

The Prevalence of Sarcopenia in Patients with Schizophrenia

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ABSTRACT

Objective: In this study, we aimed to investigate the frequency of sarcopenia in patients with schizophrenia and the risk factors that may be associated with sarcopenia.

Methods: We recruited 72 schizophrenia patients who had registered in the schizophrenia specialized unit of Çukurova University. The socio-demographic variable form was filled. Each patient underwent physical mass, strength, and performance tests to confirm the diagnosis of sarcopenia (SP), which was made according to the criteria of European Consensus.

Results: Mean age of the patients was 39.50 (19-65) years for the possible sarcopenia group and 37.00 (21-65) years for without SP group. Possible sarcopenia was 36.1% ($n=26$), and SP and severe SP were 0.0% in schizophrenia patients. Total body water (TBW) (37.60 vs. 43.90) and bone mineral density (2.70 vs. 3.10) values were significantly lower in the possible SP group compared to the non-sarcopenia group ($P=.011$ and $P=.025$, respectively). However, it was found that muscle mass (kg) (51.05 vs. 58.65) and muscle strength (kg/kg) (20.70 vs. 33.15) were significantly lower in the possible SP group compared to the non-sarcopenia group ($P=.042$ and $P=.001$, respectively). Compared to the non-sarcopenia group, patient exercising was less in the possible SP group (4 vs. 9, $P=.001$), while walking speeds (m/s) were statistically faster in the possible SP group (6.74 vs. 5.98, $P=.010$).

Conclusion: This is the first study that investigated SP in schizophrenia patients. Sarcopenia was found more frequently in schizophrenia patients than in the general population.

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INTRODUCTION

Sarcopenia (SP) is a comorbid syndrome defined as progressive loss of muscle mass and strength that can cause fractures, disability, falls, and death. Although SP can be seen at an early age secondary to a sedentary life, chronic diseases, and malnutrition, it is primarily prevalent at the age of 65 and over.¹ In young individuals, it may develop due to conditions such as inactivity, malnutrition, and cachexia.²

“Possible SP”, newly introduced in AWGS 2019, is defined as low muscle strength with or without reduced physical performance. Individuals who get positive results in the case-finding algorithm and screening tests (CC, SARC-F questionnaire, and SARC-CalF) require further evaluation through muscle strength or physical performance tests. Possible cases of SP were classified as low muscle strength (28 kg for men; 18 kg for women) according to handgrip strength or low physical performance (12 s for both genders) according to the 5-time sit test. AWGS 2019 describes “SP” as low muscle strength plus low muscle mass or low physical performance and “severe SP”

as low muscle strength, low muscle mass, and low physical performance.³

The SP prevalence increases with age. From the beginning of the fourth decade, muscle mass decreases linearly. The loss rate is higher in men than in women.⁴ The prevalence of sarcopenia varies depending on the method used.⁵ According to age-related variations and region, the prevalence of sarcopenia in the population has been reported to be 1-29%, 14-33% in long-term care populations and 10% in hospital-based acute care populations.⁶

Physical inactivity, insufficient protein intake, changes in the neuroendocrine system, and increased inflammation have been shown as causes of sarcopenia.^{7,8} In many studies, muscle loss has been reported as a result of increased exposure to reactive oxygen products and increased oxidative stress.⁹⁻¹¹ Quality of life is adversely affected in patients with sarcopenia.¹⁰ According to our knowledge, nutrition and physical exercise are the most important factors in preventing sarcopenia.¹²

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Schizophrenia is an early-onset, often chronic disease and may result in intensive care needs, long-term treatment, disability, high disease burden, low quality of life for many years, and reduced life expectancy of 15-20 years.¹³⁻¹⁵ Additionally, it has been suggested that people with schizophrenia already suffer from an accelerated aging process when it comes to functioning as they do at a young age. For example, cognitive tasks and both basic and instrumental activities of everyday life are at the same level or weaker than healthy older adults.¹⁶

Schizophrenia patients have reduced aerobic capacity and report subjective muscle weakness.^{17,18} Both are likely to play an important role in physical adaptation to daily life activities, such as walking, climbing stairs, and lifting chairs. Previous research has shown that impaired performance in activities of daily living in schizophrenia patients is associated with overweight, metabolic complications, smoking behavior, negative symptoms, and lower physical self-perception.^{19,20} An impaired functional walking capacity has also been associated with health-related poor quality of life.²¹ Although the decrease in muscle fitness may contribute to daily life disorders, the prevalence of muscle weakness in schizophrenia patients compared to healthy individuals compatible with age, gender, and body mass index (BMI) and its relation with performing daily life activities such as walking, as far as we know, has not been studied.

Male patients with mood disorders reported an increased prevalence of SP in recent years.²² Schizophrenia is an early-onset, often chronic, illness which is considered a worldwide public health problem. People with schizophrenia generally have low aerobic capacity.²³ Many studies have reported that reactive oxygen products and oxidative stress increase in schizophrenia.²⁴ Oxidative stress may also be a possible etiological factor in SP.²⁵ When these 2 are taken together, it can be thought that SP can also be seen in schizophrenia, because this is a chronic disorder and oxidative stress is associated with both diseases. In the current study, we aimed to investigate the frequency of sarcopenia in patients with schizophrenia and the risk factors that may be associated with SP.

MATERIALS AND METHODS

Study Sample

Patients diagnosed with schizophrenia who met the *Diagnostic and Statistical Manual of Mental Disorders*,

Fifth Edition (DSM-5) criteria and received outpatient or inpatient treatment in Çukurova University School of Medicine, Department of Mental Health and Diseases between October 15, 2019 and April 15, 2020 constitute the sample group of the study. In our schizophrenia specialized unit, an average of 15 patients apply on Mondays, and an average of 2-3 schizophrenia patients per day visit routine polyclinics as inpatients. Approximately 250 patient applications are expected within 3 months. The study protocol was approved by the Çukurova University Local Research Ethics Committee (Approval number: TR-92/11).

Inclusion and Exclusion Criteria

Participants have given their written informed consent. Patients were recruited among those who accepted the study. Those with a history of neurological disorders, diabetes mellitus, myopathy, goiters, kidney or liver disease, inflammatory rheumatic disorders, complex regional pain syndrome, osteomalacia, osteoporosis, depression, or a history of psychiatric disorder, and patients who had received any medical therapy for neuropathic or nociceptive pain in the last 1 month were excluded from the study.

Procedure

Written informed consent was obtained from the volunteers who agreed to participate in the study. To determine the sample size of the study G Power 3.1.9.2 program was used²⁶; 72 people in the group with medium effect size (Cohen's d : 0.50), 0.95 power, and 0.05 margin of error ($P=.05$) constitute the sample group of the study. Positive and negative symptoms rating scales (SAPS-SANS) were applied to the patients. The participants' walking speed (6 m walking time), muscle strength (to be measured by CAMRY Digital Hand Dynamometer), and muscle mass (to be measured by Tanita body analysis device) were measured. Scores measured in schizophrenia patients were evaluated according to the diagnostic criteria of SP, the frequency of SP was calculated, and risk factors that could be associated with sarcopenia were investigated.

Measurement Tools

Sociodemographic Data Form: A data form was designed for the study, which included questions about age, gender, marital status, education status, employment status, place of residence, smoking status, cigarette package/year, alcohol (yes), substance use (yes), medication (antipsychotics), hospitalization, number of hospitalizations, disease duration (month), and mental illness in the family (yes).

Anthropometric Parameters: Height, weight, and BMI of all participants were measured using a precision digital scale up to 0.1 kg and a standardized gauge up to 0.1 cm. Participants took off socks, shoes, and heavy clothes before evaluations were taken. BMI was defined as body

KEY POINTS

- The rate of possible SP was 36.1% in schizophrenia patients.
- The patients with schizophrenia are in the high-risk group for sarcopenia in advanced ages.
- Working rate, exercise rate, bone mineral density, muscle strength and muscle mass are lower, while walking speeds (m/s) were statistically faster in patients with schizophrenia with possible SP.

weight in kilograms divided by height squared in meters. All measurements were guided by trained staff.

Body Composition: A bioelectrical impedance analyzer (Tanita SA165 A0950 U-3, Netherlands) was used to evaluate the body composition parameters. Bioelectrical impedance analysis (BIA) was performed after fasting for at least 2 hours and with an empty bladder. Total skeletal muscle mass was measured by the estimation equation defined by Jannssen et al.²⁷ Skeletal muscle mass index (SMMI) was measured as complete SMM (kg)/height square (m²).²⁸ The cut-off rates defined by Bahati et al.²⁹ for the Turkish population were used to define low SMMI as 7.4 and 9.2 kg/m² in men and women.²⁹

Physical Performance: For normal walking speed assessment, an 8 m long corridor was used, in which a 4 m tape was recorded from the end of the second meter to the end of the sixth meter. Therefore, the corridor was divided into 3 parts: the first 2 m acceleration zone, the second 4 m timing area, and the third 2 m deceleration zone. Participants were asked to walk at their regular pace. The time to pass through the central area was evaluated with a stopwatch. If the rated speed is less than 0.8 m/s, it is considered low walking speed.

Muscle Strength: The grip strength of the dominant hand was used to describe muscle strength. For this, a Jamar dynamometer with an authorized protocol was used.^{30,31} The evaluation was made in the sitting position, the wrist in a neutral position, and the elbow at 90 degrees of flexion. In the sitting position, the participants squeezed as many times as possible (30-s rest intervals) and were listed as the highest holding strength. For the diagnosis of sarcopenia, the cut-off thresholds of 20 and 30 kg handgrip strength were used for men and women recommended by Bahat et al.²⁹ for the Turkish population, respectively.²⁹

Statistical Analysis

All analyses were done using Statistical Package for the Social Sciences (SPSS) version 25.0 (IBM SPSS Corp.; Armonk, NY, USA). *P* values less than .05 were considered significant. The normality control of the data was done with the Shapiro-Wilk test. Descriptive analyses were performed using median and (min-max) values for variables that were not normally distributed. We run Mann-Whitney *U* test to identify the differences between groups. For correlation analysis, Spearman test for normally distributed numerical variables and Spearman correlation tests for non-normally distributed variables were used.

RESULTS

Sociodemographic Characteristics of the Sample

Mann-Whitney *U* test was used to determine whether there was a difference between the possible SP group and non-SP group in terms of age, gender, marital status, education

status, employment status, place of residence, smoking status, cigarette package/year, alcohol (yes), substance use (yes), medication (antipsychotics), hospitalization, number of hospitalizations, disease duration (month), and mental illness in the family (yes). The mean age of the patients was 38.00 ± 12.53 years (19-65). The mean age of the patients was 39.50 (19-65) years for the possible SP group and 37.00 (21-65) years for without SP group. Among the participants 17 (23.6%) were female, and 55 (76.4%) were male. Possible SP was 36.1% (*n*=26), SP and severe SP were 0.0% in schizophrenia patients. The prevalence of possible SP in schizophrenia patients was 65.4% in men and 34.6% in women.

Comparison of demographic and clinical parameters of groups in schizophrenia patients was shown in Table 1. The percentage of males in the possible SP group and the non-SP group were higher, but there was no statistically significant difference between the groups. In addition, there was no statistically significant difference between the groups in terms of age, gender, marital status, education status, place of residence, smoking status (yes), cigarette package/year, alcohol (yes), substance use (yes), medication (Antipsychotics), hospitalization, number of hospitalizations, disease duration (month), and mental illness in the family (yes) (*P* > .05). However, it was found that there was a statistically significant difference between the groups in terms of employment status (*P* = .024). The percentage of 100.0% of the patients in the possible SP group were non-working (Table 1).

Comparison of Anthropometric Parameters

Comparison of anthropometric parameters of groups in schizophrenia patients was shown in Table 2. Total body water (TBW) (37.60 vs. 43.90) and bone mineral density (BMD) (2.70 vs. 3.10) values were significantly lower in the possible SP group compared to the non-sarcopenia group (*P* = .011 and *P* = .025, respectively). However, it was found that muscle mass (kg) (51.05 vs. 58.65) and muscle strength (kg/kg) (20.70 vs. 33.15) were significantly lower in the possible SP group compared to the non-SP group (*P* = .042 and *P* = .001, respectively). Compared to the non-SP group, patient exercising was less in the possible SP group (4 vs. 9, *P* = .001), while walking speeds (m/s) was statistically faster in the possible SP group (6.74 vs. 5.98, *P* = .010). There was no statistically significant difference between the groups in terms of metabolic age, height, weight, BMI, TBW percentage, fat mass, and visceral mass (*P* > .05) (Table 2).

The Relationship Between Possible SP and Parameters in Schizophrenia Patients

Spearman correlation analyses were performed to examine the relationship between possible SP and parameters in schizophrenia patients. Correlation coefficients between possible SP and parameters in schizophrenia patients were shown in Table 3. There was a negative correlation

Table 1. Comparison of Demographic and Clinical Parameters of Groups in Schizophrenia

Demographic and Clinical Parameters	Possible SP (<i>n</i> = 26, 36.1%)		Non-SP (<i>n</i> = 46, 63.9%)		Statistics <i>t</i> / <i>x</i> ²	<i>P</i> Value*
	<i>N</i>	Min-Max/%	<i>N</i>	Min-Max/%		
Age (year)	39.50	19-65	37.00	21-65	0.814	.722
Gender					0.101	.127
Female	9	34.6	8	17.4		
Male	17	65.4	38	82.6		
Marital status					0.615	.615
Single	18	69.2	29	63.0		
Married	6	23.1	13	28.3		
Divorced	2	2.0	4	8.7		
Education status					0.930	.813
Primary	8	30.8	10	21.7		
Secondary	4	15.4	10	21.7		
High School	7	26.9	16	34.8		
University	7	26.9	10	21.7		
Employment status					0.084	.024
Working	0	0.0	5	10.9		
Not-working	26	100.0	41	89.1		
Place of residence					0.506	.510
City center	20	76.9	32	69.9		
Rural	6	23.1	14	30.4		
Smoking status (yes)	11	42.3	21	45.7	0.785	.787
Cigarette package/year	20.0	5-60	15	1-80	0.593	.751
Alcohol (yes)	4.0	15.4	3.0	6.5	0.226	.281
Substance use (yes)	1.0	3.8	1.0	2.2	0.680	.683
Medication (Antipsychotics)	26	100.0	46	100.0	1.000	1.00
Hospitalization	17	65.4	29	63.0	0.844	.845
Number of hospitalizations	1.0	0-10	2.0	0-14	0.814	.930
Disease duration (month)	10.0	1-38	12.0	1-30	0.756	.934
Mental illness in the family (yes)	13	50.0	14	30.4	0.102	.113

*Mann-Whitney *U* test was used. SP: Sarcopenia.

between possible SP and TBW (r : -0.329, P = .005), BMD (r : -0.276, P = .019), muscle mass (r : -0.246, P = .037), and muscle strength (r : -0.767, P = .001). However, there was a positive correlation between possible SP and walking speed (r : 0.307, P = .009). In addition, no statistically significant difference was found between the groups in terms of age, gender, employment status, exercise, height, weight, and BMI (P > .05) (Table 3).

DISCUSSION

To our knowledge, this is the first study that investigated SP in schizophrenia patients. In the current study, we found that the rate of possible SP was 36.1% in schizophrenia patients. This ratio shows that patients with schizophrenia are in the high-risk group for SP in advanced ages. In addition, working rate, exercise rate, BMD, muscle strength, and muscle mass are lower, while

walking speeds (m/s) were statistically faster in patients with schizophrenia with possible SP.

As far as we know, this is the first study that investigated SP in schizophrenia patients. In the current study, possible sarcopenia was 36.1%, and SP and severe SP were 0.0% in schizophrenia patients. In the health care system in the United States in 2000, the money spent for diseases associated with SP and SP is about 18 billion dollars and is thought to account for 1.5% of total health spending.^{32,33} Therefore, SP is an important health problem in our country, whose life expectancy is rapidly increasing. SP prevalence increases with age. Studies have showed that the SP prevalence is 8-40% in 60 years and older, 5-13% between 60 and 70 years of age, and 11-50% in 80 years and older.^{34,35} The SP incidence is low in the young population (20-39 years). Krzymska-Siemaszko et al.³⁶ showed that the prevalence of SP was 16.28% for males and 2.62% for females in the young

Table 2. Comparison of Anthropometric Parameters of Groups in Schizophrenia Patients

Anthropometric Parameters	Possible SP (n=26)		Non-SP (n=46)		Statistics t/x^2	P Value*
	N	Min-Max/%	N	Min-Max/%		
Metabolic age (year)	39.50	12.0-70.0	43.00	17.0-75.0	-0.616	.513
Height (cm)	169.00	152.0-192.0	170.0	153.0-184.0	-0.557	.799
Weight (kg)	77.90	50.8-148.5	83.75	61.3-124.9	-1.630	.225
BMI (kg/m ²)	26.30	17.6-51.4	29.00	21.3-51.3	-1.624	.325
TBW (L)	37.60	29.4-49.7	43.90	27.6-55.6	-2.558	.011
TBW percentage	51.80	38.4-69.5	52.60	38.8-62.8	-0.433	.874
BMD	2.70	2.2-3.6	3.10	2.1-3.9	-2.247	.025
Fat mass (kg)	19.85	2.8-78.0	21.70	8.1-59.0	-0.082	.981
Muscle mass (kg)	51.05	40.1-71.32	58.65	38.1-75.7	-2.034	.042
Visceral mass (kg)	7.0	1-39	9.0	2-20	-1.893	.429
Muscle strength (kg/kg)	20.70	13.5-28.7	33.15	21.4-42.8	-6.466	.001
Exercise (yes)	4	15.4	9	19.6	-4.440	.001
Walking speed (m/s)	6.74	4.34-9.12	5.98	3.84-7.91	-2.585	.010

*Mann-Whitney *U* test, SP, sarcopenia; TBW: total body water; BMD: bone mineral density; BMI: body mass index.

population.³⁶ In our study, while the mean age was 38.00 ± 12.53 years (19-65), the rate of possible SP was 36.1% in schizophrenia patients. Ozturk et al.³⁷ reported that the prevalence of SP was 21.8% in men and 8.7% in women.³⁷ In our study, the prevalence of possible SP in schizophrenia patients was 65.4% in men and 34.6% in women. However, the percentage of males in the possible SP group and the non-SP group were higher, but there was no statistically significant difference between the groups.

Lately, there has been an increased interest in physical rehabilitation in the treatment of schizophrenia patients.³⁸ International guidelines report that physical activity could be one of the cornerstones of

multidisciplinary treatment.³⁹ The inability to increase physical activity in patients with schizophrenia is explained by sociodemographic, somatic, and motivational factors such as the presence of negative and depressive symptoms.⁴⁰ So, a prerequisite for supervised physical activity programs in schizophrenic patients is information about the mental and physical health status, including the presence of negative and depressive symptoms, the extent of the impairment in aerobic capacity and functional exercise capacity, and metabolic and muscular fitness.⁴⁰ While only a few previous studies have depicted the relationship between quality of life and muscle strength, Öztürk et al.³⁷ stated that both walking speed and muscle strength were positively correlated in SP patients.³⁷ In our study, there was a negative correlation between possible SP and TBW ($r: -0.329, P=.005$), BMD ($r: -0.276, P=.019$), muscle mass ($r: -0.246, P=.037$), and muscle strength ($r: -0.767, P=.001$). However, there was a positive correlation between possible SP and walking speed ($r: 0.307, P=.009$) in schizophrenia patients. Since BMD is lower in possible SP, it may be a risk factor for the development of bone fractures and osteoporosis in schizophrenia patients in the future.

While it is well known that most medical disorders are affected by body composition, it is also stated that body composition is associated with the occurrence of general mood disorders such as schizophrenia, anxiety, and depression.⁴¹ However, the possible muscle movements and the elements of body composition vital to health and vitality have largely remained unexplored. The validity of this basis stems from the evidence of general pathophysiological pathways for schizophrenia and SP that involves inflammation and oxidative stress as well as neurotrophins and are modulated by lifestyle behaviors.^{42,43} It has been reported that mechanisms related

Table 3. Correlation Coefficients Between Possible SP and Parameters in Schizophrenia Patients

	<i>r</i>	<i>P</i> value
Age	0.043	.722
Gender	-0.195	.101
Employment status	-0.205	.084
Exercise	-0.052	.663
TBW	-0.329**	.005
BMD	-0.276*	.019
Height	-0.066	.581
Weight	-0.193	.104
BMI	-0.193	.105
Muscle mass	-0.246*	.037
Muscle strength	-0.767**	.001
Walking speed	0.307**	.009

TBW: total body water; BMD: bone mineral density; BMI: body mass index; *r*: Spearman correlation coefficients. *Correlation is significant at the 0.05 level. **Correlation is significant at the 0.01 level.

to the inflammation and anti-inflammatory defense system play a role in the development of schizophrenia (Ramirez-Jirano et al.,⁴⁴ Citocinas y sistema nervioso: relacion con la esquizofrenia/2019).⁴⁴ In the current study, employment status (not working), BMD, and TBW deficiency associated with inflammation and oxidative stress were found to be lower in possible SP patients than those without SP in schizophrenia.

Studies have shown that total fat mass, visceral fat, and BMI are increased as a result of irregular nutrition and low physical activity, although muscle mass decreases.^{40,45,46} Most of these findings are also seen in elderly patients with sarcopenia.^{2,47,48} In the current study, exercise, muscle strength, and muscle mass values were significantly lower in the possible SP group compared to the non-SP group in schizophrenia. In addition, it was found that walking speed values were higher in the possible SP group compared to the non-SP group. There was a negative correlation between possible SP and muscle mass and muscle strength, although a positive correlation was observed between possible SP and walking speed.

There are some limitations in our study. First, sampling was not randomized. Second, for the patient group of participants, it would be better to increase the number of participants for further studies. Third, neurotrophins and oxidative stress parameters could not be measured.

In conclusion, this is the first study that investigated SP prevalence in schizophrenia patients. The high frequency of SP in schizophrenia is interesting. SP was found more frequently in schizophrenia patients than in the general population. In our next research, we aim to clarify what measures will be evaluated in the treatment of in-patients with schizophrenia with possible SP. Since schizophrenia is a chronic disease, it causes serious disability. When SP is added to schizophrenia, functionality will deteriorate greatly, and this will lead to an increase in the treatment burden. Precautions to be taken for possible SP in these patients in the early period will contribute to the reduction of disability in patients. As a result, as schizophrenia is described as a degenerative and chronic disorder and degeneration was demonstrated in gray and white matter in the brain,⁴⁹ the outcomes of the study may add a new point of view of degeneration that is seen in muscles in patients with schizophrenia.

Ethical Committee Approval: Ethical Committee Approval was received from the local research ethics committee of Çukurova University for this study (TR-92/11).

Informed Consent: Informed consent was obtained in the study from the research participants.

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