Are Hyperlipidaemia and Insulin Resistance Risks For Sarcopenia?

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ABSTRACT

Objective: To investigate whether insulin resistance and lipid metabolism disorders could be associated with sarcopenia.
Study Design: Cross-sectional descriptive study.
Place and Duration of the Study: Department of Physical Medicine and Rehabilitation, Sanliurfa Training and Research Hospital, Sanliurfa, Turkiye, from December 2023 and May 2024.
Methodology: The study included 135 patients who met the inclusion and exclusion criteria. Data such as age, gender, body mass index (BMI), lipid profile, fasting blood glucose, C-peptide, and insulin levels were collected. Following sarcopenia screening, participants were divided into two groups for further examination, and the correlation between sarcopenia and other parameters was assessed.
Results: BMI levels were significantly higher in the sarcopenia group ($p = 0.003$). Triglyceride levels were also significantly elevated in the sarcopenia group ($p = 0.001$). The number of patients with dyslipidaemia in the sarcopenia group was higher compared to the non-sarcopenia group ($p = 0.003$). Correlation analysis revealed a positive association between sarcopenia and BMI, insulin resistance, high triglyceride levels, and the presence of dyslipidaemia ($p = 0.002$, $p = 0.032$, $p = 0.002$, $p = 0.004$, respectively).
Conclusion: This study suggests that high triglyceride levels may represent a risk factor associated with sarcopenia and that sarcopenia may be associated with conditions such as high BMI, insulin resistance, and dyslipidaemia. Controlling lipid levels could be beneficial in reducing the risk of sarcopenia.

Key Words: *Chronic disease, Hyperlipidaemia, Hypertriglyceridaemia, Insulin Resistance, Sarcopenia.*

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INTRODUCTION

Sarcopenia is a degenerative condition of the skeletal system that impairs muscle strength, mass, and physical performance, thereby increasing the risk of injury and mortality. It results from factors such as immobility, malnutrition, polypharmacy, sedentary lifestyles, and advanced age.[1]

According to the European Working Group on Sarcopenia in Older People (EWGSOP), muscle mass, muscle strength, and physical performance should be assessed together when staging sarcopenia. A reduction in muscle mass alone, without any impact on muscle strength or physical performance, is referred to as 'probable sarcopenia'; a decrease in muscle mass coupled with a reduction in muscle strength is termed 'confirmed sarcopenia'; and a decline in muscle mass, muscle strength, and physical performance collectively is classified as 'severe sarcopenia.[2]

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Multiple risk factors combined lead to an increased incidence of sarcopenia. While older individuals often experience primary sarcopenia as a consequence of advanced age, secondary sarcopenia can result from chronic illnesses, malnutrition, prolonged inactivity, and a sedentary lifestyle. Distinguishing between primary and secondary sarcopenia can present a challenge for clinicians.[3]

The literature appears limited in terms of investigating the relationship between sarcopenia, insulin resistance, and lipid profile disorders. The aim of this study was to explore the hypothesis that insulin resistance and lipid profile disorders, both of which are associated with numerous diseases, may serve as risk factors for sarcopenia.

METHODOLOGY

The study was approved by the Harran University Clinical Research Ethics Committee (HRU/23.24.25). It was conducted in accordance with the principles outlined in the Declaration of Helsinki, and written informed consent was obtained from all participants included in the study. Volunteers who visited the endocrinology outpatient clinic between December 2023 and May 2024 were eligible for inclusion.

Participants who attended the endocrinology outpatient clinic without a prior diagnosis were included in the research. The

following conditions were set as exclusion criteria: Diabetes, dyslipidaemia, thyroid hormone dysfunction, heart failure, respiratory failure, chronic obstructive pulmonary disease, breathing difficulties, autoimmune diseases such as systemic lupus erythematosus, vasculitis, inflammatory conditions, arthritis, fibromyalgia, cerebrovascular disease, multiple sclerosis, myopathy, infectious diseases, and individuals with recent diagnoses of these conditions or those receiving long-term medication. Additionally, patients who had been hospitalised for any reason within the past year, those with a history of surgery, individuals who actively engage in sports to enhance their fitness, and those whose musculoskeletal pathologies impaired physical performance (such as polio sequelae, brachial plexus injury, advanced gonarthrosis, paraplegia, tetraplegia, surgically treated lumbar disc herniation, polyneuropathies, myelopathies, myopathies, short stature, congenital musculoskeletal disorders, etc.), and those with a history of substance use (such as alcohol or smoking) that could negatively impact health were excluded from the study. Participants aged under forty or over sixty-five were also excluded due to the low prevalence of sarcopenia in younger individuals and the higher frequency of sarcopenia in older populations. Patients whose tests were requested by the endocrinologist were then evaluated for sarcopenia by the physiatrist. The patients were evaluated by the Endocrinology and Physical Therapy physician on the same day and consecutively.

Body Mass Index (BMI) was calculated by dividing a person's body weight (in kilograms) by the square of their height (in metres). BMI classification was used to categorise participants and provide an estimate of the excess weight and body fat they carried. The classification process based on BMI (kg/m^2) was 18.5 and below: weak, 18.5 - 24.9: normal weight, 25.0 - 29.9: overweight, 30.0 - 34.9: obese (1^{st} degree obesity), 35.0 - 39.9: extremely obese (2^{nd} degree obesity), and 40 and above: morbidly obese (3^{rd} degree obesity).

After fasting for eight to ten hours, the following parameters were measured: Fasting blood glucose, insulin, triglycerides, total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was used to calculate insulin resistance. HOMA-IR is calculated by multiplying the fasting blood glucose level by the insulin level and dividing by 405. A result above 2.5 is considered indicative of insulin resistance.[4]

The lipid profile was generally assessed in terms of isolated cholesterol elevation, isolated triglyceride elevation, or combined triglyceride and cholesterol levels. Triglyceride levels below 150 mg/dl are considered normal, between 150 and 499 mg/dl are classified as borderline high, and levels above 500 mg/dl are considered high. Total cholesterol levels below 200 mg/dl are regarded as normal, between 200 - 239 mg/dl as borderline high, and above 240 mg/dl as high. LDL cholesterol levels are considered normal below 100 mg/dl, borderline high between 130 - 159 mg/dl, and high at 160 mg/dl or above. In men, HDL cholesterol levels of 60 mg/dl or higher are considered normal, 40 - 59 mg/dl as borderline low, and 40 mg/dl or below as low. In women, HDL cholesterol levels of 60 mg/dl or higher are regarded as normal, 50 - 59 mg/dl as borderline low, and 50 mg/dl or below as low. Dyslipidaemia refers to a lipid profile with one or more abnormalities.[5]

All patients were assessed by a physiatrist in terms of their musculoskeletal system, and a Simple Questionnaire to Rapidly Diagnose Sarcopenia (SARC-F) test (in Turkish) was performed.[6] In clinical practice, SARC-F is used as a screening tool to assess the risk of sarcopenia. The SARC-F survey consists of five self-report questions related to strength, walking, rising from a chair, climbing stairs, and falls. The total score ranges from 0 to 10, with a score of 4 or higher indicating an increased risk of sarcopenia. According to the SARC-F results, patients scoring 4 or above were classified as having sarcopenia.

Patients were then divided into two groups based on the presence or absence of sarcopenia as determined by the SARC-F test. The groups were compared with respect to BMI, lipid profile, and insulin resistance. Potential associations between lipid profile abnormalities, insulin resistance, and sarcopenia were explored.

The G*Power 3.1.9.2 software was used to calculate the sample size for the study. The study titled "The Association of Lipid Metabolism and Sarcopenia Among Older Patients: A Cross-Sectional Study" was used as a reference. Based on this, it was determined that a minimum of 40 patients should be included, comprising at least 20 patients with sarcopenia and 20 patients without sarcopenia, in order to achieve a 95% confidence interval and 95% statistical power.

Statistical analyses were performed using the Statistical Package for the Social Sciences (version 22.0; SPSS, Chicago, IL). Both visual methods (histograms and probability plots) and analytical techniques (Kolmogorov-Smirnov test) were employed to assess the distribution of the data. It was determined that the data did not follow a parametric distribution. Numerical data are presented as median [interquartile range (IQR)], while categorical data are expressed as numbers (%). The sociodemographic and clinical characteristics of the participants were compared using the Pearson's Chi-square test, Fisher's exact test, and the Mann-Whitney U test for categorical and numerical data, respectively.

Spearman's correlation analysis was used to investigate the potential association between sarcopenia and clinical and sociodemographic variables. A correlation coefficient of 0.1 - 0.29 was considered weak, 0.3 - 0.49 as moderate, and 0.5 - 1.0 as strong. Multiple logistic regression analysis was conducted to identify risk factors for the development of sarcopenia, including variables that were found to be statistically significant at the $p < 0.05$ level in univariate analysis. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 135 participants' data were evaluated in the study. Of these, 35 (25.9%) were males and 100 (74.1%) were females. According to the SARC-F test, 68 individuals were classified as

having sarcopenia and were assigned to Group 1. A total of 67 individuals were not diagnosed with sarcopenia based on the SARC-F test and were categorised as Group 2. In the group comparison, the sarcopenia group was found to have significantly higher BMI, insulin resistance, triglyceride levels, and a higher prevalence of dyslipidaemia ($p = 0.003$, $p = 0.025$, $p = 0.001$, $p = 0.003$). The data are presented in Table I.

A correlation analysis was performed, revealing a weak positive correlation ($r = 0.184$ - 0.268) between sarcopenia and insulin resistance, triglyceride levels, obesity stage, BMI, and dyslipidaemia. However, no significant correlation was found between age, gender, total cholesterol, HDL, LDL, and sarcopenia ($p > 0.05$). The results of the correlation analysis are shown in Table II.

A binary logistic regression analysis was conducted to identify risk factors for the development of sarcopenia. The analysis revealed that elevated triglyceride levels were a significant risk factor (Odds ratio - 95% confidence interval: 3.19 - 1.05/9.71, $p = 0.041$). Although BMI, obesity stage, insulin resistance, and dyslipidaemia were significantly higher in the sarcopenic group compared to the non-sarcopenic group, these variables were not found to be significant risk factors for the development of sarcopenia ($p > 0.05$). The regression analysis results are summarised in Table III.

Table I: Comparison of sociodemographic and clinical variables according to sarcopenia.

Parameters	Sarcopenia (-) n = 67	Sarcopenia (+) n = 68	p-value
Age, year, median (IQR)	53.0 (12.0)	57.0 (10.8)	0.139[a]
Gender, n(%)			
Female	50 (74.6)	50 (73.5)	0.884[b]
Male	17 (25.4)	18 (26.5)	
BMI, kg/m^2, median (IQR)	26.8 (5.3)	28.5 (6.5)	0.003[a]
Obesity stage, n (%)			0.039[b]
<18.5	1 (1.5)	0 (0.0)	
18.5-24.9	21 (31.3)	10 (14.7)	
25.0-29.9	33 (49.3)	32 (47.1)	
30.0-39.9	10 (14.9)	22 (32.3)	
>40.0	2 (3.0)	4 (5.9)	
Insulin resistance, n (%)			
None	25 (37.3)	14 (20.6)	0.025[c]
Yes	42 (62.7)	54 (79.4)	
Triglyceride, n (%)			
Optimal limit	43 (64.2)	24 (35.3)	0.001[b]
Borderline high	22 (32.8)	44 (64.7)	
High	2 (3.0)	0 (0.0)	
Total cholesterol, n (%)			
Optimal limit	42 (62.7)	32 (47.1)	0.189[b]
Borderline high	20 (29.9)	29 (42.6)	
High	5 (7.4)	7 (10.3)	
HDL, n (%)			
Optimal limit	13 (19.4)	6 (8.8)	
Borderline low	27 (40.3)	27 (39.7)	0.144[b]
Low	27 (40.3)	35 (51.5)	
LDL, n (%)			
Optimal limit	45 (67.2)	42 (61.8)	
Borderline high	19 (28.4)	20 (29.4)	0.571[b]
High	3 (4.4)	6 (8.8)	
Dyslipidaemia, n (%)			
None	36 (53.7)	20 (29.4)	0.003[c]
Yes	31 (46.3)	48 (70.6)	

BMI, Body mass index; HDL, High density lipoprotein; LDL, Low density lipoprotein; IQR, Interquartile range. Fisher's Exact Test (c), Pearson's Chi-square Test (b), and Mann-Whitney U Test (a).

Table II: Correlation of sociodemographic and clinical variables with sarcopenia.

Parameters	Sarcopenia	
	Spearman rho (r)	p-value
Age	0.128	0.140
Gender	0.013	0.885
BMI	0.259	0.002
Obesity stage	0.267	0.002
Insulin resistance	0.184	0.032
Triglyceride	0.268	0.002
Total cholesterol	0.152	0.079
HDL	0.154	0.075
LDL	0.068	0.435
Dyslipidaemia	0.247	0.004

Abbreviations: LDL, Low-density lipoprotein; HDL, High-density lipoprotein; and BMI, Body mass index.

DISCUSSION

In this study, high triglyceride levels were found to be a significant factor for sarcopenia when examining the relationship between insulin resistance, hyperlipidaemia, and sarcopenia. Individuals with sarcopenia experience a loss of muscle mass and strength, yet the condition is often underdiagnosed. This represents a considerable public health concern due to the increased risk of falls, functional disabilities, frailty, illness, mortality, and the associated healthcare costs, highlighting the need for further research. Therefore, identifying the risk factors that contribute to the development of sarcopenia is essential for its prevention.[7]

Table III: Analysing binary logistic regression to identify risk factors for the emergence of sarcopenia.

Parameters	Odd ratio	95% Confidential interval	p-value
BMI	1.03	0.89 / 1.20	0.663
Obesity stage			
25.0 - 29.9	0.72	0.02 / 30.56	0.866
30.0 - 39.9	0.85	0.04 / 18.82	0.918
>40.0	2.02	0.15 / 26.95	0.597
Insulin resistance (+)	0.49	0.20 / 1.19	0.116
Dyslipidaemia (triglyceride high)	3.19	1.05 / 9.71	0.041
Other dyslipidaemias (+)	1.22	0.37 / 4.01	0.744

Abbreviations: BMI, Body mass index (+): It is positive.

Studies have demonstrated that the pathophysiology of sarcopenia is multifactorial. Neurological disorders, muscle protein turnover, hormonal changes, oxidative stress, chronic diseases, malnutrition, low physical activity, and obesity are all considered risk factors for sarcopenia.[8] In this study, the elevated BMI and insulin resistance observed in the sarcopenia group supported these findings.

Lipid accumulation and its derivatives within muscle cells contribute to insulin resistance, leading to sarcopenia. This process increases oxidative stress, inflammatory cytokine production, and mitochondrial dysfunction.[9,10] Findings of this study are consistent with the literature, as the authors observed significant elevations in triglycerides and dyslipidaemia in the sarcopenic group.

Insulin resistance and dyslipidaemia were found to be positively correlated in this study. Regression analysis further revealed that dyslipidaemia is a potential risk factor for insulin resistance. Results of this study which align with previous research, suggest that hyperlipidaemia may serve as a predictive factor for sarcopenia. The literature explains that insulin resistance in muscle cells, accompanied by myosteatosis, leads to a vicious cycle, resulting in systemic insulin resistance.[9] This study shows, the elevated levels of both insulin resistance and lipid derivatives in the sarcopenic group supported this explanation. The high level of insulin resistance in this study's participants may have been secondary to the elevated lipid derivatives.

In sarcopenic obesity, muscle cells can differentiate into adipocytes due to paracrine signals from fat tissue infiltration, which impairs muscle regeneration, increases fat infiltration, and perpetuates a vicious cycle. Obesity can exacerbate sarcopenia, and vice versa, further amplifying the cycle.[11] In this study, sarcopenia was more prevalent among patients whose BMI fell within the obesity range, and the present findings are consistent with the existing literature.

Research has shown that increased lipid derivatives induce a chronic inflammatory process that leads to sarcopenia.[9] One limitation of this study is that the authors did not assess inflammatory markers, which could have provided additional insights.

The results of the study revealed a weak positive correlation (r = 0.184-0.268) between sarcopenia, insulin resistance, triglyceride levels, obesity stage, BMI, and dyslipidaemia. This finding is consistent with the literature.[12]

Lin *et al*.'s study on patients receiving statin treatment for chronic renal disease found a lower incidence of sarcopenia among these individuals. The present findings align with these results, showing a decreased risk of sarcopenia in patients with dyslipidaemic conditions treated with statins.[13,14]

It is well-established in the literature that statins, used in the treatment of hyperlipidaemia, may be associated with myopathy-like muscle diseases. In a study of stroke patients, statin use was negatively correlated with muscle strength, although no significant relationship was found between muscle mass and statin use. However, sarcopenia was strongly associated with hyperlipidaemia. This supports the conclusion that hyperlipidaemia plays a crucial role in the development of sarcopenia.[15,16]

In a retrospective sarcopenia study involving 2,697 participants, it was demonstrated that elevated triglyceride (TG) levels and fasting blood glucose may serve as risk factors for sarcopenia. Since fasting blood glucose was not measured in this study, a direct comparison cannot be made. However, the observed relationship between elevated triglycerides and sarcopenia in this study appears to be consistent with the findings of the aforementioned research.[17]

Age has been recognised in the literature as an important predictor of sarcopenia; however, this study did not find a significant correlation between age and sarcopenia ($p > 0.05$). The authors believe that the inclusion of participants under the age of 65 and the broad inclusion criteria of the study may account for this finding. Despite the absence of a significant correlation between gender and sarcopenia in this study's investigation, previous research has suggested that females are more likely than men to develop sarcopenia.[17,18]

The major limitation of this study is the inability to investigate parameters such as muscle mass and nutritional status, which are important in sarcopenia research. The lack of muscle mass measurement devices at the clinic where the study was conducted, along with the low socio-economic status of the region, can be cited as reasons for this limitation. On the other hand, although the study was conducted with a sample size larger than those suggested by the power analysis, the number of patients appears to be limited. Addi-

tionally, the fact that this is a cross-sectional study further limits the scope of the research.

CONCLUSION

In this study, high triglyceride levels were identified as a risk factor for sarcopenia, consistent with the existing literature. It was found that, despite being significantly higher in the sarcopenic group compared to the non-sarcopenic group, both BMI and insulin resistance did not appear to be significant risk factors for the development of sarcopenia.

ETHICAL APPROVAL:
The study was approved by the Clinical Research Ethics Committee of the Harran University, Sanliurfa, Turkiye (Approval No. HRU/23.24.25 Dated on 25.12.2023). This research was conducted by the ethical standards of the institute and in line with the 1964 Helsinki Declaration and its later amendments.

PATIENTS' CONSENT:
All individual participants signed a general research consent form, approved by the Institutional Review Board.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
MT, BKA, HI: Conception, study design, data acquisition, and drafting and revision of the manuscript.
MT: Data analysis and interpretation.
All authors approved the final version of the manuscript to be published.

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