

# Frequency and independent risk factors of sarcopenia in type 2 diabetes

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## Abstract

**Background:** Diabetes is a growing public health problem with the increasing obesity prevalence, and aging world population. Many comorbidities, frailty, and deteriorations in both quality of life and the health status of these patients are associated with a compound outcome of increased body mass index, aging and sarcopenia. Sarcopenia has particular importance, since it is both a cause and an outcome in these patients.

**Aim:** The aim of this study is to evaluate the sarcopenia frequency, and to determine the independent predictors of sarcopenia in patients with type 2 diabetes.

**Methods:** Patients between 18 to 65 years of age that followed-up at the Endocrinology Department of Istanbul Bakirkoy Dr. Sadi Konuk Education and Research Hospital with a diagnosis of type 2 diabetes mellitus were evaluated retrospectively.

**Results:** A total of 86 patients (F/M 60/26) with a mean age of 52.9±12.4 years were included. Fifty-four patients (62.8%) had sarcopenia (70% of females and 46.2% of males; p=0.040), and albumin levels were significantly higher in those patients (p=0.037). Multivariate analyses revealed that females (OR: 3.9; p=0.020), and increased BMI (OR: 1.1 per unit increase; p=0.040), albumin (OR: 2.7 per unit increase; p=0.028) and LDL (OR: 1.02 per unit increase; p=0.016), and decreased Tg (OR: 1.01 per unit decrease; p=0.004) levels were independent determinants of sarcopenia.

**Conclusion:** Results of this current study confirmed the previous knowledge on the subject, moreover contributes to the available evidence with reporting the increased albumin as a novel risk factor for the sarcopenia.

**Keywords:** sarcopenia, diabetes, frequency, risk factors

## 2 ТИП ҚАНТ ДИАБЕТИМЕН АУЫРАТЫН ПАЦИЕНТТЕРДЕ САРКОПЕНИЯ КЕЗДЕСІ ЖИЛІГІ ЖӘНЕ ПАЙДА БОЛУ ҚАУПІНІң ТӘУЕЛСІЗ ФАКТОРЛАРЫ

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### ТҰЖЫРЫМДАМА

**Кіріспе:** Диабет — бұл әлем халқының семіруі мен қартаюын кең таратып келе жатырған қоғамдық денсаулық сақтаудың күн сайын күрделеніп келе жатқан проблемасы болып табылады. Бұл аурумен ауыратын пациенттердің көптеген ілеспе аурулары, әлсіздігі және өмір сапасы мен денсаулық жағдайының нашарлауы ағза салмағының көбеюімен, қартаюмен және саркопениемен байланысты. Саркопение ерекше маңызға ие, өйткені ол осы пациенттер ауруының себебі де, нәтижесі де болып табылады.

**Мақсаты:** Осы зерттеудің мақсаты саркопенияның кездесу жиілігін бағалау және 2 типті диабетпен ауыратын пациенттерде тәуелсіз болжамдық факторларды айқындау болып табылады.

**Әдістері:** Дәрігер Сади Конук атындағы Ыстамбұл Бакыркөй ғылыми-зерттеу клиникасының Эндокринология бөлімінде 2 типті қант диабеті диагнозымен емделген 18 және 65 жас аралығындағы пациенттер осы ретроспективті зерттеуге енгізілді.

**Нәтижелері:** Зерттеуге барлығы 86 пациент енгізілді (ә/е:60/26), орташа жастары 52.9±12.4 жас құрады. Елу төрт пациентте (62.8%) саркопения болды (70% әйелдер және 46.2% ерлер; p=0.040), сондай-ақ бұл пациенттерде альбумин деңгейі айтарлықтай жоғары болды (p=0.037). Көп факторлы талдау саркопенияның тәуелсіз көрсеткіштері мыналар болғанын көрсетті: әйелдер (OR: 3.9; p=0.020), дене салмағының ұлғайған индексі (OR: 1.1 бірлікке ұлғаю; p=0.040), альбумин деңгейлері (OR: 2.7 бірлікке ұлғаю; p=0.028) және ЛПНП (OR: 1.02 бірлікке ұлғаю; p=0.016), және Тг төмендеген деңгейі OR: 1.01 бірлікке ұлғаю; p=0.004).

**Қорытынды:** Осы зерттеу нәтижелері пән бойынша бұрын алған білімдерді тиянақтады, одан бөлек альбуминнің жоғарылаған деңгейі саркопенияның қауіп факторы болып табылатынына дәлел келтіру үшін үлес қосады.

**Негізгі сөздер:** саркопения, қант диабеті, кездесу жиілігі, қауіп факторлары

# ЧАСТОТА ВСТРЕЧАЕМОСТИ И НЕЗАВИСИМЫЕ ФАКТОРЫ РИСКА САРКОПЕНИИ У ПАЦИЕНТОВ С САХАРНЫМ ДИАБЕТОМ 2 ТИПА

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## РЕЗЮМЕ

**Введение:** Диабет — это растущая проблема общественного здравоохранения с увеличивающейся распространенностью ожирения и старения населения мира. Многие сопутствующие заболевания, уязвимость и ухудшения как в качестве жизни, так и состоянии здоровья этих пациентов связаны со сложным исходом увеличенного индекса массы тела, старения и саркопении. Саркопения имеет особое значение, так как это является и причиной и исходом заболевания данных пациентов.

**Цель:** Целью данного исследования является оценка частоты встречаемости саркопении, и определение независимых прогностических факторов саркопении у пациентов с диабетом 2 типа.

**Методы:** Пациенты в возрасте от 18 до 65 лет, которые наблюдались в отделении эндокринологии Стамбульской научно-исследовательской клиники Бакыркёй имени доктора Сади Конук с диагнозом сахарный диабет 2 типа были включены в данное ретроспективное исследование.

**Результаты:** В исследование было включено всего 86 пациентов (ж/м: 60/26), средний возраст которых составил 52.9±12.4 года. У пятидесяти-четырех пациентов (62.8%) была саркопения (70% женщин и 46.2% мужчин;  $p=0.040$ ), а также у этих пациентов уровень альбумина был значительно выше ( $p=0.037$ ). Многофакторный анализ показал, что независимыми показателями саркопении оказались следующие: женщины (OR: 3.9;  $p=0.020$ ), увеличенный индекс массы тела (OR: 1.1 увеличение на единицу;  $p=0.040$ ), уровни альбумина (OR: 2.7 увеличение на единицу;  $p=0.028$ ) и ЛПНП (OR: 1.02 увеличение на единицу;  $p=0.016$ ), и сниженный уровень Тг (OR: 1.01 снижение на единицу;  $p=0.004$ ).

**Заключение:** Результаты настоящего исследования подтвердили ранее полученные знания по предмету, более того они вносят вклад в имеющиеся доказательства, сообщая о том, что увеличенный уровень альбумина является новым фактором риска саркопении.

**Ключевые слова:** саркопения, сахарный диабет, частота встречаемости, факторы риска

## Introduction

Excessive muscle loss and associated functional deteriorations are defined as sarcopenia [1]. Muscle loss is related with many diseases, but it can occur naturally due to aging, which is associated with deteriorated muscle functions. Under physiologic conditions, approximately 1% of the total muscle mass losses each year after 30 years-of-age [2]. With recent modifications, sarcopenia definition now includes decreased walking speed and grip strength along with the decreased muscle mass [3-5].

Current literature suggests that diabetics have an increased risk for development of sarcopenia [6]. Previous research on this topic has provided evidence about the effects of diabetes on muscle mass [7, 8]. Particularly for the patients with type 1 diabetes, insulin deprivation is the major stimulant for the increased catabolism of skeletal muscles [9, 10]. Despite the fact that the mechanism in type 2 diabetes is not so apparent like this, previous cross-sectional studies found that older diabetic adults have altered body composition and low skeletal muscle strength, and lost their knee extensor strength more rapidly than their non-diabetic counterparts [11]. Also, multivariate analyses assessing the associations between diabetes and sarcopenia controlling for the body-mass index (BMI) revealed that the difference between diabetics and non-diabetics regarding muscle density was significantly attenuated after adjustment for the BMI, which suggests that the fat density in the muscle mass was an important factor for the muscle dysfunctionality [12]. The aim of this study was to evaluate the frequency of sarcopenia in diabetic patients and evaluating the independent risk factors in sarcopenia.

## Material and methods

This study was conducted at the Endocrinology Department of Istanbul Bakirkoy Dr. Sadi Konuk Education and Research Hospital. Patients with Type-2 diabetes between 18 to 65 years of age were searched from the patient records retrospectively. Demographic data including age and sex; anthropometric evaluations including height, weight and body mass index (BMI); and, laboratory analyses including routine biochemistry, complete blood count, 25-OH-vitamin D levels, neutrophil/lymphocyte and platelet/lymphocyte ratios, and hemoglobin

A1c levels were recorded from the patient files. Cases below 18 years of age and older than 65 years of age were not included in the analyses.

Sarcopenia was diagnosed in patients according to the definitions of The European Working Group on Sarcopenia in Older People (EWGSOP).

## Statistical Analysis

Descriptive data were presented as frequency and percent for categorical variables, and mean and standard deviation for numerical variables. Comparisons of data between patients with and without sarcopenia were performed with Mann-Whitney U test, and Chi-Square test for numerical and categorical variables, respectively. Independent predictors of sarcopenia were evaluated by a logistic regression model, and Omnibus test and Hosmer-Lemeshow tests were used to evaluate the model fit. A  $p$  value  $<0.05$  was considered as statistically significant. All analyses were performed with SPSS 21 (IBM Inc., Armonk, NY, USA).

## Results

A total of 86 patients (F/M 60/26) with a mean age of 52.9±12.4 years were evaluated retrospectively. The comparisons of demographic, anthropometric, and laboratory analyses between males and females revealed that ages of patients were similar, but metabolic ages were significantly lower in males ( $p=0.009$ ). Males were taller ( $p<0.001$ ), and had lower BMIs than females ( $p=0.017$ ). Laboratory analyses revealed that TSH ( $p=0.004$ ), fT4 ( $p=0.011$ ), urea ( $p=0.003$ ), uric acid ( $p=0.044$ ), and creatinine ( $p<0.001$ ) levels were higher in males. All other parameters were found to be similar between sexes (Table 1).

The measurements regarding muscle mass revealed that 54 patients (62.8%) had sarcopenia. For the sex distribution, 70% of females had sarcopenia, whereas this was 46.2% for males, and the difference was statistically significant ( $p=0.040$ ). Comparisons of other demographic characteristics, anthropometric measurements, and laboratory analyses between patients with and without sarcopenia revealed that only albumin levels were significantly higher in sarcopenia group ( $p=0.037$ ) (Table 2).

Table 1

Comparison of general characteristics of patients between sexes

	Male n=26	Female n=60	p
Age	52±15.9	53.3±10.7	1.000
Metabolic age	54.4±15.7	64.2±11.9	0.009
Height	169.5±7.3	159.7±5.4	0.000
Weight	94.1±27	91.2±16.7	0.873
BMI	32.8±9.1	35.4±6.6	0.017
25-OH-VitD3	20.6±13.6	21.9±16.8	1.000
TSH	5.1±2.7	3.3±2.3	0.004
FT4	2.1±0.7	1.7±0.5	0.011
WBC	9.1±4.1	8.7±2.2	0.862
Hgb	13.4±1.5	13.5±1.4	0.573
Htc	40.6±4.7	41.4±4.6	0.557
MPV	8±2	7.9±1.6	0.873
MCV	84.5±9.2	87±4.7	0.229
Plt	289.5±82.4	281.7±71	0.602
Urea	40.8±18.8	30.6±11.5	0.003
Uric acid	6.3±1.3	5.5±1.9	0.044
Creatinine	1.1±0.4	0.8±0.2	0.000
Albumin	3.4±0.6	3.4±0.6	0.589
CRP	3.4±5.2	1.8±1.4	0.789
Cortisol	11.8±4.6	11.5±5.7	0.299
HgbA1c	8.1±1.3	8±1.6	0.679
LDL	145.1±29.2	135.8±38.9	0.323
HDL	39.5±10.4	41.7±13.2	0.785
Tg	259.5±130.9	260.4±128.3	0.796
Homocysteine	39.6±29.2	51.2±36.9	0.165
HOMA-IR	12.4±8.5	11.8±8.3	0.689
FBG	165.8±88.3	151.3±78.5	0.478
PLR	22.2±4.5	22.1±3.8	0.847
NLR	1.9±2.6	1.4±2.3	0.789
Fasting insulin	14.6±7.7	14.8±8.1	0.959

Table 2

General characteristics of patients with and without sarcopenia

	Sarcopenia (-) n=32	Sarcopenia (+) n=54	p
Sex			0.040
<i>Male</i>	14 (53.8)	12 (46.2)	
<i>Female</i>	18 (30)	42 (70)	
Age	52.8±13.7	52.9±11.7	0.792
Metabolic age	59.1±15.5	62.5±12.8	0.472
Height	162.2±8.7	162.9±6.8	0.693
Weight	87.9±17	94.5±21.7	0.344
BMI	32.9±6.9	35.6±7.7	0.180
25-OH-VitD3	23.8±16	20.2±15.7	0.255
TSH	3.9±2.6	3.8±2.5	0.879
FT4	1.8±0.5	1.8±0.7	0.671
WBC	8.9±1.9	8.8±3.3	0.456
Hgb	13.5±1.5	13.5±1.4	0.876
Htc	40.9±5.1	41.3±4.4	0.652
MPV	7.9±1.9	7.9±1.6	0.251
MCV	87±4.3	85.8±7.4	0.802
Plt	292±89.3	279.3±64.1	0.549
Urea	34.3±16	33.4±14.2	0.876
Uric acid	5.7±1.6	5.8±1.9	0.932
Creatinine	0.9±0.5	0.8±0.2	0.655
Albumin	3.2±0.6	3.5±0.6	0.037
CRP	2.3±2.8	2.3±3.4	0.491
Cortisol	10.8±3.8	12±6.1	0.617
HgbA1c	8.4±1.6	7.9±1.5	0.086
LDL	134.3±37.3	141.2±35.8	0.442
HDL	37.4±9.6	43.2±13.4	0.055
Tg	293.2±146.1	240.5±113.5	0.133
Homocysteine	46.1±34.5	48.7±35.6	0.626
HOMA-IR	12.5±9.3	11.7±7.7	0.979
FBG	171.8±93.7	146.1±72.4	0.221
PLR	21.7±4.1	22.4±3.9	0.294
NLR	1.9±2.8	1.4±2.2	0.288
Fasting insulin	15.1±8.5	14.6±7.7	0.813

The independent determinants of sarcopenia were evaluated by a stepwise logistic regression model, with the possible prognostic factors from univariate analyses including sex, age, BMI, albumin, LDL, HDL, TG, TSH, 25-OH-and VitD3. Final model revealed that females (OR: 3.9; p=0.020), and increased BMI (OR: 1.1 per unit increase; p=0.040), albumin (OR: 2.7 per unit increase; p=0.028) and LDL (OR: 1.02 per unit increase; p=0.016), and decreased Tg (OR: 1.01 per unit decrease; p=0.004) levels were independent determinants of sarcopenia. The final model was found to be valid and fit (Omnibus test p<0.05; Hosmer-Lemeshow test p>0.05) (Table 3).

## Discussion

In parallel to the increasing obesity prevalence and aging of the world population, the prevalence of type 2 diabetes is also increasing progressively. The Turkish Statistical Institute released the population statistics of 2016 recently, and reported that the proportion of population over 65 years is 8.3% in Turkey [13]. Another recent report by this institution was the recent health survey of Turkey in 2016, which revealed that the obesity prevalence is 19.6% over 15 years of age (23.9% for women, and 15.2% for men) [14]. For the same time period, Ministry

Table 3

Independent predictors for sarcopenia

	OR	95% CI	p
Initial model			
<i>Sex (female vs. male)</i>	4.943	1.407 - 17.366	0.013
<i>Age</i>	0.994	0.951 - 1.04	0.807
<i>BMI</i>	1.089	0.996 - 1.19	0.061
<i>Albumin</i>	2.224	0.874 - 5.662	0.094
<i>HDL</i>	1.029	0.977 - 1.083	0.283
<i>LDL</i>	1.021	1.003 - 1.039	0.021
<i>Tg</i>	0.991	0.986 - 0.997	0.004
<i>TSH</i>	1.179	0.918 - 1.514	0.197
<i>25-OH-VitD3</i>	1.005	0.972 - 1.039	0.772
<i>Constant</i>	0.008	-	0.015
Final model			
<i>Sex (female vs. male)</i>	3.903	1.244 - 12.242	0.020
<i>BMI</i>	1.090	1.004 - 1.183	0.040
<i>Albumin</i>	2.656	1.112 - 6.342	0.028
<i>LDL</i>	1.021	1.004 - 1.039	0.016
<i>Tg (per unit decrease)</i>	1.008	1.003 - 1.013	0.004
<i>Constant</i>	0.001	-	0.005

of Health reported that the prevalence of diabetes mellitus over 15 years of age was 9.1% (10.9% for females, and 7.1% for males) [15]. As can be seen from these figures, obesity and type 2 diabetes possess a significant health burden in Turkey, as in the rest of the World. The consequences of combination of aging, obesity, and diabetes may be debilitating for the patients. Some of these are deteriorated quality of life, decreased mobility, and increased rates of comorbidities associated with these health problems including sarcopenia. In this study, we have evaluated the independent determinants of sarcopenia in patients with diabetes, which is important for identification of preventive measures, particularly prior to the onset of the disease.

With the recent modifications in the definition of the sarcopenia, now it includes the decreased muscle mass, and the decreased strength and functionality [16]. Historically, aging-related functional deteriorations were thought to be associated with significantly decreased muscle mass, but research on the topic showed that functional decline is much more related with loss in muscle strength than the muscle mass [17]. These physiological changes may be monitored by routine evaluation methods including clinical and biochemical assessments, and may be accounted as independent determinants of sarcopenia. Our analyses for evaluating this hypothesis revealed that diabetic patients with sarcopenia were predominantly female, and had elevated albumin levels in the univariate analyses. Muscle loss with increasing age is more pronounced for males in the literature. For the situations like aging and/or other diseases, testosterone deficiency is more associated with a catabolic response, which also plays a major role for sarcopenia [18]. On the other hand, estrogen deficiency was found to be more related with sarcopenia particularly in postmenopausal women [17]. In our study, we have not evaluated if the women were pre- or postmenopausal, but our analyses revealed the female predominance in the sarcopenia group. This may also be associated with the nutritional status, obesity or body fat composition, and mobility and exercise status of the patients.

Secondly, we found that albumin levels were increased in patients with sarcopenia. The albumin levels in elderly patients are commonly measured for the assessment of nutritional status or disease severity [19]. The current evidence suggests that serum albumin levels may decrease in stress conditions, renal diseases, liver diseases, inflammation and following surgical interventions [20, 21]. Since it is biologically plausible for using this biomarker for assessment of muscle mass, the literature data

and currently available evidence do not suggest its utilization for this purpose [22]. Nevertheless, previous studies showed a decline in albumin levels in conditions with muscle loss. This is contradictory to our results that showed that patients with sarcopenia had elevated levels of albumin levels. But, despite the statistical significance between the albumin levels of patients with and without sarcopenia, the difference was not clinically meaningful.

The multivariate analyses for evaluating the independent determinants of sarcopenia showed that female gender, increased BMI, albumin, and LDL levels, and decreased triglyceride levels were associated with increased sarcopenia risk. BMI and increased fat levels were found to be associated with the muscle loss and sarcopenia in previous studies. Our patients were all diabetics, and diabetes itself is known as a major risk factor for functional disability, obesity, and immobility. The body fat composition significantly changes in these patients, and possess a risk for the muscle loss. Another mechanism is the insulin resistance, which also increases with aging, and defective insulin signaling can lead to reduced muscle synthesis and functioning [23]. Moreover, these patients are prone to increased oxidative stress, and this may also an underlying mechanism of the development of sarcopenia [24]. Other contributors of sarcopenia in this patient group may include sex hormone changes, [25] IGF-1 status [26], and aging-related functional loss in neuronal network and impaired re-innervation [27]. According to our results, elevated cholesterol levels and increased BMI are significant contributors to sarcopenia. But increased albumin levels as a risk factor is a striking finding, which has not been reported previously, and should be confirmed in prospective studies.

## Conclusion

Results of this current study confirmed the previous knowledge on the subject, moreover contributes to the available evidence with reporting the increased albumin as a novel risk factor for the sarcopenia.

The major limitation of this study is the retrospective design, which constrains us to make further conclusions. Thus, our striking finding of albumin as a potential risk factor of sarcopenia in diabetic patients should need confirmation in prospective studies with large sample sizes.

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