

Novel lateral whole-body dual-energy X-ray absorptiometry of lumbar paraspinal muscle mass: results from the SarcoSpine study

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Abstract

Background Here, we aimed to propose novel lateral whole-body dual-energy X-ray absorptiometry (lateral DXA) as a simple tool for measuring spinal muscle mass and investigate the feasibility of lateral DXA to measure lumbar paraspinal muscle (LPM) mass compared with lumbosacral spine three-dimensional magnetic resonance imaging (3D MRI).

Methods Twenty consecutive participants were enrolled from a prospective observational cohort (SarcoSpine study). Lateral DXA was scanned with each participant in the lateral decubitus position. The region of interest was defined to analyse the LPM mass. LPM total volume, LPM cross-sectional area at the L3 mid-vertebra and L4/5 mid-disc levels and each signal intensity were measured by 3D MRI. Isokinetic and isometric back extensor muscle strengths as well as back extensor endurance were examined. The correlation between lateral DXA-based mass (weight) and 3D MRI-based LPM volume was analysed.

Results The mean age of the 20 participants (15 women, 5 men) was 72.2 ± 4.9 years. LPM mass by lateral DXA was positively correlated with LPM volume by 3D MRI ($\beta = 0.333$, $r = 0.692$, $p < 0.001$) and negatively correlated with signal intensity of the total LPM ($\beta = -0.263$, $r = -0.530$, $p = 0.016$). LPM mass was also correlated with appendicular limb muscle mass, handgrip strength and gait speed as well as back extensor endurance ($r = 0.620$, $p = 0.004$).

Conclusions Our data suggest that LPM mass assessed by lateral DXA was positively correlated with LPM volume by 3D MRI in older adults. Lateral DXA may be a potential substitute for the cross-sectional area measurement of LPM mass. Further studies are required to validate this lateral DXA technique.

Keywords absorptiometry; photon; body composition; paraspinal muscles; sarcopenia; spine

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Introduction

Spinal sarcopenia is a phenomenon involving atrophy of and fatty changes to paraspinal muscles induced by skeletal muscle ageing.¹ Although muscle mass measurements used to

define sarcopenia have mainly been based on the sum of limb muscle mass, it is questionable whether limb muscle mass is directly associated with paraspinal muscle mass. It is necessary to measure paraspinal muscle mass to define spinal sarcopenia. Truncal muscle mass can be measured by dual-

energy X-ray absorptiometry (DXA) or bioimpedance analysis (BIA), both of which are usually used to determine conventional sarcopenia.² However, paraspinal muscle mass alone cannot be separated in these body composition analysis techniques because the skeletal muscles around the spine cannot be distinguished from the visceral muscles of the internal organs in the trunk.

Several studies have suggested measuring the cross-sectional area (CSA) of the paraspinal muscles using computed tomography (CT), magnetic resonance imaging (MRI) or ultrasonography (US). The CSA and intramuscular fat infiltrations of the paraspinal muscles measured by CT are affected by age and disc level.^{3–5} One cohort study also demonstrated that the fatty infiltration ratio of the erector spinae in the upper lumbar spine was associated with the presence of low back pain using an MRI-defined paraspinal muscle morphology analysis.⁶ However, the CSA in one section might be unable to represent the total muscle mass like the other limb muscles because the paraspinal muscles are among the most elongated muscles of the human body. Another study compared the CSA measurements of the quadriceps femoris muscle to a volumetric assessment in patients who underwent anterior cruciate ligament reconstructions.⁷ They reported that the CSA showed different correlations with the total muscle volume according to measured level. A combination of anatomical CSA and length measurements, not CSA alone, of the lower limb muscles was also suggested to be able to estimate muscle volume in patients with cerebral palsy.⁸ Thus, the use of the CSA alone has limited ability to evaluate the entire muscle volume and does not necessarily correlate with muscle function. In one study, paraspinal muscle volume was calculated by three-dimensional (3D) reconstruction by MRI scanning to evaluate the mass of the entire paraspinal muscle. They reported paraspinal muscle volume and lumbar spinal canal volume using 3D MRI image reconstruction in a lumbar spinal stenosis population.⁹ However, this is possible in the research field, not in clinical practice. Therefore, feasible measurement tools such as DXA or BIA used to diagnose conventional sarcopenia should be developed to define spinal sarcopenia.

In this study, we propose a novel technique for measuring paraspinal muscle mass that uses whole-body DXA in the lateral direction (lateral DXA). This study aimed to investigate the feasibility of lateral DXA for measuring lumbar paraspinal muscle (LPM) mass and determine its correlation with 3D reconstructed MRI-based volume or CSA of the LPM.

Materials and methods

Study population

The SarcoSpine study is a prospective observational cohort study of spinal sarcopenia conducted in a single centre.¹

Eligibility criteria included older (≥ 65 years old) community-dwelling individuals who are able to walk with or without assistive devices. Individuals with low back pain of moderate severity (numeric rating scale 5+) or history of any type of lumbar spinal surgery were excluded. The institutional review board of Seoul Metropolitan Government Seoul National University Boramae Medical Center approved the study (no. 20-2019-19), and all participants provided informed consent. The study protocol has been registered at Clinicaltrials.gov (NCT03962530). Of the recruited participants, 20 consecutive individuals who completed the baseline survey, examinations and imaging studies were enrolled in this study.

DXA and body composition analysis

DXA (Lunar iDXA for Bone Health; GE Healthcare, Schenectady, NY, USA) was used to analyse body composition including lean body and fat masses. Anteroposterior (AP) and lateral whole-body scans were performed in accordance with the enCORE-based X-ray Bone Densitometer User Manual (Revision 5; part number: LU43616EN; Jan 2010). In whole-body AP DXA, appendicular limb muscle mass (ALM) was calculated by obtaining the sum of the lean mass of the bilateral upper and lower extremities¹⁰ and standardized by being divided by the squared height value (ALM/ht^2 in kg/m^2). Whole-body lateral DXA was scanned with the subject in the lateral decubitus position with a lateral positioner placed over the back rail of the table (*Figure 1A*). The lateral positioner and the instructions below are intended to position the lumbar spine straight and parallel to the scanner table: (1) place a pillow under the subject's head, (2) allow the subject to lie on the left side and the lower limb joint to be as comfortable as possible, (3) position the subject's back and hips flat against the positioner, and (4) position the subject's arms at a 90° angle from the chest. After the lateral DXA scan was performed, the region of interest (ROI) was defined to analyse the body composition of the LPM as follows: (1) upper line, the posterior costophrenic angle that represents the T12/L1 level; (2) lower line, the top of the iliac wing that represents the L4/5 level; and (3) anterior line, the transverse process of the lumbar vertebrae¹¹ (*Figure 1B*). Lean body and fat masses were calculated in the ROI of the LPM. ROI measurements of lateral DXA were repeated two times by each of two radiological technologists with more than 5 years' experience in charge of DEXA test and analysis to ensure the reliability of the method.

Lumbosacral spine MRI (3D) with volume and signal intensity measurements

All participants underwent MRI on a 1.5 T system (Intera Achieva, Philips Healthcare, Best, The Netherlands) using a

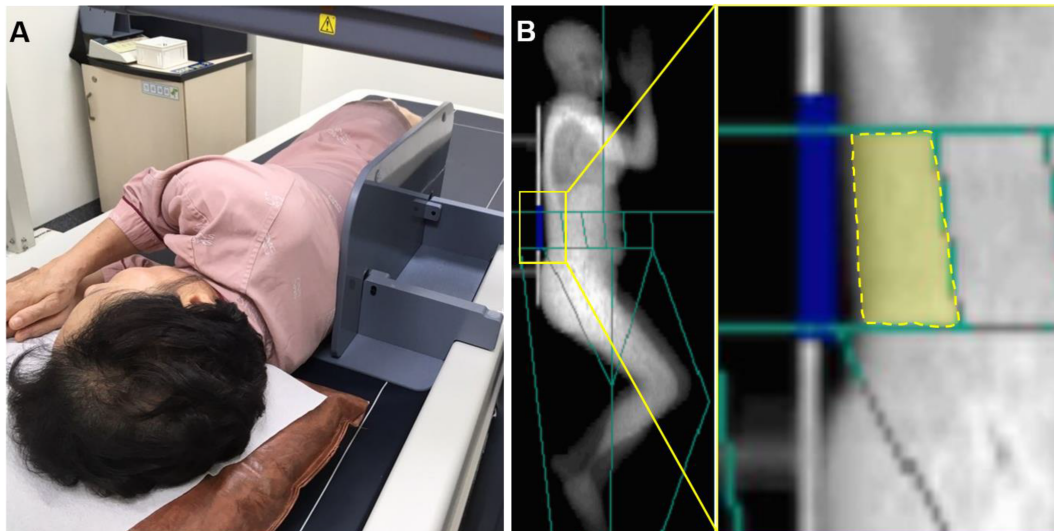


Figure 1 Measurement for body composition of lumbar paraspinal muscle by whole-body dual-energy X-ray absorptiometry in the lateral direction (lateral DXA): (A) lateral decubitus position with a lateral positioner over the back rail of the table, (B) defined region of interest (yellow dotted tetragon) to analyse the body composition.

12-channel spinal coil. All spine MRI examinations were performed with one 1.5-T MR scanner because we aimed to maintain the homogeneity of our sample. The participants were placed in the supine position with the lumbar spine in a neutral position. Spine MRI was performed with a 3D volume isotropic turbo spin-echo acquisition sequence with coronal imaging plane (repetition time, 2000 ms/echo; echo time, 120 ms; echo-train length, 97; section thickness, 2 mm; slice interval, 1 mm; and field of view, 300 × 300). The scan coverage spanned (1) from the front of the psoas muscle to the back of the erector spinae muscle (in anterior to posterior direction), (2) from the superior endplate of T12 vertebral body to the apex of coccyx (in the vertical direction) and (3) within the whole trunk (in the transverse direction).

3D segmentation of the paraspinal muscles was performed to measure the volume and mean signal intensity of the LPM (bilateral multifidus and erector spinae). The right and left LPM compartments were separately segmented from the mid-disc level of T12/L1 to the mid-disc level of L4/5. A semi-automated random walk 3D segmentation algorithm, a magic cut tool for segmentation work with a radiological software (AVIEW Research; Coreline, Seoul, South Korea), was used to volumetrically segment the LPM.¹² During the segmentation, the experienced radiologist repeatedly modified the procedures and confirmed the segmentation results. In this process, the ROI was placed at the muscle contour with care taken to avoid the accidental inclusion of subcutaneous fat or the muscle-fat interface. Bilateral LPM compartments were combined to determine the mean signal intensity and muscle volume (Figure 2). The mean signal intensity of the LPM reflects the intramuscular fat content because the signal intensity increased as the fat content increased.

CSA and signal intensity analysis of LPM

CSA and signal intensity analyses were also performed at the L3 mid-vertebra and L4/5 mid-disc levels.¹³ In the 3D multiplanar image mode, coronal and sagittal images were used to reformat the axial images, which were parallel to the L3 endplates in the L3 mid-vertebra and L4 inferior and L5 superior endplates in the L4/5 mid-disc level. Then, using the 3D segmentation ROI information, the CSA and signal intensity of the LPM were measured in these reformatted axial images (Figure 2).

Back muscle strength and endurance

The isokinetic and isometric back extensor muscle strengths were examined. Briefly, an isokinetic dynamometer (Biodex multi-joint system; Biodex Corporation, Shirley, NY, USA) was used to measure the torque of the back extensors.¹⁴ All participants were instructed to execute flexion and extension of the back at maximal effort 10 times at an angular velocity of 60°/sec after a five-repetition warm-up session. The range of motion of the isokinetic dynamometer arm was adjusted individually according to the subject's maximal flexion and extension. The largest value was used among the 10 measurements. Isometric back muscle strength test was measured with a handheld dynamometer (PowerTrack II; JTECH Medical, Salt Lake City, UT, USA). Standing in full extension with the back to a wall midway between two vertically oriented anchor rails and the feet flat on the floor with the heels touching the wall, the participants were instructed to flex forward at the hips approximately 15° so the handheld dynamometer can be positioned posterior to the spinous

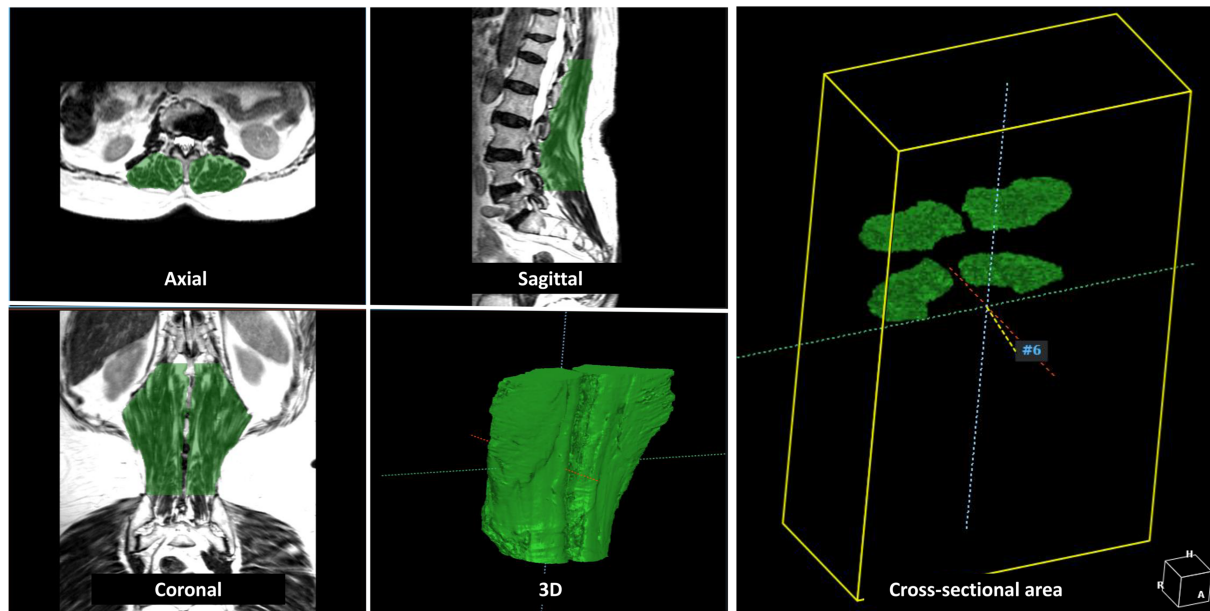


Figure 2 Three-dimensional segmentation of lumbar paraspinal muscles in L-S spine magnetic resonance imaging.

process of the seventh thoracic vertebrae. In this way, counter-pressure was provided by the fixed wall behind the participant's back to avoid variations in resistance by an examiner.¹⁵ Once positioned, each participant performed two submaximal practice trials for familiarization. Measurements were performed three times, and there was a 30-s rest period between trials. The largest value was also used among the three measurements. The prone isometric chest raise (PICR) test was done with the participant in the prone position with a pad under the abdomen and the arms along the sides to test back extensor endurance.¹⁶ They were instructed to lift the upper trunk about 30° from the table while flexing the neck and holding the sternum off the floor as much as possible. The duration (seconds) that the participant could sustain this position was measured.

Functional and performance tests

Handgrip strength was measured using a handgrip dynamometer (T.K.K.5401; Takei Scientific Instruments, Tokyo, Japan)¹⁷ as described previously.¹⁸ Gait speed was measured using 6-m usual gait speed (m/s) as recommended by the Asian Working Group for Sarcopenia,¹⁹ and sarcopenia or possible sarcopenia was defined as the updated consensus of the group.²⁰ The short physical performance battery was conducted using three objective physical function tests (i.e. time taken to cover 4 m at a comfortable walking speed, time taken to stand from sitting in a chair five times without stopping and ability to maintain balance for 10 s in three different foot positions at progressively more challenging levels).²¹ The

back performance scale, which consists of five tests (sock test, pickup test, roll-up test, fingertip-to-floor test and lift test), was also performed.²² The timed up and go test has shown excellent test–retest reliability in older adults.²³ The participants were given verbal instructions to stand up from an arm chair, walk 3 m as fast as possible, turn back at a cone set out by the researchers, walk back and sit down in the chair. Balance and fall risk were assessed using the Berg Balance Scale (BBS) (range, 0–56; lower score indicating worse outcome).²⁴

Statistical analysis

Descriptive statistics of the study population were calculated of the demographic characteristics and functional outcomes. Means and standard deviations were computed for continuous variables. Correlations between sarcopenic indices and functional outcomes were measured by Pearson's correlation coefficient. Cronbach's alpha test was used to verify the inter-rater reliability of ROI in lateral DXA measurements between two radiological technologists analysed in blinded state. Linear regression models were used to study the correlation between 3D reconstructed MRI-based volume (cm³) and lateral DXA-based weight (g) of the paraspinal muscle. The beta (β) coefficient between the two variables could be the skeletal muscle density (weight/volume). Because the physical density of the skeletal muscle^{25,26} is about 1.055 g/cm³, we hypothesized that the value might be around 1.0. SPSS Statistics software Version 26.0 (IBM Corporation, NY,

USA) was used for all analyses. p -Values < 0.05 were considered statistically significant.

Results

The baseline characteristics of the 20 older adults (15 women, 5 men) are shown in *Table 1*. The mean participant age was 72.2 ± 4.9 years, and the mean body mass index was 24.9 ± 2.6 kg/m². In conventional sarcopenic indices, ALM/ht², handgrip strength and gait speed were 7.30 ± 0.91 kg/m², 27.6 ± 9.1 kg and 1.20 ± 0.19 m/s, respectively. Among them, 18 had no sarcopenia, and two had possible sarcopenia. Of those two, only one was diagnosed with sarcopenia.

The reliability test of two measurements of LPM in lateral DXA by two blinded evaluators resulted in a Cronbach's alpha value of 0.949. LPM mass by lateral DXA showed a positive correlation with LPM volume by 3D MRI ($\beta = 0.333$, $r = 0.692$, $p < 0.001$) and a negative correlation with the mean signal intensity of LPM ($\beta = -0.263$, $r = -0.530$, $p = 0.016$) (*Figure 3*). LPM mass was significantly correlated with all three sarcopenic indices (ALM/ht², handgrip strength and gait speed), whereas both LPM volume and L3 LPM CSA were correlated with only two indices (ALM/ht² and handgrip strength). In addition, the signal intensity of total LPM by 3D

MRI and L3 LPM were significantly correlated with three sarcopenic indices (*Table 2*). Isokinetic back extensor strength and BBS total score were significantly negatively correlated with the signal intensities of total, L3 and L4/5 LPM. Back extensor endurance assessed on the PICR test showed a stronger correlation with LPM mass by lateral DXA ($r = 0.620$, $p = 0.004$) than with LPM volume by 3D MRI ($r = 0.468$, $p = 0.037$) (*Table 3*).

Discussion

In this study, we proposed measuring the paraspinal muscle mass using lateral whole-body DXA and investigating its feasibility versus 3D reconstructed MRI-based volume. The most important finding of this study was that LPM mass determined by lateral DXA was significantly correlated with LPM volume by 3D MRI in 20 community-dwelling older adults. LPM mass correlated with ALM/ht², handgrip strength and gait speed. Back muscle endurance was also correlated with LPM mass. Although LPM mass and volume are not directly equivalent and will require further validation, this is the first study to apply a novel lateral DXA technique to measure LPM and identify its clinical feasibility.

Site-specific muscle mass measurements are needed to evaluate the effect of skeletal muscle on the site. Lower

Table 1 Baseline characteristics of 20 participants

	Mean \pm SD
Age (years)	72.2 \pm 4.9
Sex	Male 5; female 15
Height (cm)	157.0 \pm 8.0
Weight (kg)	61.7 \pm 10.1
Body mass index (kg/m ²)	24.9 \pm 2.6
Waist circumference (cm)	90.0 \pm 9.2
Conventional sarcopenic indices	
ALM/ht ² by DXA (kg/m ²)	7.30 \pm 0.91
Handgrip strength (kg)	27.6 \pm 9.1
Gait speed (m/sec)	1.20 \pm 0.19
Lateral DXA	
Muscle mass (g)	662.1 \pm 237.3
Fat mass (g)	382.1 \pm 152.3
L-S spine 3D MRI	
L3 lumbar paraspinal muscle CSA (mm ²)	2963.1 \pm 521.6
L3 lumbar paraspinal muscle mean signal intensity	436.6 \pm 109.0
L4/5 lumbar paraspinal muscle CSA (mm ²)	3147.7 \pm 667.5
L4/5 lumbar paraspinal muscle mean signal intensity	510.3 \pm 129.4
Lumbar paraspinal muscle volume (cm ³)	507.0 \pm 118.8
Lumbar paraspinal muscle mean signal intensity	472.2 \pm 132.2
Back muscle strength/endurance	
Isokinetic back extensor strength (torque)	71.5 \pm 38.9
Isometric back extensor strength (N)	44.3 \pm 16.7
Prone isometric chest raise test (sec)	30.2 \pm 28.0
Functional test	
Short physical performance battery (0–12)	11.3 \pm 1.0
Back performance scale (0–15)	2.8 \pm 1.7
Berg Balance Scale (0–56)	53.5 \pm 2.5
Timed up and go test (sec)	8.9 \pm 1.2

3D MRI, three-dimensional reconstruction by magnetic resonance imaging; ALM, appendicular limb muscle mass; CSA, cross-sectional area; DXA, dual-energy X-ray absorptiometry; ht, height.

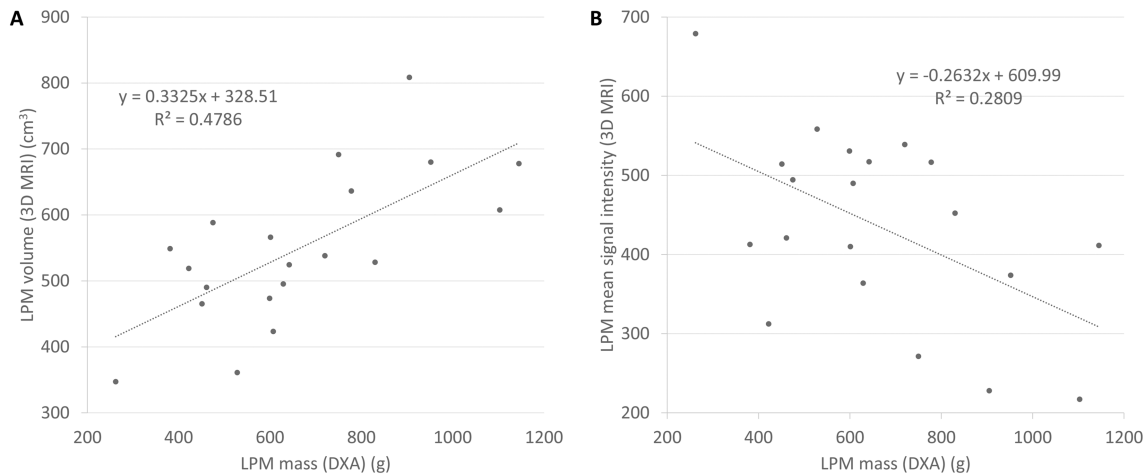


Figure 3 Scatter grams and regression lines showing correlations between lumbar paraspinal muscle mass (DXA) and lumbar paraspinal muscle volume (MRI) (A) and mean signal intensity (B). LPM, lumbar paraspinal muscle; DXA, dual-energy X-ray absorptiometry; 3D MRI, three-dimensional reconstruction by magnetic resonance imaging.

Table 2 Correlations between sarcopenic indices and lumbar paraspinal muscle values

	ALM/ht ²	Handgrip strength	Gait speed
LPM mass (DXA)	0.660 **	0.595 **	0.537 *
Lumbar fat mass (DXA)	0.530 *	0.323	0.347
LPM volume (3D MRI)	0.579 **	0.703 **	0.389
LPM signal intensity (3D MRI)	-0.457 *	-0.685 **	-0.529 *
L3 LPM CSA	0.560 *	0.655 **	0.208
L3 LPM signal intensity	-0.454 *	-0.697 **	-0.478 *
L4/5 LPM CSA	0.183	0.257	0.308
L4/5 LPM signal intensity	-0.350	-0.655 **	-0.491 *

3D MRI, three-dimensional reconstruction by magnetic resonance imaging; ALM, appendicular limb muscle mass; DXA, dual-energy X-ray absorptiometry; ht, height; LPM, lumbar paraspinal muscle.

**p* < 0.05 (in bold and italic).

***p* < 0.01 by Pearson correlation coefficient (in bold and italic).

Table 3 Correlations between paraspinal muscle values and back strength/functional outcomes.

	Isokinetic back extensor strength	Isometric back extensor strength	Endurance test (PICR)	SPPB	TUG	BBS	BPS
LPM mass (DXA)	0.117	0.345	0.620 **	0.387	-0.213	0.114	-0.077
Lumbar fat mass (DXA)	-0.117	0.002	0.508 *	0.317	-0.203	0.051	0.206
LPM volume (3D MRI)	0.405	0.545 *	0.468 *	0.354	-0.045	0.287	-0.159
LPM signal intensity (3D MRI)	-0.569 **	-0.284	-0.676 **	-0.252	-0.069	-0.529 *	0.215
L3 LPM CSA	0.428	0.545 *	0.303	0.162	0.128	0.349	-0.201
L3 LPM signal intensity	-0.618 **	-0.273	-0.614 **	-0.128	-0.169	-0.616 **	0.259
L4/5 LPM CSA	0.235	0.253	0.364	0.332	-0.255	0.070	-0.199
L4/5 LPM signal intensity	-0.630 **	-0.341	-0.679 **	-0.418	0.133	-0.649 **	0.380

3D MRI, three-dimensional reconstruction by magnetic resonance imaging; BBS, Berg Balance Scale; BPS, back performance scale; DXA, dual-energy X-ray absorptiometry; LPM, lumbar paraspinal muscle; PICR, prone isometric chest raise test; SPPB: short physical performance battery; TUG, timed up and go test.

**p* < 0.05 (in bold and italic).

***p* < 0.01 by Pearson correlation coefficient (in bold and italic).

limb, but not upper limb, muscle mass was correlated with symptomatic knee osteoarthritis.²⁷ ALM was not associated with hip joint or lumbar spine degeneration, in contrast with knee joint degeneration.²⁸ Loenneke et al.²⁹ suggested

that a site-specific muscle estimation with a measurement of muscle strength/performance can provide a more complete picture about the muscle changes that occur with ageing. One large cross-sectional study of 1507 adults also

reported that specific muscles showed prominent sarcopenia among eight muscles measured by US.³⁰ In other words, it is necessary to measure the specific muscle in order to evaluate the muscle function of the specific region rather than the sum of the limb muscles (ALM) conventionally used to diagnose sarcopenia. Therefore, direct measurement of the paraspinal muscles is essential to determine the impact of the skeletal muscles on the spine. However, few simple and feasible tools are available to measure the paraspinal muscles.

Lateral DXA has already been used to measure bone mineral density, and the superiority over DXA in AP direction has been investigated in several studies. Finkelstein et al.³¹ compared lateral and AP spine DXA in the diagnosis of osteopenia in trabecular bone. They concluded that lateral DXA measurements more often identify individuals with osteopenia than AP DXA and that the former more accurately estimates trabecular bone mass with high reproducibility. One study also suggested that lateral DXA identified considerably more men as having osteoporosis and was more sensitive for detecting age-related bone loss than AP DXA.³² Because the validity of lateral DXA for the bone mineral density measurement was sufficiently revealed through these studies, we aimed to extend it to be used for body composition analysis whether it is possible to analyse the LPM. This study confirmed that the LPM mass determined by lateral DXA was strongly correlated with the LPM volume determined by 3D MRI. LPM mass was also associated with three sarcopenic indices (ALM/ht², handgrip strength and gait speed). It was also correlated with back muscle endurance ($r = 0.620$, $p = 0.004$) with greater significance than that of the LPM volume analysed by 3D MRI ($r = 0.468$, $p = 0.037$). Thus, lateral DXA is a simple and feasible way to measure the entire LPM and a potential substitute for CSA of the LPM.

The European Working Group on Sarcopenia in Older People 2 recommend the use of lumbar muscle CSA determined on CT or MRI to measure skeletal muscle mass.¹³ L3 lumbar muscle CSA has been studied as a potential predictor for mortality, discharge disposition and the intensive care unit (ICU) utilization in elderly ICU patients.³³ It could also predict post-operative length of stay and infection but is not associated with survival after liver transplantation.³⁴ In this study, we measured the CSA and signal intensity of LPM at the L3 mid-vertebra and L4/5 mid-disc levels. The L3 LPM CSA correlated with isometric back extensor strength. Furthermore, the signal intensity of the L3 and L4/5 LPM was correlated with isokinetic back extensor strength as well as BBS score. These results indicate that the qualitative variable 'signal intensity' is more strongly correlated with muscle strength and body function than the CSA, a quantitative variable. Therefore, the CSA and signal intensity measurements of the lumbar spine using MRI and CT are valuable site-specific muscle measurements that should be used in future research and clinical studies. However, a CSA analysis of the LPM can only be

performed through an imaging study such as MRI or CT, which have distinct limitations. In addition, a post-processing analysis that draws the ROI is needed. Therefore, a method is needed that can more easily measure LPM in clinical practice, and the results of the current study suggest that lateral DXA is a candidate method.

Our study had several limitations. First, it is possible that the area scanned by the lateral DXA also contains other trunk muscles (such as the quadratus lumborum and latissimus dorsi) or retroperitoneal organs like posterior parts of the kidney. Therefore, the LPM mass measured by DXA may be relatively larger than the LPM volume precisely measured by 3D MRI. Second, the ROI defined on lateral DXA of the LPM might be incorrect. In particular, it was difficult to accurately discriminate the lumbar level because whole-body DXA had poor resolution. Therefore, the upper line of the ROI was designated the costophrenic angle and judged to be the T12/L1 level. However, as there are individual variations in lung size, it would be impossible to define the costophrenic angle in a single batch. And finally, the sample size ($n = 20$) is insufficient to provide good prediction in the regression model³⁵ because it was a preliminary study. In addition, only one of the 20 participants had sarcopenia. Therefore, individuals with more various muscle conditions should be recruited in future studies, and the future results of the SarcoSpine cohort study will be noted.

Conclusions

Our data suggest that LPM mass measured by this lateral DXA technique was positively correlated with LPM volume determined by 3D MRI in older adults. Lateral DXA may be a potential substitute for the CSA measurement of LPM mass. Further studies are required to validate this lateral DXA technique.

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Ethical statement

The study conforms to the declaration of Helsinki. All participants provided written informed consent. The manuscript complies with the ethical guidelines for authorship and publishing in the *Journal of Cachexia, Sarcopenia and Muscle*.³⁶

Conflict of interest

The authors declare no conflicts of interest.

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