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Original Article

Sarcopenia in Patients with Diabetes Mellitus

Yannis Dionyssiotis[1], Panagiotis Athanassiou[2], Jannis Papathanasiou[3,4], Efstathios Efstathopoulos[5], Konstantinos Prokopidis[6], Georgios Trovas[7], Ifigenia Kostoglou-Athanassiou[8]

[1] *Spinal Cord Injury Rehabilitation Clinic, Patras University Hospital, Patras, Greece*

[2] *Rheumatology Department, Aghios Pavlos General Hospital, Thessaloniki, Greece*

[3] *Department of Kinesiotherapy, Faculty of Public Health, Medical University of Sofia, Bulgaria*

[4] *Department of Medical Imaging, Allergology & Physiotherapy, Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria*

[5] *Medical Physics Unit, 2nd Department of Radiology, University General Hospital "Attikon", School of Medicine, National and Kapodistrian University of Athens, Greece*

[6] *Department of Musculoskeletal Biology, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom*

[7] *Laboratory for Research of the Musculoskeletal System, National and Kapodistrian University of Athens, Kifissia, Greece*

[8] *Endocrinology Department, Asclepieio General Hospital, Voula, Greece*

Corresponding author: Yannis Dionyssiotis, Spinal Cord Injury Rehabilitation Clinic, Patras University Hospital, Patras 26504, Greece; Email: yannis_dionyssiotis@hotmail.com; Tel.: +30 6946469759

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Abstract

Introduction: Diseases such as diabetes mellitus may be associated with adverse changes in body composition. Sarcopenia is characterized by a progressive and generalized loss of skeletal muscle mass and functionality.

Aim: To investigate the relationship between type 2 diabetes mellitus (T2DM) and sarcopenia.

Materials and methods: In a retrospective, non-randomized study, 35 T2DM patients, aged 20-80 years, were assessed for sarcopenia prevalence compared to controls (n=16). Appendicular skeletal mass (ASM) (kg) was measured, and sarcopenia was defined as SMI <7.0 and <5.7 kg/m^2, in males and females, respectively, using the European Working Group on Sarcopenia in Elderly (EWGOSP) definition. Low physical performance was defined as a walking speed of <0.8 m/s.

Results: Incidence of sarcopenia was significantly higher in T2DM patients vs. controls (27% vs. 20%, p=0.01) and elderly vs. young participants (40% vs. 12%, p<0.001), respectively. Walking velocity was significantly lower in T2DM patients compared to male and female controls (1.08±0.22 vs. 1.23±0.18 and 1.07±0.26 vs. 1.26±0.16, respectively, p<0.001,).

Conclusions: A moderate prevalence of sarcopenia in patients with type 2 diabetes mellitus was observed, which appeared to increase significantly in older men. Finally, incidence of T2DM displayed decreased physical performance in both genders.

Keywords

aging, diabetes mellitus, elderly, sarcopenia, whole body DXA

INTRODUCTION

As life expectancy increases and an increasing percentage of the population reaches old age, research in clinical medicine is increasingly focused on age-related health complications.[1] Diabetes mellitus (DM) is a complex, chronic disease that requires ongoing medical care that should include strategies aiming to regulate blood glucose levels and reduce potential comorbidities. The high DM prevalence is steadily rising worldwide, triggered by the increased global prevalence of obesity and unhealthy lifestyle. Type 2 diabetes mellitus (T2DM) affects 90%-95% of all people with DM.[2,3]

Sarcopenia is one of the main issues associated with the process of aging. It is more common in sedentary individuals, but may also affect those who remain physically active throughout their lifespan, indicating that physical inactivity is not the sole causal factor of reduced muscle mass and strength.[4]

In older subjects with sarcopenia, the development of insulin resistance and type 2 diabetes mellitus is well established.[5] Sarcopenia and diabetes are linked, given that insulin-mediated glucose uptake targets muscle tissue, whereby during aging process, glucose uptake sites are less efficient.[6] Skeletal muscle is the primary site of glucose deposition, and decreased muscle mass plays a key role in impaired glucose metabolism in patients with insulin resistance and type 2 diabetes.[7] Skeletal muscle resistance to insulin action appears to be the link between type 2 diabetes (T2DM) and sarcopenia. Hyperglycemia is a metabolic dysfunction, which may potentially damage muscle cells.[8] Insulin deficiency leads to substantial muscle catabolism. Some of the metabolic defects may be reversed by exogenous insulin administration.[9]

Furthermore, the metabolic disorder in diabetics can be managed by hypoglycemic agents, diet, and physical activity and physical ability may be restored through musculoskeletal system rehabilitation. Therefore, timely diagnosis of sarcopenia may lead to interventions that can prevent muscle mass and strength declines, and reduced lifestyle quality overall.[10-12] According to the results of the afore-mentioned studies, it is inconclusive whether sarcopenia leads to the metabolic dysfunction in diabetes, or sarcopenia is a consequence of diabetes.[13]

AIM

The aim of the present study was to investigate the prevalence of sarcopenia in patients with diabetes mellitus and the relationship between these two entities.

MATERIALS AND METHODS

Study participants

A group of 35 patients, aged 20-80 years old, 18 males and 17 females with type 2 diabetes mellitus, and a control group with the same demographic characteristics, participated in the study. All patients fulfilled the 2019 criteria of the American Diabetes Association for diagnosis of diabetes mellitus. In summary, patients either had a fasting plasma glucose ≥126 mg/dL, or 2 h plasma glucose ≥200 mg/dL during an oral glucose tolerance test, or a HbA1c≥6.5%, or in a patient with symptoms of hyperglycemia, a random plasma glucose >200 mg/dl.[14] Type 2 diabetes mellitus (T2DM) participants were previously examined by an endocrinologist. All T2DM participants had well controlled blood glucose levels and were on treatment with oral hypoglycemic agents mainly metformin and/or low doses of sulfonylureas.

The control group consisted of community people who visited the endocrinology outpatient clinic for a routine checkup or with non-diabetic individuals.

We excluded from the study subjects with a history of cerebrovascular events, a heart stent, an artificial cardiac pacemaker, or other metallic implant, a malignant tumor, peripheral neuropathies, macroangiopathies of the peripheral arteries of the lower extremities, liver disease, end stage chronic kidney disease, a thyroid disorder, carpal tunnel syndrome, or those who had received special dietary supplements such as protein powder, during the last three months.

Demographic characteristics (age, gender, medical history) were collected through a general questionnaire. Height and weight were measured with standard equipment, with the patients wearing light clothes and no shoes on. Body mass index (BMI) was defined as the body weight in kilograms divided by the square of body height in meters. Obesity was defined as BMI≥30 kg/m^2 and overweight as BMI>25 and <29.9 kg/m^2.[15] Collection of data and medical history was performed by trained researchers. Written informed consent was obtained from all subjects, prior to participating in this study. The protocol was designed according to the Declaration of Helsinki and approved by the Ethics Committee of the University authorities (NCT04407819).

Estimation of skeletal muscle mass and physical performance

Muscle mass was estimated via whole body DXA (Hologic Horizon W). Appendicular skeletal mass (ASM) was measured, and skeletal muscle mass index (SMI) was calculated as ASM divided by the square of body height in meters. Low muscle mass was defined as SMI<7.0 and <5.7 kg/m^2, in male and female subjects, respectively.

Furthermore, participants' walking speed was estimated as a marker of physical performance. This was measured by recording the walking speed over a 4-m distance, which was completed twice. The mean value was used to estimate the walking speed. Low physical performance was defined as walking speed <0.8 m/s.

Statistical analysis

Continuous variable values were presented using the number of participants (N), the mean value (mean) and the standard deviation (SD). Regarding categorical variables, frequencies (v) and respective percentages (%) were used. The demographic and BMI data comparison between diabetic and the control group for both genders was made through an independent samples t-test. ANCOVA analysis was used whenever there were differences between the compared groups. Statistical analysis was performed using IBM SPSS statistical software, version 17.00 (SPSS Inc, Chi-

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cago, IL). All tests were two-sided and p-value <0.05 was defined as the level of statistical significance.

RESULTS

Table 1 shows the comparison in both genders of the demographic and anthropometric data, and the parameters associated with diabetes between T2DM patients and the control group. The age of patients and controls was different in the female group (p=0.002) and in the total study population (p<0.005). Male patients with T2DM had a mean age of 68.8±9.5 vs. 55.6±2 years of the control group (p=0.134). Females with T2DM had a mean age of 60.9±5.5 vs. 42.5±11.9 years of the control group (p=0.002), while the total T2DM patients' mean age was 65.1±8.9 vs. 46.6±15.5 years of control group overall (p<0.005). No other significant difference was observed in demographics except for the variation in weight (p=0.07), which was 84.1±12 vs. 76.5±10.6 kg in diabetics vs. controls, respectively. BMI was high in each group and T2DM patients were within obesity ranges. In addition, no statistically significant difference of demographic data between males and females in the control group was observed. In each group, weight values were similar, although there was a difference in BMI due to height discrepancies.

Moreover, walking speed was significantly lower in patients with T2DM compared to male and female control group subjects (1.02±0.34 vs. 1.25±0.15, p<0.001 and 1.01±0.22 vs. 1.27±0.12, p<0.001, respectively).

There was no significant difference in appendicular muscle mass/height^2 = skeletal muscle index (SMI) between the patients and the control group in men and women **(Table 2)**.

Table 1. Demographic data of the participants in total, and those of male and female subjects within the control and patient group specifically by gender. Control group vs. T2DM patients. Homogeneity between compared groups (controls vs. T2DM patients) stratified by gender

Subjects	Men			Women			Total		
Parameters	**T2DM patients (n=18)**	**Controls (n=5)**	***p*-value**	**T2DM patients (n=17)**	**Controls (n=11)**	***p*-value**	**T2DM patients (n=35)**	**Controls (n=16)**	***p*-value**
Age (years)	68.8±9.5	55.6±20.0	0.134	60.9±5.5	42.5±11.9	0.002	65.1±8.9	46.6±15.5	<0.005
Height (m)	173.8±5.5	169.2±9.3	0.286	162.4±5.7	163.8±4.9	0.590	168.5±8.0	165.5±6.7	0.271
Weight (kg)	84.9±13.2	75.2±7.7	0.169	83.3±11.5	77.0±12.00	0.288	84.1±12.0	76.5±10.6	0.070
BMI (kg/m^2)	28.0±3.1	26.4±3.7	0.411	31.7±5.3	28.6±3.6	0.156	29.7±4.5	27.9±3.7	0.225

Table 2. Comparison of appendicular skeletal mass/height^2 between T2DM patients and controls stratified by gender

Subjects	Men			Women*			Total*		
Parameters	**T2DM patients (n=18)**	**Controls (n=5)**	***p*-value**	**T2DM patients (n=17)**	**Controls (n=11)**	***p*-value**	**T2DM patients (n=35)**	**Controls (n=16)**	***p*-value**
Appen. lean/ height^2 (kg/m^2)	6.5±1.2	7.6±1.0	0.110	6.9±0.8	6.3±0.6	0.604	6.7±0.5	6.6±0.4	0.826

* ANCOVA analysis adjusted for age, all values are presented as adjusted mean±SE; T2DM: type 2 diabetes mellitus; Appen. lean/ height^2: appendicular skeletal mass/height^2 = SMI

However, regarding appendicular muscle mass/ height^2 = SMI, a difference was found between the two genders in the control group only (7.6 vs. 6, in men and women, respectively, p=0.004) **(Fig. 1)**.

Sarcopenia prevalence in the control group was 20% in men and 18% in women, displaying non-significant difference between the two genders. On the contrary, sarcopenia prevalence in T2DM patients was 22% in men and 12% in women (p=0.001) and was significantly higher in older (≥70 years) vs. younger participants (40% vs. 12%, p<0.001).

DISCUSSION

This study aimed to contribute to a better understanding of the relationship between diabetes mellitus and sarcopenia; a field which requires further investigation. At present, a small number of observational studies have displayed decreased muscle strength in diabetic elderly men compared to control groups.

Several studies have indicated that patients with T2DM had a greater loss of muscle mass, endurance, and functional ability in the course of the disease compared to non

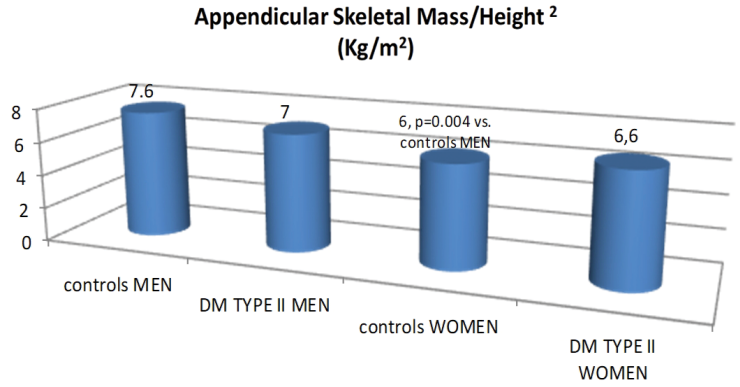

Figure 1. Appendicular muscle mass/height^2 index and statistical significance within the female control group.

T2DM individuals, although no study until now has specifically determined the correlation between T2DM and sarcopenia, using the new EWGSOP criteria.[16-20]

Furthermore, the BMI of diabetics was higher compared to the control group. Overweight people were the majority, even in the control group. BMI in general was high in each group, and T2DM patients were all obese. The control group did not show any statistical difference regarding their demographic data, indicating great homogeneity. In all groups, the weight was similar, however, due to the difference in height between women and men, BMI was found higher in women.

The prevalence of sarcopenia in the control group was not statistically significant as opposed to the patient group. Interestingly, sarcopenia prevalence was significantly higher in male patients with T2DM and significantly greater in elderly participants (>70 years old) compared to the younger participants. This can be explained because in the present study, male patients with T2DM were older. It is worth mentioning that 50% of T2DM male patients were institutionalized, and although ambulatory, male patients were often the most impaired with lower physical performance and mass. This sub-group had a greater mean age (>70 years) compared to the total number of male T2DM patients. The explanation may lie in the reduced protein supplies relative to needs in older persons leading to increased risk for sarcopenia related to low protein intake. Malnutrition is a big challenge in long-term care due to variable reasons such as disease related as well as psychosocial.[21,22]

In the Wang et al. study, the prevalence of sarcopenia was 11.2% in the control group (13.1% in men and 9.6% in women), which is slightly higher than two recent reports in Chinese populations, using the AWGS (Asian Working Group Sarcopenia) criteria.[23] Gao et al.[24] reported a total dominance of 98% (12.0% in women and 6.7% in men) in rural and urban areas, and Han et al.[25], reported a prevalence of 6.4% in men and 11.5% in older women who lived in suburbs. In the present study, which used the EWGSOP criteria, the results were incompatible with the AWGS criteria which practice different sarcopenia thresholds for muscle mass (7 kg/m^2 for men and 5.4 kg/m^2 for women via DXA, and 5.7 kg/m^2 for women via bioelectrical impedance analysis).

Despite the differences in the T2DM group, there was an agreement in the prevalence of sarcopenia in women with other studies. The increased prevalence in men of our study is attributed to increased age and the inclusion of institutionalized patients. Although our study found a significantly greater sarcopenia prevalence in males compared to females, further research is required to clarify gender differences.

There was no significant difference regarding the appendicular muscle mass/height^2 (SMI) index between the patients and the control group, except for the elderly men sub-group (>70 years old). Likewise, Leenders et al. suggested that skeletal muscle mass, lower extremities of muscle strength, and physical performance were reduced to a greater extent in elderly T2DM patients compared to controls, which consisted of euglycemic people of similar ages.[20] However, a statistical difference between the two genders regarding Appendicular Muscle Mass/Height^2 in the control group was found, indicating that BMI may not be an accurate assessment tool of obesity in this group, considering that no differences were observed.

Additionally, walking speed was significantly lower in patients with T2DM than the control group. Park et al. reported that diabetic elderly patients display a 30% greater reduction in muscle power of lower extremities following a 3-year interval, in comparison to healthy people of the same age.[10]

Furthermore, in the Korean Sarcopenic Obesity Study (KSOS), the authors reported that T2DM participants had a greater decrease in muscle mass and walking speed compared to those without diabetes, which is in line with our study.[17] Furthermore, the greatest decrease in muscle mass and function in elderly T2DM patients is independent of disease duration, metabolic control and chronic complications, although evidence is conflicting.[26-29]

An explanation in our study sample could be that community men visit later the special clinics and receive the required medication, when the deterioration is already marked. As far as women are concerned, they were younger, as they appear to attend the related clinics earlier in the course of the disease.

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Some limitations were present in this study. The sample size of patients with T2DM was relatively small due to the strict inclusion criteria. Some older T2DM patients had increased prevalence of serious complications relevant to diabetes, including incidence of cerebrovascular accident, end stage kidney disease and heart failure, which limited their physical activity and total energy intake. Therefore, those patients were excluded from our study to reduce potential confounding factors that would alter muscle mass and function measurements. Furthermore, this is a retrospective study, which does not determine causation between T2DM and increasing sarcopenia risk. Co-morbidities in patients with T2DM, restricting their physical activity may intervene with the relationship between sarcopenia and T2DM compared to the control group who may have had healthier overall diet and exercise habits.

Lastly, our sample originated from specific endocrinology units, which may have overestimated sarcopenia prevalence in comparison to the general population.

Although we managed to match cases and controls in age and sex and adjust a variety of significant variations in the multifactorial statistical analysis, we could not eliminate completely these limitations.

CONCLUSIONS

This study observed greater prevalence of sarcopenia in patients with type 2 diabetes mellitus compared to healthy individuals. Although the main mechanisms of increased risk of sarcopenia in older age are not distinct, our data suggest the utilization of urgent preventative strategies against sarcopenia in older T2DM individuals, aiming to improve blood glucose profile and physical activity levels. Potentially, further investigation of dietary protein malabsorption, glucose intolerance, pro-inflammatory cytokine production, vitamin D deficiency and sedentary lifestyle to evaluate the adverse effects of age on body composition of diabetic patients and to plan thorough therapeutic interventions is warranted.

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Саркопения у больных сахарным диабетом

Янис Дионисиотис[1], Панайотис Атанасиу[2], Янис Папатанасиу[3,4], Ефстатиос Ефстатопулос[5], Константинос Прокопидис[6], Георгиос Тровас[7], Ифигения Костоглу-Атанасиу[8]

[1] Клиника реабилитации после травм спинного мозга, Университетская больница Патры, Патры, Греция
[2] Отделение ревматологии, Больница „Агиос Павлос", Салоники, Греция
[3] Кафедра кинезиотерапии, Факультет общественного здравоохранения, Медицинский университет Софии, Болгария
[4] Кафедра медицинской визуализации, аллергологии и физиотерапии, Стоматологический факультет, Пловдивский медицинский университет, Болгария
[5] Отделение медицинской физики, 2-е отделение радиологии, Университетская больница общего профиля «Аттикон», Медицинский факультет, Национальный и Каподистрийский университет в Афинах, Греция
[6] Кафедра скелетно-мышечной биологии, Институт жизненных процессов и медицинских наук, Ливерпульский университет, Ливерпуль, Соединенное Королевство
[7] Лаборатория исследований опорно-двигательной системы, Национальный и Каподистрийский университет Афин, Кифисья, Греция
[8] Отделение эндокринологии, Больница „Асклепий", Вула, Греция

Адрес для корреспонденции: Янис Дионисиотис, Клиника реабилитации после травм спинного мозга, Университетская больница Патры, Патры, Греция; Email: yannis_dionyssiotis@hotmail.com; Тел.: +30 6946469759

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Резюме

Введение: Такие заболевания, как сахарный диабет, могут быть связаны с неблагоприятными изменениями в составе тела. Саркопения характеризуется прогрессирующей и генерализованной потерей массы и функциональности скелетных мышц.

Цель: Исследовать взаимосвязь между сахарным диабетом 2 типа (СД2) и саркопенией.

Материалы и методы: В ретроспективном нерандомизированном исследовании 35 больных СД2 в возрасте 20–80 лет оценивали распространённость саркопении по сравнению с контрольной группой (n=16). Была измерена аппендикулярная скелетная масса (АСМ) (кг), а саркопения была определена как SMI <7.0 и <5.7 kg/m^2 у мужчин и женщин, соответственно, с использованием определения Европейской рабочей группы по саркопении у пожилых людей (EWGOSP). Низкая физическая работоспособность определялась как скорость ходьбы <0.8 м/с.

Результаты: Частота саркопении была значительно выше у пациентов с СД2 по сравнению с контрольной группой (27% против 20%, p=0.01) и пожилых участников по сравнению с молодыми (40% vs. 12%, p<0.001) соответственно. Скорость ходьбы была значительно ниже у пациентов с СД2 по сравнению с мужчинами и женщинами контрольной группы (1.08±0.22 против 1.23±0.18 и 1.07±0.26 против 1.26±0.16 соответственно, p<0.001).

Заключение: Наблюдалась умеренная распространённость саркопении у пациентов с сахарным диабетом 2 типа, которая, по-видимому, значительно увеличивалась у пожилых мужчин. Наконец, заболеваемость СД2 показала снижение физической работоспособности у обоих полов.

Ключевые слова

старение, сахарный диабет, пожилой возраст, саркопения, DXA-сканирование всего тела