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Predicting the Occurrence of New Vertebral Fractures Using the Vertebral Bone Quality Score

A Prospective Cohort Study Using 11-Year MRI Follow-up Data from the Minami-Aizu Study

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Background: Previous studies have recognized the potential of the Vertebral Bone Quality (VBQ) score for predicting fractures. However, these studies often have lacked longitudinal perspectives and have not focused on community populations. Our study aimed to enhance the predictive capacity of the VBQ score by investigating its correlation with new vertebral fractures (NVFs) that were detected 11 years later in a community-based cohort and by developing a comprehensive prediction model.

Methods: This study was a population-based study conducted in the Minami-Aizu area in Fukushima Prefecture, Japan. One hundred and thirty participants voluntarily underwent T1-weighted magnetic resonance imaging (MRI) of the lumbar spine in 2004 and 2015. VBQ scores were ascertained from the 2004 scans. NVFs that occurred between 2004 and 2015 were detected based on a ≥20% reduction in vertebral height on the midsagittal sections of the MRI. Other predictors that were considered included age, sex, body mass index, smoking history, heart disease, cerebrovascular disease, respiratory disease, and existing vertebral fractures (EVFs). A logistic regression analysis was conducted.

Results: The logistic regression analysis indicated that the VBQ score, age, sex, and EVFs were significant predictors of NVFs. The prediction model showed an area under the curve of 0.84, suggesting excellent discriminatory power. The calibration capacity was confirmed using the Hosmer-Lemeshow test.

Conclusions: The VBQ score was significantly correlated with the long-term incidence of NVFs in a community population. The prediction model exhibited satisfactory discrimination and calibration capacities, highlighting the use of the VBQ score as a potential tool for long-term prediction of NVFs.

Level of Evidence: Prognostic Level II. See Instructions for Authors for a complete description of levels of evidence.

Osteoporosis management relies primarily on the assessment of 2 crucial factors: bone mineral density (BMD) and bone quality. Although the U.S. National Institutes of Health reported the importance of bone quality[1], its quantifiable assessment remains challenging. The Vertebral Bone Quality (VBQ) score, determined from T1-weighted magnetic resonance imaging (MRI) of the lumbar spine[2], has recently emerged as a promising tool in this regard. It has a weak negative correlation with bone density, and a high VBQ score means poor bone quality. The VBQ score can predict future fractures independently of BMD[3].

Ehresman et al. highlighted the potential of the VBQ score. In their retrospective study with a mean follow-up period of 12.5 years, they observed higher VBQ scores in the group that experienced fractures, thus affirming the possibility of using the VBQ score for fracture prediction[3]. Although they substantially

Disclosure: No external funding was received for this work. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJSOA/A657).

clarified the role of the VBQ score, the retrospective nature of their study and the specific population involved necessitate further exploration to validate the applicability of VBQ scores in a more generalized setting.

We conducted a longitudinal study to validate the predictive ability of the VBQ score over an extended period of time in a community-based cohort in the Minami-Aizu area in Fukushima Prefecture, Japan. We analyzed MRI data from local residents over 11 years. Our study builds upon the initial findings of Ehresman et al.[3] and validates the use of the VBQ score as a reliable predictor of future vertebral fractures in a broader population over a substantial duration of time. Moreover, we aimed to contribute to the early identification of individuals at elevated risk for fracture, thereby enabling timely intervention.

Materials and Methods

The study was conducted in accordance with the Declaration of Helsinki and was approved by both the institution's data protection officer and the ethics committee of our university (certification number: CRB2200002; reference number: 1880). All of the patients and participants provided written informed consent to undergo MRI and participate in the study.

Participants

This prospective cohort study was based on data from the Minami-Aizu study[4-6], which involved a follow-up time of approximately 11 years and 1,862 participants (697 men and 1,165 women) who had been enrolled in specific health checkups that were conducted in 2004. The participants were residents of Tadami-cho, Tateiwa-mura, and Ina-mura within Fukushima Prefecture, Japan. The age of the patients ranged from 19 to 93 years. Among these 1,862 individuals, 459 underwent MRI of the lumbar spine in 2004, and 200 individuals underwent follow-up MRI of the lumbar spine in 2015. This study only utilized MRI scans from 2004 and 2015 because this was a secondary analysis that used existing data from the Minami-Aizu study.

The study included several exclusion criteria: participants with missing data (from information obtained from specific health checkups), those whose MRI from 2004 did not include the T11-L5 vertebrae, and participants for whom the VBQ score could not be calculated using the MRI from 2004. A total of 70 participants were excluded: 41 because of missing data, 26 because of insufficient imaging from 2004, and 14 because the VBQ score could not be measured. Some participants met multiple exclusion criteria. The application of our inclusion and exclusion criteria led to a final sample size of 130 participants (Fig. 1).

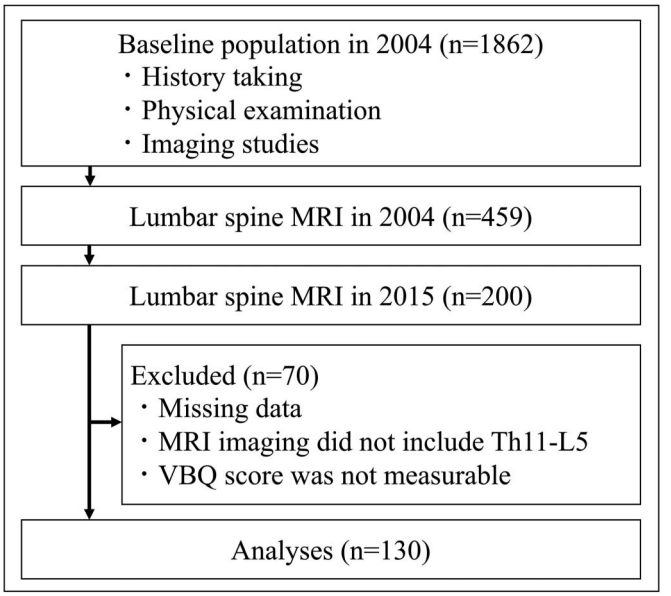

Fig. 1

Flowchart for the MRI evaluations. Of the 1,862 participants in the 2004 health checkups in the Minami-Aizu area of Fukushima Prefecture who voluntarily participated in this study, 200 had MRI data for the lumbar spine available in both 2004 and 2015, and after applying the exclusion criteria, 130 were included in the analysis.

Assessment

Potential predictors of new vertebral fractures (NVFs) were assessed at the start of the study (2004). These predictors included the VBQ score, age, sex, body mass index (BMI), current smoking status, and presence of an existing vertebral fracture (EVF), as well as a history of heart disease (HD), respiratory disease (RD), and cerebrovascular disease (CVD). The detailed measurement methods and definitions of the outcome and various predictors are described below.

In this study, the outcome was an NVF occurring within 11 years of 2004. We defined an NVF as a reduction in the vertebral height of ≥20%[7] when comparing the midsagittal MRI scans of the lumbar spine from 2004 and 2015. Both the principal investigator (T.Y.) and a collaborator (Y.E.) assessed the NVFs, and the reliability of the measurements was evaluated using the diagnostic concordance rate and the kappa coefficient. For the analysis, patients who were identified as having NVFs by either of the investigators were classified in the NVF group, while all of the other patients were classified in the no-NVF group.

First, VBQ scores were measured from MRI scans that had been acquired in 2004; however, VBQ scores were not determined for scans that had been acquired in 2015. We measured the VBQ score for each participant using the MRI scans according to the method described in a previous study[2,3] (Fig. 2). Detailed information on the MRI systems that were used in 2004, including the magnetic field strength, is shown in Table I[4]. The assessment involved evaluating the intramedullary signal intensity (SI) in T1-weighted MRI from lumbar vertebrae 1 to 4 (SI L1-L4) and the SI of the spinal fluid at level 3 of the lumbar spine (SI L3). We carefully excluded regions of osteosclerosis associated with degeneration when measuring the SI in the vertebral bodies, and we excluded the cauda equina and nerve roots from the SI fluid measurements. We then computed the VBQ score by dividing the SI L1-L4 by the SI L3.

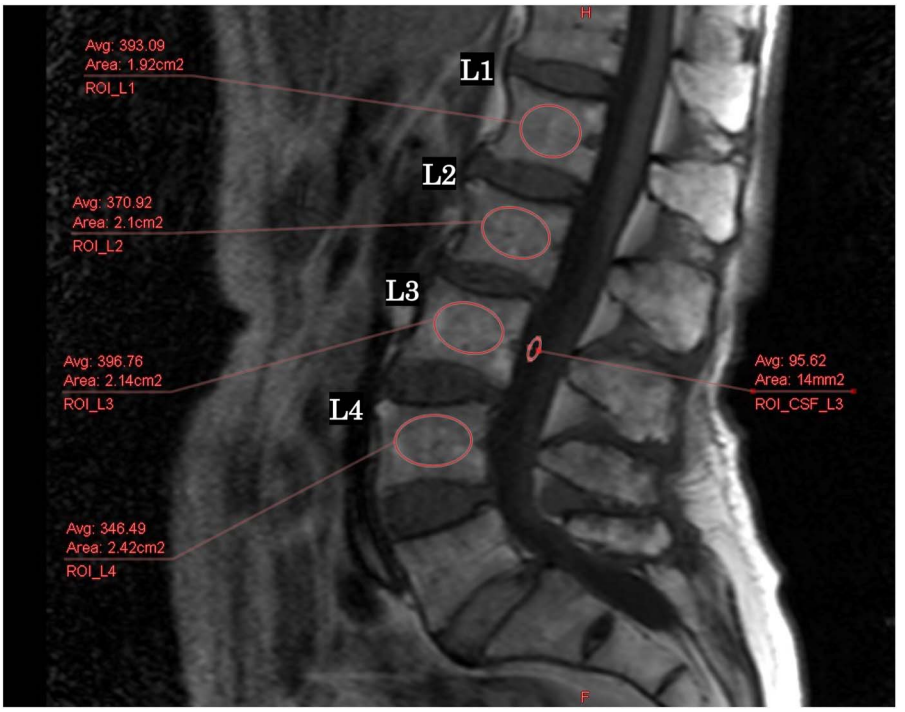

Fig. 2

The VBQ score was measured using T1-weighted MRI of the lumbar spine. In the midsagittal section, the VBQ score was calculated by dividing the average signal intensity in the L1-L4 vertebrae by the cerebrospinal fluid signal intensity in the L3 vertebra. ROI = region of interest, Avg = mean signal intensity in the ROI, Area = area of the ROI, and CSF = cerebrospinal fluid.

The VBQ scores were independently measured by the principal investigator (T.Y.) and a collaborator (Y.E.). We calculated the intraclass correlation coefficient (ICC) to assess the reliability of the VBQ score measurements. The average VBQ scores were analyzed. All of the VBQ scores were measured using ZioCube software (ZioSoft).

Information on the status of current smokers and any history of HD, RD, and CVD were collected through interviews that were conducted by well-experienced public health nurses in 2004. The presence or absence of an EVF was determined based on the findings from a midsagittal MRI scan of the lumbar spine in 2004. The diagnostic criteria for an EVF were established using a semiquantitative method[7]. An EVF was determined to be present if a vertebra in the T11 to L5 range had a vertebral height that had been reduced by ≥20%.

TABLE I MRI Specifications and Utilization*

Manufacturer	Philips	Toshiba
Product name	Gyroscan Intera Power	EXCELART/P2 Pianissimo
Tesla	1.0 T	1.5 T
Slice thickness *(mm)*	5	5
Slice gap *(mm)*	0.5	1.0
TE *(ms)*	120	108
TR *(ms)*	4,500	4,000

*MRI = magnetic resonance imaging, TE = echo time, and TR = repetition time. Reproduced, with modification, from: Fushimi Y, Otani K, Tominaga R, Nakamura M, Sekiguchi M, Konno SI. The association between clinical symptoms of lumbar spinal stenosis and MRI axial imaging findings. Fukushima J Med Sci. 2021 Dec 21; 67(3):150-60. Reproduced with permission.

Development of the Prediction Model

We performed multiple logistic regression analysis based on the outcome and aforementioned predictors. VBQ score, age, and BMI were considered continuous variables, while sex, current smoker status, presence of EVFs, and history of HD, RD, and CVD were categorical variables.

Moreover, we developed a prediction model based on the beta coefficients that were obtained from the analysis. The prediction model was able to calculate the probability of long-term vertebral fractures. We evaluated the performance of the prediction model by assessing both its discriminative and calibration capacities. The model's discrimination performance was evaluated by constructing a receiver operating characteristic (ROC) curve and calculating the area under the curve (AUC). The calibration capacity was assessed using the Hosmer-Lemeshow test and by creating a calibration plot.

Statistical Analysis

To analyze participant characteristics, t tests were used for normally distributed continuous variables, Wilcoxon signed-

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rank tests were used for non-normally distributed continuous variables, and chi-square tests or Fisher exact tests were used for categorical variables. The statistical analysis was conducted with SPSS Statistics (version 28.0.0.0; IBM). P values of <0.05 were considered to be significant.

Results

Number of NVFs

Of the 130 participants, 24 experienced NVFs. The diagnostic concordance between the 2 examiners was 89.3%, with a kappa coefficient of 0.574, suggesting moderate agreement.

VBQ Score

The mean VBQ score (and standard deviation) was 4.0 ± 0.8. The ICC between the 2 examiners was 0.819, indicating high interrater reliability.

Participant Characteristics

The participants' characteristics are listed in Table II. Significant differences were observed in terms of age, sex, EVFs, and VBQ score. The NVF group, in comparison with the no-NVF group, was older, included more women, and had more EVFs and higher VBQ scores.

The Prediction Model

The multiple logistic regression analysis demonstrated significant differences in age, sex, EVFs, and VBQ score, with odds ratios of 1.1 (95% confidence interval [CI]: 1.0 to 1.2), 16.7 (95% CI: 1.7 to 162.8), 3.4 (95% CI: 1.0 to 11.6), and 2.4 (95% CI: 1.2 to 5.0), respectively (Table III). The established prediction model is shown in Figure 3.

Discriminatory Power

The AUC was 0.84 (95% CI: 0.75 to 0.92), indicating excellent discriminatory power (Fig. 4).

TABLE II Characteristics of the Participants*

Characteristics	No NVF (N = 106)	NVF (N = 24)	P Value
Age *(yr)*	63.5 ± 8.9	69.7 ± 6.5	<0.001
Female sex	73 (68.9%)	23 (95.8%)	0.005
BMI *(kg/m²)*	22.8 ± 2.6	23.7 ± 2.9	0.171
Current smoker	10 (9.4%)	1 (4.2%)	0.688
EVF	23 (21.7%)	12 (50%)	0.010
Heart disease	15 (14.2%)	3 (12.5%)	1
Respiratory disease	1 (0.9%)	0 (0%)	1
Cerebrovascular disease	2 (1.9%)	1 (4.2%)	0.461
VBQ score	3.9 ± 0.8	4.3 ± 0.7	0.024

*Vaues are given as the mean ± standard deviation or number (%). NVF = new vertebral fracture, BMI = body mass index, EVF = existing vertebral fracture, and VBQ score = Vertebral Bone Quality score.

TABLE III Results of the Multiple Logistic Regression Analysis*

Characteristic	β	Standard Error	Odds Ratio	P Value
Age in yr	0.11	0.04	1.12	0.007
Female sex	2.82	1.16	16.7	0.015
BMI in kg/m²	0.04	0.10	1.05	0.66
Current smoker	−1.15	1.32	0.32	0.38
EVF	1.24	0.62	3.44	0.046
Heart disease	−0.92	0.84	0.40	0.28
Respiratory disease	−20.1	40193	0.00	1
Cerebrovascular disease	0.07	1.38	1.07	0.96
VBQ score	0.89	0.37	2.44	0.014
Constant	−16.2	4.32	0.00	<0.001

*BMI = body mass index, EVF = existing vertebral fracture, and VBQ score = Vertebral Bone Quality score.

Calibration Capacity

The Hosmer-Lemeshow test, which compared the measured and predicted probabilities of NVFs, did not reveal a significant difference. The calibration plot demonstrated a slope of 1.0484 and an intercept of 0.0089 (Fig. 5). This indicated that the model is well-calibrated, as the predicted probabilities aligned closely with the observed probabilities.

Discussion

The results of this study demonstrated that higher VBQ scores were associated with the occurrence of NVFs. Furthermore, a prediction model was developed using VBQ scores over a period of 11 years, which accurately predicted the likelihood of NVFs. This prediction model exhibited good discriminatory and calibration capability, making it a valuable tool.

Compared with the Trabecular Bone Score (TBS)[8] and blood and urine pentosidine levels[9,10], the VBQ score is a more recent method for assessing bone quality[2,3]. It evaluates the intramedullary vertebral signal intensity on T1-weighted MRI, with a high VBQ score indicating bone marrow fatty infiltration. Previous studies have demonstrated a weak negative correlation between the VBQ score and BMD[2], as well as an association between high VBQ scores and the occurrence of new fractures[3]. Several studies have also suggested that high VBQ scores contribute to the loosening of surgical instrumentation[11,12], highlighting the importance of the VBQ score as an indicator of bone quality and strength.

Ehresman et al. developed an innovative MRI-based approach, the VBQ score, for evaluating bone quality[2]. This score, based on the understanding that adipose infiltration into the bone marrow epitomizes the pathophysiology of bone attrition,

$$\text{Probability} = \frac{1}{1+\exp(-(0.89 \times \text{'VBQ score'} + 0.11 \times \text{'age'} + 2.82 \times \text{'sex'} + 1.24 \times \text{'EVF'} - 16.2))}$$

Fig. 3

The prediction model. This formula allows for the calculation of the probability of an NVF occurring within 11 years. The equation incorporates 4 predictors, including the VBQ score, age, sex, and presence of an EVF.

shows important potential for predicting fracture risk and enabling personalized therapeutic approaches, specifically for patients with a heightened risk of osteoporosis. Despite the potential limitations of that prior study, such as its retrospective design and probable selection bias due to the focus on high-risk patients, the VBQ score is a potential candidate for predicting fracture risk. In our study, a prospective cohort analysis was performed in a generalized setting (community residents rather than hospital patients), and our findings strengthen the evidence for the validity of the VBQ score for predicting the occurrence of NVFs. Furthermore, our prediction model using the VBQ score showed excellent discrimination and calibration, thus supporting its potential for clinical application.

We selected clinically assessable predictors that are commonly used in clinical practice as adjusting factors in multiple logistic regression analysis. The results of the multiple logistic regression analysis revealed that the VBQ score and also age, sex, and the presence or absence of an EVF were significant in predicting the occurrence of NVFs. The prediction model that incorporates the VBQ score and those other 3 predictors exhibited strong discriminatory and calibration capabilities. As age and sex are typically known before the MRI examination and an EVF can be diagnosed using MRI, the model enables the calculation of the 11-year risk of the occurrence of an NVF without the need for additional tests besides MRI. Therefore, we think that this model is highly practical for clinical use.

We believe that the VBQ score has several notable advantages. First, VBQ scores may represent bone strength more accurately than other scores. Previous studies have shown that

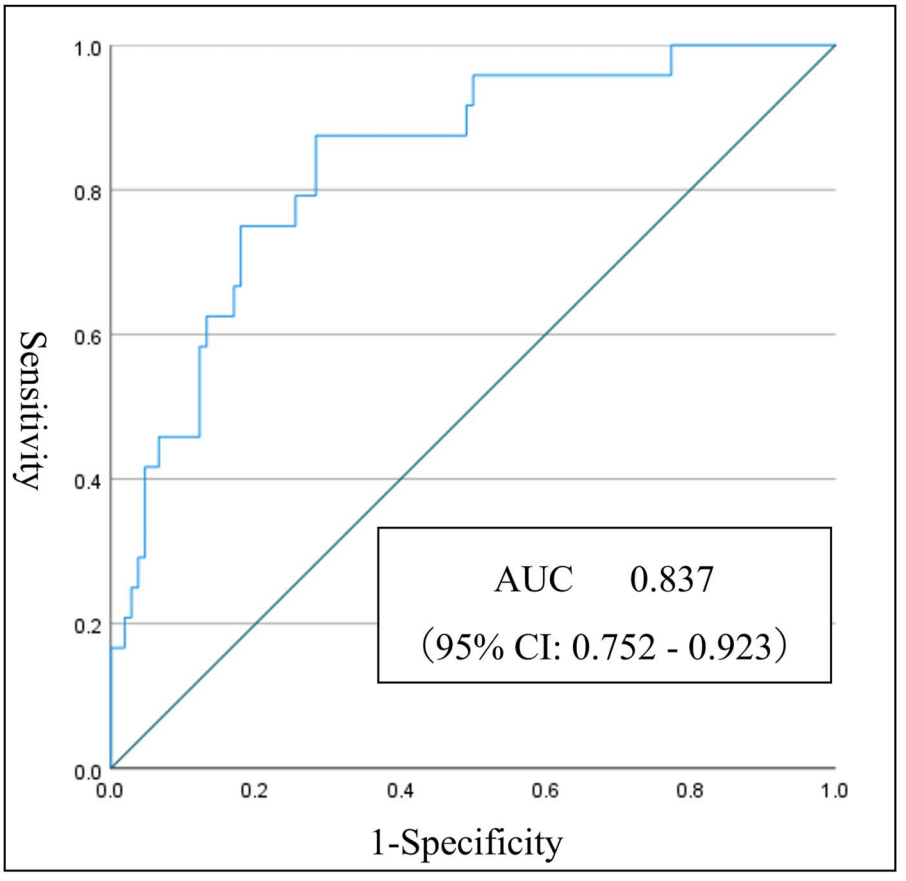

Fig. 4

An ROC curve assessing the ability of the prediction model based on the VBQ score to correctly predict the occurrence of an NVF within 11 years. The resulting AUC was 0.837, which indicates excellent discriminatory power. CI = confidence interval.

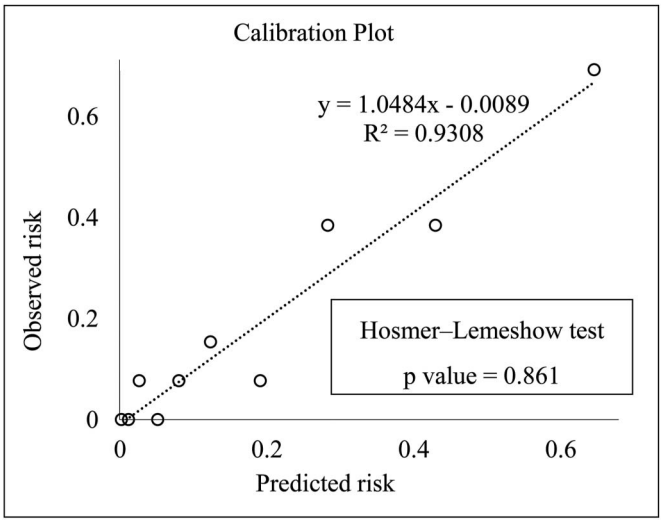

Fig. 5

No significant differences were observed in the Hosmer-Lemeshow test. The estimate made from the calibration plot was close to y = x. The calibration of the prediction model was considered excellent.

the VBQ score had better fracture prediction ability than DXA (dual x-ray absorptiometry)[3]. Additionally, studies on spinal surgery have demonstrated that VBQ scores are useful for predicting screw loosening, comparable with the Hounsfield units obtained from computed tomography scans[11]. In a large-scale cohort study that was conducted in Japan, a prediction model combining the Fracture Risk Assessment Tool (FRAX), BMD, and TBS for predicting hip fractures within 10 years exhibited excellent discriminatory ability, with an AUC of ≥0.8[13]. Although the outcomes and populations may differ, the prediction model using the VBQ score in our study also had an AUC of >0.8. Although our prediction model does not incorporate FRAX information, a prediction model with high discriminatory ability can be developed by incorporating the FRAX. However, adding FRAX information may impose limitations on the ease of use of the prediction model. Therefore, addition of the FRAX has both advantages and disadvantages. Second, an important advantage of the VBQ score is that it is based on MRI, which involves no radiation exposure. As mentioned earlier, our prediction model exhibited high discriminatory ability, enabling convenient assessment of fracture risk without radiation exposure.

However, previous studies have suggested that accurately predicting fracture risk using VBQ scores is challenging in patients with a history of vertebral fractures[14]. These patients may have low VBQ scores, which seem to contradict their actual poor bone health. Our data also indicated that, in 2004, participants with EVFs had lower average VBQ scores than those without EVFs (see Appendix). This inconsistency, where VBQ scores may not align with a patient's fracture history, corresponds with outcomes from logistic regression analyses. The low VBQ scores after vertebral fractures can potentially be attributed to factors such as the influence of bone healing or the effects of postinjury osteoporosis treatment. However, verifying the true cause of these decreases in VBQ scores remains unattainable at present. Further exploration of the validity of the VBQ score, such as tracking changes in scores after osteoporosis treatment, can offer valuable insight and an enhanced understanding of this topic.

Additionally, previous studies have indicated that predicting repetitive vertebral fractures solely based on the VBQ score can be challenging in patients with EVFs[14]. However, the prediction model developed in this study was designed to account for such repetitive fractures. By incorporating other predictors in the model, we believe that the VBQ score becomes sufficiently useful for predicting recurrent vertebral fractures.

Limitations

This study relied on secondary data from a previous study and therefore has limitations in terms of the selection of predictors and sample size. However, the findings based on 11 years of MRI follow-up data from the local population provide valuable insights.

Selection bias should be considered, as participants were from the Minami-Aizu area and voluntarily participated in this study. Moreover, some individuals with underlying medical conditions or difficulties in performing daily activities might have been excluded. Additionally, the occurrence of NVFs may have been underestimated because some participants may not have been followed after subsequent vertebral fractures, potentially reducing the number of participants classified in the NVF group.

Furthermore, this study focused on vertebral fractures and may not accurately predict nonvertebral fragility fractures in the hip, forearm, or humerus. Collecting information about fractures at different anatomical sites and incorporating additional data could potentially help develop a prediction model for fragility fractures that is not limited to only vertebral fractures.

Detailed information about the timing and symptoms of vertebral fractures was not available in this study. Such information would have been valuable in evaluating the quality of this prediction model. However, in osteoporosis management, screening patients with asymptomatic vertebral fractures is crucial. Vertebral fractures often exhibit subtle or no symptoms, making their assessment challenging through patient interviews and with clinical information. In this study, we relied on diagnostic assessments based on morphological evaluation using MRI data, allowing for the collection of cases of both asymptomatic and symptomatic vertebral fractures.

The information that was available for our study did not include a patient history of osteoporosis, treatment records, or the presence of osteoporosis interventions over the 11-year period; this could have influenced the quality of our prediction model. Additional investigations incorporating these factors are warranted.

Conclusions

This study developed a long-term prediction model for the occurrence of NVFs using the VBQ score. This prediction model shows great potential and supports the applicability

of the VBQ score for predicting fragility fractures. However, further validation is necessary to confirm these findings.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A658). ■

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