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Original Article

Reference Skeletal Muscle Mass Values at L3 Vertebrae Level Based on Computed Tomography in Healthy Turkish Adults

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SUMMARY

Background: Sarcopenia which is described as decreased muscle strength, skeletal muscle mass (SMM), and muscle function is related with poor clinical outcomes. The cut-offs for the diagnosis of low SMM based on computed tomography (CT) have been previously reported in several populations. However, in order to investigate the presence of sarcopenia, it is recommended to use normative data of the study population instead of other reference populations. There is lack of normative SMM data based on CT in Turkish population. Therefore, our aim was to define the sex-specific cut-off values of healthy Turkish population on CT.
Methods: Skeletal muscle index (SMI) and psoas muscle mass index (PMI) in 270 healthy kidney donors (20–60 years old) were measured at L3 vertebrae level on CT. Sex-specific SMI-L3 and PMI-L3 distribution was assessed, and cut-off values using two standard deviations to define low SMM in both total study population and younger subjects aged 20–40 years were determined.
Results: Sex-specific SMI-L3 cut-off values were calculated as 44.98 and 36.05 cm^2/m^2 for males and females, respectively in the 20–60 years old donor group. PMI-L3 cut-off values were calculated as 2.63 and 2.02 cm^2/m^2 for males and females, respectively. In the 20–40 years old subgroup data (88 subject), SMI-L3 cut-off values were 45.47 and 36.19 cm^2/m^2, and PMI-L3 cut-off values were 3.2 and 2.87 cm^2/m^2 for males and females, respectively.
Conclusion: Our data established the sex-specific cut-off values of SMM in healthy Turkish population and that could be applicable for defining sarcopenia in Turkish population.

1. Introduction

Decreased whole body skeletal muscle strength and muscle mass (quantity) and/or quality together is described as sarcopenia and is a significant aspect for the detection of malnutrition.[1] Sarcopenia is a common finding in subjects with malignancy which is related with poor clinical outcomes and increased mortality in many disorders.[2–5] Consensus recommendations for the detection of sarcopenia includes both low skeletal muscle quantity or quality and low skeletal muscle strength. If these conditions are accompanied by low physical performance, it indicates severe sarcopenia.[6] For the detection of sarcopenia, in addition to handgrip test for muscle strength and gait speed for muscle performance, computed tomography (CT) is used as a gold standard method for non-invasive assessment of skeletal muscle mass or quantity.[4,6–8] Quantitative measurement of cross-sectional skeletal muscle area (SMA) and index (SMI = SMA/height^2) on CT are useful for the assessment of SMM and the detection of sarcopenia. SMA at the level of the 3rd lumbar vertebra (SMA-L3) is prevalently used in sarcopenia assessments and highly correlates with whole body SMM.[3,4,5,9] To classify patients as sarcopenic or not, sex-specific cut-off values of SMI at L3 (SMI-L3) were suggested in various studies.[10–13] Furthermore, psoas muscle area (PMA) and index (PMI) at L3 level (PMA-L3 and PMI-L3) have been reported to reflect the status of whole body SMM.[14] However, the use of psoas muscle in the diagnosis of sarcopenia is controversial because it is relatively a small muscle.[6]

Body composition varies between ethnicities and the European Working Group on Sarcopenia in Older People (EWGSOP) proposes using normative data of the study population rather than other reference populations to investigate the presence of sarcopenia.[6] Cut-off values for SMI-L3 on CT have been previously reported for Caucasian,[10] American,[11,12] and Asian[13] populations, and for PMI-L3 in an Asian population.[14] However, no data is available for Turkish population yet. Therefore, our aim was to define the sex-specific reference cut-off values of SMI-L3 and PMI-L3 in Turkish population on CT and to contribute to literature.

2. Materials and methods

The institutional ethics committee approved the study and a waiver of the requirement for informed consent was granted.

2.1. Study population

Individuals who underwent abdominal computed tomography

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(CT) examination as a part of the evaluation for kidney donation in the Radiology Department of Pamukkale University Hospital between January 2008 and July 2018 retrospectively investigated. Patient's descriptive information (weight, height age and gender) was obtained from their latest medical record just before the date of CT examination. Subjects who had unenhanced CT images and descriptive information recorded in the archive and had fully visible abdominal muscles on CT at L3 level, who were deemed healthy enough to kidney donation were included in the study.

2.2. Computed tomography acquisition

Computed tomography (CT) examinations were performed in supine position using a multi-detector CT scanner (16-detector row, Brilliance; Philips Healthcare, Netherlands). CT protocols were performed using parameters as follows: tube voltage; 120 kV, tube current; 50–120 mA, matrix; 512 × 512, pitch; 1, rotation time; 0.75 s and slice thickness; 5 mm. The tube current was automatically modulated to the patient's body mass.

2.3. Evaluation of computed tomography images

Before the quantitative measurements, all CT images were assessed for the presence of artifacts that hinder muscle area measurement at L3 vertebrae level by a board-certified radiologist (F.U.). Patients with insufficient CT image quality for muscle area measurement were excluded.

For the quantitative measurements, all CT images were exported to a personal computer and measurements were done using Osirix software (v10.0.0; Pixmeo SARL, Bernex, Switzerland). All measurements were performed in two different sessions with one-week interval to prevent recall. In the first session, skeletal muscle was identified and quantified by using the threshold values of –29 to +150 Hounsfield unit. We followed the method described by Prado et al.[7] to measure area of skeletal muscle (SMA), at the lower part of the L3 level (SMA-L3). In the second session, we also measured the psoas muscle area (PMA-L3) manually, which was described by Jones et al.[15] All CT images were evaluated by a single trained radiologist (F.U.) (Fig. 1). Cross-sectional areas (SMA-L3 and PMA-L3; cm^2) were computed for each image, and these values were divided by the square of the heights in meters (m^2) for each subject in order to normalize them for stature (skeletal muscle index [SMI] and psoas muscle index [PMI]; cm^2/m^2). Body mass index (BMI) was also computed as the weight divided by the height squared (kg/m^2).

2.4. Statistical analysis

Continuous variables are represented as mean with standard deviation (SD) or median with range, in normally and non-normally distributed data, respectively. Categorical variables are represented as percentage (%). Mann-Whitney U test or Student's t-Test was used for analyzing continuous data. Spearman's correlation and linear regression analyses were used for assessing correlations between the continuous variables. To describe the distribution of SMA-L3, PMA-L3, SMI-L3, and PMI-L3 values percentiles (p5 to p95) were used for the young subjects (aged 20–40 years) and whole study population. A low PMA-L3, PMI-L3, SMA-L3 and SMI-L3 was considered as a value below 5^{th} percentile.[10,14,16] SPSS Version 21.0 for Windows (Armonk. NY: IBM Corp.) was used for analyses and a *p* value ≤ 0.05 was considered statistically significant.

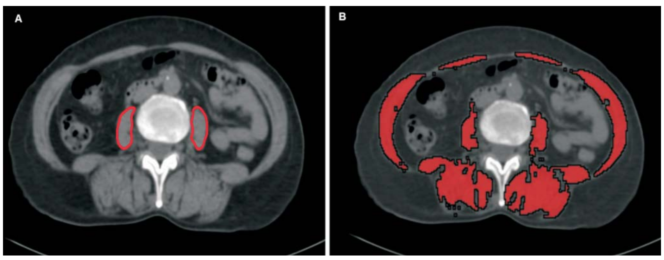

Fig. 1. Cross-sectional computed tomographic images at the third lumbar vertebra level. (A) Bilateral psoas muscle areas were measured by manual tracing. (B) Entire skeletal muscle area was quantified by using the threshold values of –29 to +150 Hounsfield unit.

3. Results

Of the 390 healthy subjects medically approved as potential living kidney donors, 270 individuals were included the study (aged between 20–60 years, mean age, 44.7 ± 10 years). In the evaluation of the study group; there were no significant differences in mean BMI (26.4 vs. 25.4 kg/m^2, p = 0.476) and mean age (44.3 vs. 45 years, p = 0.629) between males and females. Males were significantly (p < 0.001) heavier (75.8 vs. 67 kg) and taller than females (169.6 vs. 161 cm) (Table 1).

Based on the 20–60 years old donor data, we determined the sex-specific SMI-L3 cut-off values as 44.98 and 36.05 cm^2/m^2 for males and females, respectively. PMI-L3 cut-off values were 2.63 and

Table 1
Characteristics of the study population.

Aged 20–40 years	All subjects	Male	Female	*p* value
Number of subjects	88	48	40	
Age				
Mean ± std (years)	32.3 ± 5.3	30.9 ± 5.8	34 ± 4.2	0.065*
Median (years)	33	31	34	
Range (years)	20–40	24–40	26–40	
Weight				
Mean ± std (kg)	70.5 ± 13.5	76.4 ± 10.5	63.4 ± 13.5	0.006*
Median (kg)	72	73	70	
Range (kg)	39–99	56–99	39–77	
Height				
Mean ± std (cm)	168 ± 11	173.5 ± 9.3	162.3 ± 9.8	0.0001
Median (cm)	171	173	162	
Range (cm)	148–191	153–191	148–179	
Body mass index				
Mean ± std (kg/m^2)	24.7 ± 3.5	25.3 ± 3.5	23.9 ± 4.2	0.184
Median (kg/m^2)	24.1	25.1	23.4	
Range (kg/m^2)	17.1–31.2	21.8–31.1	17.1–31.2	
Aged 20–60 years	**All subjects**	**Male**	**Female**	***p* value**
Number of subjects	270	134	136	
Age				
Mean ± std (years)	44.7 ± 1.6	44.3 ± 11.2	45 ± 8.6	0.629*
Median (years)	48	48	48	
Range (years)	24–60	24–60	26–60	
Weight				
Mean ± std (kg)	71.4 ± 11.2	75.8 ± 11.1	67 ± 9.6	0.0001*
Median (kg)	72	77	69	
Range (kg)	39–99	56–99	39–87	
Height				
Mean ± std (cm)	165.1 ± 8.9	169.6 ± 8.6	161 ± 6.7	0.0001
Median (cm)	165	170	160	
Range (cm)	148–191	148–191	148–179	
Body mass index				
Mean ± std (kg/m^2)	26.1 ± 3.5	26.4 ± 3.5	25.4 ± 3.6	0.476
Median (kg/m^2)	26	26.4	25.4	
Range (kg/m^2)	17.1–36.5	21–36.5	17.1–31.6	

* Mann Whitney U test was used. Std, standard deviation.

2.02 cm^2/m^2 for males and females, respectively. Based on the younger 20–40 years old subgroup data (88 individual), SMI-L3 cut-off values were 45.47 and 36.19 cm^2/m^2 for males and females, respectively. PMI-L3 cut-off values were 3.2 and 2.87 cm^2/m^2 for males and females, respectively. Sex-specific mean, standard deviation (SD), median, minimum, maximum and percentile values for SMA-L3, PMA-L3, SMI-L3 and PMI-L3 are shown in Table 2. Comparisons of mean SMA-L3, SMI-L3, PMA-L3 and PMI-L3 values in both sexes are shown in Table 3.

4. Discussion

Based on the younger data (aged 20–40 years), we suggest that SMI-L3 values less than 45.47 cm^2/m^2 for males and 36.19 cm^2/m^2 for females, can be used to diagnose low SMM in Turkish population. Also, we suggest that PMI-L3 values less than 3.2 cm^2/m^2 for males and 2.87 cm^2/m^2 for females can be used to diagnose low SMM in Turkish population.

The EWGSOP defined sarcopenia as generalized and progressive loss of SMM and muscle performance.[6] SMM and adipose tissue mass of the body, can be assessed using several methods, such as Dual energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI), CT and bioelectrical impedance analysis (BIA).[6,17,18] The EWGSOP recommended computed tomography (CT) as the gold standard for assessing muscle mass or quantity, as this method is a very precise imaging tool that can clearly separate the skeletal muscle from the body fat.[6] Additionally, CT with or without positron emission tomography is usually used for cancer staging, preoperative diagnoses of abdominal disorders and follow ups. Therefore, evaluation of sarcopenia by CT does not incur additional costs or burden of radiation for those patient groups.

It has been shown that the survival rate and pulmonary functions were significantly lower in sarcopenic patients than in patients with normal SMM who underwent living donor liver transplantation.[19–21] Therefore, in some centers the diagnosis of severe sarcopenia (in the presence of all these: low muscle quantity or quality, low muscle strength and low physical performance) is started to be used as exclusion criteria in lung transplantation and living donor liver transplantation patients.[14] We suggest that the data in our study, which will be expanded with the contribution of literature findings, would help in determining the exclusion criteria for organ transplantation in Turkey.

Table 3

In the evaluation of differences of SMA, SMI, PMA and PMI values at L3 level between males and females in the individuals aged 20–40 years and 20–60 years.

	Male	Female	*p* value
Aged 20–40 years			
SMA mean (cm^2)	155.41	110.67	0.028
PMA mean (cm^2)	17.52	14.47	0.024*
SMI mean (cm^2/m^2)	51.66	42.28	0.0001*
PMI mean (cm^2/m^2)	5.78	5.4	0.22*
Aged 20-60 years			
SMA mean (cm^2)	145.53	106.34	0.0001
PMA mean (cm^2)	14.92	11.91	0.0001*
SMI mean (cm^2/m^2)	50.51	41.32	0.0001
PMI mean (cm^2/m^2)	5.12	4.64	0.026*

* Mann-Whitney U test was used. SMA, skeletal muscle area; PMA, psoas muscle area; SMI, skeletal muscle index; PMI, psoas muscle index.

Table 2

Gender specific measurement results and percentiles for skeletal muscle parameters at L3 level for the total study population (aged 20–60 years) and subjects aged 20–40 years.

20-40 years	All subjects				Male				Female			
	SMA	PMA	SMI	PMI	SMA	PMA	SMI	PMI	SMA	PMA	SMI	PMI
Mean	135.07	16.13	47.40	5.61	155.41	17.52	51.66	5.78	110.67	14.47	42.28	5.40
Median	136.94	15.16	48.02	5.15	156.81	15.46	52.01	5.37	111.94	12.97	40.54	4.65
Std.	25.55	5.90	6.37	1.72	14.24	5.39	3.58	1.54	9.12	6.19	5.08	1.94
Minimum	90.42	7.14	36.14	2.85	121.71	8.53	45.20	2.85	90.42	7.14	36.14	2.86
Maximum	176.13	27.21	58.21	9.10	176.13	27.21	58.21	8.98	122.63	27.21	54.96	9.10
Percentiles												
p5	95.91	7.49	37.89	2.92	125.52	9.46	45.47	3.20	90.61	7.14	36.19	2.87
p10	102.27	8.86	41.77	3.53	136.94	12.93	46.40	4.37	94.81	7.32	37.23	3.13
p25	112.53	11.80	48.02	4.34	144.00	13.76	49.27	4.81	103.80	11.16	38.19	4.21
p50	136.94	15.16	52.14	5.15	156.81	15.46	52.01	5.37	111.94	12.97	40.54	4.65
p75	159.61	17.47	55.01	6.52	168.37	22.11	54.16	7.06	118.80	15.50	45.34	6.52
p90	171.21	27.20	57.76	8.54	174.33	27.20	57.44	8.45	122.40	26.85	50.57	9.00
p95	175.23	27.21	37.89	9.07	176.13	27.21	58.18	8.98	122.63	27.21	54.75	9.10
20-60 years	All subjects				Male				Female			
	SMA	PMA	SMI	PMI	SMA	PMA	SMI	PMI	SMA	PMA	SMI	PMI
Mean	125.79	13.41	45.88	4.88	145.53	14.92	50.51	5.12	106.34	11.91	41.32	4.64
Median	118.80	12.38	45.48	4.60	143.83	15.19	50.55	5.11	106.05	10.80	40.77	4.21
Std.	23.84	5.32	5.99	1.77	17.30	5.22	3.95	1.57	8.27	5.02	3.72	1.94
Minimum	90.42	3.80	33.79	1.73	103.47	3.80	43.23	1.73	90.42	5.48	33.79	2.01
Maximum	181.58	27.21	59.47	9.12	181.58	27.21	59.47	8.98	122.63	27.21	54.96	9.12
Percentiles												
p5	95.04	5.94	37.08	2.46	114.71	7.37	44.98	2.63	93.20	5.57	36.05	2.02
p10	98.20	7.77	38.25	2.86	124.79	8.39	45.42	2.82	95.07	7.14	37.10	2.85
p25	104.74	8.97	40.53	3.46	133.18	10.72	47.05	3.79	99.61	8.53	39.14	3.27
p50	118.80	12.38	45.48	4.60	143.83	15.19	50.55	5.11	106.05	10.80	40.77	4.21
p75	143.83	16.34	50.63	6.00	156.23	17.47	52.88	6.06	112.58	14.51	43.10	5.96
p90	161.58	20.91	54.17	7.45	170.41	21.59	55.79	7.00	116.45	20.79	46.02	8.19
p95	170.41	24.36	55.79	8.98	176.13	27.19	58.16	7.91	119.79	23.65	49.20	9.10

SMA, skeletal muscle area; PMA, psoas muscle area; SMI, skeletal muscle index; PMI, psoas muscle index; Std, standard deviation.

In 2016, a study by Bahat et al.[17] from Turkey proposed the whole body SMM cut-offs to define the low SMM measured by bioelectrical impedance analysis (BIA); 9.2 and 7.4 kg/m^2 in males and females, respectively. However, cut-offs for SMM at L3 on computed tomography (CT) in Turkey have yet to be specified. Although reference skeletal muscle mass values based on CT (SMA-L3, SMI-L3, PMA-L3 and PMI-L3) are lacking in healthy Turkish population, cut-off values in healthy American,[11,12] Caucasian[10] and Asian[13,14] populations have recently been defined. van der Werf et al.[10] reported the cut-off values of SMI-L3 as 41.6 cm^2/m^2 for males and 32 cm^2/m^2 for females, respectively in a Caucasian population (the vast majority of European). When fifth percentile (two standard deviations) is considered as the cut-off valuein the total study population (20–60 years aged), we found SMI-L3 cut-off values 45 cm^2/m^2 for males and 36 cm^2/m^2 for females. We suggest that the small differences between those studies may be related to the variety between ethnicity, lifestyle and physical activity among populations, as previously described.[6,9–14,22,23] Because skeletal muscle mass may differ between ethnicities, the percentiles in our study are representative for the Turkish population. Comparison of studies investigating muscle mass on CT in healthy individuals is shown in Table 4.

Cut-off values of SMM (such as SMI-L3 or PMI-L3) on CT have been defined in many studies based on optimum stratification for prognosis.[4,7,15,24–26] Prado et al.[7] reported that, cut-off values for SMI at L3 level are associated with poor prognosis in obese (BMI equal to or greater than 30 kg/m^2) population (n = 250) with a solid tumor and they defined the cut-offs as 52.4 and 38.5 cm^2/m^2 in males and females, respectively.[7] Furthermore, Yuri et al.[25] also studied in subjects with hepatocellular carcinoma and reported the PMI-L3 cut-off values (6.31 cm^2/m^2 for males and 3.91 cm^2/m^2 for females) can be useful for predicting outcomes. The mortality based SMI-L3 and PMI-L3 cut-off values that were defined[7,15,24–26] are higher than our predicted fifth percentile in healthy males and females aged 20–40 years. The comparison of healthy population skeletal muscle mass values and other studies in which mortality or outcome-based cut-off values of muscle mass have been defined, would not be proper but makes it feasible to detect the prevalence of low SMM. We suggest that other factors (such as variations in body size, lifestyles, and ethnicities) may contribute to diversity in cut-off values. Thus, we would like to reiterate again the importance of ethnicity and sex-specific reference values for proper diagnosis of low SMM.

It has been shown that CT examination parameters may influence skeletal muscle mass measurements and it should preferably be unenhanced and performed at 120 kV for comparison of the results.[10] In our study, 120 kV was used for CT examinations and only patients with unenhanced CT scans were included in the study. Using different software programs for SMA-L3 and PMA-L3 measurements may give slightly different results between studies. However, it has been shown that different software programs showed perfect inter-software agreement for skeletal muscle area measurements thus results from different software programs may reliably be compared.[9] Comparison of studies investigating muscle mass on CT in healthy individuals with different software programs is shown in Table 4.

This study has several limitations. First, subject's descriptive data were retrospectively collected. However, there was no missing data (individuals with missing data were excluded from the study) minimizing the weakness of the study. Second, we did not identify the subject's status of physical activity, which could affect SMM, and muscle functional analyses (strength or performance) were not performed as part of this study. However, CT is a one of the most precise technique for detecting low SMM.[6] Third, our study only included individuals who are a potential kidney donor, and this may introduce selection bias. For instance, extremely obese subjects (BMI higher

Table 4

Comparison of studies investigating muscle mass at L3 level on computed tomography in healthy individuals.

Study	Origin of study	Number of subjects	Population	Age range (years)	Mean weight (kg) (female/ male)	Mean height (cm) (female/ male)	BMI (kg/m^2) (female/ male)	Software	Male p5				Female p5			
									SMA	SMI	PMA	PMI	SMA	SMI	PMA	PMI
van der Werf et al. [10]*	Germany	420 (246 Females)	PKD	20–82	72/86.2	168/182	25.5/26.1	SliceOmatic	134	41.6	–	–	89.2	32	–	-
van der Werf et al. [10]*	Germany	300 (174 Females)	PKD	20–60	–	–	–	SliceOmatic	138.2	43.1	–	–	96.2	32.7	–	-
Derstine et al. [11]	United States of America	604 (347 Females)	PKD	18–40	72.6/87.8	164/179	26.8/27.4	Matlab	141.7	44.6	–	–	91.2	34	–	-
Derstine et al. [12]	United States of America	735 (410 Females)	PKD	18–40	72.7/88.7	164.2/179.1	26.9/27.6	Matlab	144.3	45.4	–	–	92.2	34.4	–	-
Kim et al. [13]	Korea	1422 (872 Females)	PWCD	20–89	56.6/71.5	158/171	22.8/24.5	Manual tracing	–	–	–	3.31–5.92[+]	–	–	–	1.48–4[+]
Hamaguchi et al. [13]	Japan	230 (114 Females)	PLD	20–49	56.6/71.5	158/171	22.8/24.5	Manual tracing	–	–	–	6.36	–	–	–	3.92
Present Study*	Turkey	88 (40 females)	PKD	20–40	63.4/76.4	162.3/175.5	23.9/25.3	Osirix	125.52	45.47	9.46	3.2	90.61	36.19	7.14	2.87
Present Study*	Turkey	270 (136 females)	PKD	20–60	67/75.8	161/169.6	25.4/26.4	Osirix	114.71	44.98	7.37	2.63	93.20	36.05	5.57	2.02

PKD, potential kidney donor; PWCD, patients without known chronic disease; SMA, skeletal muscle area; PMA, psoas muscle area; SMI, skeletal muscle index; PMI, psoas muscle index; BMI, body-mass index.

* Studies investigating cut-off values in the whole and young population separately. [+] Cut-off values were described for each decade of the population.

than 35 kg/m^2) were not represented within our study population due to contraindication for kidney donation. Lastly, our Turkish population-based cut-off values have not been tested against clinical outcomes. Therefore, more studies are needed to define cut-off values based on mortality.

In conclusion, this is the first study to measure sex-specific SMA-L3, SMI-L3, PMA-L3 and PMI-L3 values on CT in a population of healthy subjects from Turkish population and to establish skeletal muscle cut-off values that may be used to define sarcopenia in Turkish population. We suggest these results may contribute other researchers to extract clinically useful data.

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Declarations of interest

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