1 **Title Page**

2 **Original Article**

3 Relationship Between Vertebral Instability And The Cross-Sectional Area Of Lumbar Muscles In

4 Postmenopausal Acute Osteoporotic Vertebral Fractures

5

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11 Shun Okuwaki wrote and prepared the manuscript, and Toru Funayama and Akira Ikumi participated in

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1 **Abstract**

2 **Introduction:** Vertebral instability (VI) in osteoporotic vertebral fractures (OVFs) varies from mild to severe. The
3 relationship between the VI of OVFs and independent factors, such as bone mineral density (BMD) and lumbar
4 muscle volume, is unclear. This study aimed to investigate whether BMD and the cross-sectional area (CSA) of
5 lumbar muscles are related to VI in OVFs.

6 **Methods:** On the basis of the thoracolumbar lateral radiographs of 95 acute OVFs in postmenopausal women (mean
7 age 80.6 years; range: 64–103 years), supine and standing vertebral collapse rates (CRsp and CRst, respectively)
8 were determined. Subsequently, VI was defined as follows: $VI = CRst - CRsp$.

9 Using axial T2-weighted magnetic resonance imaging (MRI), CSA of the psoas major, erector spinae, and
10 multifidus muscles at the L3/4 intervertebral disc level were measured. The BMD of the lumbar spine and proximal
11 femur (total hip) was measured for all participants using dual-energy X-ray absorptiometry. The patients were
12 classified into group 1 ($VI < 20\%$) and group 2 ($VI \geq 20\%$).

13 **Results:** We observed a negative correlation between VI and CSA of the erector spinae muscle ($r = -0.3962$,
14 $P < 0.0001$). No significant correlations were observed between VI and BMD. The CSA of the erector spinae muscle
15 in group 2 was significantly lower than that in group 1 ($P = 0.0002$). No significant difference in the BMD or the

CSA of the psoas major or multifidus muscles was observed between the two groups. A multivariable analysis of factors of VI was performed. Both age (odds ratio [OR], 1.099; 95% confidence interval [CI], 1.015–1.189; $P = 0.020$) and the CSA of the erector spinae (OR, 0.996; 95% CI, 0.993–0.999; $P = 0.020$) were significant predictors of high VI.

Conclusions: Although the severity of OVFs was related to the CSA of the erector spinae muscle, it was not associated with BMD.

Keywords: osteoporotic vertebral fractures, cross-sectional area, lumbar paraspinal muscles, vertebral instability, standing and supine radiographs

1 **Introduction**

2 Osteoporotic vertebral fractures (OVFs) are fragility fractures associated with osteoporosis. Osteoporosis
3 commonly affects postmenopausal women because estrogen deficiency after menopause induces rapid bone loss,
4 and OVFs are a major cause of morbidity and reduce activities of daily living among the elderly¹. Previous studies
5 indicated that sarcopenia was significantly associated with osteoporosis and was a risk factor for OVFs²⁻⁴.

6 Sarcopenia is considered one of the main features of the aging process. It is characterized by a reduction in muscle
7 mass and strength⁵. Observational studies have shown that sarcopenia and a decreased cross-sectional area (CSA) of
8 the paraspinal muscle are risk factors for OVFs². Weakened psoas major muscles have been found to lessen hip
9 flexion velocity, cause gait disturbances, and be closely related to falling when walking⁶. Similarly, studies have
10 reported a relationship between the quality of paraspinal muscles, such as the erector spinae and multifidus, and the
11 maintenance of a stable standing position⁷. Additionally, muscular imbalance may deteriorate the sagittal curvature
12 of the vertebrae and limit the range of motion³.

13 Vertebral instability (VI) in OVFs varies from mild to severe. Changes in vertebral height from standing to supine
14 radiographs shortly after the initial injury frequently reveal the instability of the fracture.

Muscular strength is proportional to the CSA of the muscle, and the CSA measurement is typically used to evaluate lumbar muscular strength⁸. Although many studies have reported that weaknesses of lumbar muscles are related to OVFs^{9,10}, there is uncertainty on the association between the CSA of lumbar muscles and VI.

In this study, we aimed to assess the relationship between the VI of OVFs in postmenopausal women, bone mineral density (BMD), and the CSA of lumbar muscles in an acute setting using quantitative volumetric measurements.

Materials and Methods

Informed consent was obtained from all participants prior to the start of the study. The study was approved by our Institutional Review Board and was conducted according to the principles of the Declaration of Helsinki.

In total, 95 acute OVFs at the thoracolumbar junction (Th10–L2) in postmenopausal women (mean age: 80.6 years, range 64–103 years) were included in this study. Fractures were considered acute if the interval between the onset of symptoms and the admission was <2 weeks, the standing and supine thoracolumbar lateral radiographs showed vertebral collapse, and magnetic resonance imaging (MRI) showed an abnormal signal change in the vertebral body. Trauma more severe than a simple fall from a standing position on level ground, secondary osteoporosis,

postoperative status, pathological fractures, infection, lumbar scoliosis (Cobb angle >20), and diffuse idiopathic skeletal hyperostosis were excluded.

Patient demographics included age, body mass index (BMI), and fracture level. (When more than one fracture was present, the one that was more collapsed was used.) Standing and supine radiographs were obtained on admission.

The heights of the anterior and posterior walls of the fractured vertebrae were measured on the lateral standing radiograph (A1 and P1, respectively) and the supine radiograph (A2 and P2, respectively) (Figure 1). The standing and supine vertebral collapse rates (%) (CRst and CRsp, respectively) were defined as follows:

$CRst = (1 - A1/P1) \times 100$ and $CRsp = (1 - A2/P2) \times 100$, respectively. VI (%) was defined as the difference in vertebral collapse rates between the standing and supine collapse rates: $VI = CRst - CRsp^{11,12}$.

All MRI scans were performed using 3.0-T scanners (Magnetom Skyra, Siemens Healthineers, Erlangen, Germany). Using axial T2-weighted MRI images at the L3/4 intervertebral disc level, the bilateral psoas major, erector spinae, and multifidus muscles were measured, and the mean values were adopted for each muscle.

Moreover, the total CSA of all these muscles was recorded^{13,14}. For each image, the region of interest was drawn using the hospital picture archiving and communication system (I-PACS, NEOVISTA I-PACS, ver. 1.09 R04; KONICA MINOLTA, Japan) to outline the bilateral muscles separately (Figure 2). The fat infiltration of the para-

spinal muscle was measured semi-quantitatively with three visual scale grades¹⁵. The scale defined the mild, moderate, and severe grades as a fat portion <10%, between 10% and 50%, and >50%, respectively.

A dual-energy X-ray absorptiometry scan (Lunar Prodigy; GE Healthcare, Chicago, IL, USA) was performed to measure the BMD of the lumbar region of the spine (L1–L4) and the proximal femur (total hip). Instead, of vertebral BMD, proximal femur BMD was used for data analysis because vertebral fractures and osteophytes are known to lead to falsely high BMD values.

According to our previous report¹², we classified patients into a VI of 20%, which was calculated as the threshold value for resistance to conservative treatment. We classified patients into two groups according to the calculated VI: group 1 (VI <20%) and group 2 (VI ≥20%). We compared the BMD and CSA of each muscle between the groups (Table 1).

Because the samples were not normally distributed and the data are presented as the median and range, nonparametric tests were used for further analyses. The Mann–Whitney U test was used to compare the unpaired groups. The Spearman correlation coefficient was calculated to assess the relationship between variables. To determine the risk factors for high VI (VI ≥20%), multivariable regression analysis was performed. Differences were

considered to be statistically significant at $P < 0.05$, and all statistical analyses were performed using the Prism8 statistical package (GraphPad Software, USA) and IBM SPSS Statistics ver. 26.0 (IBM Co., USA).

Results

The relationship between the CSA of lumbar muscles and BMD in the OVFs is shown in Figure 3. Although BMD was positively correlated with the CSA of the psoas major ($r = 0.2950$, $P = 0.041$), erector spinae ($r = 0.3854$, $P = 0.0001$), and total muscle ($r = 0.4390$, $P < 0.0001$), it was not significantly correlated with the CSA of the multifidus muscle ($r = 0.1960$, $P = 0.0597$).

The relationship between BMD and CRst was not significant ($r = -0.1099$, $P = 0.2945$). Similarly, the relationship between BMD and VI was not significant ($r = -0.2018$, $P = 0.0524$) (Figure 4). CRst was not significantly correlated with the CSA of the psoas major ($r = -0.1773$, $P = 0.0857$), erector spinae ($r = -0.1572$, $P = 0.1282$), multifidus ($r = -0.01613$, $P = 0.1694$), and total muscle ($r = -0.1734$, $P = 0.0928$) (Figure 5). A negative correlation was observed between VI and the CSA of the erector spinae ($r = -0.3962$, $P < 0.0001$) and total muscle ($r = -0.3772$, $P = 0.0002$). The CSAs of the psoas major and multifidus muscles did not significantly correlate with VI ($r = -0.1575$, $P = 0.1275$ and $r = -0.1847$, $P = 0.0731$, respectively) (Figure 6). No statistically significant difference in BMD ($P = 0.7102$) or CSA of the psoas major ($P = 0.1804$) or multifidus ($P = 0.2505$) muscles was observed

between the groups. However, group 2 had a significantly smaller mean CSA of the erector spinae ($P = 0.0002$) and total muscle ($P = 0.0009$) than group 1. Three grades were evaluated on the basis of the fat infiltration of the paraspinal muscle. The number of patients with mild grade was 23 (34.3%) in group 1 and 4 (14.2%) in group 2. Patients with moderate and severe grades were 31 (46.3%) and 13 (19.4%) in group 1 and 13 (46.4%) and 11 (39.3%) in group 2, respectively. Additionally, patients in group 2 tended to have a higher grade of fat infiltration than those in group 1 ($P = 0.020$) (Table 2). Multivariable analysis was performed. The dependent variable was the severity of VI (either $VI \geq 20\%$ or $VI < 20\%$). Covariates were age, BMI, CSA of psoas major, CSA of erector spinae, and fat infiltration. Both age (odds ratio [OR], 1.099; 95% confidence interval [CI], 1.015–1.189; $P = 0.020$) and the CSA of the erector spinae (OR, 0.996; 95% CI, 0.993–0.999; $P = 0.020$) were significant predictors of high VI (Table 3).

Discussion

The CSA of the erector spinae was negatively correlated with increased VI in OVFs. This result provides the first quantitative evidence that a smaller erector spinae muscle may contribute to VI of OVFs in postmenopausal women. We observed a close relationship between BMD and the CSAs of the psoas major and erector spinae muscles. The relationship between BMD and the collapse rate or VI was not significant. The mean CSA of the erector spinae

muscle was significantly lower in group 2 than in group 1, suggesting that this muscle is typically smaller in patients with severe VI of OVFs. The age and fat infiltration differed significantly between groups 1 and 2. Multiple logistic regression analysis revealed that both age and erector spinae affect the severity of OVFs.

Both muscle and bone are important in maintaining skeletal structure and strength. Muscle mass contributes to bone mineral mass¹⁶. Sarcopenia has been reported to be an independent risk factor for a low BMD of the femoral neck and lumbar spine¹⁷. With increasing age, the weakening of muscle contractions results in a decrease in bone marrow longitudinal stress¹⁸. Reduced loading, mechanical stimulation, and relative immobility can cause decreased bone formation. Clinical studies have shown that loss of muscle mass occurs concurrently with osteoporosis¹⁹.

Previous studies have reported that the risk factors of a delayed union in OVFs are the thoracolumbar junction location, the presence of a posterior wall fracture with displacement, and diffuse low- and high-signal changes on T2-weighted MRI^{20,21}. Other studies have reported that VI is involved in conservative resistance in OVFs^{11,12}. We believe that cases with severe VI are refractory to conservative treatment, associated with clinical findings, and reflect severity.

Lumbar extensor muscles influence the compression fracture of vertebrae as a stabilizer^{22,23}, and an association between OVFs and paraspinal muscle atrophy and fat infiltration was reported². In our study, the atrophy of the

erector spinae muscle was correlated with VI. A reduction in the size of the erector spinae muscle may decrease the protective factor of the spine from trauma, leading to VI. Muscle atrophy and fat infiltration progress with aging and, thus, sarcopenia. In this study, besides aging, multivariate analysis showed that the atrophy of the erector spinae muscle was significantly associated with VI. This confirms that the erector spinae plays a role in protecting the vertebrae.

To our knowledge, this is the first study investigating the relationship between BMD, CSA of lumbar muscles, and VI in OVFs. We observed a negative correlation between the CSA of the erector spinae muscle and VI of OVFs. Moreover, it was observed that the CSA of the erector spinae muscle decreased significantly when the VI was $\geq 20\%$. These results indicate that smaller erector spinae muscles may contribute to the poor stabilizing ability of the spine, resulting in greater vulnerability to OVFs, ultimately playing a role in the severity and prognosis of OVFs.

The present study has several limitations. First, this study is cross-sectional and not longitudinal. Second, we included only slim Japanese women with low BMDs. Similarly, this study is retrospective in nature because of the sampling problems that are inherent to this mode of investigation. Third, this study used only the MRI images at the L3/4 intervertebral disc level; therefore, it is necessary to measure those at other levels in future studies and conduct related investigations. Fourth, we did not conduct a quantitative evaluation of fat infiltration; thus, additional

research will be required in the future. Finally, this study did not consider confounding factors affecting OVFs, such as osteoporosis treatment. In the future, it will be necessary to consider patient matching to remove the influence of confounding factors.

Further studies are needed to demonstrate a correlation between lumbar muscle volume and VI both in terms of physio-pathological and clinical aspects. Increasing the awareness of these conditions will improve the therapeutic approach that counteracts the onset of disabling complications.

Conclusions

The study results suggest that there is a correlation between decreased BMD and CSA of erector spinae and psoas major muscles in postmenopausal women with OVFs. The CSA of the erector spinae muscle is negatively correlated with VI.

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1 Tables

2 Table 1: Patient demographic data

3 Data are expressed as mean $\pm$ standard deviation.

4 BMI, body mass index; BMD, bone mineral density

5

6 Table 2: BMD and CSA differences between groups 1 and 2

7 Data are expressed as mean $\pm$ standard deviation.

8 BMD, bone mineral density; CSA, cross-sectional area

9

10 Table 3 Multiple logistic regression analysis of factors associated with the severity of vertebral instability

11 BMD, bone mineral density, CI, confidence interval

12

13

1 **Figure Legends**

2 Figure 1 Lateral radiographs of thoracolumbar spine

3 Anterior and posterior vertebral body height of standing (A1 and P1, respectively) and supine (A2 and P2,
4 respectively) lateral radiographs.

5 Figure 2 A magnetic resonance axial image

6 A magnetic resonance axial image shows the cross-sectional area of the muscles at the L3/4 disc level. Cross
7 sections of the psoas major, erector spinae, and multifidus muscles are drawn.

8 Figure 3: The relationship between bone mineral density (BMD) and the cross-sectional area (CSA) of lumbar
9 muscles

10 BMD is positively correlated with the CSA of the psoas major, erector spinae, and total muscle.

11 Figure 4: The relationship between BMD and radiographic parameters

12 The relationship between BMD and collapse rate or vertebral instability is not significant.

13 Figure 5: The relationship between standing collapse rate and the CSA of lumbar muscles

- 1 The standing collapse rate is not significantly correlated with the CSA of the psoas major, erector spinae, multifidus,
- 2 and total muscle.
- 3 Figure 6: The relationship between vertebral instability and the CSA of lumbar muscles
- 4 The CSA of the erector spinae and total muscle is negatively correlated with vertebral instability.

Variable	Number of patients (n = 95)	Group 1 (n = 67)	Group 2 (n = 28)	P value
Average age (yr)	80.6 (64–103)	78.9 (64–96)	84.8 (70–103)	0.0009
BMI (kg/m ²)	22.0 (16.0–31.2)	22.1 (12.0–32.2)	21.7 (15.6–29.8)	0.6190
Level (n)				
T10	4	3	1	
T11	8	5	3	
T12	36	26	10	0.3339
L1	36	28	8	
L2	11	5	6	

	Number of patients (n = 95)	Group 1 (n = 67)	Group 2 (n = 28)	P value
BMD (g/cm ²)	0.662 ± 0.13	0.663 ± 0.11	0.631 ± 0.11	0.2226
Psoas major (mm ²)	506.67 ± 133.74	511.44 ± 86.03	495.27 ± 55.08	0.1804
Erector spinae (mm ²)	1080.20 ± 229.99	1135.7 ± 142.58	947.42 ± 211.58	0.0002
Multifidus (mm ²)	304.49 ± 82.45	313.21 ± 35.33	283.61 ± 146.93	0.2505
Total (mm ²)	1891.36 ± 338.04	1960.34 ± 337.06	1726.29 ± 277.86	0.0009
Fat infiltration				
Mild	27	23	4	
Moderate	44	31	13	
Severe	24	13	11	0.020

Variable	B	Odds ratio	95%CI	P value
Age (yr)	0.094	1.099	1.015–1.189	0.020
BMD (g/cm ²)	−0.973	0.378	0.001–128.920	0.744
Psoas major (mm ²)	0.002	1.002	0.998–1.006	0.400
Erector spinae (mm ²)	−0.004	0.996	0.994–0.999	0.020
Fat infiltration	0.160	1.173	0.556–2.476	0.675