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Research article

Multi-compartment mesenchymal tissue segmentation in pelvic MRI examinations of women: Anthropomorphic and clinical correlations

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ABSTRACT

Aim: To investigate the reliability of multicompartmental volumetric mesenchymal segmentations on MRI and their correlations with anthropomorphic and clinical parameters.

Materials and methods: A consecutive series of middle-age (35–50 year old) female volunteers with variable body mass index (BMI) and MRI scans performed as a part of the Dallas Heart Study were included. A semi-automatic segmentation tool was used to partition different mesenchymal tissues- fat, muscle, and bone on MRI of pelvis. Total volumes of each compartment were calculated and compared between overweight/obese (BMI > = 25 kg/m^2) and non-obese (BMI < 25 kg/m^2) groups, and with physical performance measurements, i.e. mean activity counts per minute (MVPA) and cardiorespiratory fitness (CRF) estimated by submaximal treadmill test (TT). Kruskal Wallis, Mann-Whitney U test, intraclass correlation coefficient (ICC) and Spearman correlations were used. P value < 0.05 was considered statistically significant.

Results: There were statistically significant positive correlations between fat volume and BMI ($p < 0.0001$), muscle volume and height ($p = 0.03$), and bone volume and height ($p < 0.0001$). Significant inverse correlations were found between bone volume and BMI ($p = 0.002$). Fair to good interobserver reliability was seen with muscle and fat volumes (ICC = 0.43–0.64) and excellent reliability was seen with bone volumes (ICC = 0.78–0.79). Statistically significant inverse correlations were found between MVPA and age ($p = 0.01$), and TT with BMI and weight ($p = 0.01, 0.03$).

Conclusion: Multi-compartment mesenchymal tissue volume quantification on pelvic MRI is reliable in females. Inverse correlation of bone volume with BMI has potential implications for future risk of fracture.

1. Introduction

The prevalence of obesity has increased dramatically in the last three decades, rising across each of the fifty US states among men and women of all age groups [1]. Currently, an alarming 69% of US adults are either overweight or obese, and 36% are obese [2]. A rise in obesity levels has been linked to increased risks of metabolic syndrome, diabetes, and cardiovascular disease [3,4]. In women, obesity leads to additional risks of polycystic ovary syndrome, and postmenopausal breast and endometrial malignancies [5,6]. Increasing evidence links obesity to the development of sarcopenia through fatty infiltration of skeletal muscle and loss of muscle quantity and quality, a process termed as sarcopenic obesity (SO) [7,8].

Research on sarcopenia and obesity is hampered by the lack of accepted definitions for both, leading to a wide array of differing criteria for their diagnostic evaluation [9,10]. Although muscle volume is most commonly utilized to characterize sarcopenia, bone mineral density and body mass index (BMI) measurements have also been used [11–13]. This has increased the need to collectively assess body composition and height in order to better define SO [14,15]. Similarly, there is disagreement regarding the most accurate definition of obesity, ranging from BMI measurement for generalized obesity to abdominal adiposity for central obesity, to physical performance measurements [16,17]. Therefore, there is a need for reliable and feasible imaging tools that provide accurate body composition analysis.

Among available methods of tissue quantification, computed tomography (CT), dual X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) are considered the most accurate and useful

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[18,19]. We chose MRI for segmentations as it is a non-invasive imaging modality with excellent soft tissue contrast. It also has the added advantage of being radiation free (when compared to CT and DXA). In this study, we aimed to test the inter-reader reliability of a semiautomatic soft tissue segmentation in the quantification of various soft tissue components in pelvic MRI of women and correlated them with anthropomorphic and physical performance measurements.

2. Materials and methods

2.1. Study design and patient population

This retrospective study was conducted using information from the Dallas heart study (DHS) population data base. From this population, a randomly selected group of 120 volunteers [ages 35 to 50 years, divided into 39 obese (BMI 30–50 kg/m^2), 40 non-obese (BMI 18–24.9 kg/m^2) and 39 over-weight (BMI 25–29.9 kg/m^2) females] and their pelvic MRI scans were evaluated.

The DHS is a multiethnic population-based probability sample of Dallas County adults, weighted to include approximately 50% African-American and non-African-American participants. The study was initiated in 2000, and all original participants were invited for a repeat evaluation in 2008–2009 (DHS-2). All participants were enrolled as volunteers and had provided written informed consent in compliance with the Health Insurance Portability and Accountability Act (HIPAA). Physical performance measures and pelvic MRI scans were obtained prospectively as a part of the same study. Physical performance measures were obtained in DHS and DHS-2 populations while MR scans were obtained only on DHS-2 population. All participants were originally screened for polycystic ovary (PCO) disease in DHS, but in our sample, none of them had PCO disease.

2.2. Clinical data

All clinical examination and physical performance measurements were performed as part of DHS, DHS-2 and data was obtained from DHS-2 data base records. Height and weight were measured using a standard physician's scale without shoes and in light clothing. BMI was calculated as weight in kilograms divided by height in meters squared. An accelerometer (Philips Respironics, Bend, OR) was used to record physical activity. The accelerometer mean activity counts per minute (MVPA) variable represents average time in minutes per day spent in moderate-to-vigorous activity (defined as > 4000 accelerometer counts per minute) and it correlates with overall activity level [represented by average counts per minute (CPM)] [20]. The treadmill 4-minute walk test (TT) was performed to determine the cardiorespiratory fitness (CRF). CRF level was determined from the estimated peak oxygen uptake (VO_{2max}) and the units of fitness were in ml/kg/min. [21,22].

2.3. Imaging technique

All MRI pelvis scans included T1W and T2W images and these were performed on a 3-Tesla whole body scanner (Philips Achieva, Ingenia, Best, Amsterdam, the Netherlands) using a Torso XL coil linked to the posterior spine coils. Axial nonfat suppressed T1W images (TR:600ms, TE: 5–6 ms, turbo spin echo sequence, slice thickness- 5 mm, inter-slice gap – 10%, matrix- 256 × 256, in plane resolution 0.6 mm, and field of view from L5 vertebra to lesser trochanters) were used for segmentation and evaluation. No scans were excluded due to motion or breathing artifacts. All scans were loaded on departmental research picture archiving and communications system (PACS, IntelliSpace, Philips Healthcare, Amsterdam, the Netherlands).

2.4. Image analysis

The image analysis was performed independently by two readers (RK-medical student, RD- radiologist with 8 years of experience) blinded to the demographic data, anthropomorphic and clinical information. Under the supervision of a fellowship trained musculoskeletal radiologist, both readers were trained on a separate set of 10 scans before the final reading and segmentation procedures. Employing SliceOmatic software (TomoVision v 4.3, Chicago, USA), each axial image was segmented into fat (including subcutaneous and visceral fat), muscle, and bone compartments using a combination of semi-automated segmentation tools. The threshold tool was used to first separate each image into muscle and fat compartments, then the region growing tool was then used to segment bone areas. Intermittent editing was performed by comparing the original MR slice with the segmented version to verify the integrity of each sub-region and edit aberrant voxels. Final volumes of fat, muscle, and bone were calculated for each volunteer by summating the total number of axial images in the pelvic region (varied between 4–8 images depending upon the size of patient) (Figs. 1 and 2). Total time spent for collective image segmentation and editing were recorded for each volunteer. The calculated volumes, patient demographics (age, height, BMI), and physical performance measurements (accelerometer and treadmill data) obtained as part of the DHS-2 protocol were recorded on an encrypted Excel file (Microsoft, Seattle, 2013) and correlated to each other.

2.5. Statistical analysis

Statistical analysis was performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Descriptive statistics were used to calculate range, mean, and standard deviation (SD) for patient age, BMI, and height. Total volumes of each compartments were calculated and compared among the three groups (normal, overweight, and obese) using Kruskal Wallis test. Patients were then divided into two groups per BMI as normal (BMI < 25 kg/m^2) and overweight/obese (BMI ≥ 25 kg/m^2). When the Kruskal Wallis test was statistically significant, ad-hoc multiple comparisons were performed with Bonferroni adjustment, while Mann-Whitney U test was used to assess differences between two independent groups (normal vs overweight/obese).

Correlations between total volumes of each compartments with BMI, physical performance measurements (MVPA and TT) were assessed by Spearman correlation coefficient. Intra-class correlation (ICC) was used to evaluate the inter-reader agreement. Agreement was considered as poor for ICC less than 0.40, fair for ICC between 0.40 and 0.59, good for ICC between 0.60 and 0.74, and excellent for ICC of 0.74 or greater. P value of less than 0.05 was considered statistically significant.

3. Results

3.1. Age, BMI, and height

Ages ranged from 35 to 49, 37 to 49, and 35 to 50 years among normal, overweight, and obese groups respectively. Mean ages were 42 ± 4.4, 44 ± 3.8, and 43 ± 4.7 years among normal, overweight, and obese groups respectively. BMI ranged from 19.6 to 24.9, 25 to 30, and 30.3 to 48.1 kg/m^2 among normal, overweight, and obese groups respectively. Mean BMIs were 22.5 ± 1.6, 27.7 ± 1.5, and 35.8 ± 4.9 kg/m^2 among normal, overweight, and obese groups respectively. Height ranged from 1.5 to 1.8, 1.2–1.8, and 1.5–1.7 meters among normal, overweight, and obese groups respectively. Mean heights were 1.6 ± 0.07, 1.6 ± 0.1, and 1.6 ± 0.06 m among normal, overweight, and obese groups, respectively.

3.2. Multicompartment volumetry

All segmentations took a total 20 ± 5 min (mean + / − SD) for each volunteer. Mean total fat volumes were 2584 ± 619, 3513 ± 910, and 5683 ± 1430 cm^3, mean total muscle volumes were 2228 ± 477,

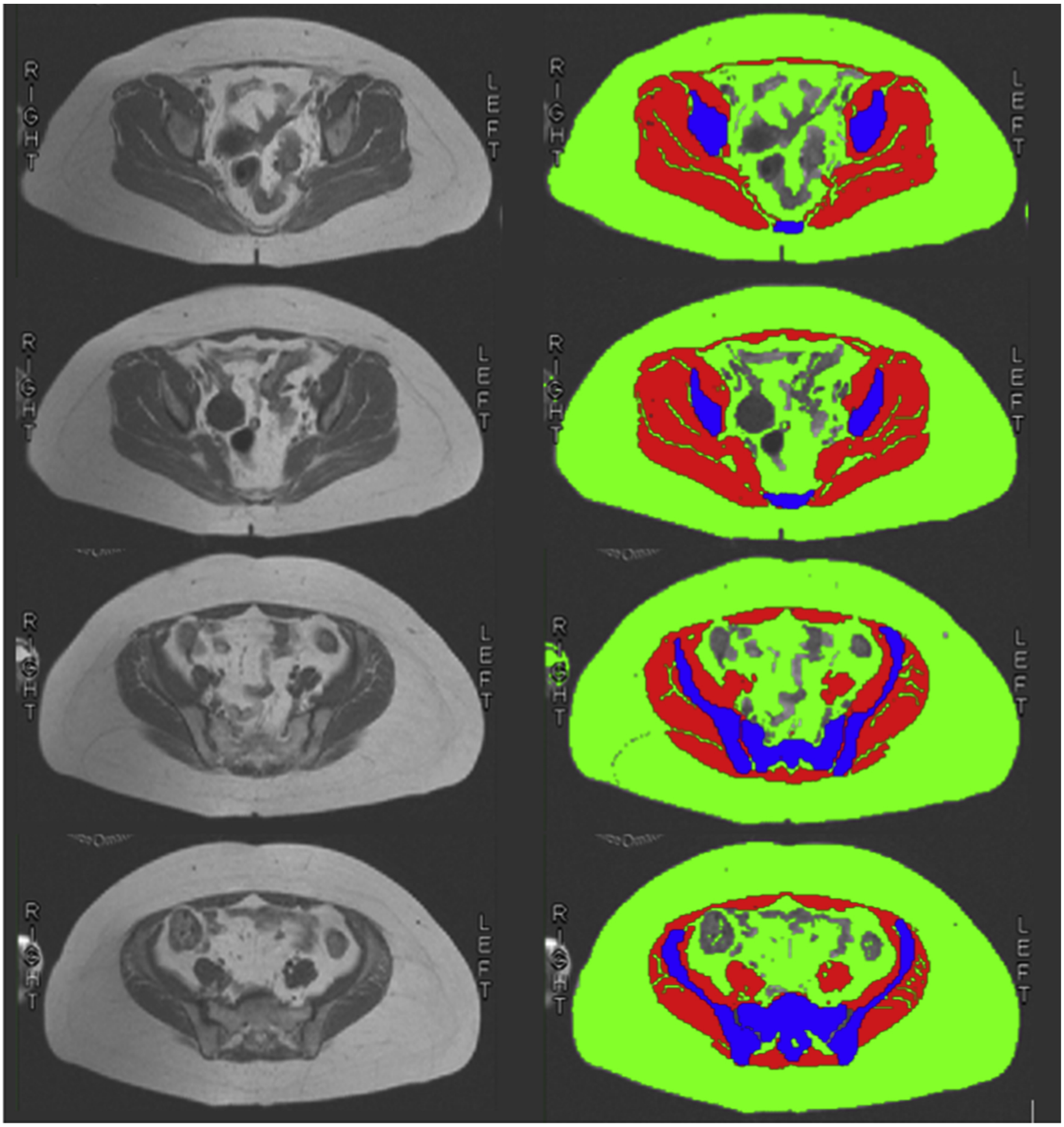

Fig. 1. Axial MRI images with multicompartmental soft tissue segmentations in obese volunteer (BMI = 32.61 kg/m^2). Fat = green, Muscle = Red and Bone = Blue. Fat volume = 4446cm^3, muscle volume = 1203 cm^3 and bone volume = 377.9 cm^3.

2221 ± 488, and 2141 ± 580 cm^3, and mean total bone volumes were 526 ± 95, 503 ± 109, and 473 ± 99 cm^3 among normal, overweight, and obese groups, respectively. (Table 1a). When no differences were found among muscle measurements in the three individual groups (normal, overweight, and obese), the patients were divided into two groups (normal, overweight/obese) and results were calculated accordingly. Differences in mean total fat and bone volumes among obese/overweight and non-obese subjects were statistically significant (p values < 0.0001 and 0.03 respectively) (Table 1b, Fig. 3).

3.3. Interobserver performance

For inter-reader agreements, the ICC was excellent, fair and good for total bone, fat and muscle measurements in the normal weight group; and excellent, good and fair for total bone, fat and muscle measurements in the obese/overweight group (Table 2).

3.4. Correlations between volumetric and performance parameters with different anthropomorphic measurements

There were statistically significant positive correlations of total fat volume with BMI and weight ($p < 0.0001$) and total muscle volume with height ($p = 0.03$) (Table 3). The total bone volume showed statistically significant inverse correlation with BMI ($p = 0.002$) and positive correlation with height ($p < 0.0001$). The MVPA showed inverse correlation with age ($p = 0.01$), and TT also showed statistically significant inverse correlations with increasing BMI and weight ($p = 0.01$ and 0.03 respectively).

3.5. Correlations between volumetric measurements and different physiological parameters

There was statistically significant inverse correlation of fat volume

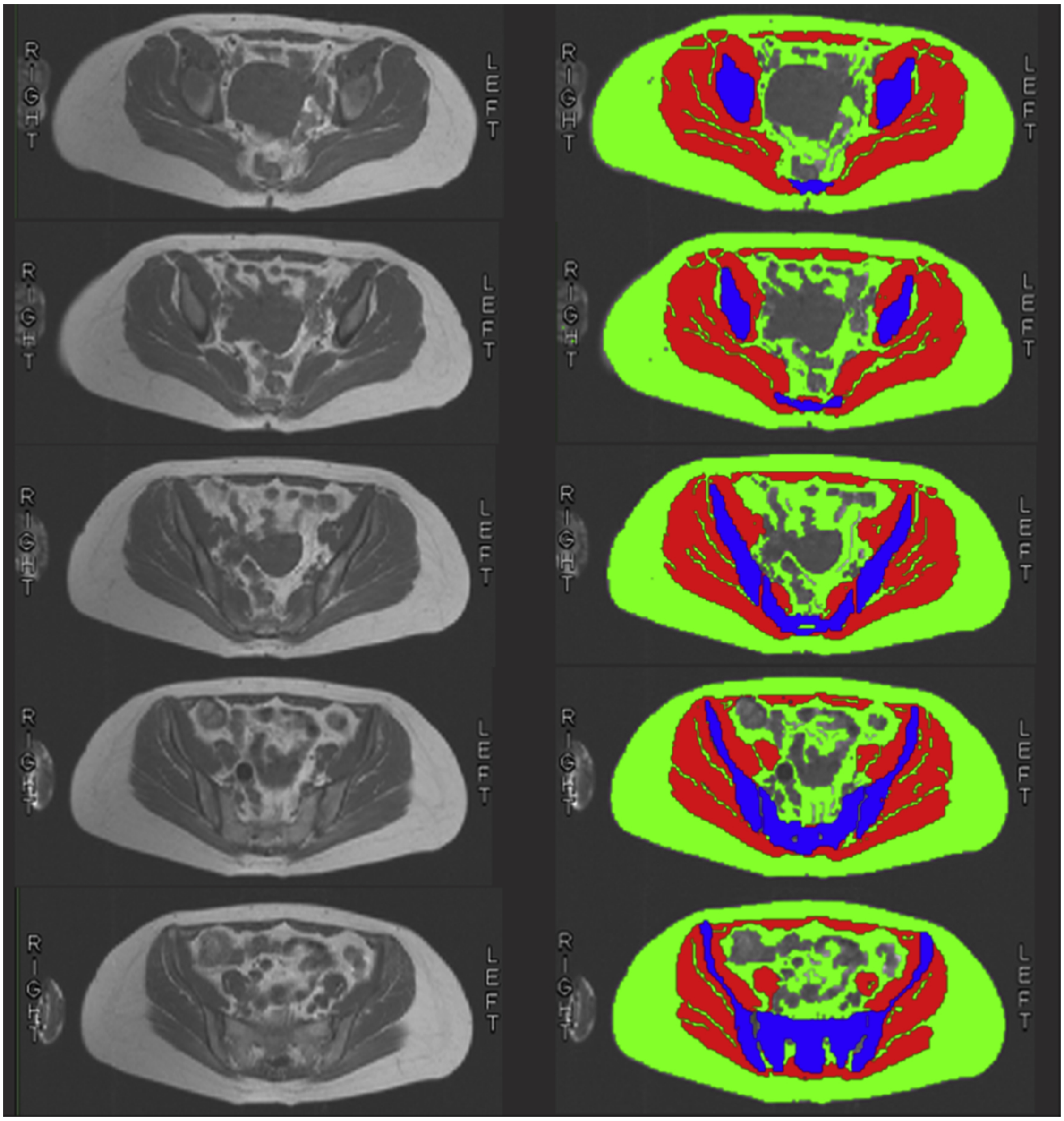

Fig. 2. Axial MRI images with multicompartmental soft tissue segmentations in normal weight volunteer (BMI = 24.59 kg/cm²). Fat = green, Muscle = Red and Bone = Blue. Fat volume = 2654cm³, muscle volume = 1409 cm³ and bone volume = 407.6 cm³.

Table 1
a) Total Tissue Volume in Normal weight, Overweight and Obese and total Tissue Volume in b) Normal weight versus Overweight/ obese.

Variable	Normal Weight (n = 40)	Overweight (n = 41)	Obese (n = 39)	P value
Total Fat Volume (cm³)	2584 ± 619	3513 ± 910	5683 ± 1430	< 0.0001
Total Muscle Volume (cm³)	2228 ± 477	2221 ± 488	2141 ± 580	0.85
Total Bone Volume (cm³)	526 ± 95	503 ± 109	473 ± 99	0.03

Variable	Normal Weight (n = 40)	Overweight/Obese (n = 80)	P value
Total Fat Volume (cm³)	2584 ± 619	4571 ± 1611	< 0.0001
Total Muscle Volume (cm³)	2228 ± 477	2182 ± 533	0.66
Total Bone Volume (cm³)	526 ± 95	488 ± 105	0.03

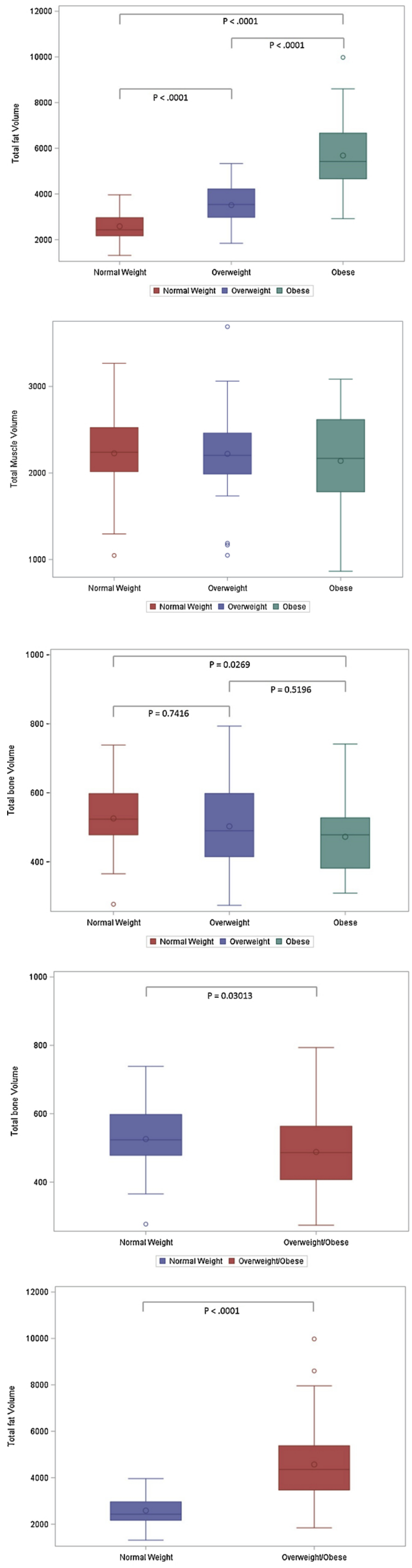

Fig. 3. Differences in a) total fat, b) muscle and c) bone volumes in normal, overweight, and obese subjects. Differences in d) total bone and e) fat volumes in normal versus overweight/obese subjects (significant differences are represented for each plot). The bottom and top edges of each box represent the 1st and 3rd quartiles (Q1, Q3) with interquartile range (IQR) in between. The central dot and line inside the box indicates the mean and median values. Outliers are observations that are more extreme than the upper and lower fences (± 1.5 IQR).

Table 2
Inter-observer performance in volumetric measurements.

		ICC	95% Confidence Interval	
Normal Weight	Bone	0.78	0.63	0.88
	Fat	0.43	0.15	0.65
	Muscle	0.64	0.42	0.80
Obese and Overweight	Bone	0.79	0.64	0.88
	Fat	0.62	0.38	0.78
	Muscle	0.44	0.14	0.66

with TT ($p = 0.01$). However, there were no significant correlations between physiologic parameters and total muscle or bone volumes (all p-values > 0.05) (Table 3).

4. Discussion

Sarcopenia is the presence of low muscle mass with or without reduced muscle power or performance [23,24]. Clinically, a combination of low fat and high muscle mass is considered healthy, while a combination of low muscle mass (sarcopenia) and high fat mass (obesity) is the most concerning. The condition known as SO is the one where sarcopenia and obesity coexist [25]. Recent studies have shown an estimated prevalence 5–10% for SO [25]. The importance of SO lies in the fact that, with age, patients with SO have higher risks of mobility disability [26,27], metabolic diseases [28,29], hypertension [30], cardiovascular diseases [31,32] and mortality [33,34], which results in rising healthcare costs [35].

Recent literature has discussed the definition and diagnosis of SO [14,15,25], exploring its relationship with various risk factors [34,36,37]. Fewer studies have explored imaging modalities to quantitatively diagnose sarcopenia [10,11,23]. To date, little is known about reliability of quantitative volumetric multicompartment measurements obtained on cross sectional imaging and their correlations with various clinical parameters in SO. Our study showed that multilevel volumetric tissue segmentations without exposure to ionizing radiation is possible as opposed to other studies, in which only one axial slice on CT or a numeric density measurement on DXA scans was obtained [23,38,39]. It took about 20 ± 5 min to segment an average of 6 axial MRI cuts and it became faster as the reader became more facile with software. Identification of various tissue types (bone, muscle and fat) did not seem difficult, which is reflected in fair to good ICC for fat and muscle and excellent ICC for bone volumes between experienced and non-experienced readers. Potentially, technologists can be trained in the future to perform bone, muscle and fat segmentations in a semi-automated or automated fashion, rendering volumetric segmentation translation feasible in future clinical practice.

We found statistically significant positive correlations between total fat volumes with BMI and weight. This agrees with previous cross sectional studies showing strong correlations between fat volumes and BMI [40]. Statistically significant inverse correlations were

Table 3
Spearman correlations of volumetric measurements with anthropomorphic measurements and physical performance parameters.

Parameter	value	BMI	Age	Height	Weight	MVPA	TT
Total Fat volume	Rho	0.82	0.02	0.02	0.85	−0.01	−0.22
	P-value	< 0.0001	0.86	0.83	< 0.0001	0.94	0.02
Total Muscle volume	Rho	−0.08	−0.05	0.20	−0.02	0.01	0.03
	P-value	0.40	0.55	0.03	0.87	0.90	0.71
Total Bone volume	Rho	−0.28	0.04	0.37	−0.18	0.05	0.03
	P-value	0.002	0.69	< 0.0001	0.05	0.60	0.73
MVPA	Rho	0.01	−0.22	−0.15	−0.01		
	P-value	0.92	0.02	0.11	0.96		
TT	Rho	−0.23	−0.15	0.11	−0.19		
	P-value	0.01	0.11	0.21	0.03		

demonstrated between bone volumes and BMI. This is an important finding, since it demonstrates the importance of quantification of bone volumes in obesity and agrees with studies showing that sarcopenic patients are at higher risk for fractures [13]. Significant correlations were found between muscle volumes and height, but no significant correlations were found between muscle volumes and physiologic parameters. This did not agree with the recent literature on sarcopenia and could be attributed to various aspects of the study population, such as inclusion of relatively young volunteers making them less likely to exhibit abnormal muscle bulk.

Statistically significant inverse correlations were found between MVPA and age, and TT with BMI and weight. These results are consistent with known facts of decreasing activity levels and slowing of cardiac activity with obesity. Decreasing CRF with increasing BMI has important implications in terms of increasing risks of cardiovascular disease and metabolic syndromes.

This study has several limitations. First, subjects were included as volunteers taking part in multicenter trial (DHS) and were not clinically suspected to have SO. We attempted to mitigate this limitation by including and comparing three cohorts, one normal, one overweight, and one obese group. Second, only females were included, introducing a gender bias. Although this represented the cohort of the DHS (from which we obtained our data), it also reduces inherent variations in tissue composition expected between males and females. In addition, their clinical activity and heart rate parameters were uniformly recorded as part of DHS-2 study protocols. The MRI protocols were uniform however there were no 3-dimensional or volume imaging. Furthermore, the use of unedited DICOM images (which sometimes including other body parts outside the pelvis) and semi-automated techniques for segmentations (including extra or less fat, muscle and bony components), can lead to some errors in volume calculation. These were carefully corrected with minimal, if any contamination into the final volume calculation. In the future, volumetric isotropic MR acquisitions might render segmentations more reliable and dedicated MRI segmentation software may become commercially available.

To summarize, initial results of this study show that multi-compartmental tissue volume quantification on MRI is reliable in females. Findings of significant inverse correlations of bone volume with BMI, and fat volume with cardiorespiratory fitness provide baseline data for future studies investigating the role of tissue segmentation as a predictor of future fracture risk and cardiovascular disease among women.

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Disclosures

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Conflict of interest

None.

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