Brain and Spine 3 (2023) 102684

Contents lists available at ScienceDirect

Brain and Spine

journal homepage: www.journals.elsevier.com/brain-and-spine

Correlation between MRI-based spinal muscle parameters and the vertebral bone quality score in lumbar fusion patients

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ARTICLE INFO

Handling Editor: Prof F Kandziora

Keywords:
Cross-sectional area
Osteoporosis
Sarcopenia
Osteosarcopenia
VBQ score

ABSTRACT

Introduction: The vertebral bone quality (VBQ) score that is based on non-contrast enhanced T1-weighted MRI was recently introduced as a novel measure of bone quality in the lumbar spine and shown to be a significant predictor of healthy versus osteopenic/osteoporotic bone.
Research question: This study aimed to assess possible correlations between the VBQ score and the functional cross-sectional area (FCSA) of psoas and lumbar spine extensor muscles.
Material and methods: Patients who underwent fusion surgery between 2014 and 2017 and had lumbar MRI and CT scans within 6 months prior to surgery were included. The FCSA was assessed at L3-L5 using a pixel intensity threshold method. The VBQ score was calculated by dividing the signal intensity (SI) of the vertebrae L1-L4 through the SI of the cerebrospinal fluid at L3. Volumetric bone mineral density (vBMD) was assessed by quantitative CT.
Results: 80 patients (58.8% female, median age 68.8 years) were included. Overall prevalence of osteopenia/osteoporosis was 66.3%, with no significant differences between men and women. The mean (SD) VBQ score was significantly smaller in men, at 2.26 (0.45) versus women at 2.59 (0.39) ($p = 0.001$). After adjusting for age and BMI, a significant negative correlation was seen between the VBQ score and psoas FCSA at L3 ($\beta = -0.373$; $p = 0.022$), but only in men.
Conclusion: Our results highlight sex differences in the VBQ score that were not demonstrated by vBMD and suggest a potential role of this novel measure to assess not only bone quality, but also spinal muscle quantity.

1. Introduction

Implant stability within bone is important for the success of spinal fusion. Bone strength not only depends on bone quantity, typically expressed through bone mineral density (BMD) that primarily measures bone mineral content, but also on bone quality that is characterized by the geometry and shape of bone, its trabecular microarchitecture, bone turnover, and bone collagen properties (Viguet-Carrin et al., 2006). Dual X-ray absorptiometry (DXA) is considered the gold standard for the assessment of BMD and the diagnosis of osteopenia/osteoporosis (Kanis et al., 2002), and the association between BMD and instrumentation efficacy in spine surgery is well established (Khalid et al., 2020; Kim et al., 2021). The vertebral bone quality (VBQ) score based on lumbar magnetic resonance imaging (MRI) was recently introduced as a novel measure for bone quality and was reported to be predictive of osteopenia/osteoporosis in spine surgery patients with an accuracy of 81% (Ehresman et al., 2020). Furthermore, the VBQ score has been shown to be predictive of fragility fractures in at-risk patients with low BMD

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https://doi.org/10.1016/j.bas.2023.102684
Received 3 May 2023; Accepted 29 September 2023
Available online 30 September 2023

(Ehresman et al., 2021), of vertebral compression fractures among patients with spinal metastases (Ehresman et al., 2019), and of cage subsidence following transforaminal lumbar interbody fusion (Hu et al., 2022; Soliman et al., 2022). Haffer et al. were the first to show an association between the VBQ score and trabecular bone microstructure determined by microcomputed tomography (μCT) in lumbar fusion patients (Haffer et al., 2022). Despite the traditional focus on BMD in the spinal literature, the investigation of paraspinal muscles as predictors of spinal surgical outcome has gained attention (Bokshan et al., 2016, 2017; Hirase et al., 2021; Inose et al., 2018; Li et al., 2021), particularly for metastatic spine disease where sarcopenia or tumor cachexia are frequently present (Bourassa-Moreau É et al., 2020; Zakaria et al., 2020). Negative effects of sarcopenia on spinal surgical outcomes have been reported by several authors (Bokshan et al., 2016; Hirase et al., 2021; Inose et al., 2018). While sarcopenia refers to low muscle strength, low muscle quantity or quality, and low physical performance (Cruz-Jentoft et al., 2019), osteosarcopenia describes the additional presence of osteopenia/osteoporosis in affected individuals (Kirk et al., 2020). A non-invasive assessment tool for both bone quality and spinal muscle quantity would be of interest, particularly for patients scheduled to undergo lumbar fusion. For this study, we hypothesized that the VBQ score is associated with the functional cross-sectional area (FCSA) of psoas or posterior paraspinal muscles in lumbar fusion patients.

2. Material and methods

2.1. Patient population

This was a retrospective cross-sectional single-center study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The present study was approved by the Institutional Review Board of Hospital for Special Surgery (New York, United States) and individual consent for this retrospective analysis was waived. Study subjects and their clinical data were retrieved from a retrospective database of 296 adult patients undergoing primarily posterior lumbar fusion for degenerative conditions at a single academic institution between 2014 and 2017. Patients with both preoperative lumbar MRI and computed tomography (CT) scan obtained within 6 months prior to surgery at the author's institution were considered eligible. Exclusion criterion was a lumbar Cobb angle of $>20^{\circ}$ on preoperative anteroposterior standing radiographs because of expected asymmetric degeneration of spinal muscles (Shafaq et al., 2012; Yagi et al., 2016). Demographic data included age, sex, race, body mass index (BMI), volumetric bone mineral density (vBMD) of the lumbar spine, and history of previous lumbar decompression (laminectomy). Additional data on presurgical symptoms was retrospectively collected by patient chart review. Asynchronous quantitative CT (QCT) was used to assess average vBMD at L1/2 using Mindways QCT Pro Software (Mindways Software, Inc., Austin, TX, USA) (Brown et al., 2021). Prevalence of osteopenia/osteoporosis was determined by the vBMD-threshold of $\leq$120 mg/cm^3 published by the American College of Radiology (ACR) (American College of Radiology - ACR–SPR–, 2018). This study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

2.2. Muscle measurements

Muscle measurements consisted of the FCSA and were conducted on axial T2-weighted MR images at the superior endplates of the L3-L5 vertebrae for the psoas and for the combined *multifidus and erector spinae* muscles (posterior paraspinal muscles). Segmentations of these muscles were performed on both sides using ITK-SNAP (version 3.8.0) (Fig. 1A). A custom-written Matlab™ program (version R2019a, The MathWorks, Inc., Natick, MA, USA) was used to calculate pixel intensity thresholds within these segmentations (Fig. 1B), as previously described (Moser et al., 2022, 2023; Otsu, 1979). This method of quantitatively assessing the FCSA has shown excellent intra-rater and inter-rater reliability, with an interclass correlation coefficient (ICC) of 0.988 and 0.963, respectively (Moser et al., 2023).

2.3. VBQ measurements

VBQ measurements were conducted using Picture Archiving and Communication Systems (PACS) software Sectra IDS7 (version 22.1, Sectra AB, Linköping, Sweden) and included the signal intensity of the medullary portion of the vertebrae L1-L4 and the cerebrospinal fluid (CSF) at L3 on mid-sagittal T1-weighted MR images (Fig. 2), as previously described by Ehresman et al. (2020). All MRI scans used for this study were obtained at the author's institution on one of the following 1.5 or 3.0 T MR scanners: GE Signa HDxt, GE Optima MR450w, or GE Discovery MR750 (General Electric Healthcare, Chicago, IL, USA). The VBQ score was calculated by dividing the median signal intensity of L1-L4 through the signal intensity of the CSF. The inter-rater reliability for calculating the VBQ score in this manner has been reported to be good to excellent, with an ICC ranging from 0.800 to 0.910 (Aynaszyan et al., 2022; Ehresman et al., 2020; Mierke et al., 2022; Schilling et al., 2021).

2.4. Statistical analysis

Fisher's exact test and χ^2 test were used for the comparison of categorial variables. The Shapiro-Wilk test was applied to check the normality of continuous variables. Mean and standard deviation (SD) or median and interquartile range [IQR] were summarized for continuous variables depending on their distribution, and comparisons were performed utilizing either *t*-test or Mann-Whitney *U* test. Receiver

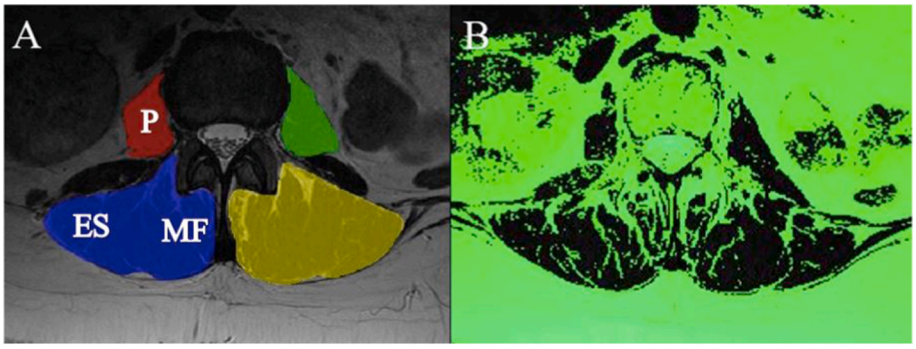

Fig. 1. Radiographic muscle measurements at L3 in a 60 y/o female patient. A: Bilateral manual segmentation of psoas (P) and posterior paraspinal muscles (*erector spinae* (ES) and *multifidus* (MF)) on axial T2-weighted MRI. B: Pixels above the automated pixel intensity threshold (high intensity pixels). Low intensity pixels (shown in dark) were used to calculate the functional cross-sectional area of muscles.

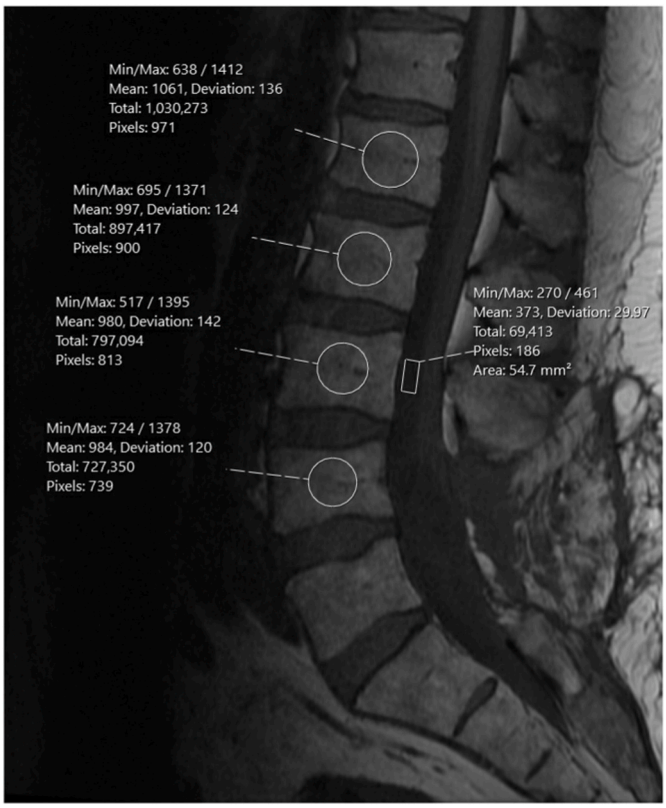

Fig. 2. Sagittal T1-weighted MRI showing regions of interest for VBQ measurements in a 60 y/o female patient. To calculate the VBQ score, the median signal intensity (SI) of the medullary portion of the vertebrae L1-L4 was divided through the SI of the cerebrospinal fluid (CSF) at L3.

operating characteristic (ROC) analysis was performed to determine the area-under-curve (AUC) of the VBQ score to predict the presence of osteopenia/osteoporosis. Box-cox transformation was used for non-normally distributed FCSA outcomes (L5 psoas and L4 posterior paraspinal muscles in women; $\lambda = 0$) and natural log transformation was applied. Multivariable linear regression analysis with adjustments for age and BMI was utilized to examine the association between the VBQ score and the FCSA of muscles of interest. All analyses were stratified by sex. Analyses were conducted using SPSS Statistics version 23.0 (IBM Corp., Armonk, New York, USA) and SAS version 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Patient population

Out of 148 eligible patients, 80 (58.8% female) were included in the final analysis (Fig. 3). The patient population was 93.8% Caucasian with a median [IQR] age at surgery of 68.8 [59.4; 75.1] years and a mean (SD) BMI of 29.3 (6.9) kg/m^2. Patient demographics and preoperative characteristics are listed in Table 1.

3.2. Vertebral bone quality score and volumetric bone mineral density

The overall prevalence of osteopenia/osteoporosis was 66.3%, with no significant difference between men and women. Mean (SD) VBQ score was found to be significantly smaller in men at 2.26 (0.45) when compared to women at 2.59 (0.39) ($p = 0.001$) (Table 2). The VBQ score showed a significant negative correlation with vBMD in men ($\rho = -0.586$; $p < 0.001$), and osteopenic/osteoporotic men had significantly higher VBQ scores (2.44 (0.43) vs 1.96 (0.32); $p = 0.002$). Based on ROC curve analysis, the prognostic accuracy of the VBQ score to predict the presence of osteopenia/osteoporosis in men was 0.813 (95% CI 0.667–0.960; $p = 0.003$) (Fig. 4). In women, the correlation between the

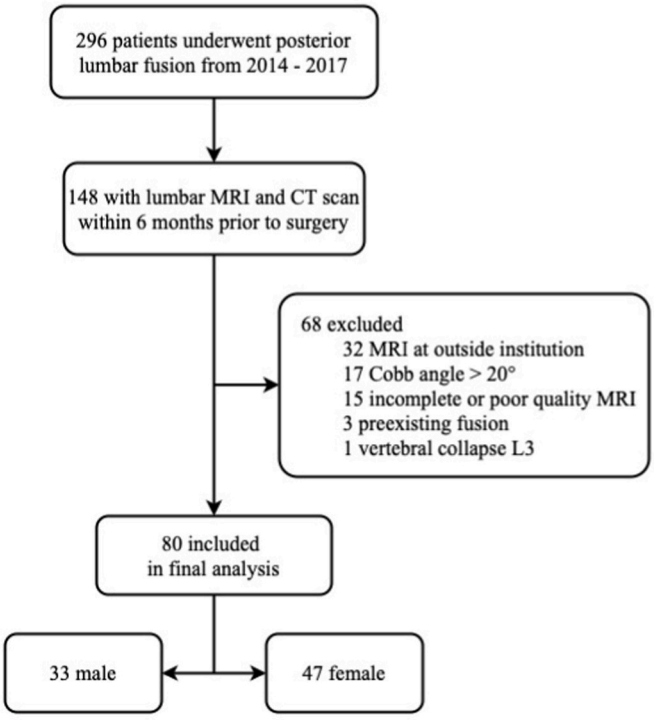

Fig. 3. Flow diagram depicting inclusion and exclusion criteria of study population.

Table 1
Patient demographics and preoperative characteristics stratified by sex.

	Total	Men	Women	*p* value
No. of patients	80	33	47	
Age, Median [IQR]	68.8 [59.4; 75.1]	65.3 [54.1; 74.4]	70.6 [60.9; 77.1]	0.068
BMI (kg/m^2), Mean (SD)	29.3 (6.9)	30.4 (6.5)	28.6 (7.1)	0.245
L1/2 vBMD (mg/cm^3), Median [IQR]	105.9 [90.6; 136.1]	105.9 [91.3; 132.9]	103.3 [91.2; 136.6]	0.980
Osteopenia/Osteoporosis (≤120 mg/cm^3), n (%)	52 (65)	22 (66.7)	30 (63.8)	1.000
Race, n (%)				
Caucasian	75 (93.8)	31 (93.9)	44 (93.6)	0.531
African American	1 (1.3)	1 (3.0)	0 (0)	
Asian	1 (1.3)	0 (0)	1 (2.1)	
Other	3 (3.8)	1 (3.0)	2 (4.3)	
Previous lumbar laminectomy, n (%)	6 (7.5)	4 (12.1)	2 (4.3)	0.380
Symptoms[a], n (%)				
Low back pain	71 (88.8)	28 (84.8)	43 (91.5)	0.708
Low back pain >12 weeks	67 (83.8)	26 (78.8)	41 (87.2)	0.532
Radicular leg pain	42 (52.5)	19 (57.6)	23 (48.9)	0.622
Radicular leg pain >12 weeks	39 (48.8)	18 (54.5)	21 (44.7)	0.446
Motor deficit	14 (17.5)	9 (27.3)	5 (10.6)	0.105
Sensory deficit	29 (36.3)	13 (39.4)	16 (34.0)	1.000
Neurogenic claudication	39 (48.8)	19 (57.6)	20 (42.6)	0.119

BMI, body mass index; IQR, interquartile range; SD, standard deviation; vBMD, volumetric bone mineral density.
[a] Some patients had multiple diagnoses. Boldface type indicates statistical significance ($p < 0.05$).

Table 2
VBQ score and muscle measurements stratified by sex.

	Total	Men	Women	*p* value
VBQ Score, Mean (SD)	2.46 (0.44)	2.26 (0.45)	2.59 (0.39)	**0.001**
FCSA (mm^2), Median [IQR]				
L3 psoas	1292.1 [926; 1801.8]	1909.3 [1582.1; 2150.4]	989.8 [821.3; 1186.5]	< **0.001**
L4 psoas	1889.8 [1603.8; 2844.9]	3049.5 [2515.1; 3555.0]	1625.2 [1440.5; 1846.5]	< **0.001**
L5 psoas	2223 [1883.9; 3201.7]	3290.4 [2623.6; 3787.1]	1949.3 [1729.6; 2227.1]	< **0.001**
L3 paraspinal	2888.4 [2240.5; 3491.2]	3574.2 [2995; 4231.6]	2456.1 [2041.6; 2897.6]	< **0.001**
L4 paraspinal	2760.7 [2224.8; 3547.1]	3627.2 [3047.1; 4587.2]	2406 [2059.5; 2827.4]	< **0.001**
L5 paraspinal	2119.9 [1593.4; 2852.4]	2435.8 [2016; 3154.4]	1892.7 [1493.3; 2438.6]	**0.004**

Boldface type indicates statistical significance ($p < 0.05$).
FCSA, functional cross-sectional area; IQR, interquartile range; SD, standard deviation; VBQ, vertebral bone quality.

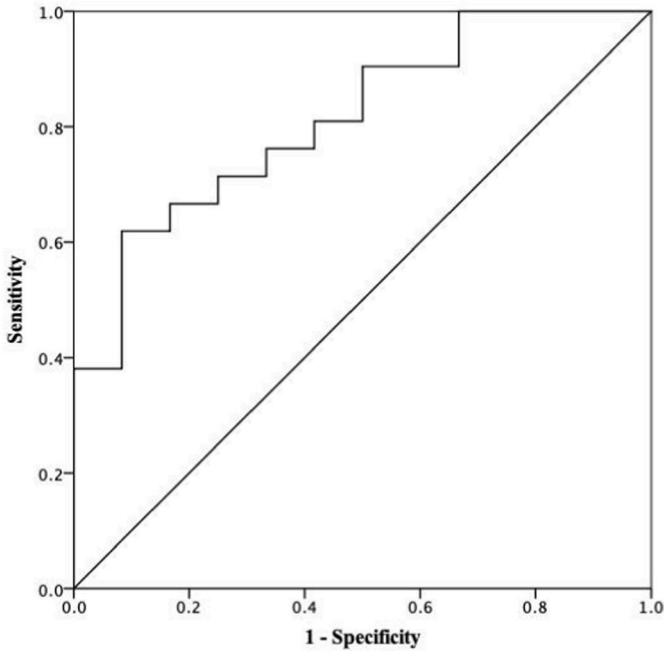

Fig. 4. Receiver operating characteristics curve of the VBQ score for predicting the presence of osteopenia/osteoporosis in male patients.

VBQ score and vBMD was weaker and did not reach statistical significance ($\rho = -0.271$; $p = 0.065$), and osteopenic/osteoporotic women did not have higher VBQ scores (2.65 (0.37) vs 2.47 (0.41); $p = 0.144$). Overall, there was no difference in VBQ scores between 1.5 and 3.0 T MRI scans, with 2.54 (0.49) vs 2.44 (0.43) ($p = 0.420$), respectively.

3.3. Vertebral bone quality score and functional cross-sectional areas

All muscle measurements were significantly greater in men (Table 2). In the simple (unadjusted) analysis, a significant negative correlation was seen between the VBQ score and psoas FCSA at L3-L5 in men. After adjusting for age and BMI, a significant negative association was seen between the VBQ score and psoas FCSA at L3 ($\beta = -0.373$; 95% CI −0.687 to −0.058; $p = 0.022$) (Table 3). In women, a significant negative correlation was seen between the VBQ score and paraspinal FCSA at L3 in the simple (unadjusted) analysis ($\rho = -0.367$; 95% CI −0.607 to −0.042; $p = 0.011$), but significance was lost after adjusting for age and BMI (Table 4).

4. Discussion

In this study we investigated the association between the VBQ score and the FCSA of spinal muscles in patients undergoing lumbar fusion surgery. In accordance with our hypothesis, a significant negative association was found between the VBQ score and psoas FCSA at L3 that was irrespective of age and BMI, but only among men. Our results highlight sex differences in the VBQ score that were not observed for vBMD or categorial bone status and suggest a potential role of this novel measure to simultaneously assess bone quality and spinal muscle quantity in male individuals. Although DXA scanning is considered the international gold standard for measuring BMD and a reference standard for measuring body muscle mass (Buckinx et al., 2018; Link and Lang, 2014), it is not routinely performed for patients undergoing spine surgery, and the prevalence of osteopenia/osteoporosis is likely underrecognized in this population (Dipaola et al., 2009). MRI scans, on the other hand, are frequently obtained before spinal surgical consultation and may be used as an opportunistic screening tool for osteosarcopenia in these patients. Given the demographic changes and the continuous increase in spinal fusion procedures (Martin et al., 2019), such non-invasive and widely available screening would be highly appreciated in clinical practice. While the ACR has established thresholds for diagnosing osteopenia/osteoporosis based on QCT measurements (American College of Radiology - ACR–SPR–, 2018), there is no consensus on cutoff values for diagnosing sarcopenia, and measurement techniques vary considerably (Buckinx et al., 2018). QCT-derived average vBMD estimates of the L1/2 vertebrae have been shown to highly correlate with all lumbosacral vertebrae (Salzmann et al., 2019), an important finding as the majority of spinal fusion procedures typically involves lower lumbar segments and the lumbosacral junction. Because the VBQ score is based on the median signal intensities of the L1-L4 vertebrae, it may also be referred to as a marker of global lumbar bone quality rather than a segmental marker. Our results showed that women had higher VBQ scores than men, consistent with greater fatty infiltration of the lumbar trabecular bone, which is known to negatively correlate with vBMD (Baum et al., 2012; Cordes et al., 2016; Patsch et al., 2013), although we could only observe a trend towards a weak negative correlation in our female cohort. This might be related to the small sample size and inherent selection bias of our study population, where patients with severely decreased vBMD, particularly women, would be less likely to undergo fusion. The VBQ score of 2.65 in our osteopenic/osteoporotic female group was considerably lower than the 3.50 reported by Ehresman et al. for fragility fractures in a predominantly female at-risk population (Ehresman et al., 2021). In men, the VBQ score showed a moderate negative correlation with vBMD, but with an AUC of 0.813 for predicting the presence of osteopenia/osteoporosis. This predictive accuracy is in accordance with the 81% reported by Ehresman et al. using femoral neck and total hip DXA T-scores of < -1.0 in spine surgery patients (Ehresman et al., 2020), but one strength of our study is that we were able to compare VBQ scores with site-specific lumbar vBMD measurements instead of extraspinal DXA measurements. As a marker of bone quality, the VBQ score may only be partially linked to bone mineral content, and as seen in our female cohort, fatty infiltration of bone marrow can be present irrespective of decreased vBMD. In this regard, Aynaszyan et al. recently reported high-density lipoprotein to be positively associated with the VBQ score (Aynaszyan et al., 2022).

Given the limited availability of whole-body DXA scanning for spinal surgical consultation, areal psoas measurements based on CT scans are often used as surrogate parameters to assess skeletal muscle mass. These

Table 3
Correlations between VBQ score and FCSA of psoas and posterior paraspinal muscles in men, adjusted for age and BMI.

FCSA	Unadjusted			Adjusted		
	Rho	95% CI	*p* value	*Beta*	95% CI	*p* value
L3 psoas	−0.487	−0.766–−0.084	**0.004**	−0.373	−0.687–−0.058	**0.022**
L4 psoas	−0.405	−0.673–−0.009	**0.019**	−0.319	−0.673–0.034	0.075
L5 psoas	−0.451	−0.731–−0.079	**0.008**	−0.278	−0.637–0.081	0.124
L3 paraspinal	−0.321	−0.610–0.017	0.069	0.047	−0.277–0.372	0.768
L4 paraspinal	−0.183	−0.506–0.220	0.309	0.151	−0.217–0.519	0.408
L5 paraspinal	−0.109	−0.409–0.195	0.546	0.101	−0.281–0.483	0.594

Boldface type indicates statistical significance ($p < 0.05$).
BMI, body mass index; CI, confidence interval; FCSA, functional cross-sectional area; VBQ, vertebral bone quality.

Table 4
Correlations between VBQ score and FCSA of psoas and posterior paraspinal muscles in women, adjusted for age and BMI.

FCSA	Unadjusted			Adjusted		
	Rho	95% CI	*p* value	*Beta*	95% CI	*p* value
L3 psoas	0.036	−0.272–0.330	0.812	−0.078	−0.372–0.217	0.597
L4 psoas[a]	−0.017	−0.339–0.295	0.911	−0.147	−0.439–0.146	0.317
L5 psoas[a]	−0.086	−0.405–0.239	0.566	0.838	0.610–1.150	0.266
L3 paraspinal	−0.367	−0.607–−0.042	**0.011**	−0.112	−0.354–0.131	0.357
L4 paraspinal[a]	−0.261	−0.533–0.055	0.076	0.960	0.748–1.232	0.742
L5 paraspinal	−0.241	−0.530–0.077	0.103	−0.073	−0.374–0.228	0.627

BMI, body mass index; CI, confidence interval; FCSA, functional cross-sectional area; VBQ, vertebral bone quality.
[a] Non-normal distribution according to the Shapiro Wilk test. For L4 psoas FCSA, non-standardized and standardized residuals were normally distributed. For L5 psoas FCSA ($\lambda = 0$) and L4 paraspinal FCSA ($\lambda = 0$) natural log transformation was used for the adjusted regression analysis and re-transformed results are reported.
Boldface type indicates statistical significance ($p < 0.05$).

include the total cross-sectional area (CSA) (Bokshan et al., 2016, 2017; Zakaria et al., 2020), or the CSA normalized either to the vertebral body area (Bourassa-Moreau É et al., 2020; Gakhar et al., 2015), or body height (Charest-Morin et al., 2018; Hirase et al., 2021). Of note, the CSA of skeletal muscle and adipose tissue at L3 measured on axial MRI has shown the highest correlation with whole-body muscle mass and adipose tissue for both sexes (Schweitzer et al., 2015). In this regard it is of particular interest that we found a significant association between the VBQ score and psoas FCSA at L3 in men. Nevertheless, the significance of sarcopenia on spinal surgical outcome remains controversial. While some authors reported on significantly increased in-hospital complications, hospital length of stay, 30-day re-operation and re-admission rates, and discharge to a facility in sarcopenic patients after thoracolumbar spine surgery (Bokshan et al., 2016; Hirase et al., 2021), others could not correlate sarcopenia with adverse events, length of stay, discharge home, or death in non-complex lumbar spine surgery performed for degenerative conditions (Charest-Morin et al., 2018).

This study isn't without limitations. The retrospective study design with specified inclusion and exclusion criteria, and the low sample size must be critically considered when interpreting our results. We only included patients with MRI and CT scans obtained within 6 months prior to surgery, as significant changes in bone mineral content, fatty infiltration of bone marrow or spinal muscle mass would be less likely to occur during this short period of time. But half of the patients screened for this study did not have appropriate imaging, and this selection bias might limit the generalizability of our study results. Furthermore, patients with severely decreased vBMD or clinically advanced sarcopenia/cachexia are less likely to undergo instrumented fusion surgery. MR spectroscopy is considered the gold-standard for assessing bone marrow fat content due to its elimination of partial volume effects (Cordes et al., 2016), but this imaging modality is not universally available and not routinely performed in lumbar fusion patients. The same might be true for whole-body DXA scanning to assess skeletal muscle mass (Buckinx et al., 2018). We only performed a presurgical radiographic assessment study and did not report on surgical outcome or adverse events in this population. Larger high-quality studies are needed to corroborate our findings in terms of external validity and to examine the clinical utility of the VBQ score in assessing osteosarcopenia for both sexes, including its impact on spinal surgical outcome. In this regard, future studies might also investigate the role of preemptive measures like prehabilitation and nutritional supplementation for lumbar fusion outcomes (Debono et al., 2021).

5. Conclusions

We found the VBQ score to be negatively associated with psoas FCSA at L3 among male individuals, irrespective of age and BMI. Our results highlight sex differences in the VBQ score that were not demonstrated by vBMD or categorial bone status and suggest a potential role of this novel measure to assess not only bone quality, but also spinal muscle quantity. Further studies are needed to assess the clinical utility of the VBQ score as a non-invasive screening tool for osteosarcopenia.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

Conception and design: Moser. Acquisition of data: Moser, Albertini Sanchez, Adl Amini, Oezel, Salzmann, Muellner, Haffer. Analysis and interpretation of data: Moser, Hughes. Drafting the article: Moser. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hughes. Statistical analysis: Moser. Administrative/technical/material support: Tan, Shue. Study supervision: Hughes.

Declaration of competing interest

Authors MM, LAS, DAA, LO, SNM, MM, HH, ETT, and JS have no relevant financial or non-financial interests to disclose.

Author AAS declares financial interests: Royalties: Ortho Development, Corp.; Private Investments: Vestia Ventures; MiRUS Investment,

LLC; ISPH II, LLC; ISPH 3, LLC; and VBros Venture Partners X, Centinel Spine; Consulting Fees: Clariance, Inc., Kuros Biosciences AG, Medical Device Business Service, Inc.; Speaking and Teaching Arrangements: DePuy Synthes Products, Inc.; Scientific Advisory Board: Clariance, Inc., and Kuros Biosciences AG; Trips/travel: Medical Device Business; Research Support: Spinal Kinetics, Inc.

Author FPC declares financial interests: Royalties: Accelus; Private Investiments: Orthobond Corporation, Spine Biopharma, LLC; Healthpoint Capital Partners, LP; Tissue Differentiation Intelligence, LLC; VBVP VI, LLC; VBVP X, LLC; Woven Orthopedic Technologies; 4WEB Medical, Inc; ISPH II, LLC; ISPH 3 Holdings, LLC; Ivy Healthcare Capital Partners, LLC; Medical Device Partners II, LLC; Medical Device Partners III, LLC; Consulting Fees: Accelus, DePuy Synthes, NuVasive, Inc; Spine Biopharma, LLC; Board Member: Medical Device Partners, LLC; Orthobond Corporation, Spine Biopharma, LLC; Woven Orthopedic Technologies; Healthpoint Capital Partners, LP; Research Support: 4WEB Medical, Inc; Camber Spine, Centinel Spine, Mallinckrodt Pharmaceuticals.

Author FPG declares financial interests: Royalties: NuVasive, Inc.; Ortho Development Corp., DePuy Synthes Spine; Private Investments: Bonovo Orthopedics, Inc.; Healthpoint Capital Partners, LP; Tissue Differentiation Intelligence; BICMD; Consulting Fees: OrthoDevelopment Corp; Spineart USA, Inc.; NuVasive, Inc; DePuy Synthes Spine; Ethicon, Inc.; Advisory Board: Spineart USA, Inc.; Healthpoint Capital Partners, LP.

Author APH declares financial interests: Research Support: NuVasive, Inc.; Kuros Biosciences AG; Fellowship Support: NuVasive, Inc.; Kuros Biosciences AG.

Acknowledgements

The authors would like to thank Jiaqi Zhu, MA for statistical advice regarding the Box-Cox transformation.

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