1) Title page

Title: The relationship between sarcopenia and oral sarcopenia in elderly people

Short running head: Relation to sarcopenia and oral sarcopenia

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2) Abstract and key words

Abstract:

Objective(s): The purpose of this study is to clarify the relationship between generalized sarcopenia and oral sarcopenia in the elderly in order to facilitate the establishment of a method for assessing oral sarcopenia.

Methods: 54 elderly persons participated in this study. We examined the skeletal muscle mass index (SMI), grip strength (GS), and walking speed (WS) as the index of generalized sarcopenia, and the cross-sectional area of the geniohyoid muscle (CSG), tongue pressure (TP), and oral diadochokinesis (ODK) as the index of oral sarcopenia.

Results: We found a moderate correlation between CSG and SMI, a weak correlation between GS and TP, and a moderate correlation between WS and ODK. CSG, TP, and ODK were significantly smaller in the sarcopenia group than in the non-sarcopenia group. By Multiple regression analysis, SMI and TP were significantly associated with CSG. ODK, BMI, and CSG were significantly associated with TP. WS and SMI were significantly associated with ODK.

Conclusion: CSG, TP, and ODK were confirmed as endpoints of oral sarcopenia. All endpoints of oral sarcopenia were influenced by those of generalized sarcopenia.

Keywords: Sarcopenia, Oral sarcopenia, Geniohyoid muscle, Tongue pressure, Oral diadochokinesis,

3) Text

1. Introduction

In the aging society, sarcopenia, in which muscle strength and motor function decline with age, has attracted attention, and many researchers have investigated different testing and treatment methods [1-6]. Aspiration resulting from reduced swallowing function is a problem in the elderly, and aspiration pneumonia significantly deteriorates the life prognosis and QOL [7]. As sarcopenia is involved in the onset of dysphagia [8, 9], the relationship between sarcopenia and dysphagia has attracted attention.

Dysphagia is caused by several factors, such as a decreased maximum tongue pressure, decreased skilled tongue movements, decreased mass of swallowing-related muscles, decreased tongue elevation, and decreased opening of the esophageal orifice [10]. In particular, the tongue plays an important role in swallowing. Therefore, sarcopenia in the oral region, including the tongue, leads to declined swallowing function and dysphagia. Thus, we focused on the tongue to examine the concept of oral sarcopenia.

Similar to generalized sarcopenia, oral sarcopenia is examined mainly by assessing muscle mass and strength, and motor function. Tamura et al. [11] reported that the tongue muscle mass, i.e., the thickness of the tongue, was correlated with triceps skinfolds (TSF) and arm muscle area (AMA) in the elderly. Maeda et al. [12] found that the tongue muscle strength, i.e., decreased tongue pressure, was correlated with dysphagia due to sarcopenia in hospitalized elderly patients without a history of diseases associated with dysphagia. Kikutani et al. [13] demonstrated that the motor function of the tongue of the elderly was affected by age-related changes. Thus, muscle mass and strength, and motor function in the oral region were separately examined. However, these three factors have not been examined together, and the relationship between generalized and oral sarcopenia remains unclear. Therefore, we aimed to clarify the relationship between generalized and oral sarcopenia in the elderly in order to facilitate the establishment of a method for assessing oral sarcopenia.

2. Methods

2.1. Subjects

There were 54 participants (16 men and 38 women), with a mean age of 78.8 ± 7.1 years, from nursing homes in Sasayama–city, communities in Sasayama City, Hyogo Prefecture, Japan, or Osaka Dental University Hospital, Osaka Prefecture, Japan. Pacemaker wearers, non-ambulatory persons, and those lacking in communication skills were excluded from the subjects. This study was approved by the ethics committee of Osaka Dental University (Approval No.110970).

2.2. Information collection and measurement

Basic information and endpoints of generalized and oral sarcopenia were surveyed.

2.2.1. Basic information

Information (age, sex, basic disease, medical history, and medications) was obtained from interviews with the participants and clinical records. The body mass index (BMI) was calculated by dividing the weight by the square of the height. The oral examination was performed by a dentist to assess the number of remaining teeth excluding stump of teeth. To assess the independence of daily life, basic daily movements were examined using a questionnaire on the Barthel Index (BI) [14]. To assess nutritional status, interviews were performed using a Mini Nutritional Assessment-Short Form (MNA-SF) questionnaire [15]. To assess eating and swallowing functions, interviews were performed using the questionnaire of Eating Assessment Tool-10 (EAT-10) [16].

2.2.2. Generalized sarcopenia

The skeletal muscle mass index (SMI) was calculated by measuring the mass of extremity skeletal muscles by bioelectrical impedance analysis (BIA). For the measurement, the In Body S10 (In Body Japan, Tokyo, Japan) was employed. The measurement was performed in a standing position with electrodes attached to the thumbs and middle fingers of both hands and the ankles of both legs. The subjects were instructed not to speak or move during the measurement. The standard values for reduction in SMI were ≤ 7.0 and < 5.4 kg/m^2 for males and females, respectively (AWGS [4]).

The grip strength (GS) was measured using a digital grip strength tester (Takei Scientific Instruments Co., Ltd., Niigata, Japan). After adjusting the second joint of the subject's index finger at a right angle to the grip of the grip tester, the subjects were instructed to hold the tester without shaking their arm. The measurement was performed twice, alternating between the left and right. The maximum value was taken as the GS. The standard values for reduction in GS were <26 and <18 kgf for males and females, respectively (AWGS [4]).

The walking speed (WS) was measured by walking 9 meters (Cesari et al. [17]). The subjects were instructed to walk as usual without being told about the WS measurement. The 9 meters consisted of 2 meters at the start and end points as a preparatory route, and 5 meters for the measurement of WS. For the measurement, the start and 2-, 7-, and 9 (goal) -meter points were marked to be recognized by the measurer. The measurement time was determined when one foot touched the 2- and 7-meter points. The WS was calculated by dividing 5 meters by the measurement time. The measurement was performed twice, and the faster WS was taken as the measured value. The standard value for the reduction in the WS was <0.8 m/s for both males and females (AWGS [4]).

The subjects were classified according to the diagnostic criteria for generalized sarcopenia based on the measured SMI, GS, and WS [4]. Those with decreased muscle mass and decreased muscle strength or motor function were classified as having sarcopenia, whereas the others were classified as the non-sarcopenia group.

2.2.3. Oral sarcopenia

The cross-sectional area of the geniohyoid muscle (CSG), involved in swallowing function [18], was measured as an indicator of muscle mass in oral sarcopenia. The geniohyoid muscle was measured using an ultrasonic diagnostic system (Shimizu et al. [19]). Each subject was seated in a comfortable posture on a reclining chair at an angle of 30 degrees from the floor, with a 3.5 MHz convex probe ultrasonic diagnostic system (miruco®; NIPPON SIGMAX Co., Ltd, Tokyo, Japan) attached perpendicularly to the lower surface of the geniohyoid muscle in the center of the mouth floor. The probe was not in contact with the thyroid cartilage, but the probe surface was in close contact with the bottom of the jaw. Ultrasonic gel was sufficiently used to not compress the soft tissue under the probe. On the B-mode sagittal cross-sectional plane (frequency: 3.5 MHz), the hyoid bone and mandible with acoustic shadows and the geniohyoid muscle attached to both were depicted on a single screen to save the resting state as a still image. The ultrasound image stored in the ultrasound diagnostic device was loaded into a personal computer. Using Image J software (NIH, Maryland, USA), the geniohyoid muscle depicted between the mandible and the hyoid bone on the ultrasound image was plotted, and the surrounded area was measured. The same examiner (RK) performed ultrasonography and measured CSG.

Tongue pressure (TP) was measured using a tongue measuring instrument (JMS, Hiroshima, Japan) as the indicator of muscle strength in oral sarcopenia. The measurement was performed as previously reported [20]. Before the measurement, calibration was performed, and the concave part of the dedicated TP probe was held with the upper and lower front teeth, with the probe held by the examiner. Each subject was instructed to press and crush the vinyl bulge at the tip of the probe against the palate with a maximum tongue force. Each subject underwent sufficient training for measurement. The measurement was performed three times with sufficient rest between measurements. The average of three measurements was taken as the TP.

Oral diadochokinesis (ODK) was measured as an indicator of the motor function of oral sarcopenia. The pronunciation of /ta/ accompanied by the movement of the tongue tip was selected as the task. Each subject was instructed to repeat the pronunciation of /ta/ as rapidly as possible in five seconds and to take breaths as needed. The measurement was performed by the calculator method. The measurement was performed three times with sufficient rest between measurements. The ODK value of /ta/ was calculated as the mean number of pronunciations per second of the three measurements.

2.3. Statistical analysis

The muscle mass and strength, and motor function of generalized and oral sarcopenia were examined using Pearson's correlation coefficient. A t-test was performed to examine whether CSG, TP, and ODK were significantly different between the sarcopenia and non-sarcopenia groups (significance level: <0.05). Multiple regression analysis was performed with CSG, TP, ODK as dependent variables, and age, sex, BMI, number of remaining teeth, BI, SMI, GS, WS, CSG, TP, and ODK as independent variables (significance level: <0.05). Statistical analysis was performed using SPSS Statistics 22 (IBM, New York, USA).

3. Results

The basic information for each subject is shown in Table 1. The muscle mass and strength, and motor function were examined in relation to generalized and oral sarcopenia. The correlations among SMI, GS, WS, CSG, TP, and ODK are shown in Table 2. A moderate correlation was found between CSG and the SMI (r = 0.48, p = 0.00). A weak correlation was found between the GS and the TP (r = 0.29, p = 0.03). A moderate correlation was found between the WS and ODK (R = 0.50, p = 0.00).

CSG, TP, and ODK were compared between the sarcopenia and non-sarcopenia groups using the Student's or Welch's t-test. CSG was significantly smaller in the sarcopenia group than in the non-sarcopenia group (254.2 ± 65.7 mm^2 versus 212.7 ± 37.4 mm^2, p = 0.01) (Figure 1). The TP was significantly lower in the sarcopenia group than in the non-sarcopenia group (31.4 ± 6.8 kPa versus 22.8 ± 5.7 kPa, p = 0.00) (Figure 2). ODK was significantly lower in the sarcopenia group than in the non-sarcopenia group (6.2 ± 0.7/s versus 5.4 ± 0.9/s, p = 0.00) (Figure 3).

Multiple regression analysis was performed to identify factors that influenced the endpoints of oral sarcopenia, i.e., CSG, TP, and ODK. Stepwise regression analysis was performed with CSG as a dependent variable, and age, sex, BMI, number of remaining teeth, BI, SMI, GS, WS, TP, and ODK as independent variables, demonstrating that SMI (β = 0.39, p = 0.003) and TP (β = 0.27, p = 0.04) were significantly associated with CSG (Table 3). Stepwise regression analysis was performed with TP as a dependent variable, and age, sex, BMI, number of remaining teeth, BI, SMI, GS, WS, CSG, and ODK as independent variables, demonstrating that ODK (β = 0.30, p = 0.02), BMI (β = 0.26, p = 0.04), and CSG (β = 0.25, p = 0.04) were significantly associated with TP (Table 3). Stepwise regression analysis was performed with ODK as a dependent variable, and age, sex, BMI, number of remaining teeth, BI, SMI, GS, WS, CSG, and TP as independent variables, demonstrating that WS (β = 0.42, p = 0.001) and SMI (β = 0.32, p = 0.009) were significantly associated with ODK (Table 3).

4. Discussion

In the present study, the basic information and data on the endpoints of generalized and oral sarcopenia were examined to clarify the relationship between generalized and oral sarcopenia in the elderly, revealing a correlation between generalized sarcopenia and oral muscle mass and motor function. In addition, the multivariate multiple regression analysis demonstrated that the endpoints of oral sarcopenia were influenced by those of generalized sarcopenia. The present study was the first to examine the relationships of muscle mass and strength, and motor function with generalized and oral sarcopenia.

Males and females aged ≥65 were included. Exclusion criteria were a history of marked causative disease of dysphagia, pacemaker wearers contraindicated for the use of SMI measurement equipment, and inability to measure WS. In addition, for the BI, MNA-SF, and EAT-10, those unable to communicate were excluded. As those with reversible sarcopenia were included in the study, those with severe dysphagia or malnutrition were excluded.

The present study was conducted according to the AWGS criteria [4]. As the muscle mass of generalized sarcopenia, the SMI was calculated using BIA. BIA is convenient, and the validity of the prediction formula for multi-ethnic adults, and a high correlation between BIA and MRI have been reported [21]. GS was measured to assess the muscle strength of generalized sarcopenia. GS measurement represents muscle strength assessment, and has been employed by the EWGSOP [22] and the AWGS [4]. The usual WS was employed as the motor function of generalized sarcopenia. The usual WS is a predictor of disability, providing an assessment method for elderly people [23, 24].

In the present study, muscle mass and strength, and motor function were examined in both generalized and oral sarcopenia. CSG was examined for muscle mass, maximum TP for muscle strength, and ODK for motor function. Several imaging methods (e.g., MRI and CT) [25, 26] are employed to measure the mass of swallowing-related muscles. However, their clinical use is limited by radiation exposure and cost. In addition, the BIA method cannot be easily applied to local swallowing-related muscles because it calculates muscle mass using electrical resistance between electrodes. Therefore, in the present study, CSG was measured using an ultrasound system to measure the muscle mass. The following point should be considered as a reason for selecting the geniohyoid muscle among the swallowing-related muscles. The swallowing-related muscles mainly originate from the branchial arch. The muscles originating from the branchial arch are potentially activated periodically by stimuli input from the respiratory center, and are therefore unlikely to undergo muscle atrophy after disuse [27, 28]. However, the geniohyoid muscle is not activated periodically, and exhibits muscle loss with age [29]. Thus, in the present study, the mass of the geniohyoid muscle was measured. To measure its cross-sectional area, Shimizu et al. determined the mass using an ultrasonic diagnostic device, enabling reliable and appropriate assessment of the muscle mass [19]. Our measurement method was as reported by Shimizu et al. [19]. The maximal TP was measured to assess muscle strength. Although the TP upon swallowing does not differ with age, the maximum TP decreases with age [30]. In addition, the reduction of maximum TP was significantly associated with sarcopenia and dysphagia due to sarcopenia [12]. Therefore, in the present study, the maximum TP was measured to determine muscle strength. Oral motor function was assessed by measuring ODK. Danila et al. [31] demonstrated a correlation between ODK and chewing time. The pronunciation of /ta/ is carried out by lightly touching the tip of the tongue to the anterior part of the palate, which involves a raising motion of the anterior part of the tongue. In addition, tongue elevation is a movement required for feeding a food bolus. In the present study, the ODK of /ta/ was measured as an indicator of oral motor function.

A moderate positive correlation was noted between the SMI and the CSG, indicators of muscle mass in generalized and oral sarcopenia, respectively ($r = 0.49$, $p = 0.00$). The mass of the geniohyoid muscle decreases with age [29]. A moderate positive correlation was also noted in the present study, suggesting that CSG should be employed as an indicator of muscle mass in oral sarcopenia. A weak positive correlation was noted between GS and TP, indicators of muscle strength in generalized and oral sarcopenia, respectively ($r = 0.29$, $p = 0.03$). Buehring et al. [32] and Sakai et al. [33] reported a correlation between TP and GS. Our results and previous reports suggest that TP can be suitably employed as an indicator of muscle strength in oral sarcopenia. A moderate positive correlation was noted with WS, an indicator of motor function in generalized sarcopenia, and ODK, an indicator of motor function in oral sarcopenia ($r = 0.50$, $p = 0.00$). Danila et al. [31] reported a positive correlation between ODK and the time from chewing to swallowing. ODK can be suitably employed as an indicator of oral motor function.

In the present study, the subjects were divided into two groups, i.e., a sarcopenia group (severe sarcopenia and sarcopenia) and a non-sarcopenia group (pre-sarcopenia and normal) depending on the conceptual sarcopenia stages of the EWGSOP [4], to conduct a population mean difference test on CSG, TP, and ODK between the two groups.

CSG was significantly smaller in the sarcopenia group than in the non-sarcopenia group. Shimizu et al. reported that CSG was significantly smaller in the dysphagia group than in the non-dysphagia group [34]. All of the subjects in the study were 65 years or older, independent in their daily lives, and able to orally ingest food without dysphagia. However, CSG was smaller in the generalized sarcopenia group. Thus, the measurement of CSG is a valid indicator of oral sarcopenia, and may also be effective in finding those who are likely to have dysphagia. The TP was significantly lower in the sarcopenia group than in the non-sarcopenia group. Maeda et al. [12] reported that a low TP was significantly associated with sarcopenia. Moreover, in the present study, TP was significantly lower in the sarcopenia group. ODK in the sarcopenia group was significantly lower in the sarcopenia group than in the non-sarcopenia group. Danila et al. [31] reported that the assessment of skilled oral movements in ODK was correlated with the time from chewing to swallowing. In the present study, TP was also significantly lower in the sarcopenia group, suggesting that the assessment of ODK serves as an endpoint of oral sarcopenia.

Multiple regression analysis was performed on the endpoints of muscle mass and strength, and motor function in oral sarcopenia, i.e., CSG, TP, and ODK. SMI ($\beta = 0.39$, $p = 0.003$) and TP ($\beta = 0.27$, $p = 0.04$) were significantly associated with CSG. Thus, CSG was affected by the skeletal muscles of the entire body. ODK ($\beta = 0.30$, $p = 0.02$), BMI ($\beta = 0.26$, $p = 0.04$), and CSG ($\beta = 0.25$, $p = 0.04$) were significantly associated with TP. As /ta/ is pronounced with the tip of the tongue in contact with the palate, the region to measure skilled tongue movements may be close to that to generate TP. Kikutani et al. [20] reported that the TP increased as the thickness of the tongue increased. This may be explained by the tongue becoming larger at a higher BMI, resulting in increased TP. WS ($\beta = 0.42$, $p = 0.001$) and SMI ($\beta = 0.32$, $p = 0.009$) were significantly associated with ODK, suggesting that motor function in oral sarcopenia should be assessed by ODK.

In generalized sarcopenia, different reference values are set for skeletal muscle mass and muscle strength between males and females [4]. In oral sarcopenia, different reference values should be set for CSG and TP between males and females. However, the sample size in the present study was only 54, precluding the examination of differences between males and females. In the future, the sample size should be increased to examine the differences in muscle mass and strength in oral sarcopenia between males and females.

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6) Tables

Table 1. Characteristics of the study population

Variable	All(n=54)
Age (years)	78.5±7.0
Sex (%)	Male (30.0) Female (70.0)
BMI(Kg/m^2)	21.5±3.1
BI	99.2±2.6
MNA-SF	11.1±2.3
EAT-10	2.37±3.4
SMI (kg/m^2)	6.09±1.0
GS (Kgf)	22.4±7.1
WS (m/s)	1.07±0.29
CSG (mm^2)	240±61
TP (Kpa)	28.5±7.7
ODK (/s)	5.90±0.86

Data are given as mean ± SD.

BMI; body mass index, BI; bathel index, MNA-SF; mini nutritional assessment-short form, EAT-10; eating assessment tool-10, SMI; skeletal muscle mass index, GS; grip strength, WS; walking speed, CSG; cross section of geniohyoid muscle, TP; tongu pressure, ODK; oral diadochokinesis of /ta /

Table 2. Bivariate simple correlation analyses of each parameter

N=54	ODK	TP	CSG	WS	GS	SMI
SMI	.416**	.384**	.497**	.233	.726**	1
GF	.334*	.291*	.381**	.328*	1	
WS	.495**	.408**	.193	1		
CSG	.340*	.420**	1			
TP	.484**	1				
ODK	1					

Coefficients of correlation were calculated with Pearson's product moment correlation coefficient for parametric values.

**p value <0.01 *p value <0.05

SMI; skeletal muscle mass index, GS; grip strength, WS; walking speed, CSG; cross section of geniohyoid muscle, TP; tongu pressure, ODK; oral diadochokinesis of /ta/

Table 3. Multiple regression analysis with CSG or TP or ODK as a dependent variable.

Dependent variables	Independent variables	Beta	t	p
CSG	SMI	0.39	3.1	0.0030
	TP	0.27	2.1	0.038
TP	ODK	0.39	3.1	0.003
	CSG	0.29	2.3	0.024
ODK	WS	0.42	3.6	0.0010
	SMI	0.32	2.7	0.0090

CSG;cross section of geniohyoid muscle, SMI;skeletal muscle mass index, TP;tongu pressure, ODK; oral diadochokinesis of /ta/, WS;walking speed

7) Figures and legends

Figure legends:

Figure 1. Comparison of non-sarcopenia and sarcopenia in CSG.

CSG; cross-section of the geniohyoid muscle **p value <0.01

Figure 2. Comparison of non-sarcopenia and sarcopenia in TP.

TP; tongue pressure **p value <0.01

Figure 3. Comparison of non-sarcopenia and sarcopenia in ODK.

ODK; oral diadochokinesis of /ta/ **p-value <0.01 *p-value <0.05

Figure 1.

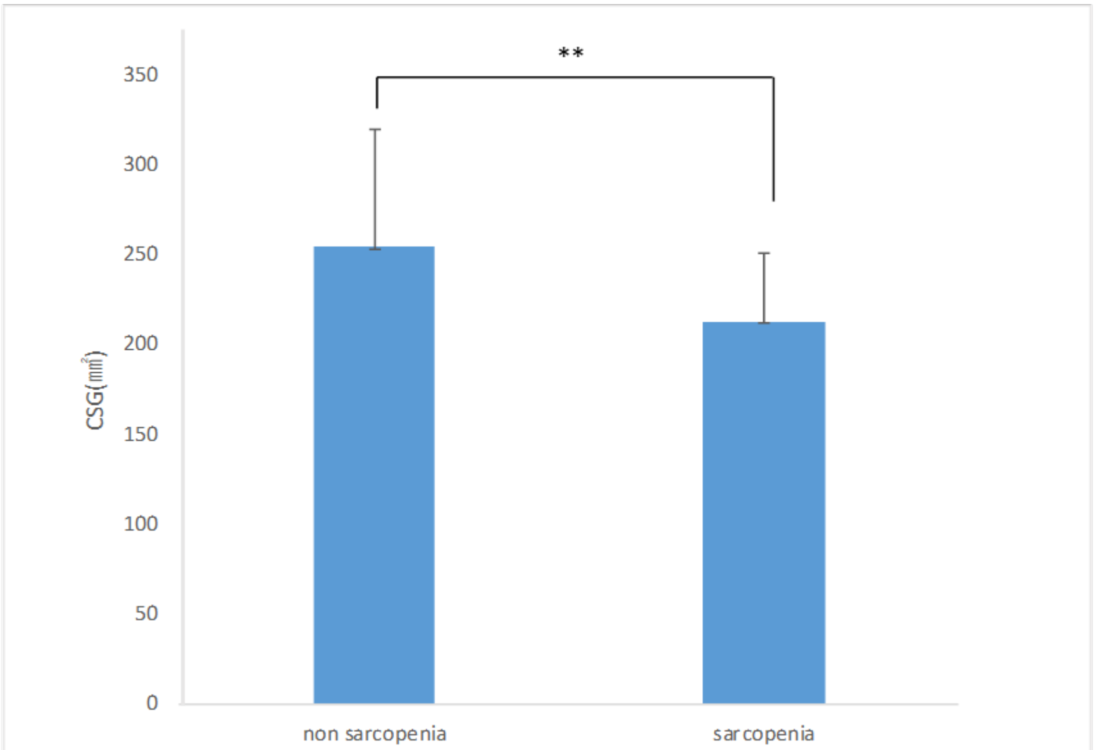

Figure 2.

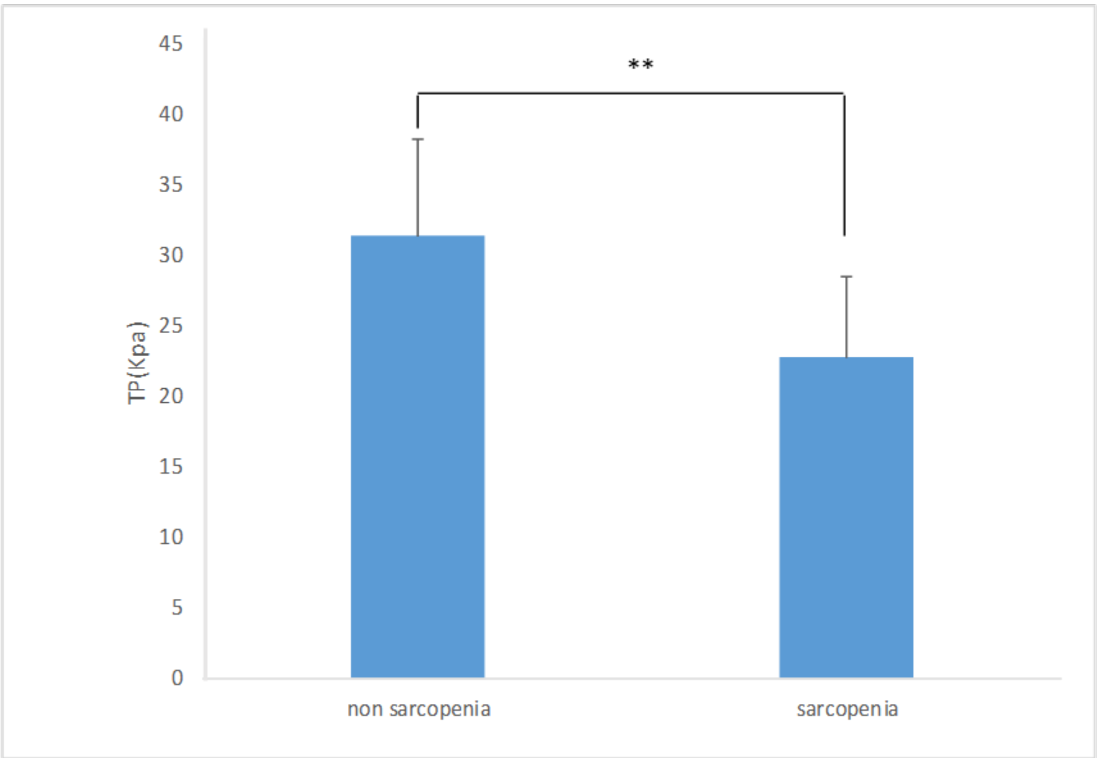

Figure 3.