненова Д.В. (ORCID ID: https://orcid.org/0000-0001-6212-4568): статистическая обработка, интерпретация результатов, редакция рукописи

Якимова Я.Л. (ORCID ID: https://orcid.org/0009-0006-1151-261X): осмотр пациентов, сбор и обработка материала, статистическая обработка

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Samoilova I.G. (ORCID ID: https://orcid.org/0000-0002-2667-4842): conceptualization, revision and final approval of manuscript

Matveeva M.V. (ORCID ID: https://orcid.org/0000-001-9966-6686): conception and design, material analysis, revision and final approval of manuscript

E.A. Khoroshunova (ORCID ID: https://orcid.org/0000-0002-3596-6732): conception and design of the study, data analysis and interpretation, manuscript writing

Podchinenova D.V. (ORCID ID: https://orcid.org/0000-0001-6212-4568): statistical processing, interpretation of results, manuscript revision

Yakimova Y.L. (ORCID ID: https://orcid.org/0009-0006-1151-261X): examination of patients, collection and processing of material, statistical processing

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