Scientific Research Publishing

Open Journal of Orthopedics, 2022, 12, 85-96
https://www.scirp.org/journal/ojo
ISSN Online: 2164-3016
ISSN Print: 2164-3008

Quantitative Evaluation of Fat Composition in Lumbar Vertebral Body and Paraspinal Muscle by Proton Density Fat Fraction with MRI

Yuji Kasukawa[1*], Michio Hongo[1], Toshihito Ebina[2], Taishi Chiba[3], Daisuke Kudo[1], Ryota Kimura[1], Yoichi Shimada[4], Naohisa Miyakoshi[1]

[1]Department of Orthopedic Surgery, Akita University Graduate School of Medicine, Akita, Japan
[2]Department of Orthopedic Surgery, Kakunodate General Hospital, Senboku, Japan
[3]Radiology Division, Kakunodate General Hospital, Senboku, Japan
[4]Independent Administrative Institution, Akita Prefectural Development and Disability Organization, Akita, Japan
Email: *kasukawa@doc.med.akita-u.ac.jp, mhongo@doc.med.akita-u.ac.jp, ebitoshi-hp18@kakunodate-hp.com, renji6481@yahoo.co.jp, dkudo@doc.med.akita-u.ac.jp, rkimura@med.akita-u.ac.jp, seikei@doc.med.akita-u.ac.jp, miyakosh@doc.med.akita-u.ac.jp

How to cite this paper: Kasukawa, Y., Hongo, M., Ebina, T., Chiba, T., Kudo, D., Kimura, R., Shimada, Y. and Miyakoshi, N. (2022) Quantitative Evaluation of Fat Composition in Lumbar Vertebral Body and Paraspinal Muscle by Proton Density Fat Fraction with MRI. *Open Journal of Orthopedics*, **12**, 85-96.
https://doi.org/10.4236/ojo.2022.123010

Received: January 28, 2022
Accepted: March 8, 2022
Published: March 11, 2022

Abstract

Purpose: Bone marrow and muscle adiposity have been considered to correlate with osteoporosis and Sarcopenia. Proton Density Fat Fraction (PDFF) can be measured by Magnetic Resonance Imaging (MRI). The purpose of the present study was to measure PDFF in the lumbar spine, paraspinal muscle and subcutaneous fat tissue. **Methods:** Participants were comprised of 30 patients (18 males, 12 females; age range, 14 - 87 years) who underwent MRI due to low back symptoms. PDFFs for the body of the fourth lumbar vertebra (L4), paraspinal muscle, and subcutaneous fat were measured. **Results:** PDFFs of the vertebral body and subcutaneous fat were significantly higher than that of paraspinal muscle ($p < 0.001$). PDFF was significantly higher for subcutaneous fat than for the vertebral body ($p < 0.001$). Although no significant differences in PDFF of the vertebral body, paraspinal muscle, and subcutaneous fat between females and males, PDFFs of the vertebral body and paraspinal muscle were significantly higher in older subjects (>63 years) than in younger subjects (<63 years; $p < 0.05$). **Conclusions:** PDFF of the vertebral body was significantly higher than that of paraspinal muscle. PDFFs of the vertebral body and paraspinal muscle were significantly lower in younger subjects than in older subjects.

Keywords

Proton Density Fat Fraction, Vertebral Body, Bone Marrow, Para-Spinal Muscle, Age, Bone Mineral Density

1. Introduction

Osteoporosis is associated with a higher risk of fragility fractures due to a loss of bone mass, microarchitecture, and strength [1]. In addition to the deterioration of bone and decrease in Bone Mineral Density (BMD), bone marrow adiposity and skeletal muscle weakness or muscle atrophy are considered to be risk factors for fragility fractures among osteoporotic elderly patients. Furthermore, obesity increases the risk of osteoporosis at the femoral neck and severe osteopenia in the lumbar spine [2]. Histomorphometric studies on bone biopsy specimens have revealed a pronounced accumulation of adipose tissue in the bone marrow of osteoporotic patients [3] [4]. Skeletal muscle weakness or muscle atrophy is characterized as sarcopenia, defined as the age-related, progressive, generalized loss of skeletal muscle masses along with impaired muscle functions [5]. Osteoporosis and sarcopenia are commonly associated with aging and are frequently closely linked to each other [6]. Wong *et al.* recently reported that bone marrow adiposity and muscle adiposity are related in postmenopausal osteoporotic women [7]. An evaluation of fat tissue in both vertebral bone marrow and skeletal muscle is thus warranted.

Noninvasive measurement of bone marrow adiposity has been improving. Magnetic Resonance Imaging (MRI) has been used to demonstrate bone marrow fat fraction, including magnetic resonance spectroscopy and chemical shift encoding-based water-fat separation (CSE)-MRI. For fat quantification, T1 bias and T2* decay effects need to be considered in order to extract the Proton Density Fat Fraction (PDFF) [8] [9] [10]. MRI-based quantification of fat in bone marrow can be expressed as the PDFF, which can be regarded as a fundamental tissue property defined as the ratio of the density of mobile protons from fat to the total density of protons from mobile fat and mobile water [11]. Several studies have demonstrated changes to the PDFF of the vertebral body or paraspinal muscle in osteoporotic patients or postmenopausal women. Kuhn *et al.* reported that the PDFF of vertebral bodies was significantly increased in osteoporosis patients compared with healthy subjects [12]. Sollmann *et al.* revealed that the PDFFs of the paraspinal muscle and bone marrow of the vertebral body were significantly higher in postmenopausal women [13].

However, no standard methods for measuring PDFF in the vertebral body or skeletal muscle have been defined. Furthermore, differences in PDFF of the vertebral body, paraspinal muscle, and subcutaneous fat tissue among sexes or with age are also unknown for the Japanese population. The purpose of the present study was to measure PDFF in vertebral bodies of the lumbar spine as well as the PDFF in paraspinal muscle and subcutaneous fat tissue with MRI. A secondary purpose was to compare PDFFs among different sites (body of the fourth lumbar (L4) vertebra, paraspinal muscle, and subcutaneous fat tissue), between females and males, and between younger and older subjects in a Japanese population.

2. Methods

2.1. Patients and Study Design

A total of 30 patients (18 male, 12 female) were enrolled in this study. Median age of patients was 63 years (range, 14 - 87 years). The number of subjects was decided based on the previous study [14]. All patients had required MRI for the investigation of clinical symptoms such as low back pain, pain or numbness in the lower extremities, or intermittent claudication in Kakunodate General Hospital from January 2020 to December 2020. Patients with severe low back pain due to acute vertebral fractures, metastatic spinal tumor, inflammatory diseases, or discitis of the spine were excluded. During regular MRI, additional scans for PDFF were performed after obtaining written informed consent from all patients. The consent from subjects aged younger than 18 years were obtained from their parent. The study protocol was approved by the ethics committee of our institute (IRB #1970). This study was conducted in accordance with the Declaration of Helsinki.

2.2. MRI

All subjects underwent MRI (Signa Explorer 1.5T; GE Healthcare, Milwaukee, WI) in the supine position during free breathing. Three-dimensional spoiled-gradient echo pulse sequences was acquired in the sagittal plane to create parametric MRI-PDFF maps of the lumbar spine using Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation-iron quantification based on previously reported methods (**Figure 1**) [14]. For later assessment of bone marrow, paraspinal muscle, and subcutaneous fat, a sagittally prescribed six-echo sequence was acquired with the following sequence adjustments: acquisition matrix = 128 × 128; first Echo time (TE) = 2.1 msec; TE spacing = 1.6 msec; Repetition time = 14.8 msec; flip angle = 5; slice thickness = 8 mm; slice spacing = 0 mm; number of slices = 10; acceleration = Auto-calibrating Reconstruction for Cartesian imaging; and acceleration factor = 1. The imaging-based PDFF map was computed from the ratio of fat signals to the sum of fat and water signals, as described previously [14] [15].

2.3. Image Analysis

Manual Regions of Interest (ROIs) were drawn on PDFF maps using measurement software (SYNAPSE OP-A, Fujifilm Medical, Co., Ltd, Tokyo, Japan) for the medical system at Kakunodate General Hospital. We measured the PDFF for bone marrow in the L4 vertebral body using two different methods. First, an elliptical ROI as large as possible within the border of bone marrow was placed in the L4 vertebral body on a slice at the level of the spinous process on sagittal PDFF maps (**Figure 2A**). Second, four square ROIs (area: 49.5 - 50.5 mm^2) were placed at anterior cranial, posterior cranial, anterior caudal, and posterior caudal positions in the L4 vertebral body on the same sagittal slice used for the elliptical ROI (**Figure 2B**). The average value from the four square ROIs was used as the

square PDFF value for L4 vertebral bone marrow. To measure PDFF for paraspinal muscle and subcutaneous fat tissue, two square ROIs (area: 49.5 - 50.5 mm^2) were placed at cranial and caudal levels of L4 in three slices at the spinous process level to the right and left on sagittal PDFF maps (**Figure 2C**, **Figure 2D** for right cranial and left caudal paraspinal muscle; **Figure 2E**, **Figure 2F** for right cranial and left caudal subcutaneous fat tissue). For the right or left PDFF of paraspinal muscle or subcutaneous fat, average PDFFs for cranial and caudal sites were used as the right or left PDFFs. Average PDFFs for paraspinal muscle or subcutaneous fat were calculated from 4 ROIs (right cranial, right caudal, left cranial, and left caudal) in comparisons between male and female patients or between younger and older age groups.

Image analysis was performed by two investigators, with both blinded to the measurements of the other reader. Intraclass correlation coefficient (ICC) of inter-observer and intra-observer reliability of elliptical ROI and four square ROIs of the PDFF for bone marrow in the L4 vertebral body were 0.996 and 0.987, respectively.

2.4. Statistical Analyses

Results are expressed as mean (standard deviation) for parametric data. The Kolmogorov-Smirnov test revealed that all data were parametric. Differences in

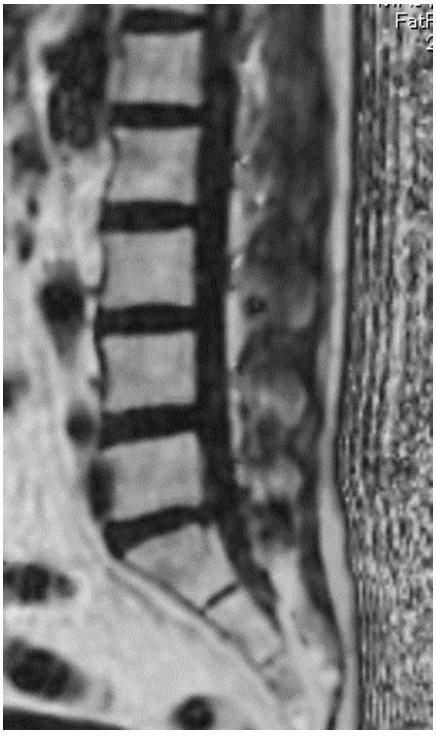

Figure 1. Sagittal proton density fat fraction (PDFF) map from chemical shift encoding-based water-fat magnetic resonance imaging (CSE-MRI). Sagittal-view CSE-MRI allowing measurement of PDFF in bone marrow of the fourth lumbar vertebral body.

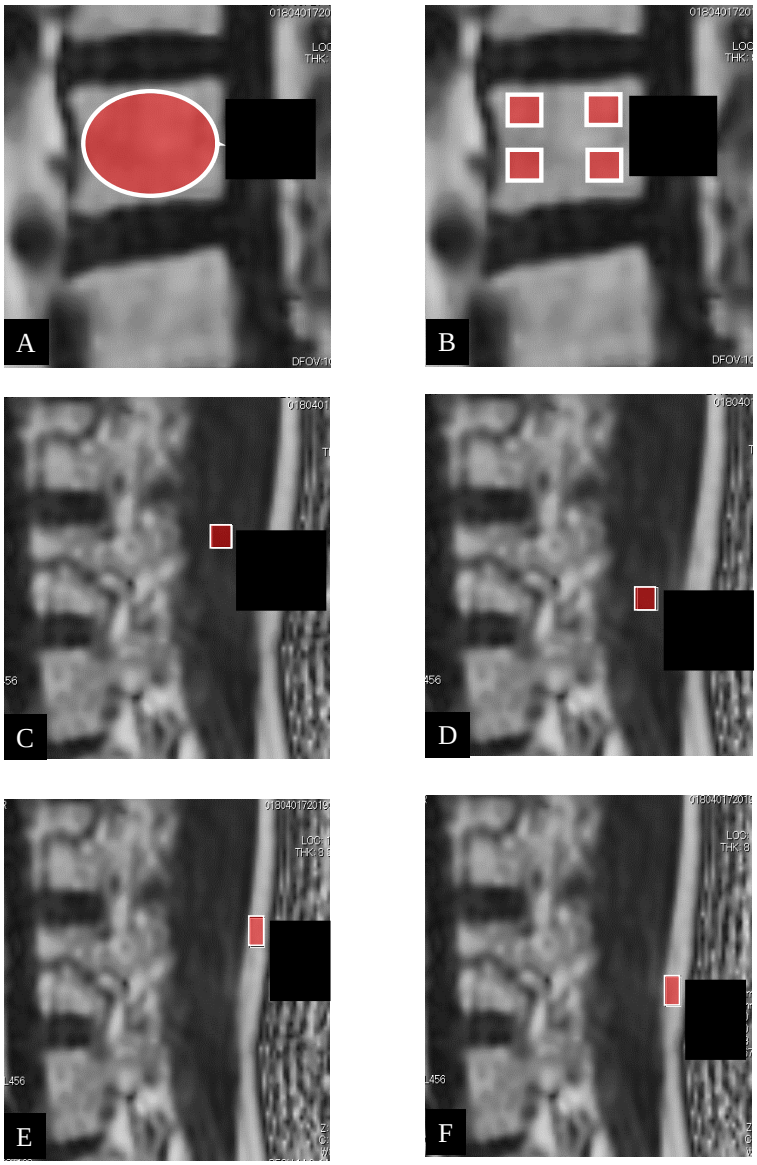

Figure 2. Regions of interest (ROIs) for proton density fat fraction (PDFF) measurements. Elliptical (A) and square ROIs (B) for PDFF in the fourth lumbar vertebral body. ROI for PDFF of paraspinal muscle at the right (C) and left ROI (D), and subcutaneous fat at the right (E) and left ROI (F).

L4 vertebral body PDFF among the four ROIs in the vertebral body as well as paraspinal muscle and subcutaneous fat tissue PDFF among the total four ROIs in bilateral muscle and fat tissues were assessed using one-way analysis of variance (ANOVA) with the Bonferroni test as a post hoc test. Differences in PDFF for the L4 vertebral body, paraspinal muscle, and subcutaneous fat were also analyzed using ANOVA and Bonferroni testing. Differences in PDFFs for the L4 vertebral body with the elliptical ROI and with the average of four square ROIs, average PDFFs for four ROIs of paraspinal muscle and subcutaneous fat between females and males were assessed using Student's *t*-test.

The median age of participants was 63 years in this study. Subjects were thus

divided into younger subject (<63 years old) and older subjects (>63 years old). Differences in averaged PDFF at the three regions of the L4 vertebral body, paraspinal muscle, and subcutaneous fat between younger and older subjects were also evaluated using Student's *t*-test. Differences showing values of $P < 0.05$ were considered statistically significant. All statistical analyses were performed using EZR statistical software (The R Foundation for Statistical Computing) [16].

3. Results

PDFFs of L4 vertebral bone marrow, paraspinal muscle, and subcutaneous fat (**Table 1**).

PDFFs for the four regions of front cranial, back cranial, front caudal, and back caudal square ROIs in the L4 vertebral body did not differ significantly (**Table 1**). PDFFs of paraspinal muscle and subcutaneous fat tissue of both sides cranially and caudally did not differ significantly among the four ROIs (**Table 1**).

Differences of PDFF in L4 vertebral bone marrow, paraspinal muscle, and subcutaneous fat (**Figure 3**)

Average PDFF for the L4 vertebral body from elliptical and square ROIs as well as for subcutaneous fat were significantly higher than that for paraspinal muscle ($p < 0.001$) (**Figure 3**). Average PDFF for subcutaneous fat was significantly higher than that for the L4 vertebral body from elliptical and square ROIs ($p < 0.001$) (**Figure 3**).

Table 1. PDFFs of L4 vertebral bone marrow, paraspinal muscle, and subcutaneous fat.

		P value by ANOVA
Vertebral bone marrow elliptical	57.83 (11.28)	
Vertebral bone marrow square		0.281
Front cranial	53.90 (10.36)	
Back cranial	59.09 (11.69)	
Front caudal	58.33 (12.61)	
Back caudal	59.07 (12.88)	
Para-spinal muscle		0.533
Right cranial	9.77 (6.09)	
Right caudal	9.00 (6.47)	
Left cranial	11.58 (7.03)	
Left caudal	10.23 (7.93)	
Subcutaneous fat		0.987
Right cranial	81.30 (8.90)	
Right caudal	81.32 (8.97)	
Left cranial	81.93 (9.45)	
Left caudal	81.92 (9.20)	

Data are represented as mean (standard deviation). *P*-values are analyzed by analysis of variance (ANOVA).

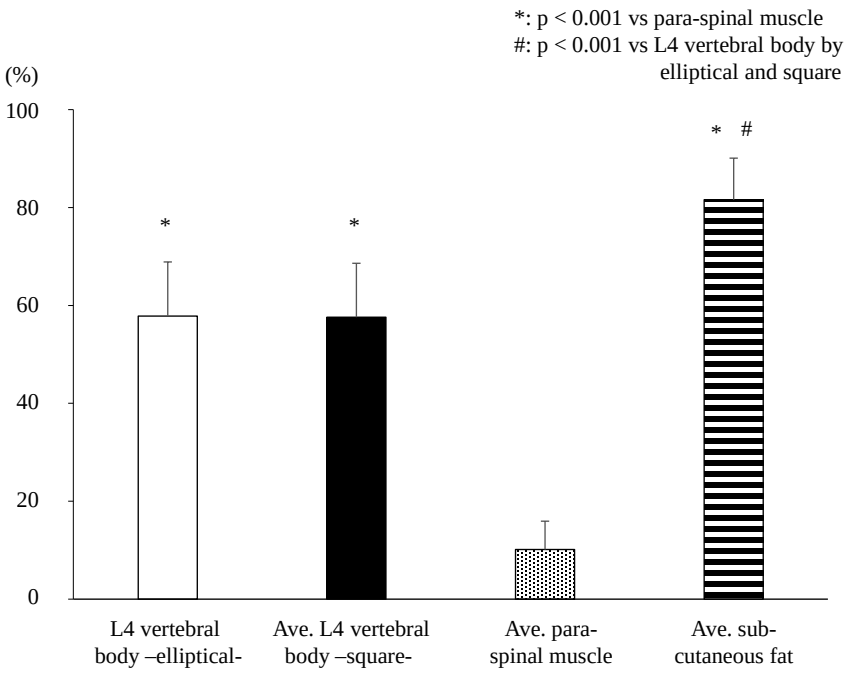

Figure 3. Difference in proton density fat fractions (PDFFs) between measurement regions. PDFF of L4 vertebral body was measured with elliptical (white bar) and squares (black bar). PDFFs of paraspinal muscle (dotted bar) and subcutaneous fat tissue (crossed bar). * $p < 0.001$ vs paraspinal muscle. # $p < 0.001$ vs L4.

Differences in PDFF of L4 vertebral body, paraspinal muscle, and subcutaneous fat between sex and age (**Figure 4**, **Figure 5**).

No significant differences in PDFF for the L4 vertebral body from elliptical and square ROIs, paraspinal muscle, and subcutaneous fat were seen between females and males (**Figure 4**). However, PDFFs of the L4 vertebral body and paraspinal muscle were significantly higher in older subjects (>63 years old) than in younger subjects (<63 years old; $p < 0.05$) (**Figure 5**). PDFF in subcutaneous fat did not differ significantly between older and younger subjects (**Figure 5**).

4. Discussion

4.1. Summary of Present Study

PDFFs of the L4 vertebral body from elliptical and square ROIs were similar, significantly higher than that of paraspinal muscle and significantly lower than that of subcutaneous fat. PDFFs of the L4 vertebral body, paraspinal muscle, and subcutaneous fat did not differ significantly between males and females in this study. Finally, PDFFs of the L4 vertebral body and paraspinal muscle were significantly lower in younger subjects than in older subjects, but PDFF of subcutaneous fat did not differ significantly by age.

4.2. Measurement of PDFF in Vertebral Bodies or Paraspinal Muscle

Several reports have described the measurement of PDFF in vertebral bodies by

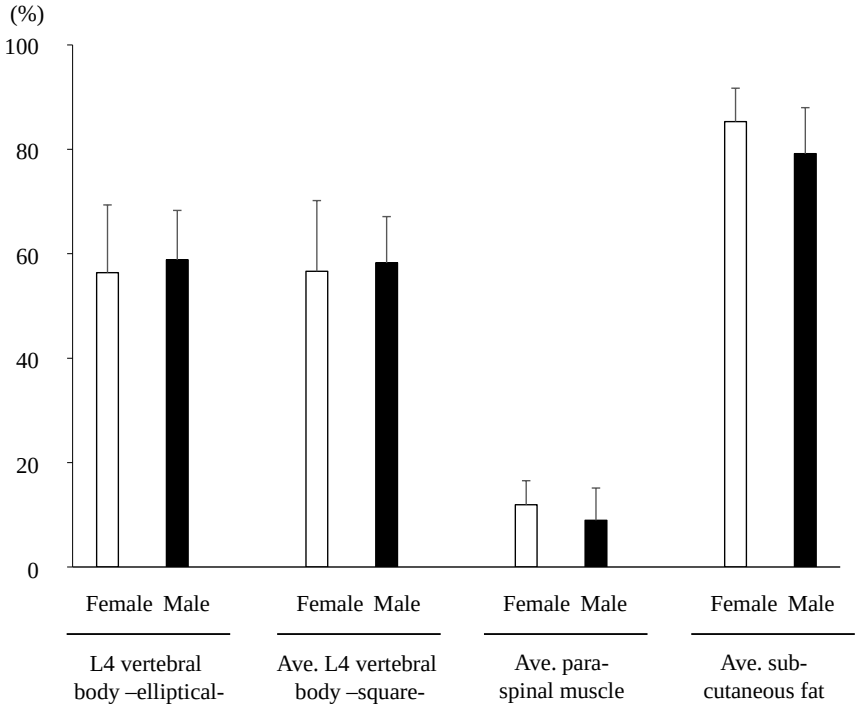

Figure 4. Differences in proton density fat fractions (PDFFs) between females and males. Differences in PDFFs for L4 vertebral body with elliptical and squares, for paraspinal muscle, and for subcutaneous fat tissue between females (white bars) and males (black bars). No significant differences are seen between females and males for any regions.

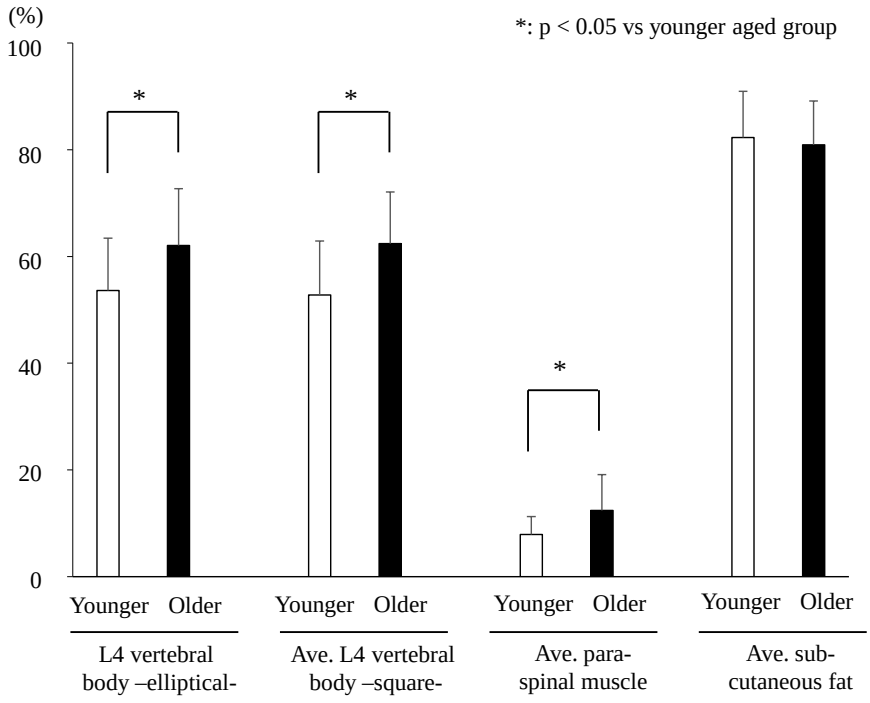

Figure 5. Differences in proton density fat fractions (PDFFs) between younger and older subjects. Differences in PDFFs for L4, paraspinal muscle, and subcutaneous fat tissue between younger (white) and older (black) groups. PDFFs for the L4 and paraspinal muscle are significantly lower in younger than in older patients. *: $p < 0.05$ vs younger.

CSE-MRI. ROIs for PDFF of the vertebral body have differed among previous studies. Kuhn *et al.* placed an elliptical ROI on vertebral bodies from L1 to L5, excluding motion artifacts, vertebral discs, cortical bone of vertebral bodies, focal lesions, venous plexuses and spinal canals [12]. We measured PDFF for the L4 vertebral body in an elliptical ROI based on that report. However, squares in vertebral body segments were placed to measure PDFF of the vertebral body in other studies [9] [13] [17] [18]. In the present study, although we compared PDFF of the vertebral body between elliptical and separated square ROIs, no significant differences were apparent between methods. We thus consider that the ROI for PDFF measurement might be sufficient using an elliptical ROI, which is easier to decide compared to square ROIs.

4.3. Differences in PDFF at the Level of the Lumbar Spine

The present study measured PDFF of vertebral bodies only at the L4 level. PDFF of the vertebral bodies increased significantly from C3 to L5 [19] or from L1 to L5 [18]. Other studies have evaluated PDFF of the vertebral body from L1 to L5 [12] [13] [18], from L1 to L3 [20] or to L4 [17]. When we measure PDFF in osteoporotic patients, vertebral fractures or collapse may influence PDFF of the vertebral body. The thoracolumbar region from T10 to L2 is the most common level of osteoporotic vertebral fractures. We thus consider that the lower lumbar spine could be appropriate for evaluating PDFF of the lumbar spine. Further, regarding an evaluation of PDFF of paraspinal muscle, axial-slice PDFF maps should be appropriate. Sollmann *et al.* measured PDFF of the right and left erector spinae muscles from the upper endplate level of L2 to the lower endplate of L5 on axial PDFF maps [13]. We need to consider whether the entire lumbar spine from L1 to L5 should be acquired to measure PDFF of vertebral bodies and paraspinal muscle in future studies.

4.4. Differences in PDFF between Sex or Age

Several studies have examined associations of PDFF by sex or age. Baum *et al.* reported PDFF of the vertebral body as significantly higher in males than in females in their twenties and thirties [17]. In the present study, PDFF of the vertebral body was no different between males and females, including all subjects between 14 and 87 years old. PDF of the vertebral body (bone marrow) and paraspinal muscle were significantly lower in premenopausal women than in postmenopausal women [13] [18]. Moderate inverse correlations were found between bone marrow fat fraction and BMD [20]. Kuhn *et al.* reported that PDFF was significantly increased in osteoporosis compared with healthy subjects [12]. Furthermore, Sollmann reported a significant correlation in postmenopausal women, but not in premenopausal women, between the PDFFs of paraspinal muscle and vertebral body bone marrow [13]. A recent study by Wong *et al.* reported that a large amount of muscle fat in the leg was associated with osteoporosis status [21]. PDFF of the vertebral body or paraspinal muscle should be changed by age or osteoporotic conditions, so future studies should investigate relationships be-

tween PDFF in bone marrow and skeletal muscle before and after treatment for osteoporosis.

4.5. Study Limitations

Several limitations need to be considered when interpreting the results from this study. First, the study cohort was rather small. Second, all patients had complaints regarding the lumbar spine, although patients with critical diseases of the lumbar spine such as acute vertebral fracture, tumor, or discitis were excluded. Third, PDFF measurement in paraspinal muscle was performed on sagittal PDFF maps. An axial PDFF maps should be appropriate to measure PDFF of the paraspinal muscle. Finally, PDFF of the vertebral body was measured only at the L4. The PDFF values of the vertebral body should be changed by the level of spine.

5. Conclusion

PDFF in the L4 vertebral body as measured by the circular ROI was significantly higher than that in paraspinal muscle and significantly lower than that in subcutaneous fat. PDFFs of the L4 vertebral body and paraspinal muscle in younger subjects were significantly lower than those in older subjects, but PDFF for subcutaneous fat did not differ significantly by the subject age.

Acknowledgements

We wish to thank the staff of Kakunodate General Hospital for helping with the collection of survey data.

CRediT Authorship Contribution Statement

Yuji Kasukawa: conceptualization, investigation, validation, visualization, writing—original draft, review & editing.

Michio Hongo: investigation, writing—review & editing.

Toshihito Ebina: investigation, validation.

Taishi Chiba: conceptualization, investigation, methodology.

Yoshinori Ishikawa: investigation, writing—review & editing..

Daisuke Kudo: investigation, formal analysis, writing—review & editing.

Ryota Kimura: investigation, formal analysis, writing—review & editing.

Yoichi Shimada: conceptualization, supervision, writing—review & editing.

Naohisa Miyakoshi: project administration, writing—review & editing.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Compston, J.E., McClung, M.R. and Leslie, W.D. (2019) Osteoporosis. *The Lancet*, **393**, 364-376. https://doi.org/10.1016/S0140-6736(18)32112-3

[2] Albrahim, T. (2018) The Relationship between Bone Mineral Density and Obesity in Women. *Foot and Nutrition Sciences*, **9**, 136-144. https://doi.org/10.4236/fns.2018.92011

[3] Yeung, D.K., Griffith, J.F., Antonio, G.E., Lee, F.K., Woo, J. and Leung, P.C. (2005) Osteoporosis Is Associated with Increased Marrow Fat Content and Decreased Marrow Fat Unsaturation: A Proton MR Spectroscopy Study. *Journal of Magnetic Resonance Imaging*, **22**, 279-285. https://doi.org/10.1002/jmri.20367

[4] Sheu, Y. and Cauley, J.A. (2011) The Role of Bone Marrow and Visceral Fat on Bone Metabolism. *Current Osteoporosis Reports*, **9**, 67-75. https://doi.org/10.1007/s11914-011-0051-6

[5] Cruz-Jentoft, A.J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A.A., Schneider, S.M., Sieber, C.C., Topinkova, E., Vandewoude, M., Visser, M., Zamboni, M., Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2 (2019) Sarcopenia: Revised European Consensus on Definition and Diagnosis. *Age Ageing*, **48**, 601. https://doi.org/10.1093/ageing/afz046

[6] Greco, E.A., Pietschmann, P. and Migliaccio, S. (2019) Osteoporosis and Sarcopenia Increase Frailty Syndrome in the Elderly. *Frontiers in Endocrinology* (*Lausanne*), **10**, 255. https://doi.org/10.3389/fendo.2019.00255

[7] Wong, A.K., Chandrakumar, A., Whyte, R., Reitsma, S., Gillick, H., Pokhoy, A., Papaioannou, A. and Adachi, J.D. (2020) Bone Marrow and Muscle Fat Infiltration Are Correlated among Postmenopausal Women with Osteoporosis: The AMBERS Cohort Study. *Journal of Bone and Mineral Research*, **35**, 516-527. https://doi.org/10.1002/jbmr.3910

[8] Wang, X., Hernando, D. and Reeder, S.B. (2016) Sensitivity of Chemical Shift-Encoded Fat Quantification to Calibration of Fat MR Spectrum. *Magnetic Resonance in Medicine*, **75**, 845-851. https://doi.org/10.1002/mrm.25681

[9] Hernando, D., Liang, Z.P. and Kellman, P. (2010) Chemical Shift-Based Water/Fat Separation: A Comparison of Signal Models. *Magnetic Resonance in Medicine*, **64**, 811-822. https://doi.org/10.1002/mrm.22455

[10] Colgan, T.J., Hernando, D., Sharma, S.D. and Reeder, S.B. (2017) The Effects of Concomitant Gradients on Chemical Shift Encoded MRI. *Magnetic Resonance in Medicine*, **78**, 730-738. https://doi.org/10.1002/mrm.26461

[11] Reeder, S.B., Hu, H.H. and Sirlin, C.B. (2012) Proton Density Fat-Fraction: A Standardized MR-Based Biomarker of Tissue Fat Concentration. *Journal of Magnetic Resonance Imaging*, **36**, 1011-1014. https://doi.org/10.1002/jmri.23741

[12] Kühn, J.P., Hernando, D., Meffert, P.J., Reeder, S., Hosten, N., Laqua, R., Steveling, A., Ender, S., Schröder, H. and Pillich, D.T. (2013) Proton-Density Fat Fraction and Simultaneous R2* Estimation as an MRI Tool for Assessment of Osteoporosis. *European Radiology*, **23**, 3432-3439. https://doi.org/10.1007/s00330-013-2950-7

[13] Sollmann, N., Dieckmeyer, M., Schlaeger, S., Rohrmeier, A., Syvaeri, J., Diefenbach, M.N., Weidlich, D., Ruschke, S., Klupp, E., Franz, D., Rummeny, E.J., Zimmer, C., Kirschke, J.S., Karampinos, D.C. and Baum, T. (2018) Associations between Lumbar Vertebral Bone Marrow and Paraspinal Muscle Fat Compositions—An Investigation by Chemical Shift Encoding-Based Water-Fat MRI. *Frontiers in Endocrinology* (*Lausanne*), **9**, 563. https://doi.org/10.3389/fendo.2018.00563

[14] Schmeel, F.C., Vomweg, T., Träber, F., Gerhards, A., Enkirch, S.J., Faron, A., Sprinkart, A.M., Schmeel, L.C., Luetkens, J.A., Thomas, D. and Kukuk, G.M. (2019) Proton Density Fat Fraction MRI of Vertebral Bone Marrow: Accuracy, Repeatability, and Reproducibility among Readers, Field Strengths, and Imaging Platforms. *Journal of Magnetic*

Resonance Imaging, **50**, 1762-1772. https://doi.org/10.1002/jmri.26748

[15] Schlaeger, S., Inhuber, S., Rohrmeier, A., Dieckmeyer, M., Freitag, F., Klupp, E., Weidlich, D., Feuerriegel, G., Kreuzpointner, F., Schwirtz, A., Rummeny, E.J., Zimmer, C., Kirschke, J.S., Karampinos, D.C. and Baum, T. (2019) Association of Paraspinal Muscle Water-Fat MRI-Based Measurements with Isometric Strength Measurements. *European Radiology*, **29**, 599-608. https://doi.org/10.1007/s00330-018-5631-8

[16] Kanda, Y. (2013) Investigation of the Freely Available Easy-to-Use Software "EZR" for Medical Statistics. *Bone Marrow Transplant*, **48**, 452-458. https://doi.org/10.1038/bmt.2012.244

[17] Baum, T., Rohrmeier, A., Syväri, J., Diefenbach, M.N., Franz, D., Dieckmeyer, M., Scharr, A., Hauner, H., Ruschke, S., Kirschke, J.S. and Karampinos, D.C. (2018) Anatomical Variation of Age-Related Changes in Vertebral Bone Marrow Composition Using Chemical Shift Encoding-Based Water-Fat Magnetic Resonance Imaging. *Frontiers in Endocrinology* (*Lausanne*), **9**, 141. https://doi.org/10.3389/fendo.2018.00141

[18] Burian, E., Subburaj, K., Mookiah, M.R.K., Rohrmeier, A., Hedderich, D.M., Dieckmeyer, M., Diefenbach, M.N., Ruschke, S., Rummeny, E.J., Zimmer, C., Kirschke, J.S., Karampinos, D.C. and Baum, T. (2019) Texture Analysis of Vertebral Bone Marrow Using Chemical Shift Encoding-Based Water-Fat MRI: A Feasibility Study. *Osteoporosis International*, **30**, 1265-1274. https://doi.org/10.1007/s00198-019-04924-9

[19] Baum, T., Yap, S.P., Dieckmeyer, M., Ruschke, S., Eggers, H., Kooijman, H., Rummeny, E.J., Bauer, J.S. and Karampinos, D.C. (2015) Assessment of Whole Spine Vertebral Bone Marrow Fat Using Chemical Shift-Encoding Based Water-Fat MRI. *Journal of Magnetic Resonance Imaging*, **42**, 1018-1023. https://doi.org/10.1002/jmri.24854

[20] Zhao, Y., Huang, M., Ding, J., Zhang, X., Spuhler, K., Hu, S., Li, M., Fan, W., Chen, L., Zhang, X., Li, S., Zhou, Q. and Huang, C. (2019) Prediction of Abnormal Bone Density and Osteoporosis from Lumbar Spine MR Using Modified Dixon Quant in 257 Subjects with Quantitative Computed Tomography as Reference. *Journal of Magnetic Resonance Imaging*, **49**, 390-399. https://doi.org/10.1002/jmri.26233

[21] Wong, A.K., Chandrakumar, A., Whyte, R., Reitsma, S., Gillick, H., Pokhoy, A., Papaioannou, A. and Adachi, J.D. (2020) Bone Marrow and Muscle Fat Infiltration Are Correlated among Postmenopausal Women with Osteoporosis: The AMBERS Cohort Study. *Journal of Bone and Mineral Research*, **35**, 516-527. https://doi.org/10.1002/jbmr.3910