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RESEARCH

# Poor bony density can independently trigger higher incidence of adjacent vertebral fracture after percutaneous vertebralplasty: a mono-center retrospective study

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## Abstract

**Objective** Symptomatic adjacent vertebral fractures (AVF) poses a challenge to patient prognosis in osteoporotic vertebral compressive fractures (OVCF) treated by percutaneous vertebralplasty (PVP). This study aimed to identify potential risk factors for AVF, thereby offering theoretical insights for refining patient management strategies and surgical protocols.

**Methods** Clinical data of PVP patients treated between March 2018 and May 2020 were retrospectively analyzed, with an average follow-up period of 30 months. Patients were stratified into two groups based on the presence or absence of recurrent symptomatic AVF. Demographic characteristics and imaging based parameters were assessed to identify potential risk factors for AVF.

**Results** Demographic parameters, including age, sex, body mass index, and fracture location (junctional or non-junctional), did not significantly differ between the two groups and were not found to be independent risk factors for AVF. However, patients with AVF exhibited significantly lower bone mineral density, as assessed by T-score and Hounsfield unit (HU) values. Notably, lower HU values emerged as an independent risk factor for AVF. Contrary to expectations, larger vertebral distraction and intervertebral disc cement leakage did not trigger higher incidence of AVF.

**Conclusion** Progression of bony density reduction emerged as the primary driver for the heightened incidence of AVF. Accordingly, anti-osteoporosis therapy should be regarded as an effective strategy for mitigating the risk of AVF in patients undergoing PVP.

**Keywords** Osteoporotic vertebral compressive fracture · Percutaneous vertebralplasty · Adjacent vertebral fracture · Intervertebral cement leakage · Hounsfield unit value

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## Introduction

As the global demographic shifts towards an increasingly aging population, there has been a concomitant rise in the prevalence of osteoporotic vertebral compressive fractures (OVCF) [1, 2], presenting a substantial burden to healthcare systems and economies worldwide. Among the array of surgical interventions developed for the management of OVCF, percutaneous vertebroplasty (PVP) remains the predominant technique due to its proven efficacy in alleviating pain, facilitating early mobilization, and enhancing patient rehabilitation [3, 4]. Despite its widespread application, the rapid escalation in PVP procedures has been paralleled by an uptick in reports of adjacent vertebral fractures (AVF), a complication that precipitates recurrent severe back pain and exacerbates spinal sagittal imbalance, thereby compromising the long-term outcomes for patients with OVCF [5, 6].

The reported incidence of AVF post-PVP exhibits significant variability across studies, with rates ranging from 3% to over 50% [7, 8]. This discrepancy underscores the complexity of identifying definitive risk factors for AVF, amidst conflicting evidence. Demographic factors such as age, sex, body mass index (BMI), and the specific location of the fracture (e.g., junctional position between thoracic vertebra 11 and lumbar vertebra 1 [T11-L1], versus non-junctional positions) have been implicated as potential contributors to AVF risk [9, 10]. Conversely, other research challenges the significance of these variables. Furthermore, there is debate regarding the biomechanical impacts of vertebral height and kyphotic angle restoration post-PVP; while some studies suggest that greater restoration may elevate AVF risk through increased strain on surrounding soft tissues, others argue that insufficient correction of vertebral height and sagittal alignment exacerbates local load transmission, thereby heightening AVF susceptibility [9, 11]. Notably, intervertebral cement leakage has emerged as a contentious factor; while some evidence suggests it acts as a catalyst for AVF, prompting consideration for prophylactic vertebroplasty of adjacent vertebral bodies, other findings downplay its influence on AVF incidence [2, 12].

This study aims to elucidate the impact of these contested factors on AVF risk through a comprehensive review of clinical and imaging data from patients treated with PVP at a single center. By dissecting the relationship between these variables and AVF occurrence, we aspire to furnish theoretical insights that will inform the refinement of treatment protocols for OVCF, ultimately ameliorating patient prognoses and minimizing the incidence of AVF.

## Methods

### Patient data collection

The clinical data of OVCF patients treated using PVP from March 2018 to May 2020 were reviewed in the study. The patients' average follow-up period was nearly 30 months. A senior spine surgeon performed all the PVP procedures. The demographic data were recorded, which included patients' age, sex, BMI and fracture positions (Junction position (T11-L1) or Non-junction position).

The patient inclusion criteria were as follows: (1) The patients who experienced severe back pain due to acute (<2 weeks) or subacute (between 2 and 8 weeks) OVCF; (2) the patients with complete medical records and related radiographic data; (3) the patients with a follow-up of nearly 30 months and with complete clinical data. The exclusion criteria for the patients were as follows: (1) the presence of a n eurological deficit; (2) pathological vertebral fractures caused by malignancies or infections; (3) unstable fractures; (4) loss of follow-up; (5) incomplete imaging data (Fig. 1) [4, 13, 14].

### Radiographic data measurement

Radiographic evaluation was conducted by a senior spine surgeon. The diagnosis of AVF was determined based on following criteria: recurrent low back pain accompanied by a hypointense signal on T1-weighted MRI images, a hyperintense signal on Short Tau Inversion Recovery MRI sequences [4, 13]. Patients were divided into two group: With and without AVF. To assess bone mineral density, dual-energy X-ray absorptiometry (DXA) was utilized to measure the T-score, complemented by a quantitative analysis of preoperative CT imaging data to determine Hounsfield unit (HU) values [14, 15]. For HU measurement consistency, CT scans were performed with a tube voltage of 120 kV and a layer thickness of 1 mm, parameters aligned with those employed in analogous studies [16, 17]. The region of interest (ROI) for HU assessment was meticulously defined to encompass the largest possible area within the cancellous bone, meticulously excluding cortical bone, bony endplates, osteophytes, and the posterior venous plexus. ROI placement was systematically executed across four planes: the midsagittal, central transverse, proximal to the superior endplate transverse, and proximal to the inferior endplate transverse planes. The mean HU value derived from these planes was designated as the vertebral body's HU value [18, 19], with the average HU value of both the cranial and caudal adjacent vertebral bodies calculated to gauge the HU value of the region proximate to the AVF.

Furthermore, the restoration of vertebral height and kyphotic angle post-PVP were evaluated via preoperative and postoperative lateral radiographs. Measurements of the anterior and posterior edges of the affected vertebral body were conducted to ascertain vertebral height, with the difference in these measurements pre- and postoperatively representing the vertebral height restoration value [11, 20]. Similarly, the alteration in kyphotic angle pre- and postoperatively was quantified to determine the kyphotic angle restoration value [5, 21]. The assessment of intervertebral disc cement leakage was performed through meticulous examination of immediate postoperative lateral radiographs [22, 23]; instances where cement extended beyond the confines of the bony endplate were classified as intervertebral bone cement leakage [9, 24].

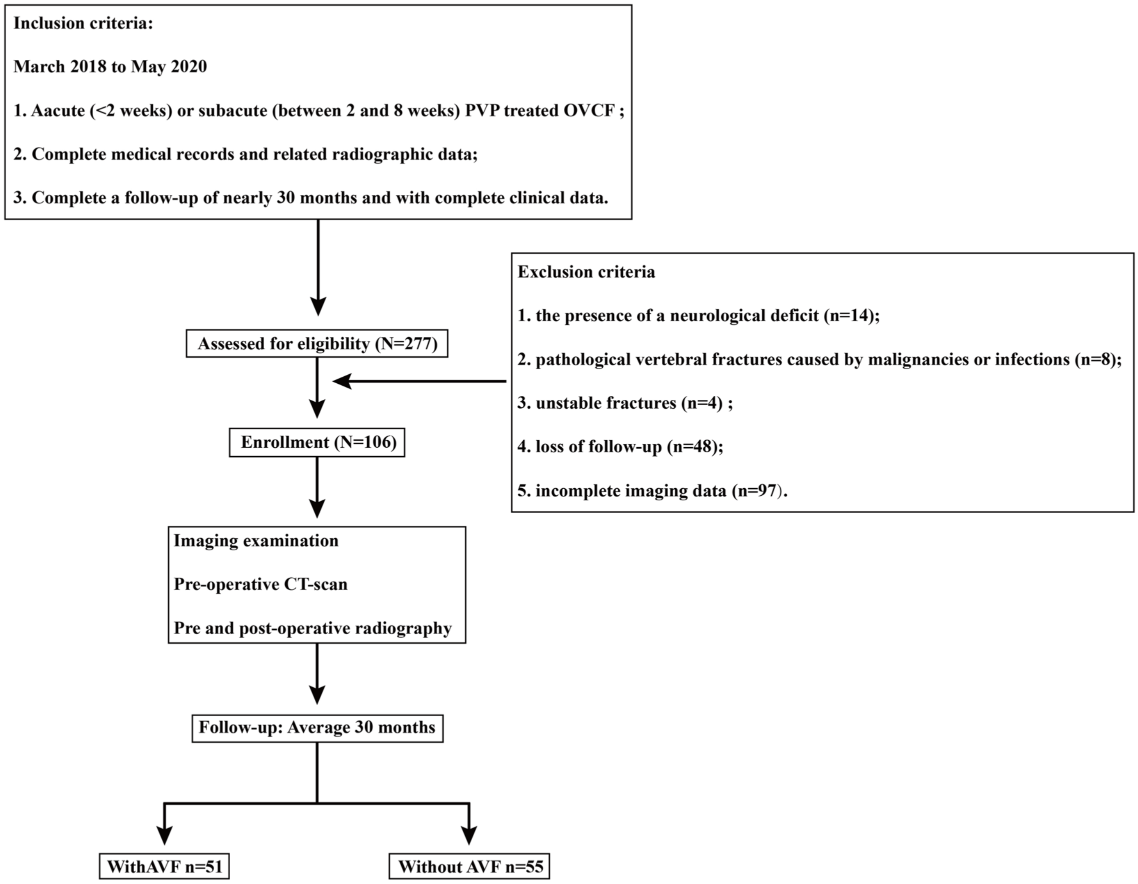


**Fig. 1** Schematic for patient inclusion and exclusion

## Statistical analysis

Indicators were expressed as mean ± standard deviation for continuous variables and number (or percentage) for categorical variables. To evaluate the interobserver and intraobserver reliability, 20 patients were selected randomly, and one week after the measurement of the imaging data, the selected patients were subjected to re-measurement of the same imaging data by a spine surgeon and an experienced radiologist [14, 25]. The intraclass correlation efficiency (ICC) was then computed to determine the repeatability of continuous variables (ICC $\geq$ 0.8 represented excellent reliability), and Kappa values was also computed to determine that of binary variable [26, 27].

When evaluating the effect of intervertebral cement leakage on the risk of AVF, cranial and caudal cement leakage and AVF status were judged separately. In contrast, when evaluating the effect of other variables on the risk of AVF, AVF of cranial and caudal sides were considered together. In this process, when comparing the difference between the groups with and without AVF, an independent-samples Student's t-test was used for continuous variables, while the chi-squared test was used for the categorical variables. A binary logistic regression analysis was performed to identify the independent risk factors for AVF. Univariate analyses were then performed for each of the identified potential risk factors, and the variables that achieved the significance level of $p < 0.1$ were used in the subsequent multivariate analyses. The variables with $p < 0.05$ in the multivariate analysis were considered independent risk factors [28, 29]. Receiver Operating Characteristic (ROC) curve analyses were performed to assess the predictive value of the HU values measured using different methods, and the area under the curve (AUC) was calculated as an indicator of the predictive performance of each imaging based parameters [30, 31].

## Results

### Patient data collection and inter and intra-observer reliability judgement

In this study, we analyzed data from 106 PVP treated OVCF patients, comprising 17 males and 90 females with an average age of 76.12 ± 6.74 years. The incidence rate of AVF

**Table 1** ICC and Kappa values of inter- and intraobserver reliability when measuring imaging based parameters

| | Interobserver | Intraobserver |
|---|---|---|
| IVD cement leakage status | 0.894 | 1 |
| HU values | 0.872 | 0.864 |
| Vertebral height restoration values | 0.896 | 0.901 |
| Kyphotic angle restoration values | 0.832 | 0.863 |

was observed in 48.11% (51/106) of patients. Interobserver and intraobserver reliability was assessed through the calculation of ICC and Kappa values, indicating excellent reliability across measurements (Table 1).

## Significant difference computations

Our analysis revealed no significant differences in demographic parameters (age, sex, BMI) between patients with and without AVF. Similarly, the location of the fracture (junction versus non-junction positions) did not significantly affect the incidence of AVF, aligning with findings from previously published studies. The rate of intervertebral cement leakage and the differences in vertebral height and kyphotic angle restoration post-PVP were also not statistically significant between the two patient groups. Notably, bone mineral density (BMD) measurements were the exception, with patients experiencing AVF exhibiting significantly lower T-scores and HU values (Fig. 2) (Table 2).

## Identification of independent risk factors for AVF

Univariate logistic regression analysis identified BMD measurement parameters (T-score and HU values) as potential predictors of AVF risk, with a P-value < 0.1. Due to a significant correlation between T-score and HU values, indicating collinearity, multivariate logistic regression was deemed inappropriate. HU values, with a $P < 0.05$, were independently associated with AVF, establishing them as a significant risk factor. T-score approached significance, with a P-value of 0.051 (Table 3).

**Table 2** Significant comparison between variates for patients with and without AVF

| | Without AVF | With AVF | *P* value |
|---|---|---|---|
| Age | 75.75 ± 6.12 | 76.74 ± 7.31 | 0.581 |
| Sex (Male / Female) | 7/44 | 10/45 | 0.532 |
| BMI | 21.25 ± 4.58 | 21.73 ± 3.15 | 0.688 |
| T-score | −2.82 ± 0.78 | −2.51 ± 0.77 | 0.045* |
| HU values | 45.93 ± 25.95 | 61.75 ± 28.99 | 0.004** |
| Vertebral height restoration | 2.29 ± 2.63 | 1.98 ± 2.13 | 0.611 |
| Kyphotic angle restoration | −0.41 ± 6.15 | 0.88 ± 4.15 | 0.284 |
| Cement-leakage status (Cranial) | 9/21 | 18/58 | 0.501 |
| Cement-leakage status (Caudal) | 3/19 | 20/64 | 0.303 |
| Fracture position (Junction/No-junction) | 21/30 | 27/28 | 0.413 |

*, statistical significance ($P<0.05$)

**, statistical significance ($P<0.01$)

**Table 3** Logistic regression analysis of AVF

| | OR | 95% CI | | *P* value |
|---|---|---|---|---|
| **Univariate analyses** | | | | |
| **Demographic characteristics** | | | | |
| Age | 1.016 | 0.96 | 1.076 | 0.577 |
| Sex (Male / Female) | 0.716 | 0.25 | 2.049 | 0.533 |
| BMI | 1.035 | 0.88 | 1.216 | 0.68 |
| Fracture position (Junction/ No-junction) | 1.248 | 0.582 | 2.678 | 0.57 |
| **BMD measurement methods** | | | | |
| T-score | 1.698 | 1 | 2.882 | 0.051# |
| HU values | 1.021 | 1.006 | 1.036 | 0.006#,* |
| **Operation-related parameters** | | | | |
| Vertebral height restoration | 0.944 | 0.759 | 1.174 | 0.604 |
| Kyphotic angle restoration | 1.052 | 0.961 | 1.152 | 0.273 |
| Cement-leakage status (Cranial) | 1.381 | 0.538 | 3.546 | 0.503 |
| Cement-leakage status (Caudal) | 0.505 | 0.135 | 1.886 | 0.31 |

#,variables that achieved a significance level of $p<0.1$ in the univariate analysis

*, statistical significance ($P<0.05$)

## Predictive value of BMD parameters

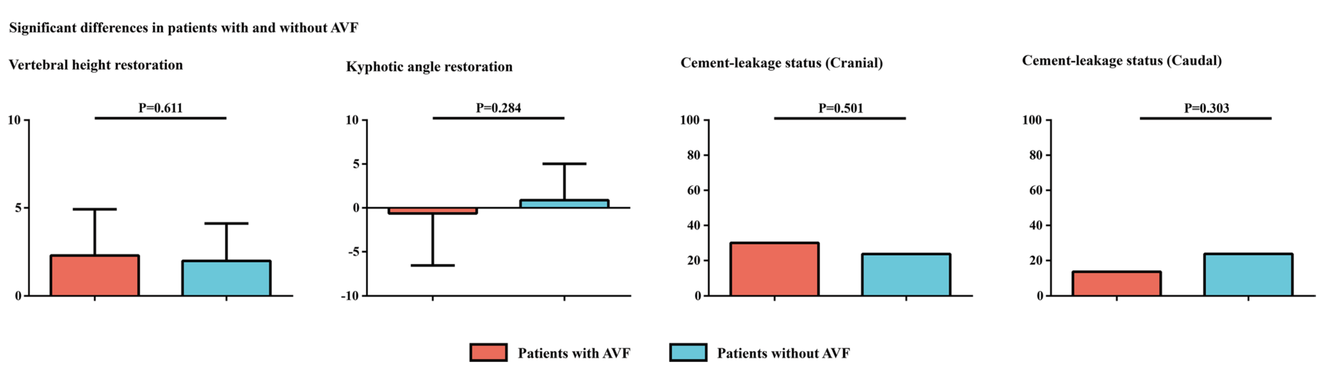


**Fig. 2** Significant differences in intraoperative indicators between the patient groups with and without AVF

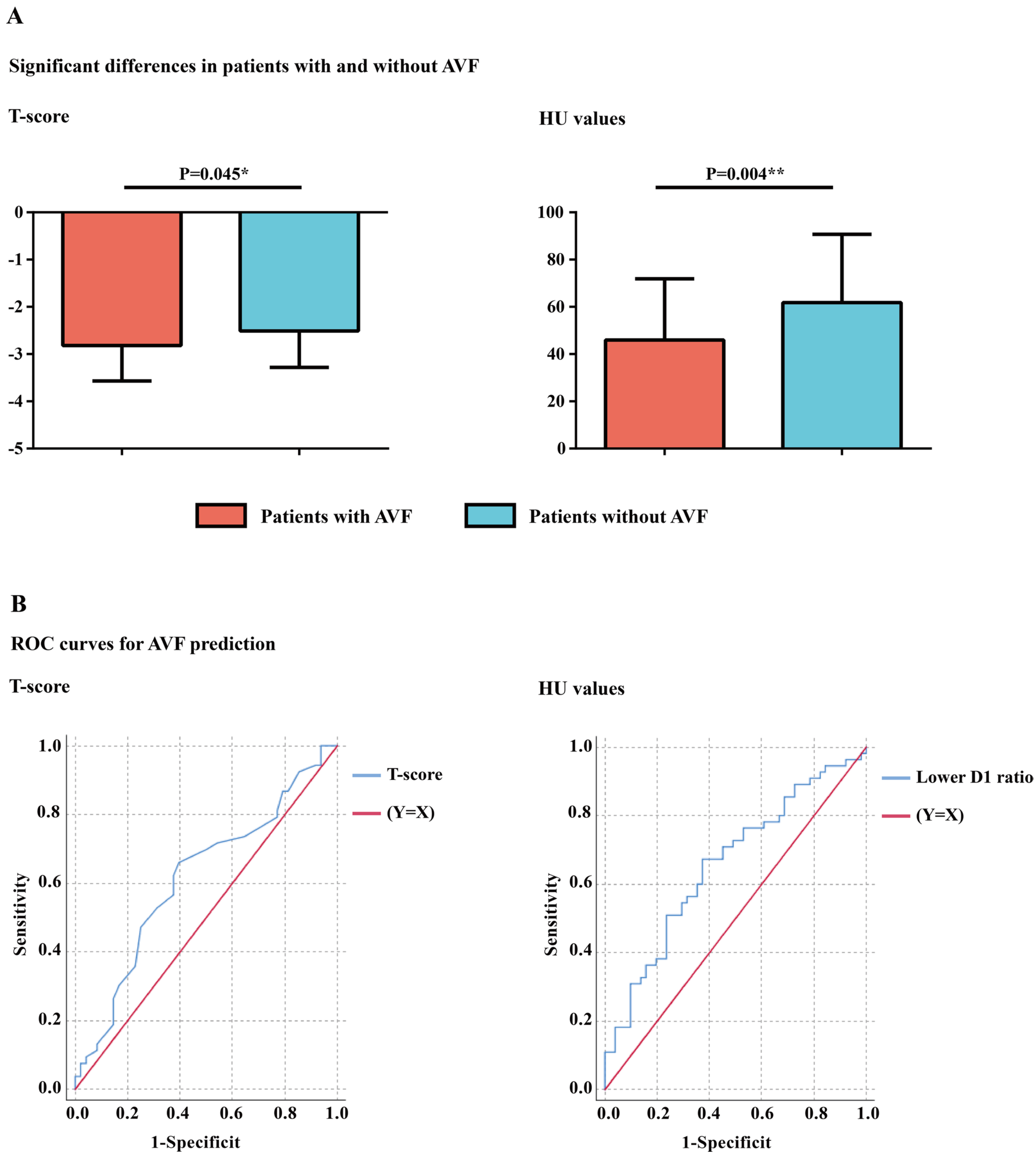


**Fig. 3** Significant differences in BMD measurement parameters between the patient groups with and without AVF, and corresponding ROC curves for AVF prediction

**Table 4** The cut-off value, sensitivity and specificity for AVF

| | T-score | HU values |
|---|---|---|
| Cut-off value | −2.75 | 56.345 |
| Sensitivity | 0.66 | 0.6 |
| Specificity | 0.604 | 0.647 |
| AUC | 0.616 | 0.658 |

ROC curve analysis was conducted to evaluate the predictive value of BMD parameters for AVF. The AUC for HU values was 0.658, and for T-score, it was 0.616, suggesting moderate predictive power (Fig. 3 and Table 4).

## Discussion

AVF emerges as a noteworthy complication in PVP treated patients, potentially precipitating a recurrence of clinical symptoms and imposing a significant socio-economic burden. Identifying the determinants of AVF is imperative for refining management strategies for OVCF patients. Our study highlights a comparably elevated AVF incidence, possibly attributed to the extended follow-up duration of 30 months, surpassing that of most extant literature [13, 32]. Contrary to previous findings, our investigation reveals no significant correlation between vertebral body distraction post-fracture and the risk of AVF. Notably, the restoration of vertebral height and kyphotic angle did not markedly influence AVF incidence, underscoring their negligible role as independent risk factors. This outcome may be ascribed to the exclusive employment of PVP in our patient cohort, a technique known for its limited distraction [33, 34]. Consequently, our findings indicate that minor vertebral distractions achieved through PVP do not significantly affect the risk of adjacent vertebral fractures (AVF). However, we acknowledge that the current conclusions cannot be directly extrapolated to cement augmentation techniques involving more pronounced vertebral distraction, such as percutaneous kyphoplasty (PKP) and vertebral body stenting (VBS). In other words, the implications of relatively large vertebral distractions in PKP or VBS procedures warrant further investigation in future studies.

Studies present that inervertebral cement leakage is an independent risk factor for AVF. From a biomechanical perspective, adjacent vertebral bodies' stress concentration emerges as a pivotal etiology of AVF [35, 36]. Given the disparity in elastic modulus between polymethylmethacrylate bone cement and the intervertebral disc (IVD), one might hypothesize that cement leakage into the IVD would augment stiffness, thereby elevating AVF risk [37, 38]. Conversely, our study demonstrating that cement leakage does not independently elevate AVF risk, with patients experiencing caudal AVF exhibiting an insignificantly lower incidence of leakage. This contradiction may root in the multifaceted biomechanical interactions within the spinal motion segment. Specifically, local stress distribution on vertebral bodies is affected by several factors, including disc degeneration phenotype (i.e., disc collapse and fibrosis), facet joint osteoarthritis, and even spinal alignment change in both coronal and sagittal plane [39, 40]. Differences in these parameters between the current patient cohort and those with disc cement leakage, who experience a higher incidence of AVF, may lead to varying clinical outcomes regarding whether disc cement leakage can indeed trigger AVF. However, these differences have yet to be elucidated and should be addressed in future studies to provide a coherent explanation for this apparent contradiction.

Furthermore, our analysis indicates significantly lower BMD values in patients with AVF, as measured by T-scores and HU values. However, logistic regression analysis revealed that while T-scores approached significance as an independent risk factor ($p=0.051$), they ultimately did not meet the threshold, potentially due to limited sample size and the inherent limitations of DXA. Specifically, DXA's two-dimensional imaging modality may fail to accurately capture osteoporosis in cancellous bone, essential for spinal load-bearing, particularly in the context of ZJOA-induced osteosclerosis [41, 42]. In contrast, CT-based HU measurements, by focusing on the cancellous bone within a refined ROI, offer superior predictive accuracy for AVF risk [43, 44]. Consequently, we advocate for the substitution of traditional DXA with preoperative CT scans for BMD assessment in OVCF patients, recommending routine HU value measurements to ascertain AVF risk. Regardless of the methodological approach to BMD assessment, the imperative for standardized medical anti-osteoporosis therapy remains undiminished to mitigate AVF risk.

It is crucial to acknowledge the limitations of our study, notably its applicability solely to PVP-treated patients with bilateral punctures. Future investigations should extend to diverse surgical modalities, including unilateral puncture, PKP, and VBS, to comprehensively elucidate the risk factors for AVF. Additionally, the biomechanical underpinnings responsible for the observed clinical phenomena warrant further exploration to substantiate our findings. Moreover, while regular anti-osteoporosis therapy is an effective approach to reducing the incidence of re-fractures, the absence of a standardized treatment protocol for anti-osteoporosis remains a significant limitation of this study. In our forthcoming prospective cohort study, we will meticulously document the subsequent anti-osteoporosis treatment regimens administered to various patients and assess their impact on the risk of AVF. Our aim is to provide a more valuable reference for enhancing patient treatment strategies.

## Conclusions

In conducting a retrospective evaluation of clinical and imaging data from PVP treated OVCF patients, this study elucidates that the progression of osteoporosis singularly precipitates the occurrence of AVF. Consequently, we advocate for the standardization of medical anti-osteoporosis therapy in OVCF patients as a strategic measure to mitigate AVF risk. This approach underscores the necessity for integrating comprehensive osteoporosis management, including pharmacotherapy and lifestyle modifications, into the therapeutic regimen for OVCF patients, thereby enhancing patient outcomes by addressing the root cause of AVF development post-PVP treatment.

**Author contributions** Conception and design: Tao Gao, and Jingchi Li; Acquisition of data: Shengyu Wan, Tao gao, Jian Zhang Hong Li, and Xu Lin; Analysis and interpretation of imaging data: Shengyu Wan, Zichuan Wu, and Jingchi Li; Statistical analysis: Shengyu Wan, and Zichuan Wu; Manuscript Preparation: Shengyu Wan, Zichuan Wu, and Jingchi Li; Manuscript modification: Xu Lin, Tao Gao, and Jingchi Li.

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**Data availability** All the data of the manuscript are presented in the paper.

## Declarations

**Ethics approval and consent to participate** Approval for this study was obtained from the Zigong Fourth People's Hospital (2024-005), informed consent was obtained from all subjects and/or their legal guardian(s).

**Consent for publication** Not Applicable.

**Competing interests** The authors declare no competing interests.



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