

ASSESSMENT OF SARCOPENIA RISK FACTORS
IN RELATION TO MUSCLE HISTOPATHOLOGY
AND MORPHOLOGY: AN AUTOPSY STUDY

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Abstract

Physical inactivity, malnutrition, smoking, excessive sleep duration, and diabetes have been associated with an increased risk of sarcopenia. This study aims to elucidate the relationship between sarcopenia risk factors and the histopathological and morphometric characteristics of striated muscles, as well as to assess the findings in light of the existing literature. Histopathological and morphometric evaluations were performed on samples taken from the deltoid, intercostal, and psoas muscles of 88 autopsy cases over one year. A statistically significant decrease in muscle fibre width was observed, particularly in psoas muscle samples, after the age of 30–50 years. In our study, the observation that muscle fibre diameters were lower in individuals classified as obese compared to other BMI groups only in the deltoid muscle group suggests that the impact of BMI may vary across different muscle groups. We believe that the effects of sarcopenia risk factors on muscle structure can be further elucidated through large-scale population-based studies examining individual cases in more detail.

Key words: sarcopenia, risk factors, muscle width, autopsy, histopathology

Introduction. The term sarcopenia was first proposed by ROSENBERG in 1988 and was defined as the progressive and generalized loss of muscle mass and

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strength [1]. In 2009, the European Geriatric Medicine Society (EUGMS) established the European Working Group on Sarcopenia in Older People (EWG-SOP) to determine diagnostic criteria for sarcopenia. Sarcopenia was defined as a syndrome characterized by generalized and progressive loss of muscle mass and strength, which can lead to adverse outcomes such as physical disability, reduced quality of life, and mortality [2]. The EWGSOP categorized sarcopenia as “primary” when no cause other than ageing was identified, and as “secondary” when one or more non-ageing-related causes were present [2]. Secondary sarcopenia has been further classified into three subgroups: activity-related, disease-related, and nutrition-related sarcopenia [2]. Physical inactivity, malnutrition, smoking, excessive sleep duration, and diabetes have been associated with an increased risk of sarcopenia [3]. In the literature, sarcopenia has been reported as a significant prognostic indicator for survival and complications in chronic diseases such as cancer, renal failure, and liver disease [4, 5].

The aim of this study is to investigate the relationship between sarcopenia risk factors and the histopathological and morphometric characteristics of striated muscles and to evaluate the findings in the context of the existing literature.

Materials and methods. Over a one-year period, 88 cases were evaluated out of 200 autopsy cases conducted at the Ordu Branch of Forensic Medicine. Cases with severe burns, carbonization, advanced decomposition findings, and dismembered bodies, as well as those under the age of 30, were excluded from the study. A preliminary questionnaire consisting of 10 questions was completed based on forensic investigation files and information obtained from the relatives of the deceased. The questionnaire included inquiries regarding gender, age, height, weight, substance abuse (if present, type of substance), presence of chronic diseases (if present, type of disease), history of hospitalization (if hospitalized, duration of hospitalization), and regular medication use. During the autopsy, three muscle samples were collected: from the intercostal muscle at the level of the fourth intercostal space, from the proximal portion of the psoas muscle, from the proximal portion of the deltoid muscle.

Muscle biopsies were fixed in 4% paraformaldehyde for 24 hours and embedded in paraffin following alcoholic dehydration. Three-micrometer-thick sections were stained with hematoxylin and eosin (H&E), and pathological evaluation was blindly performed by two pathologists. Additionally, they conducted a morphological assessment by measuring muscle fibre width (Fig. 1).

The study results were analyzed using the SPSS 22.0 statistical software. Descriptive statistics were applied, and categorical data were compared using the chi-square test. The Independent *t*-test was used for the comparison of two independent groups in quantitative data. To evaluate differences in means across multiple groups, ANOVA was performed. In cases of heterogeneous variance, the Brown–Forsythe test, which provides more robust results, was applied. When necessary, post hoc tests were conducted. Additionally, to examine the contributions

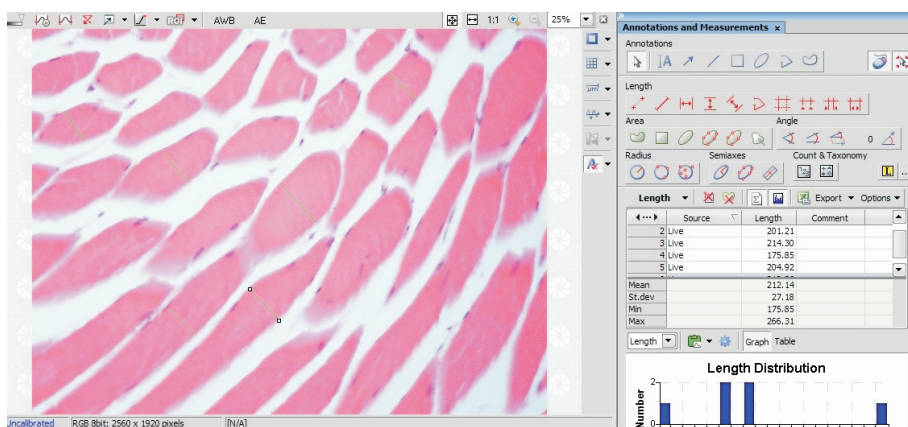


Fig. 1. Measurement of muscle fibre width

of risk factors, multiple linear regression analysis was performed.

Results. Among the 88 cases included in the study, 84.1% ($n = 74$) were male, and 15.9% ($n = 14$) were female. The youngest case was 30 years old, while the oldest was 90 years old, with a mean age of 58.46 ± 15.15 years. The mean height was 168 ± 8.69 cm, the mean weight was 76.21 ± 15.87 kg, and the mean body mass index (BMI) was calculated as 26.80 ± 4.69 .

The number of cases who died due to natural causes was 52.3% ($n = 46$), while those who died due to traumatic causes accounted for 47.7% ($n = 42$). The distribution of sarcopenia risk factors according to causes of death is presented in Table 1.

For the psoas muscle, the Brown–Forsythe test indicated a statistically significant difference in mean muscle fibre sizes across age groups (Brown–Forsythe $F(df, df) = \text{value}, p < 0.05$).

In the post hoc test, a statistically significant difference was found among all age groups. However, the most pronounced significance was specifically observed between the 30–50 age group and the 71–90 age group ($p < 0.05$).

The mean muscle fibre widths were measured as $184.76 (\pm 49.67) \mu\text{m}$ for the intercostal muscle, $191.37 (\pm 55.76) \mu\text{m}$ for the deltoid muscle, and $173.20 (\pm 48.30) \mu\text{m}$ for the psoas muscle. In the statistical distribution tests conducted separately for each muscle, a significant difference was observed only in the deltoid muscle group. Specifically, in individuals with obesity ($\text{BMI} > 30$), muscle fibre width was lower compared to other BMI groups, while no similar pattern was detected in the other muscle groups ($p < 0.05$).

No statistically significant difference was found between muscle fibre widths across all muscle groups in relation to gender, smoking and alcohol use, history of hospitalization, presence of chronic disease, or regular medication use ($p > 0.05$). However, when chronic diseases were analyzed in detail, it was observed that

T a b l e 1

Distribution of sarcopenia risk factors by causes of death

	Natural deaths		Traumatic deaths		χ^2	p
	n	%	n	%		
<i>Gender</i>					2.44	0.11
Male	36	40.90	38	43.18		
Female	10	11.36	4	4.54		
<i>Age groups</i>					6.67	0.03
30–50	10	11.36	17	19.31		
51–70	21	23.86	20	22.72		
71–90	15	17.04	5	5.68		
<i>BMI categories</i>					3.88	0.14
18.5–24.9	21	23.86	12	13.63		
25.0–29.9	14	15.90	21	23.86		
$30.0 \geq \text{BMI}$	11	12.50	9	10.22		
<i>Substance use</i>					1.01	0.31
No substance use	19	21.59	13	14.77		
Alcohol and smoking	27	30.68	29	32.95		
<i>Chronic diseases</i>					38.85	$p < 0.01$
None	4	4.54	31	35.22		
Present	42	47.72	11	12.50		
<i>Hospitalization</i>					0.20	0.65
No hospitalization	39	44.31	37	42.04		
Hospitalized	7	7.95	5	5.68		
<i>Regular medication use</i>					1.51	0.21
No medication use	32	36.36	34	38.63		
Regular medication use	14	15.90	8	9.09		

*Chi-square test (χ^2), $p < 0.05$

the smallest muscle fibre width in the psoas muscle was found in patients with Parkinson's disease, as shown in Fig. 2.

Histopathological examination revealed that in the psoas muscle group, there was a statistically significant increase in nuclear degeneration in the 71–90 age group compared to other age groups ($\chi^2 = 7.52$, $p = 0.02$). In deltoid muscle cells, the increase in connective tissue was found to be statistically significantly higher in females compared to males ($\chi^2 = 7.10$, $p = 0.02$). Additionally, in the deltoid muscle group, mononuclear cell infiltration was significantly higher in natural deaths compared to traumatic deaths ($\chi^2 = 7.52$, $p = 0.02$).

When evaluating the contribution of sarcopenia risk factors to natural death, the multiple linear regression model explained 44.8% of the variance. Statistical significance was observed in relation to BMI and the presence of chronic diseases, and the results are presented in Table 2.

Discussion. The prevalence of sarcopenia varies depending on geographic region and age, with reported rates ranging between 1% and 29% in the general

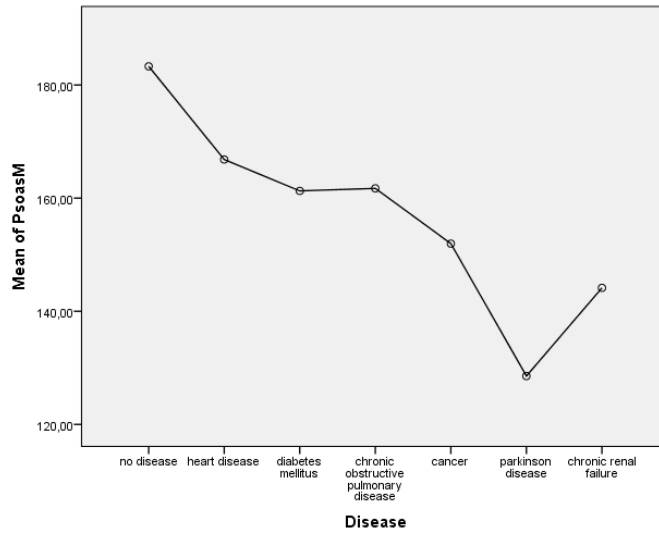


Fig. 2. Distribution of muscle fibre widths according to chronic diseases

T a b l e 2

Effect of sarcopenia risk factors on natural death cases

Model	Unstandardized coefficients		Standardized coefficients β	t	p	95.0 % CI for β		VIF
	β	Standart error				Lower bound	Upper bound	
Constant	1.06	0.31		3.39	0.00	0.44	1.69	
BMI	-0.02	0.00	-0.19	-2.33	0.02	-0.03	-0.00	1.12
Chronic diseases	0.70	0.09	0.69	7.53	0.00	0.52	0.89	1.32

population [2]. In specific patient groups, the prevalence of sarcopenia is significantly higher than in the general population. For example, studies have reported a prevalence of 18% in diabetic patients and 66% in untreated cancer patients [6, 7]. Furthermore, in patients with prolonged hospital stays, the prevalence has been documented as 33%, whereas in short-term hospitalizations, it has been reported as 10% [2].

Muscle mass and strength peak during early adulthood and gradually decline from middle age onward [8]. With ageing, there is a progressive reduction in both the number and size of muscle fibres. Between the ages of 30 and 80, muscle mass decreases by 30% in the back and arm muscles and by 40–60% in the lumbar and leg muscles [9]. The gradual decline in muscle fibres begins at the age of 50, with approximately 50% of fibres lost by the age of 80. Notably, muscle fibre atrophy is also observed in athletes [10]. Consistent with the literature, our study

demonstrated a statistically significant reduction in muscle fibre diameter in the psoas muscle, particularly between the 30–50 and 71–90 age groups.

After adjusting for muscle mass, a higher body mass index (BMI) has been identified as a risk factor for sarcopenia [5, 11]. In our study, only in the deltoid muscle group, individuals classified as obese (BMI > 30) exhibited smaller muscle fibre diameters compared to other BMI groups. This suggests that the impact of BMI on muscle morphology may vary across different muscle groups.

A meta-analysis found that smoking increases the risk of sarcopenia [12]. However, the literature suggests that there is no direct relationship between alcohol consumption and sarcopenia [12]. In our study, no statistically significant relationship was found between muscle fibre atrophy and the combined use of alcohol and tobacco.

SHEN et al. [13] identified the *LYV1* gene as a marker in tissue-resident macrophages within the skeletal muscle microenvironment, highlighting age-related changes in muscle structure. Additionally, a 2023 meta-analysis proposed that a single radiological measurement of psoas muscle morphometry could serve as a reliable predictor of frailty and trauma outcomes in elderly patients [14]. In our study, the increased nuclear degeneration observed in the psoas muscle among the 71–90 age group, compared to other age groups, was statistically significant. This finding aligns with previous research and suggests that the psoas muscle may play a crucial role in sarcopenia prognosis, potentially influenced by both phenotypic and genotypic factors.

Histological analysis of sarcopenic individuals reveals not only a decrease in muscle mass but also infiltration of muscle tissue by fat and connective tissue, a hallmark of sarcopenia [15]. One of the notable findings of our study was the significantly greater increase in connective tissue in the deltoid muscle of females compared to males. This observation may be attributed to hormonal fluctuations throughout life. However, the lack of detailed hormonal analysis represents a limitation of our study.

Another limitation may stem from the regional characteristics of the autopsy cases included in our study. Additionally, the limited number of cases with cancer and Parkinson's disease, as well as the overlap of alcohol and tobacco use, restricted the ability to conduct a more detailed evaluation of these factors. Future large-scale studies in specialized centres or longitudinal studies focusing on case-specific analyses could provide more comprehensive insights.

In conclusion, among individuals with sarcopenia risk factors, the presence of obesity appears to contribute to muscle fibre reduction, particularly in the deltoid muscle. Furthermore, as previously noted in the literature [14], histopathological and morphological changes in sarcopenic psoas muscle accelerate with ageing, which is a known risk factor for increased trauma susceptibility after the age of 50. Additionally, among the sarcopenia risk factors, chronic diseases and BMI were found to explain 44.8% of natural deaths. However, these conditions themselves

are also direct causes of mortality. Further population-based studies focusing on individual cases are necessary to better elucidate the impact of sarcopenia risk factors on muscle structure.

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