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CT-based vertebral three-dimensional Hounsfield unit can predict the new vertebral fracture after percutaneous vertebral augmentation in postmenopausal women: a retrospective study

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Abstract

Background Vertebral Hounsfield unit (HU) were regarded as a new way to predict fragility fracture. However, HU values were measured in a single plane, which is not accurate for the entire vertebral body. This study aimed to create a new CT-based metric for assessing bone mineral density, three-dimensional Hounsfield unit value (3D-HU), and to evaluate its effect in independently predicting new vertebral fracture (NVF) after percutaneous vertebral augmentation (PVA) in postmenopausal women.

Methods This study reviewed female patients with osteoporotic vertebral compression fracture (OVCF) who were treated at our hospital. Patients were divided into NVF and control groups according to whether they had NVF. 3D-HU of the L1-4 vertebrae was measured using preoperative computed tomography (CT) scanning of the lumbar spine. Demographics, procedure-related data, and radiological data were collected. Pearson correlation test was used to determine the correlation between 3D-HU and BMD T-score. The independent risk factors of NVF were determined by multivariate logistic regression analyses. Receiver operating characteristic curve (ROC) was used to evaluate the predictive performance of 3D-HU.

Results This study involved 349 postmenopausal women who were treated with PVA between January 2017 and August 2022. Among them, 61 people suffered the NVF following PVA. The mean 3D-HU was 40.64 ± 22.43 in the NVF group and 79.93 ± 25.69 in the without NVF group ($p < 0.001$). Multivariate analysis showed that lower 3D-HU (OR = 0.927; 95%CI = 0.906–0.945; $p < 0.001$) was the only independent predictor of NVF following PVA. The predictive accuracy of 3D-HU was 87.7%, which was higher than that of the HU value (82.3%), and it was highly positively correlated with BMD T-score ($r = 0.628$, $p < 0.001$).

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Conclusions Lower 3D-HU was significantly associated with NVF following PVA in postmenopausal women. In addition, vertebral 3D-HU had better predictive power than HU values. 3D-HU assessment prior to PVA may provide insight into a patient's risk for NVF.

Keywords Osteoporosis, New vertebral fracture, Computed tomography, Percutaneous vertebral augmentation

Introduction

Osteoporotic vertebral compression fracture (OVCF) is the most common osteoporotic fracture in the elderly, particularly prevalent in postmenopausal women [1]. Patients with OVCF may face clinical consequences such as severe back pain, restricted mobility, and even high comorbidity and mortality rates [2, 3]. The disease affects the elderly' s quality of life. In addition, it has an enormous financial burden on individuals, families, and society as a whole [4]. Percutaneous vertebral augmentation (PVA), as a representative technique of minimally invasive spinal surgery, is widely used in the treatment of OVCF. The procedure helps patients relieve symptoms, restore function and improve quality of life in a short period of time [5, 6]. The safety and efficacy of PVA in OVCF treatment has been demonstrated in previous studies [7]. Moreover, a number of studies have also shown that PVA has a better cost-effectiveness than conservative medical therapy in the treatment of OVCF [8, 9].

PVA has been widely applied in the treatment of OVCF [10, 11]. However, it has been reported that many patients suffered new vertebral fracture (NVF) after PVA procedures, with an incidence of 3–52% [12–15]. Undoubtedly, NVF has become an urgent and pressing issue that requires immediate attention. Studies have confirmed that most NVF occur within 1–2 years after the fracture and that 2 years is considered the "imminent" risk period for re-fracture [16]. If we can accurately identify the potential risks of NVF after PVA, we will have the opportunity to formulate more effective and timely treatment strategies. This will reduce the incidence of NVF in a limited time window for patients at high risk.

Low Bone Mineral Density (BMD) is a significant risk factor for NVF following PVA [17]. Currently, Dual-energy X-ray absorptiometry (DEXA) and quantitative computed tomography (QCT) are the two clinical techniques most commonly used for measuring BMD and assessing the risk of fragility fractures and refractures [18, 19]. However, it cannot be ignored that both techniques have their limitations. Recently, the HU values of vertebral cancellous bone have emerged as an alternative method of assessing bone mineral density that is easily accessible in clinical practice [20–22]. The greatest advantage of this method is its speed and simplicity. Additionally, it is capable of performing opportunistic measurements using CT images obtained previously without exposing the patient to additional radiation and expense.

However, in previous studies, the HU value was measured in a single plane [23], which is an inaccurate method for assessing the bone mineral density of the entire vertebral body. Therefore, this study aimed to search for a new approach to measure the HU value and introduced a new assessment for BMD, the CT-based vertebral three-dimensional Hounsfield unit (3D-HU), which was defined as the average HU value over the entire three-dimensional space of the vertebral body excluding the cortical bone. At the same time, we also evaluated its predictive value for NVF after PVA in postmenopausal women.

Materials and methods

Study population

We retrospectively analyzed clinical and imaging data on postmenopausal women with painful OVCF who underwent PVA surgery between January 2017 and August 2022 at our hospital. The diagnostic criteria for NVF were the presence of vertebral high-signal bone marrow edema on T2-weighted fat-suppressed magnetic resonance imaging (MRI) and recurrent back pain. Based on this definition, postmenopausal women were divided into the NVF group and the without NVF group. Figure 1 illustrates a representative case of NVF after PVA. Inclusion criteria included: (1) female patients aged 50 years or above; (2) low-energy trauma; (3) back pain caused by OVCF; (4) complete imaging examination data; (5) not receiving standardized anti-osteoporosis treatment; (6) follow-up period of not less than 2 years. Exclusion criteria included: (1) female aged less than 50 years; (2) high-energy trauma; (3) previous OVCF was treated with internal fixation surgery or conservatively; (4) patients with metabolic bone diseases other than osteoporosis; (5) pathological fractures; (6) insufficient radiological examinations data; (7) received standard anti-osteoporosis treatment; (8) loss of follow-up. The flowchart of patient screening is shown in Fig. 2.

Our hospital's ethical review board approved this retrospective study. Due to the retrospective nature of the study, written informed consent was not required.

Clinical data

The electronic medical record and radiographic examinations was used to obtain patient-related information. All imaging examinations were performed within one week

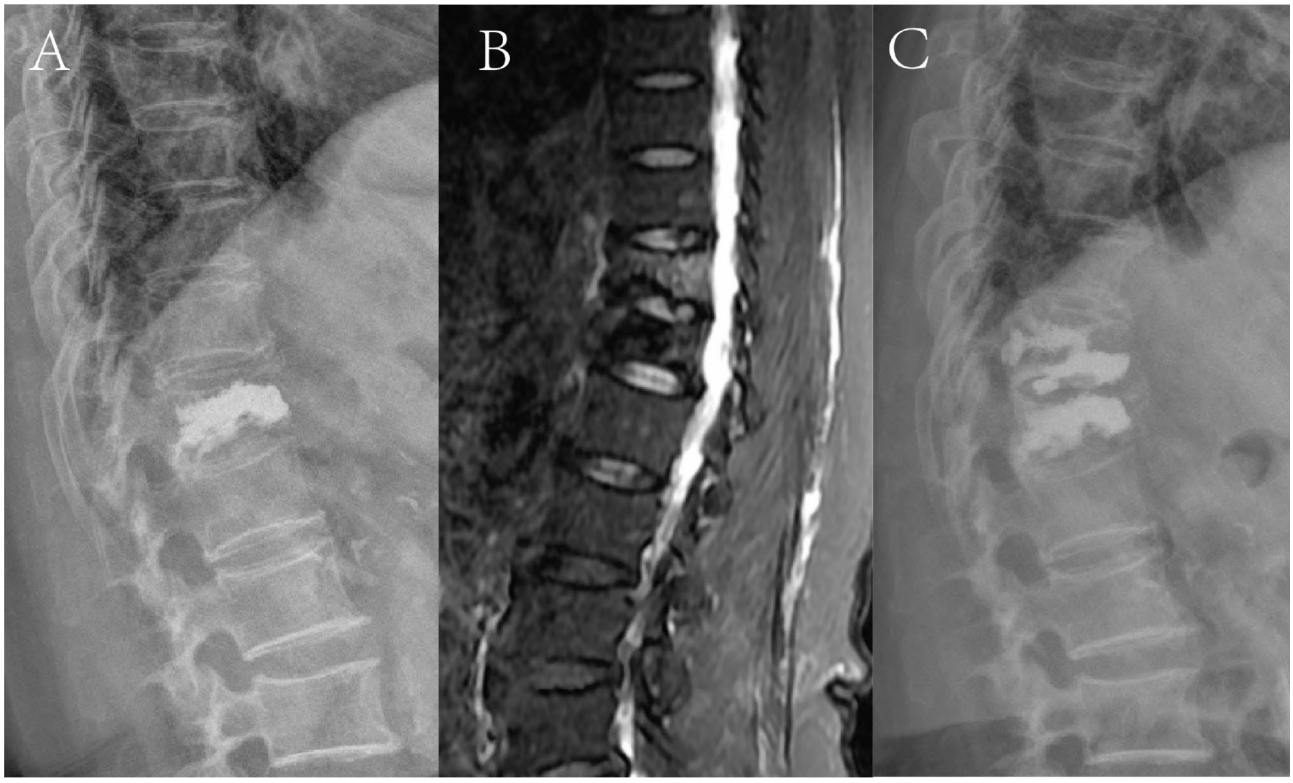

Fig. 1 A representative case of NVF following PVA (**A-C**). (**A**) X-ray revealed that the fractured T12 vertebra was treated. (**B**) MRI images indicated that the T11 vertebra fractured after eleven months postoperatively. (**C**) X-ray demonstrated the fractured T11 vertebrae were treated again

before the operation. Demographic variables include age, body mass index (BMI), history of diabetes, history of hypertension, history of anti-osteoporosis therapy and duration of follow-up. At the same time, we obtained the patient's BMD T-score. BMD in the lumbar spine was measured by dual-energy X-ray absorptiometry (Prodigy Advance; General Electric Company, USA). The mean T-scores of the L1-L4 vertebral bodies (excluding the fractured vertebral bodies) were calculated and used for all subsequent analyses. Surgical variables include the number of fractured vertebrae, location of treated vertebrae, and the method of surgery. Vertebrae treated with PVA at the T12 - L2 level were defined as the thoracolumbar junction, whereas those at the T1 - T11 and L3 - L5 levels were categorized as the non - thoracolumbar junction. Before the first PVA surgery, the number of fractured vertebrae was counted. The one-segmental fracture is a single primary fractured vertebra, whereas the multi-segmental fracture is a primary fracture where the number of fractured vertebrae exceeds one segment.

Surgical technique

During the operation, the patient remained in a prone position throughout. All patients treated received local anesthesia and low levels of sedation. With the assistance of a C-arm X-ray machine (Philips Company, Netherlands), the surgical segment is determined. At the same time, the entry position of the needle was marked on the skin surface. Then, through a unilateral or bilateral approach, an 11- or 13-gauge bone mineral biopsy needle (Kinetic, Shanghai, China) is inserted into the collapsed vertebral body until the needle tip reaches the anterior one-third of the vertebra. If necessary, it is possible to restore the height of the collapsed vertebra by inserting an expanded balloon inside it. Guided by fluoroscopy, inject the prepared bone cement into the fractured vertebral body. During this process, it is necessary to monitor whether there is bone cement leakage. Once leakage occurs, the operation should be stopped immediately.

CT acquisition and 3D-HU calculation

All enrolled patients received spinal Computed tomography (CT) scanning within the week before PVA surgery. CT scanning was performed using a multi-detector CT scanner (BrightSpeed 16, General Electric Company, WI, USA) with tube voltage of 120 kVp, tube current of 240 mA, and slice thickness of 0.63 mm. The 3D-HU was measured using IntelliSpace Portal 9.0 (Philips Company, Netherlands). The CT images were analyzed according to the following steps. First, three-dimensional reconstruction of CT scans was conducted. Second, the upper and lower borders were limited to the cancellous bone region

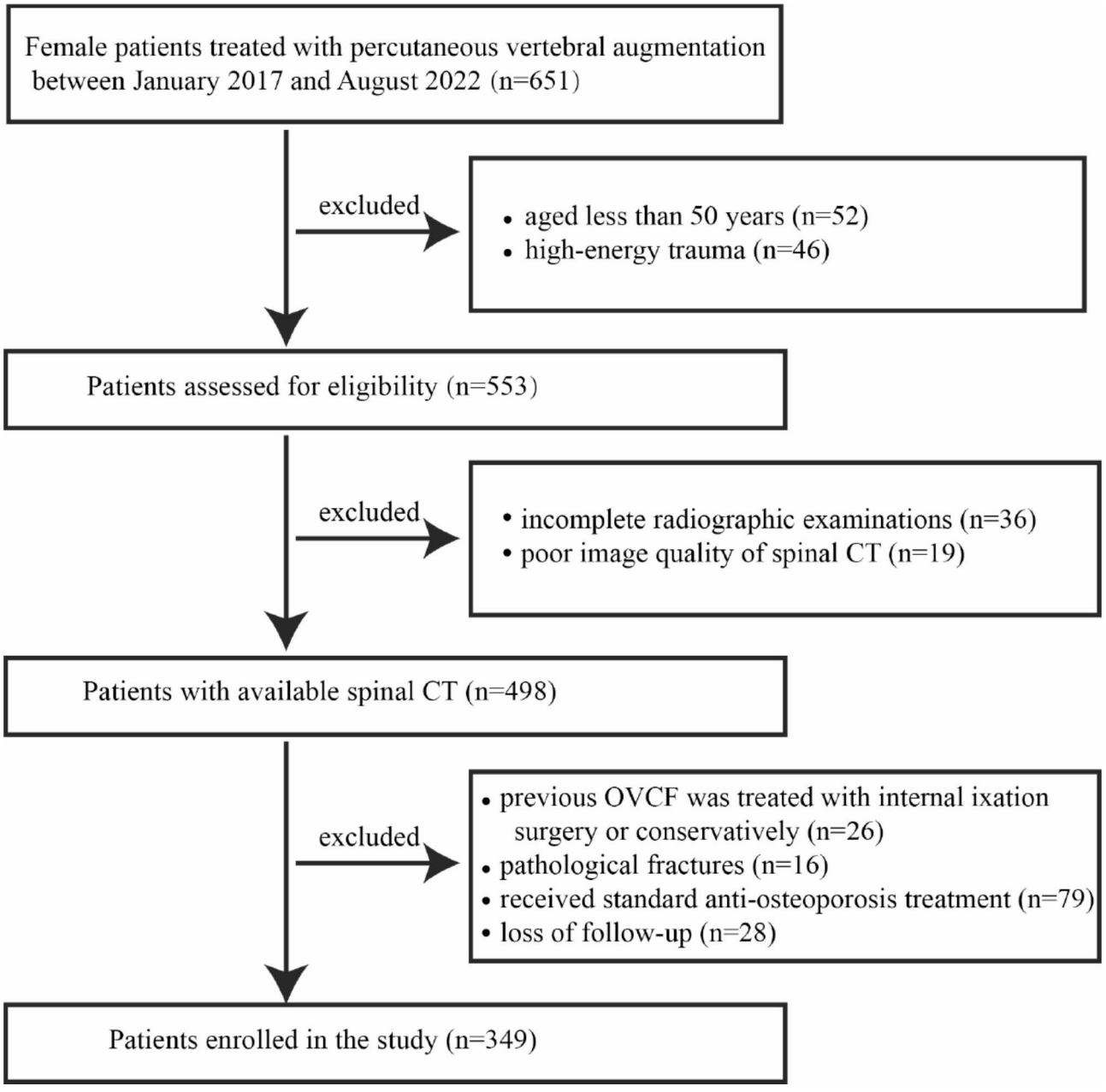

Fig. 2 Flowchart of patient selection in the study

in the sagittal and coronal images using the Tissue Segmentation tool. Third, we used the Draw ROIs tool to limit the boundary to the cancellous bone area in the axial image. Expand the boundary to the greatest extent practicable while excluding cortical bone. Fourth, it was changed to "body" in the "present" option. Finally, after the new three-dimensional image was generated, the average HU value of the entire three-dimensional model was automatically read, and this value was the 3D-HU (Fig. 3). In this study, we measured the 3D-HU of the L1-4 vertebrae and derived the mean value. Two senior spine surgeons independently evaluated the 3D-HU.

HU values measurements

Through IntelliSpace Portal 9.0 (Philips Company, Netherlands), the mean HU value of the L1-4 vertebral bodies was measured using the previously described method [23]. The HU value was measured on the CT axial image. The elliptical region of interest (ROI) containing only the cancellous bone area was located below the upper endplate, in the middle of the vertebral body, and above the lower endplate (Fig. 4). The average HU value of the three ROIs was the vertebral HU value.

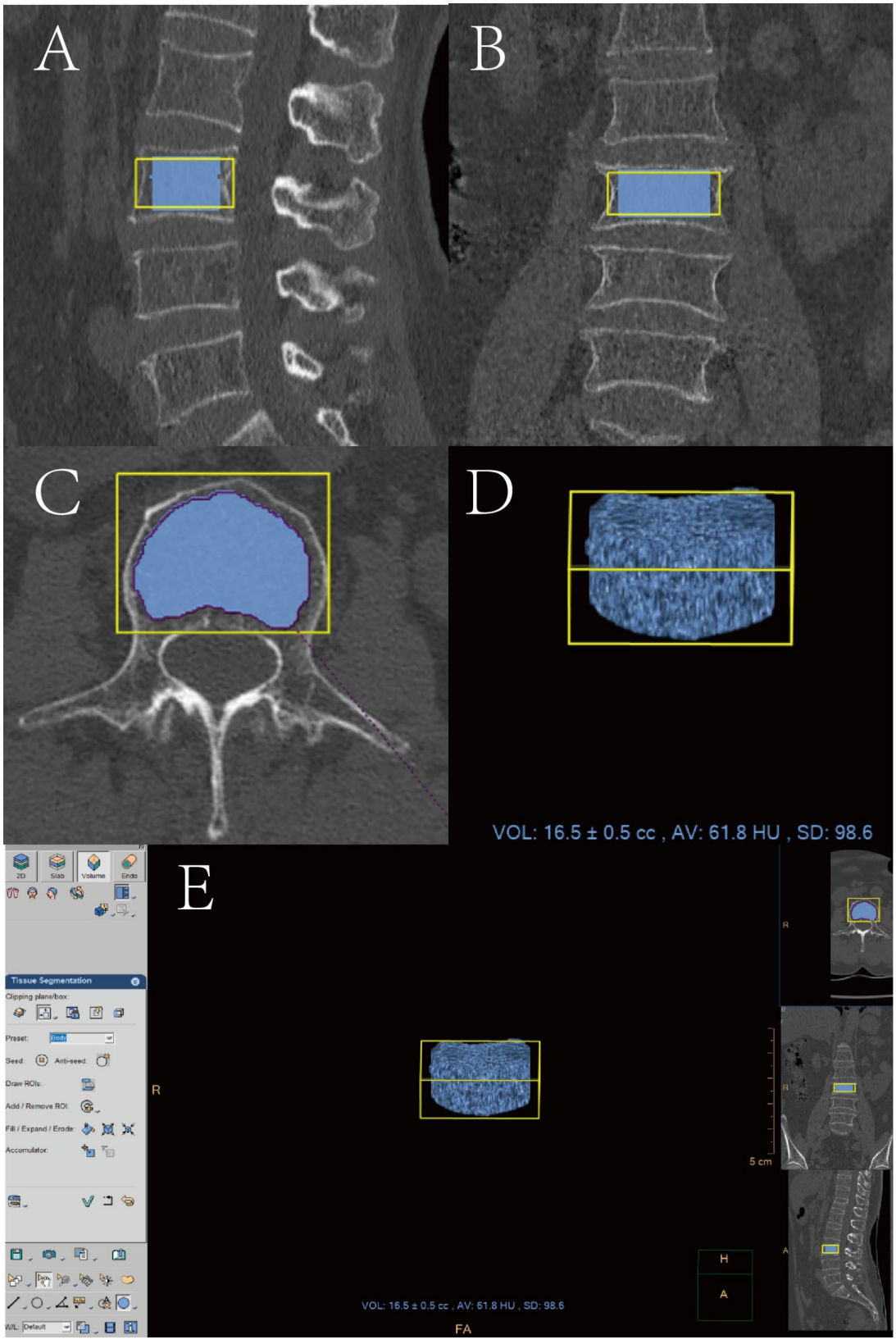

Fig. 3 3D-HU was measured on CT scans (**A-E**). (**A**, **B**) the upper and lower borders were limited to the cancellous bone region in the sagittal and coronal images using the Tissue Segmentation tool. (**C**) Used the Draw ROIs tool to limit the boundary to the cancellous bone area in the axial image. (**D**) Automatically read the average HU value over the entire three-dimensional model, which was 3D-HU. (**E**) Summary of 3D-HU measurement process

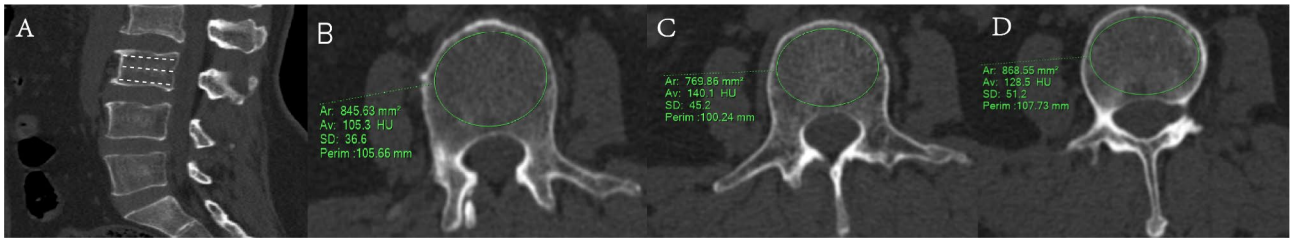

Fig. 4 HU value was measured on CT scans by the largest elliptical region of interest. (**A**) CT sagittal image shown the positions of the 3 slices. (**B**) Inferior to the upper endplate. (**C**) The middle of the body. (**D**) Superior to the inferior endplate

Table 1 Comparison of demographic and clinical characteristics between the NVF group and the without NVF group

Variables	With NVF ($n=61$)	Without NVF ($n=288$)	*P* Value
Age, years	74.75 ± 8.45	69.44 ± 8.86	**< 0.001**
BMI, kg/m^2	23.33 ± 4.24	23.51 ± 3.34	0.719
History of hypertension, n (%)			0.268
Yes	31 (50.8)	124 (43.1)	
No	30 (49.2)	164 (56.9)	
History of diabetes, n (%)			0.222
Yes	6 (9.8)	46 (16.0)	
No	55 (90.2)	242 (84.0)	
Location of treated vertebrae, n (%)			0.106
TL junction	47 (77.0)	246 (85.4)	
Non-TL junction	14 (23.0)	42 (14.6)	
Multiple vertebral fracture, n (%)			**< 0.001**
Yes	16 (26.2)	13 (4.5)	
No	45 (73.8)	275 (95.5)	
Surgical procedure, n (%)			0.714
PKP	9 (14.8)	48 (16.7)	
PVP	52 (85.2)	240 (83.3)	
BMD T-score	-3.23 ± 1.18	-2.62 ± 1.13	**< 0.001**
HU value	34.46 ± 23.44	68.15 ± 28.00	**< 0.001**
3D-HU	40.64 ± 22.43	79.93 ± 25.69	**< 0.001**

NVF, new vertebral fracture; BMI, body mass index; TL junction, the treated vertebrae located at the level of T12–L2; HU, Hounsfield unit; 3D-HU, three-dimensional Hounsfield unit;

P < 0.05 was considered statistically significant

Statistical analysis

In this study, statistical analysis and plotting of statistics was conducted with SPSS 27 (IBM Corporation, Armonk, New York, USA) and GraphPad Prism 9.5 (GraphPad Software, San Diego, California, USA). Quantitative parameters are expressed as the mean ± SD and were statistically analysed using Student's t test or the Mann–Whitney U test. As for qualitative variables, they are reported as frequency and percentage and evaluated using the chi-square test or Fisher's exact test. Variables that showed statistical significance in the univariate analysis were included in a multivariate logistic regression analysis used to identify risk factors for NVF following PVA. Pearson correlation was used to determine the relationship between the 3D-HU and BMD T-score. The interobserver reliability of the 3D-HU measurement was evaluated by intraclass correlation coefficient (ICC). Generally, when ICC ≥ 0.75, it indicates good reliability. The area under the Receiver Operating Characteristic (ROC) curve was used to assess the diagnostic efficiency for predicting the development of NVF. The optimal cut-off value was determined using the highest Youden index. The *P* value < 0.05 was considered to indicate statistical significance.

Results

A total of 349 women were included in this study. Patient-related information are shown in Table 1. Of the 349 patients, 61 cases had an NVF after the initial PVA, while 288 participants did not. The NVF group had an average age of 74.75 ± 8.45 years and a average BMI of 23.33 ± 4.24. Among them, 47 (77.0%) patients underwent PVA at TL junction, and 16 patients (26.2%) experienced multiple vertebral fractures. In the 61 patients, the mean 3D-HU was 40.64 ± 22.43, the average HU value was 34.46 ± 23.44, and the average BMD T-score was − 3.23 ± 1.18. Of the NVF group, 9 (14.8%) cases underwent percutaneous kyphoplasty (PKP), and 52 (85.2%) patients were performed with percutaneous vertebroplasty (PVP). Compared with without NVF group, the age and incidence of multiple vertebral fracture in NVF group were significantly higher ($p < 0.001$; $p < 0.001$), while the HU value, 3D-HU and BMD T-score were significantly lower ($p < 0.001$; $p < 0.001$; $p < 0.001$). Other demographic data showed no significant differences (all $p > 0.05$) (Table 1). In the validation study, the ICC for the 3D-HU demonstrated excellent performance (ICC = 0.955).

The 3D-HU and BMD T-score correlation

According to the Pearson correlation test, the vertebral 3D-HU showed a highly positive correlation with the BMD T-score ($r = 0.628$, $p < 0.001$); similarly, the HU value was moderately positively correlated with BMD T-score ($r = 0.570$, $p < 0.001$) (Fig. 5A, B).

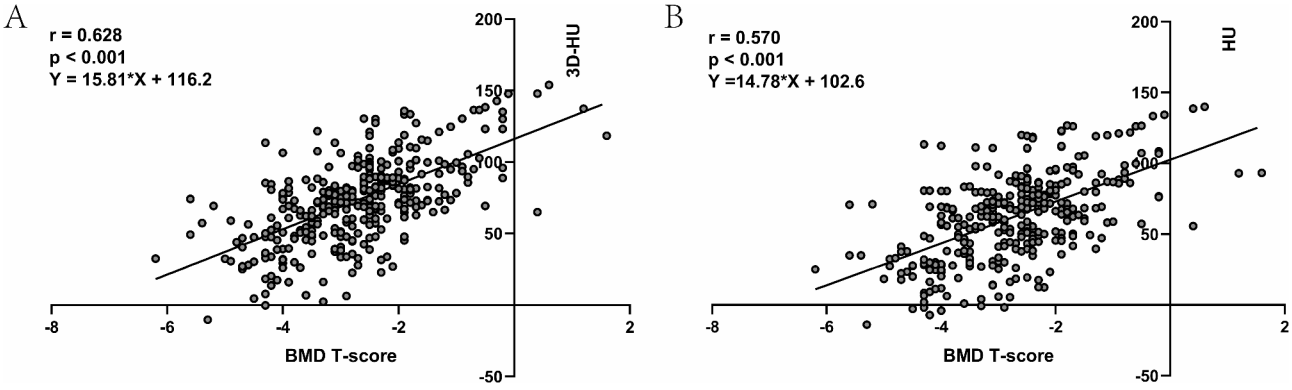

Fig. 5 (**A**) Correlation between 3D-HU and BMD T-score. (**B**) Correlation between HU value and BMD T-score

Table 2 Multivariate logistic regression analyses to evaluate the important risk factors of new vertebral fracture

Variables	Odds ratio	95% CI	*P* Value
Age	0.964	0.918–1.010	0.131
Multiple vertebral fracture	1.136	0.439–2.829	0.787
3D-HU	0.927	0.906–0.945	**< 0.001**

3D-HU, three-dimensional Hounsfield unit; CI, confidence interval.*P* < 0.05 was considered statistically significant

Table 3 The ROC curve analysis of 3D-HU and HU value for predicting the occurrence of NVF

Variables	Cut-off	Sensitivity	Specificity	AUC (95% CI)	*P* value
3D-HU	56.3	0.803	0.847	0.877 (0.831–0.923)	**< 0.001**
HU value	51.4	0.820	0.747	0.823 (0.769–0.876)	**< 0.001**

3D-HU, three-dimensional Hounsfield unit; HU, Hounsfield unit;

ROC, receiver operating characteristic; AUC, area under curve; CI, confidence interval.*P* < 0.05 was considered statistically significant

Factors predicting NVF following PVA

Multivariate regression analyses were used to identify potential predictive risk factors for NVF after PVA in postmenopausal women (Table 2), and the only significant predictor identified was the 3D-HU (OR = 0.927; 95%CI = 0.906–0.945; $p < 0.001$). In multiple studies, BMD T-score and HU value have been proven to be effective predictors of NVF after PVA [17, 24]. However, in this study, our aim was solely to compare the predictive capabilities of HU value and 3D-HU, as well as to explore the correlation between BMD T-score and 3D-HU. Therefore, we did not include HU value and BMD T-score to reduce their impact on the results of the multivariate logistic regression analysis.

Assessment of predictive value

ROC curves for 3D-HU as a predictor of NVF were constructed and compared to HU value. The area under the curve (AUC) for 3D-HU was 0.877 (95%CI = 0.831–0.923, $p < 0.001$), and the cutoff value was 56.3 (specificity 0.847; sensitivity 0.803) determined through the highest Youden index, while the area under the curve (AUC) for the HU value was 0.823 (95%CI = 0.769–0.876, $p < 0.001$), and the threshold value was 51.4 (specificity 0.747; sensitivity 0.820) (Table 3; Fig. 6A, B).

Discussion

Currently, PVA is a common procedure for OVCF, with the advantages of being minimally invasive, providing rapid pain relief, and most importantly, reducing mortality [25]. Nevertheless, a significant percentage of postmenopausal women develop the NVF after PVA [12–15]. NVF causes severe multiple traumas and heavy financial burden to patients, which is a major problem for orthopedic surgeons. In this study, we developed a novel CT-based assessment of BMD and demonstrated that the vertebral 3D-HU significantly predicted NVF after PVA in postmenopausal women and was superior to the HU value.

The predictors of NVF after PVA

In this study, the incidence of NVF following PVA was 17%, which was greater than that of Cheng' s study [24]. The discrepancy may be attributed to the difference in the mean age of patients across studies, which may be a key factor. In our study, the mean age was 70.37 ± 9.01 years, and a relatively high age could explain the high NVF rate. Additionally, one possible explanation for the high rate of NVF in this study was that the patient population did not receive normal anti-osteoporosis medication.

In postmenopausal women with OVCF, age was considered the risk factor associated with NVF following PVA [26]. Qian et al. [27] reported, however, that logistic regression analysis revealed no statistical difference according to age. This is consistent with our findings. Our study reveals that patients in the NVF group have a greater average age compared with the control group. But, according to the multivariate logistic regression

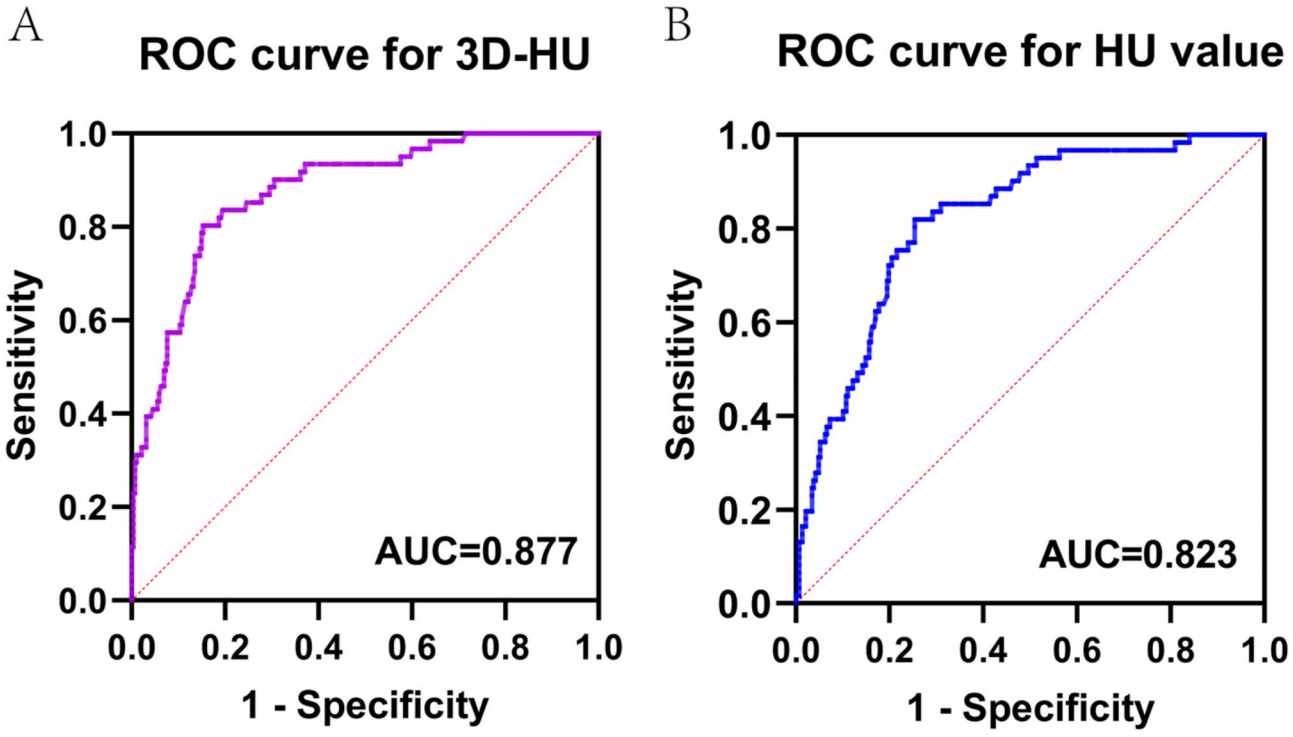

Fig. 6 (**A**) ROC curve of 3D-HU. (**B**) ROC curve of HU value

analysis, age was not an independent predictor of NVF after PVA. Due to the limited sample size and retrospective design, our study may carry a risk of bias.

Multiple vertebral fractures in the first OVCF are considered a risk factor for new OVCF after PVA [17]. However, some studies suggest that the occurrence of NVF after PVA was not related to the number of initial OVCF [28]. In this study, the incidence of multiple vertebral fractures was significantly higher in the NVF group than in the without NVF group. However, multivariate logistic regression analysis confirmed that multiple vertebral fractures were not an independent predictor in the development of NVF after PVA. The reason could be that osteoporosis patients are more prone to multi-segmental fractures, but there aren't many of them. Most studies consider BMD to be the foremost factor contributing to the occurrence of NVF after PVA. A retrospective study was carried out to explore the risk factors for NVF after PVA and demonstrated that low BMD was closely related to NVF [17]. The analysis by Dai et al. [29] also reached the same conclusion. Although DEXA is regarded as the gold standard for evaluating BMD by the WHO, the T-score measured with DEXA is inevitably affected by vessel wall calcification, implants, etc.

Quantitative computed tomography (QCT) is another commonly used clinical test for bone mineral content [18]. Because QCT measures the amount of bone mineral per unit volume of vertebral body, it is unaffected by osseous and aortic calcification [30]. Many studies have shown that QCT is more accurate than DEXA in measuring bone mineral density [31–33]. The application of QCT in screening and opportunistic measurement of osteoporosis is, however, limited because of the increased radiation exposure to patients, the need for specialist equipment, and post-processing software [34].

Recently, HU value as a measurement of BMD has been used increasingly in NVF risk assessment [24]. Vertebral HU value adequately reflects bone mass levels within cancellous bone, and its validity has been confirmed by many studies [20–22]. Spinal CT is a routine preoperative test for OVCF, therefore, the HU value has great clinical significance.

3D-HU predicts NVF after PVA

Currently, a growing number of researchers are interested in using the HU value to assess BMD [18, 19]. Similarly, the relationship between bone mass-related parameters and NVF after PVA is gradually gaining more attention. However, according to the previously mentioned methods, an accurate vertebral HU value could not be obtained [35]. Inspired by QCT volumetric BMD, we have searched for an innovative measurement method and introduced a novel index, the three-dimensional Hounsfield unit value (3D-HU). In this study, we demonstrated that the new vertebral 3D-HU has excellent predictive value for NVF following PVA in postmenopausal women. When the vertebral 3D-HU is smaller than 56.3, the risk of NVF after PVA will be significantly higher. At

the same time, we demonstrated that vertebral 3D-HU has a stronger predictive power than HU value. Thus, vertebral 3D-HU is useful in assessing the immediate risk of NVF after PVA and has great potential to become a tool in clinical practice.

The significance of the 3D-HU is as follows: (1) It provides a new and more accurate way to predict NVF after PVA in postmenopausal women; (2) It confirms that it is feasible to measure CT-based three-dimensional HU values.

Key findings of this study

To the authors' knowledge, this is the first study to develop the 3D-HU for the vertebral cancellous bone. Our findings indicated a highly positive correlation between 3D-HU and BMD T-score ($r = 0.628$, $p < 0.001$). Moreover, the accuracy of the 3D-HU (87.7%) in predicting NVF following PVA in postmenopausal women was higher than that of the HU value (82.3%).

Limitations

Our study still has some limitations. First, restricted to retrospective studies, as not all patients met the inclusion criteria, which resulted in a more limited sample size. Second, most patients did not have preoperative QCT, and as the more accurate bone mineral density assessment tool available, it is necessary to evaluate the correlation between vertebral 3D-HU and QCT. Third, limited by the available tools, which don' t completely segment the entire cancellous bone region of the vertebrae, we need better post-processing software. Fourth, In this study, adjacent vertebral fractures (AVF) were included in the definition of NVF. Although abundant research indicates that the AVF is closely related to osteoporosis, the changes in local mechanical conditions caused by bone cement cannot be ignored. In the future, we plan to specifically conduct research on the population with the AVF, focusing on the impact of bone-cement-related parameters and 3D-HU on this complication. Finally, despite keeping imaging equipment as consistent as possible, scanning results may still vary; therefore, multicenter, prospective studies are needed to confirm the validity of vertebral 3D-HU in predicting NVF after PVA.

Conclusion

In summary, we introduced a novel CT-based bone mineral density assessment. Lower vertebral 3D-HU was an independent risk factor for NVF following PVA in postmenopausal women. In addition, vertebral 3D-HU had better predictive power than HU values. Given the availability of pre-operative CT, 3D-HU assessment prior to PVA may provide insight into a patient' s risk for NVF.

Abbreviations

OVCF	Osteoporotic vertebral compression fracture
PVA	Percutaneous vertebral augmentation
DEXA	Dual-energy X-ray absorptiometry
QCT	Quantitative computed tomography
NVF	New vertebral fracture
BMD	Bone mineral density
3D-HU	Three-dimensional Hounsfield unit
PKP	Percutaneous kyphoplasty
PVP	Percutaneous vertebroplasty
ICC	Intraclass correlation coefficient

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Author contributions

R.C. and L.C. conceived and designed the study. R.C. and Z.W. collected the data. Y.W. and R.M. performed the 3D-HU measurement. R.C. and R.L. analyzed the data. F.C. and Y.Y. designed the figures. R.C. and Z.G. wrote the manuscript. All authors reviewed and revised the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was performed according to the Helsinki Declaration and approved from the Institutional Review Board of the People's Hospital of Ningxia Hui Autonomous Region, Ningxia Medical University (2024-LL-169) where the experiment was performed.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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