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Original Research

The Impact of Combination of Aerobic and Resistive Exercise on Activities of Daily Living and Risk of Fall in Osteosarcopenic Patients

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Abstract

Objectives: It is aimed to explain the impact of the combination of aerobic and resistive exercise on activities of daily living and the risk of falls in osteosarcopenic patients.

Methods: Female and male patients over 70 years of age followed up from the osteoporosis outpatient clinic were screened. Appropriate patients were evaluated for sarcopenia gait speed, grip strength and skeletal muscle mass. Patients with sarcopenia who did not have the exclusion criteria were included in the 3-month aerobic and resistive exercise program. Changes in skeletal muscle mass measurements, physical performance and balance tests were evaluated at 1 month and 3 months.

Results: Sarcopenia was screened in 91 patients with osteoporosis and osteopenia. Sarcopenia was detected in 27 patients and 23 completed the 3-month study. The mean age of the patients was 78.4±5.7 years and the number of female patients was 16 (69.6%). There was no significant change in skeletal muscle mass measurements and Katz Activities of Daily Living Scale performed at 1 and 3 months ($p>0.05$). Short Physical Performance Battery (SPPB), Timed Up and Go Test (TUGT) and Berg Balance Test (BBT) were found to improve significantly in the first month, and it continued to develop in the third month ($p<0.05$).

Conclusion: Although the combination of aerobic and resistive exercise in osteosarcopenic patients did not lead to a significant increase in skeletal muscle mass, It has a significant effect on physical performance and balance. It can be foreseen that this will increase the independence of the person while reducing the risk of falling.

Keywords: Aerobic exercise, balance, falling, osteosarcopenia, physical performance, resistive exercise

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Osteoporosis is a progressive metabolic bone disease that results in a decrease in bone mineral density (BMD) and deterioration in the microarchitecture of the bone, resulting in increased fragility and a tendency to fracture.[1] Osteoporosis was described as the most common bone disease and a major public health problem.[2] Accord-

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ing to the FRACTURK study conducted in Türkiye in 2012; over 50 years of age, the BMD score was defined as -1.0 and below in 50%, and -2.5 and below in 25%.[3]

Sarcopenia is a progressive and generalized skeletal muscle disease with important consequences such as falls, fractures, physical disability, and mortality. Over time, deterioration in muscle function accompanies low muscle mass.[4] Due to potential for personal, social, and financial concerns, sarcopenia should be addressed as well as possible.[5] Today, ICD-10MC is used in Diagnosis Code and studies and experiences in this field are also been researched. Although sarcopenia is typically common in older ages, it may also occur in the early stages of life. Muscle strength, muscle mass, and physical performance are the three factors that should be taken into account when defining sarcopenia and its severity.[6]

Osteoporosis and sarcopenia are usually seen in advanced ages and their association is common. Therefore, 'Osteosarcopenia' is defined as a new geriatric syndrome. It is not enough to treat osteoporosis alone. Sarcopenia also needs to be treated to prevent falls and improve quality of life. Although there is no clear treatment method yet, exercise is a good treatment option for decreased muscle mass, strength and function. In this study, we aimed to show the positive effects of resistive and aerobic exercise combination on activities of daily living and all risks, as well as the changes in bioimpedance analysis (BIA).

Methods

Sarcopenia was screened in 91 patients who applied to the osteoporosis outpatient clinic. Inclusion criteria: 70 years and older who have osteopenia or osteoporosis, it was determined that he/she was able to independently mobilize, had a walking speed below 0.8 m/sec, had grip strength below 20 kg for women, 30 kg for men and willing to exercise for 3 months. Presence uncontrolled hypertension (systolic blood pressure >200 mmHg, diastolic blood pressure >110 mmHg), uncontrolled diabetes mellitus, stroke in the last 6 months, hip fracture, knee and hip arthroplasty, history of spinal surgery and difficulty in cooperation, presence of a cardiac pacemaker, dialysis patients, presence of acute infection, presence of severe edema, advanced malignancy patients, presence of severe anemia (Hgb<8 mg/dL) were not included in the study. The study was approved by the University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital's ethics committee (2189/4.12.2018) and registered to ClinicalTrials.gov (NCT04526327). Informed consent was obtained from all patients prior to enrollment and it was conducted in accordance with the principles stated in the Declaration of Helsinki.

Patients with osteopenia or osteoporosis at the age of 70 years who were followed up from the osteoporosis outpatient clinic were first screened for sarcopenia. Since the patient group was of advanced age, the patients were first examined in Internal Medicine and Cardiology while using the study exclusion criteria. After measuring the blood pressure of the patients from both arms, they were evaluated by transthoracic echocardiogram (TTE). Laboratory tests were checked from the hospital system. In patients who did not have an impediment to exercising internally, the walking speed was measured first and the next step was started in patients with a walking speed of 0.8 m/sec or less. Grip strength was evaluated if the walking speed was>0.8 m/sec. The grip strength of the dominant hand was examined three times with a Jamar Hydraulic Dynamometer (Sammons Peston Rolyan, Chicago, USA). Fifteen seconds have waited between each measurement. When assessing muscle mass, we used InBody230® (Seoul, Korea) multi-frequency bioelectrical impedance body composition analyzer. BIA measurement was performed to confirm the diagnosis of sarcopenia in patients whose grip strength was found to be less than 20 kg for women and 30 kg for men. Twenty-seven patients (SMI<9.2 kg/m^2 for men and <7.4 kg/m^2 for women) who were found to have sarcopenia with a bioimpedance analyzer were included in a 3-month exercise program.

Exercise duration was determined as 3 months. The weekly exercise frequency was planned as 3 times and the duration was 45 minutes. Exercises for the first month were done once a week with a physiotherapist. The resistive exercises were given for the hip flexor, extensor, abductor, adductor, knee flexor and extensor muscles and each movement was repeated 10 times. As an aerobic exercise, it was planned to walk for 15 minutes on the treadmill. Sandbags were used for resistive exercises and increased by 1 kg weekly and a maximum of 3 kg was increased according to the patient's tolerance. Active exercises were demonstrated in the first week of the exercise, starting in the second week, working with sandbags. Walking on the treadmill started in the 2nd week. During walking, 85% of the maximum heart rate according to the age of the patients was targeted and the walking speed was determined accordingly. Pulse and saturation were monitored with the fingertip saturation probe during the exercise.

The cognitive status of the patients included in the study was evaluated with the Mini Mental State Examination (MMSE), their activities of daily living with the Katz Activities of Daily Living (ADL) Scale, their physical performances by Time Up and Go Test (TUGT), Short Physical Performance Battery (SPPB) and 5 Times Sit to Stand Test. The Berg Balance Test (BBT) was used to evaluate balance.

At 1st and 3rd month, the completed clinical scales and BIA were repeated and their effects on activities of daily living and falling were evaluated.

In the descriptive statistics of the data, mean, standard deviation, median lowest, highest, frequency and ratio values were used. The distribution of variables was measured with the Kolmogorov-Smirnov Test. In the analysis of dependent quantitative data, the paired sample T-test and the Wilcoxon Test were used. SPSS 26.0 (IBM, New York, USA) program was used in the analysis.

Results

This study was conducted from December 2018 to September 2019. We included 27 patients in the study. We completed the 3-month exercise program with 23 patients. The mean age of the patients was 78.4±5.7 years. While the number of women was 16 (69.6%), the number of men was 7 (30.4%). Participants' mean height was found to be 153.9±11.6 cm and their average weight was 53.1±11.4 kg. Body Mass Index (BMI) was calculated as 22.0±2.4 kg/m^2. It was between this value and the ideal body weight. While %87 of the participants had comorbidity, the most common comorbidity was essential hypertension (43.5%). In addition, there were 3 (13%) patients with a history of falling and 4 (17.4%) patients with a known symptomatic fracture history. The most commonly used drug other than osteoporosis treatment consisted of anti-hypertensive drugs (48.1%). When we look at the 25-OH vitamin D levels of the patients included in the study, the mean was 31.1±13 µg/L. The demographic and laboratory characteristics of the patients are shown in Table 1.

Table 1. The demographic and laboratory characteristics of the patients

	Min-Max	Median	Mean±SD/n-%
Age	70.0-91.0	78.0	78.4±5.7
Gender			
Female			18-66.7
Male			9-33.3
Heigh (cm)	134-179	154.0	153.9±11.6
Weight (kg)	35.8-75.0	52.8	53.1±11.4
Body Mass Index (kg/m^2)	17.8-25.9	21.8	22.0±2.4
Educational Background			
Illiterate			6-22.2
Literate			2-7.4
Elementary School			8-29.6
Middle School			3-11.1
High School			5-18.5
University			3-11.1
Additional Disease			
(-)		4-14.8	
(+)		23-85.2	
Diabetes Mellitus			5-18.5
Hypertension			13-48.1
Myocardial Infarction			1-3.7
Fracture			4-14.8
Syncope			1-3.7
Falling			3-11.1
Hypothyrodism			5-18.5
Others			10-37.0
Drug Use			
(-)		7-25.9	
(+)		20-74.1	
Anti-hypertensive			16-59.3
Oral Anti-diyabetic			4-14.8
Anti-aggregant			2-7.4
Thyroid drug			4-14.8
Others			7-25.9
Glucose	79.0-153.0	95.0	97.6±14.9
Hemoglobin	9.8-15.0	12.3	12.5±1.4
Albumin	3.1-4.5	4.0	4.0±0.4
Calcium	8.4-10.7	9.6	9.6±0.5
Parathormone	12.8-136.1	56.0	58.2±31.2
25-OH vitamin D	12.0-68.9	28.0	31.1±13.0
Mini Mental State Examination	18.0-30.0	24.0	23.1±4.4

The walking speed of the participants was found to be 1.1±0.3 m/sec. In the next step of sarcopenia screening, the evaluation of the grip strength was measured as 14.5±2.9 kg in women and 25.4±3.1 kg in men. The results of the walking speed, grip strength and anthropometric measurements of the patients are shown in Table 2.

Skeletal muscle mass measurements of participants made with the BIA device in shown in Table 2 and Table 3. The skeletal muscle mass index of women was calculated as 7.35±0.32 kg/m^2, while that of men was calculated as 8.53±0.67 kg/m^2. As expected, initial skeletal muscle mass and muscle mass index values were found to be significantly higher in men than in women ($p<0.05$).

In the Katz ADL Scale evaluation performed before exercise, the average was found to be 5.96±0.2 points. In the physical performance evaluation made with SPPB, the average was calculated as 8.6±2.4 points. The 5 Times Sit to Stand Test, which has a parameter in SPPB, was measured as 14.5±3.2 seconds on average. It was found to be an average of 12.3±2.1 seconds in the TUGT, which evaluates both physical performance and balance. The average value of the BBT was found 48.0 points. Pre-exercise evaluation data of our patients' activities of daily living and physical performances are shown in Table 2.

The skeletal muscle mass and skeletal muscle mass index evaluations of the patients who were repeated in 1st and

Table 2. The assessment of sarcopenia parameters and clinical scales

	Min-Max	Median	Mean±SD
Gait Speed (m/sec)	0.6-2.1	1.1	1.1±0.3
Grip Strength (kg) 1st	8.0-29.0	17.0	18.0±5.8
Grip Strength (kg) 2nd	10.0-30.0	17.0	18.3±6.2
Grip Strength (kg) 3rd	9.0-29.0	18.0	18.1±6.3
Avg. Grip Strength (kg)	9.3-29.3	16.6	17.9±6.0
SMM (kg)	12.0-30.0	17.7	18.7±4.3
Female	12.0-20.6	16.6	16.3±2.1
Male	19.5-30.0	22.9	22.8±2.2
SMM/(Heigh)^2	6.7-9.4	7.4	7.8±0.8
Female	6.7-7.4	7.4	7.4±0.3
Male	7.4-9.4	8.6	8.5±0.7
Katz ADL	5.0-6.0	6.0	6.0±0.2
SPPB	4.0-12.0	9.0	8.6±2.4
5 Times Sit to Stand Test	8.6-22.3	14.4	14.5±3.2
Timed Up and Go Test	6.6-20.8	12.3	12.3±2.6
Berg Balance Scale	35.0-54.0	48.0	46.4±4.8

SMM: Skeletal Mucle Mass; Katz ADL: Katz Activities of Daily Living; SPPB: Short Physical Performance Battery.

Table 3. Skeletal muscle mass measurement

	Min-Max	Median	Mean±SD	p*	p**
SMM (Kg)					
Pre-Exercise	12.0-30.0	17.7	18.7±4.3		
1st Month	12.8-30.1	17.2	18.7±4.7	0.715^w	
3rd Month	12.6-26.0	17.2	18.2±4.0	0.359^w	0.676^w
SMM /Heigh^2					
Pre-Exercise	6.7-9.4	7.4	7.8±0.8		
1st Month	6.3-9.4	7.4	7.8±0.9	0.709^w	
3rd Month	6.7-9.3	7.5	7.8±0.8	0.084^w	0.356^w

^{w}Wilcoxon test; p* Comparison with pre-exercise/p** Comparison with 1st month; SMM: Skeletal Muscle Mass.

3rd month after the exercise are shown in Table 3. No significant change was found in weight, BMI and skeletal muscle mass assessments performed in the 1st and 3rd months compared to the baseline (p>0.05).

Katz ADL Scale in the 1st and 3rd months after exercise did not change significantly (p>0.05) compared to pre-exercise. SPPB value in 1st and 3rd months after exercise increased significantly (p<0.05) compared to pre-exercise. In addition, the SPPB value at the 3rd month after exercise increased significantly (p<0.05) compared to the 1st month after exercise. After exercise, the 5 Times Sit to Stand Test score decreased significantly (p<0.05) compared to pre-exercise in the 1st and 3rd months. TUGT score decreased significantly (p<0.05) in the 1st and 3rd months after exercise

Table 4. Changes in clinical scales

	Min-Max	Median	Mean±SD	p*	p**
Katz ADL					
Pre-Exercise	5.0-6.0	6.0	5.96±0.19		
1st Month	6.0-6.0	6.0	6.0±0.00	0.317^w	
3rd Month	6.0-6.0	6.0	6.0±0.00	0.317^w	1.000^w
SPPB					
Pre-Exercise	4.0-12.0	9.0	8.6±2.4		
1st Month	6.0-12.0	10.5	9.7±2.2	0.000^w	
3rd Month	6.0-12.0	11.0	10.1±1.9	0.000^w	0.013^w
5 Times Sit to Stand Test					
Pre-Exercise	8.6-22.3	14.4	14.5±3.2		
1st Month	7.7-20.3	12.5	13.5±3.1	0.048^w	
3rd Month	7.6-19.6	12.0	12.7±2.7	0.000^w	0.016^w
Timed Up and Go Test					
Pre-Exercise	6.6-20.8	12.3	12.3±2.6		
1st Month	5.5-15.6	11.0	10.9±2.6	0.007^w	
3rd Month	5.5-15.2	11.2	10.5±2.3	0.001^w	0.013^w
Berg Balance Scale					
Pre-Exercise	35.0-54.0	48.0	46.4±4.8		
1st Month	12.0-56.0	52.0	48.8±8.9	0.000^w	
3rd Month	40.0-56.0	53.0	51.6±3.5	0.000^w	0.000^w

^{w}Wilcoxon test; p* Comparison with pre-exercise/p** Comparison with 1st month; Katz ADL: Katz Activities of Daily Living; SPPB: Short Physical Performance Battery.

compared to the pre-exercise. TUGT score in the 3rd month after exercise decreased significantly (p<0.05) compared to the 1st month after exercise. BBT scores at 1st and 3rd months after exercise increased significantly (p<0.05) compared to pre-exercise. BBT score increased significantly (p<0.05) in the 3rd month after exercise compared to the 1st month after exercise. Changes in clinical scales are shown in Table 4.

Discussion

Apart from the mechanical relationship between bone and muscle, there is a balance because of paracrine and endocrine interaction.[7] In many studies, sarcopenia and osteoporosis have been shown to contain common risk factors and biological pathways.[8] Sjöblom et al.[9] investigated the relationship between postmenopausal osteoporosis and sarcopenia components and found the risk of osteoporosis 12.9 times higher in sarcopenic women compared to non-sarcopenic women. They also stated that the risk of osteoporosis was 11.7 times higher in those with low grip strength and that the risk of fracture increased 2.7 times in those with sarcopenia. All these publications show that muscle and bone are a whole and muscle and bone problems should be approached on common ground. In our study, we aimed to contribute to the literature by explain-

ing the effects of exercise on clinical scales and muscle mass in patients with both osteoporosis and sarcopenia.

The awareness of sarcopenia has been increasing in recent years. According to the data published by the World Health Organization[10] in 2010, it has been declared that the population over the age of 65 is 524 million, which corresponds to 8% of the total population and it is predicted that the population over the age of 65 will be 1.5 billion in 2050. While sarcopenia is seen at a rate of 20-25% over the age of 70, it increases to 50% over the age of 80.[11,12] In a Far Eastern prevalence study involving 316 people, osteosarcopenia was found with a rate of 10.4% in men and 15.1% in women over 65 years of age.[13]

What makes sarcopenia important for us is that it has many adverse consequences, especially falling. Falling is the most common cause of morbidity and mortality over the age of 75.[14] Causes of the fall; there may be neuromuscular or cognitive deficiencies and losses in balance, coordination, muscle strength and vision.[15,16] In our study, we tried to explain the effect of exercise on balance by using BBT. We found a significant increase in BBT scores compared to pre-exercise.

Although the treatment algorithm for osteoporosis is clearly demonstrated, this is not valid yet for sarcopenia. Although lots of publications suggest that resistive exercise and nutritional support should be given together, a clear treatment algorithm has not been established yet. Of course, one reason for this situation is that the diagnosis of sarcopenia is still in the process of development and there are differences between guidelines. When we look at the literature, it has been shown that resistive exercise programs increase muscle strength, endurance, flexibility and functional autonomy.[17-19] In a review published in 2017, it was stated that regular walking alone has minimal or no effect on muscle and bone, and traditional progressive resistive studies have a protective effect on muscle mass, size and strength. In addition, it was stated that reducing the sitting time and interrupting the sitting period would help prevent muscle loss.[20] In this study by Kwon et al. [21], the changes in skeletal muscle mass, muscle strength, physical and cognitive functions were examined with resistive Thereband® exercises. Significant increases in skeletal muscle mass, muscle strength and physical performance were detected after 8 weeks of exercise. In our study, while a significant improvement was observed in physical performance, there was no significant change in skeletal muscle mass. The reason for this may be the short exercise period, the supervised exercise period being only in the first 1 month, or the lack of additional protein support. Although high-speed progressive resistive exercise (or strength exercise) is superior to traditional progressive resistive exercise on muscle strength and functional performance due to its rapid muscle contraction, its evidence is still limited.[22]

There are many studies involving the combination of resistive exercise and other exercises. A study by Eyigor et al. [23], showed that walking, balance and flexibility exercises combined with resistive exercise increased knee extensor muscle strength. Although we did not measure muscle strength directly in our study, the significant improvement in the 5 times sit-to-stand test is an indirect indicator of the increase in lower extremity muscle strength. In a meta-analysis consisting of 12 randomized controlled studies, it was stated that the combined resistive and balance exercise program was effective in preventing falls.[24] Takeshima et al.[25] showed that aerobic and resistive sequential exercises simultaneously were protective on cardiovascular fitness, muscle strength and body composition. Italian researchers recommended aerobic, resistive and strength exercises in their study about sarcopenic patients.[26] In our study, we similarly found that the combination of resistive and aerobic exercise provided improvement in the clinical scales.

In many studies conducted in patients with osteoporosis and/or sarcopenia, aerobic exercise is recommended for its many positive effects in elderly patients. Ossowski et al.[27] examined the short-term effect of the Nordic walking stuff on sarcopenia-related parameters in women with low BMD and found that it had positive effects on muscle strength and functional performance. Trappe et al.[28] gave the patients 13 weeks of resistive or aerobic exercise and then compared them with a placebo group. They found an increase in quadriceps muscle volume in the groups that received exercise compared to the placebo group. In addition, they stated that this increase was similar at the end of 12 weeks in resistive and aerobic exercise groups.

Since the patient group with osteosarcopenia is generally of advanced age, understanding and applying the given exercise and ensuring its continuity has an important place in terms of the benefit of the treatment. In a randomized controlled study by Tsekoura et al.[29], group exercise and home-based exercise group were found to be superior to the control group with functional evaluations, but group exercise was found to be significantly more effective than home-based exercise on functional performance in sarcopenic elderly. The reason we gave our patients observed exercise in the first month of our study was to ensure patient compliance and to be followed up regularly. We observed a significant improvement in physical performance tests, but we could not detect an increase in muscle mass. We can attribute this to the fact that our observed exercise program is limited to 1 month and the exercise in the last 2

months is a home-based exercise.

Being able to prevent osteosarcopenia before treating it is an important strategy. When we looked at the literature, we came across many publications emphasizing the importance of many physical activities. In the ROAD study, which is one of the most important studies on this subject; Prevention of osteoporosis is important to reduce the risk of fractures, prevent fractures and sarcopenia, osteosarcopenia alone leads to a higher fracture risk than osteoporosis, prevention of both osteoporosis and sarcopenia prevents the development of frailty, recognition when osteoporosis or osteosarcopenia is detected, appropriate treatment based on nutrition and physical activity, It has been emphasized that it should be regulated.[30] In a study by Akune et al.[31], they tried to explain the relationship between exercise habits in middle age and sarcopenia. As a result of the study, they found a lower prevalence of sarcopenia in individuals who exercised at the age of 25-50. In a published review and meta-analysis, the relationship between physical activity and sarcopenia was tried to be explained and it was stated that sarcopenia was lower in physically active groups.[32]. In another study, it was been reported that protein synthesis decreases in cases with a decrease in step duration, sedentary lifestyle and protein in the diet and this causes muscle loss.[33] Many scientists state that exercise protects against mitochondrial dysfunction that occurs with aging.[34,35] Aerobic studies have been shown to stimulate oxidative capacity and increase mitochondrial enzyme activity in human and animal models.[36,37] Therefore, exercise is both a protective and therapeutic method.

The first limitation of our study is the small number of patients and the absence of a control group. The second is that the sarcopenia diagnosis algorithm was followed according to the 2010 recommendations instead of the 2019 recommendations of EWGSOP. This is because the study started before the final recommendations were published. The reasons that make our study strong are, to be prospective, specifically to give aerobic and resistive exercise to the osteosarcopenia group, 85% of the patients stay in the study and the use of national cut-off values for skeletal muscle mass index.

Conclusion

Based on all these publications and the results of our study, we think that the combination of resistive and aerobic exercise will reduce the loss of balance and falls and increase the independence of the person. In the future, there is a need for studies with a high level of evidence on osteosarcopenia with more patient numbers and groups and with specific treatment recommendations.

Disclosures

Ethics Committee Approval: The study was approved by University of Health Sciences Türkiye, Sisli Hamidiye Etfal Training and Research Hospital's ethics committee (2189 / 4.12.2018) and registered to ClinicalTrials.gov (NCT04526327).

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