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Incidence and risk factors of adjacent vertebral fracture after percutaneous vertebroplasty or kyphoplasty in postmenopausal women: a retrospective study

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Adjacent vertebral fracture (AVF) is a serious complication of percutaneous vertebroplasty (PVP) or kyphoplasty (PKP) for osteoporotic vertebral compression fracture (OVCF). This study aimed to explore the incidence and risk factors of AVF following PVP or PKP in postmenopausal women. The incidence of AVF was determined by spinal radiographic examinations. The potential risk factors of AVF were identified by univariate analysis, followed by multivariate logistic regression analyses to determine the independent risk factors. In total, 674 postmenopausal women who were treated with PVP or PKP from December 2019 to February 2022 were enrolled in the study. Among them, 58 (8.61%) women experienced an AVF following PVP or PKP. After adjusting for confounding factors, BMI (OR [95% CI] 0.863 [0.781–0.952]; p = 0.003), previous history of OVCF (OR [95% CI] 1.931 [1.044–3.571]; p = 0.036), and Hounsfield unit (HU) value (OR [95% CI] 0.979 [0.967–0.990]; p < 0.001) were found to be independent risk factors of AVF following PVP or PKP in postmenopausal women. The ROC analysis revealed that the BMI and HU thresholds were 21.43 and 65.15, respectively. In conclusion, the incidence of AVF was 8.61%. BMI, previous history of OVCF and HU value were independent risk factors of AVF following PVP or PKP in postmenopausal women.

Keywords Osteoporotic vertebral compression fracture, Adjacent vertebral fracture, Percutaneous vertebroplasty, Percutaneous kyphoplasty, Postmenopausal women

Osteoporotic vertebral compression fracture (OVCF) is the most common osteoporotic fracture in elderly individuals, especially in postmenopausal women[1]. In addition, OVCFs are usually caused by low-energy trauma, even a fall or a cough. A series of clinical consequences may occur in patients with OVCFs, such as severe back pain, activity limitations, low quality of life, and even high comorbidity and mortality rates[2–4]. Minimally invasive spinal surgery, such as percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP), has been widely used to relieve clinical symptoms, improve physical function, and enhance quality of life[5,6]. PVP and PKP have been proven to be safe and effective in the treatment of OVCFs[7,8]. Additionally, several studies have demonstrated that PVP and PKP are more cost-effective options for treating OVCFs than conservative medical therapy[9,10].

PVP and PKP have become widely used to treat OVCFs. Consequently, adjacent vertebral fracture (AVF), a severe complication of PVP or PKP, has gradually been reported and aroused increasing concerns[11,12]. Indisputably, AVF has become an urgent and pressing issue that needs to be addressed without delay, placing an enormous burden on patients, society, and the healthcare system. Several studies have shown that some risk factors, including low bone mineral density (BMD), cement volume and bone cement leakage, were associated with AVF following percutaneous vertebral augmentation in elderly individuals[13,14]. However, to our knowledge, the risk factors of AVF after vertebral augmentation in postmenopausal women are still unknown.

The issue of AVF occurrence in postmenopausal women should receive more attention. It is crucial and essential to study the risk factors of AVF following percutaneous vertebral augmentation in postmenopausal

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women. Therefore, we conducted the present study to investigate the associations between risk factors and the occurrence of AVF, to guide orthopedists in clinical decision-making, and to provide researchers with a new perspective for future research, which may reduce the incidence of AVF or even prevent the occurrence of AVF in postmenopausal women following percutaneous vertebral augmentation for OVCFs.

Methods

Study population

A retrospective study was conducted to evaluate postmenopausal women who were treated with PVP or PKP for OVCFs from December 2019 to February 2022 in our hospital. Postmenopausal women who were enrolled in this study were classified into the AVF group and non-AVF group based on the presence or absence of AVF, respectively. The inclusion criteria were as follows: (1) aged 50 years or older; (2) back pain resulting from OVCF; (3) low-energy trauma; (4) fresh OVCF demonstrated by magnetic resonance imaging (MRI); (5) initial OVCF treated with PVP or PKP; (6) complete radiological examinations; and (7) follow-up period exceeding 12 months. The exclusion criteria were as follows: (1) less than 50 years of age; (2) high-energy trauma; (3) initial OVCF treated with pedicle screw fixation; (4) a history of previous spinal surgery; (5) spine vertebral burst fracture; (6) neurological deficiency; (7) pathological fractures; (8) insufficient images; and (9) loss to follow-up. In accordance with the Helsinki Declaration, this study was approved by our institution's Ethics Committee. Informed consent was obtained from all participants before enrollment in the study.

Data collection

Among the demographic variables collected from electronic medical records were age, body mass index (BMI), history of hypertension, history of diabetes, tobacco use, alcohol use, steroid medication, bisphosphonate therapy, previous history of OVCF, and duration of follow-up. Radiographic examinations or electronic medical records were used to obtain surgery-related parameters, including fracture location, number of fractured vertebrae, operative method, cement volume, cement distribution pattern, cement leakage and intradiscal cement leakage. Zoledronic acid, a bisphosphonate drug, was administered intravenously at a dose of 5 mg for at least 15 min. Computed tomography (CT) scanning was used to measure radiographic data, also known as Hounsfield unit (HU) value. CT scanning was performed by a General Electric 128-slice CT scanner (General Electric Company, USA) with the following parameters: a scanning tube voltage of 120 kV, a scanning tube current of 500 mA, and a scanning thickness of 1 mm. A previous history of OVCF indicated that the patient had one or more vertebral compression fractures before the initial PVP or PKP procedure. Fracture locations were categorized into three types according to the vertebral fracture segments: the thoracolumbar (TL) junction, where all fractured vertebral segments were located between the T11 and L2 vertebrae; the non-TL junction, where none of the fractured vertebral segments were located between the T11 and L2 vertebrae; and the non-TL + TL junction, where the fractured vertebral segments were partially located between the T11 and L2 vertebrae and partially not located between the T11 and L2 vertebrae. The number of fractured vertebrae was counted before the first PVP or PKP surgery. PVP and PKP are the two operative methods used for the treatment of OVCFs. The trabecular type and compact type were the two cement distribution patterns based on plain films. Cement leakage and intradiscal cement leakage were observed via X-rays or CT scans. The HU value was used to evaluate BMD and was measured on the axial CT scan via the elliptical region of interest (ROI). The locations of the elliptical ROIs were inferior to the superior endplate, middle of the vertebrae and superior to the inferior endplate of the L1 vertebrae. If the L1 vertebra was fractured, the HU value was measured in a vertebra adjacent to the L1 vertebral body. All data were recorded and measured based on electronic medical records and radiographic examinations of the first hospitalization. Radiographic examinations were carried out on all patients before and after surgery. Figures 1 and 2 illustrate representative patients who were treated with PVP and PKP surgery.

Statistical analysis

In this study, statistical analysis was conducted with SPSS 24 (IBM Corporation, Armonk, New York, USA). For quantitative parameters, the mean and standard deviation are shown, while for qualitative variables, the frequency and proportion are expressed. Univariate analysis and multivariate logistic regression analysis were performed to determine the risk factors for AVF following PVP or PKP. In the univariate analysis, Student's t test or the Mann–Whitney U test was performed to compare continuous variables, while the chi-square test or Fisher's exact test was carried out to compare categorical parameters. A multivariate logistic regression analysis model was constructed based on variables with p-values < 0.05 obtained from univariate analysis. Then, multivariate logistic regression analysis was performed to determine the independent risk factors. Furthermore, receiver operating characteristic (ROC) curves were constructed to assess the diagnostic efficiency for predicting the development of AVF. The cutoff value was calculated by the highest Youden index. A p value < 0.05 was considered to indicate statistical significance.

Results

Six hundred and seventy-four women participated in the study. Of the 674 women, 58 patients had an AVF following initial PVP or PKP, accounting for 8.61%, while 616 participants did not. Among the 58 women, the mean age was 73.74 ± 7.94 years, the average HU value was 49.86 ± 22.22, and the average BMI was 21.48 ± 2.71 kg/m^2. Twenty women (34.5%) had a previous history of OVCF. In the AVF group, 40 (69.0%) patients underwent PVP, and 18 (31.0%) patients underwent PKP. Thirteen (22.4%) individuals experienced cement leakage, and eleven (19.0%) participants experienced intervertebral disc leakage (Table 1).

According to the univariate analysis, the age of patients in AVF group was greater than that of patients in the non-AVF group, and the difference between the two groups was significant (p = 0.001). The BMI of women with

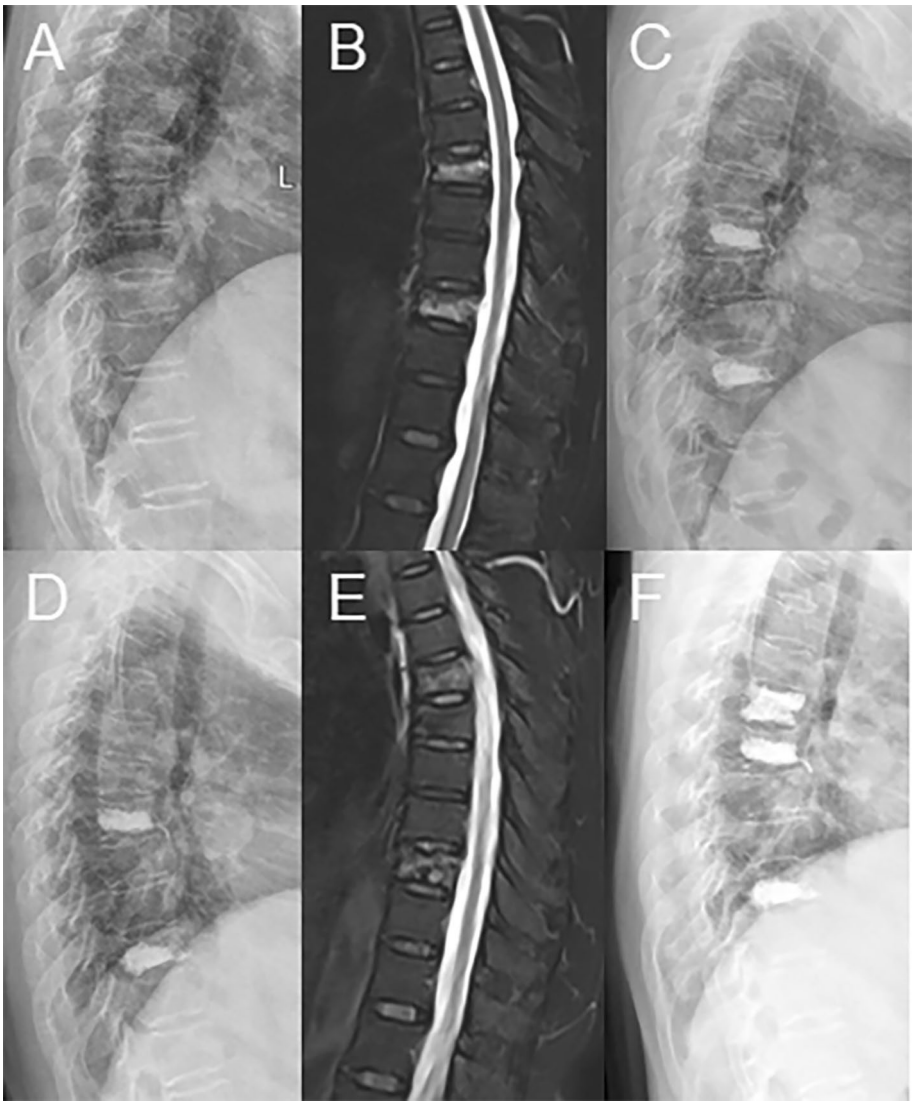

Figure 1. A representative case of AVF following PVP (**A**–**F**). (**A**,**B**) X-ray and MR images showing fractured T7 and T10 vertebrae in a 60-year-old female. (**C**) X-ray revealing that the fractured T7 and T10 vertebrae were treated. (**D**,**E**) X-ray and MR images indicating that the T6 vertebrae fractured three months after surgery. (**F**) X-ray demonstrating that the fractured T6 vertebrae was treated again.

AVF was lower than that of patients without AVF, and there was a significant difference between the two groups ($p < 0.001$). In terms of a previous history of OVCF, a significant difference was detected between the two groups ($p < 0.001$). Patients in the AVF group had lower HU values than those in the non-AVF group ($p < 0.001$). However, no significant differences were observed in the other demographic variables or surgery-related parameters (all $p > 0.05$) (Table 1).

According to the multivariate logistic regression analysis, a low BMI significantly increased the risk of AVF after PVP or PKP (OR [95% CI] 0.863 [0.781–0.952]; $p = 0.003$). A previous history of OVCF was associated with a high odds of AVF (OR [95% CI] 1.931 [1.044–3.571]; $p = 0.036$). The HU value was determined to be an independent risk factor of AVF following PVP or PKP in postmenopausal women (OR [95% CI] 0.979 [0.967–0.990]; $p < 0.001$). However, age was not an independent risk factor of AVF (OR [95% CI] 1.027 [0.991–1.063]; $p = 0.139$) (Table 2).

The ROC analysis revealed that BMI had an area under the curve (AUC) of 0.662 (95% CI 0.590–0.733, $p < 0.001$), with a cutoff value of 21.43 (specificity of 0.747; sensitivity of 0.534), and the HU value had an AUC of 0.712 (95% CI 0.653–0.771, $p < 0.001$), with a threshold of 65.15 (specificity of 0.597; sensitivity of 0.776) (Table 3, Fig. 3).

Discussion

With the widespread application of PVP and PKP surgery, AVF, a severe complication of percutaneous vertebral augmentation for the treatment of OVCFs, has gradually aroused increasing concerns. Consequently, AVF has become a significant health issue that cannot be ignored. Nevertheless, little attention has been given to the

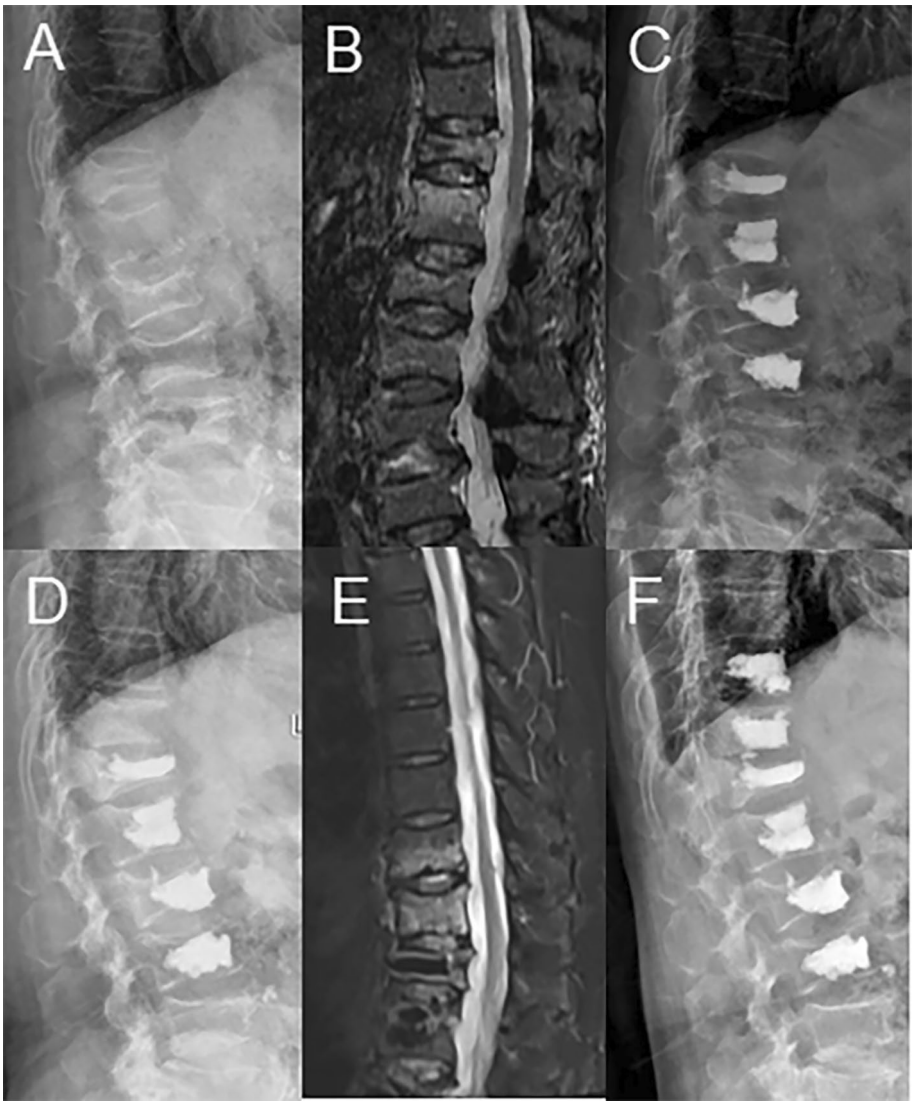

Figure 2. A representative case of AVF after PKP (A-F). (**A**,**B**) X-ray and MR images revealing fracture of the T12-L3 vertebrae in a 73-year-old female. (**C**) X-ray demonstrating that fracture of the T12-L3 vertebrae was treated. (**D**,**E**) X-ray and MR images indicating that the T10 and T11 vertebrae fractured two months after surgery. (**F**) X-ray showing that the fractured T10 and T11 vertebrae were treated again.

occurrence of AVF in postmenopausal women. Therefore, we conducted a retrospective study to identify the associations between risk factors and the occurrence of AVF and to determine the risk factors of AVF following vertebral augmentation for OVCFs in postmenopausal women. In our study, 58 postmenopausal women who experienced AVF after initial PVP or PKP accounted for 8.61% of all patients, which was less than that reported in Li's study[15]. The possible reason was that Li's study included only women who had vertebral fractures in the thoracolumbar junction which was likely to increase the incidence of AVF. According to the results of our study, BMI, previous history of OVCF, and HU value were determined to be independent risk factors of AVF following PVP or PKP in postmenopausal women (Table 4).

Previous studies revealed that age was associated with vertebral fracture in postmenopausal women[16,17]. It should be noted that few articles have reported the risk factors of for new vertebral fractures following vertebral augmentation in postmenopausal women. In a retrospective study, Takahara et al.[18] identified the risk factors of adjacent vertebral collapse following PVP in postmenopausal women. The results of the study indicated that advanced age was associated with an increased risk of new vertebral fractures in postmenopausal women after PVP. However, a retrospective study including 390 patients investigated the correlation between several potential risk factors and new vertebral fractures following PVP after menopause. This study revealed no strong association between age and new vertebral compression fractures in postmenopausal women after PVP[15], which was in consistency with our results. Our study revealed that age was not an independent risk factor of AVF after PVP or PKP in postmenopausal women.

BMI was considered an independent risk factor of AVF following percutaneous vertebral augmentation for the treatment of OVCFs. Previous studies did not support this opinion. Tao et al.[14] retrospectively reviewed

Variables	All patients (n = 674)	AVF group (n = 58)	non-AVF group (n = 616)	*P* Value
Age, years	70.20 ± 8.23	73.74 ± 7.94	69.87 ± 8.18	**0.001***
BMI, kg/m^2	22.99 ± 2.97	21.48 ± 2.71	23.13 ± 2.96	**< 0.001***
History of hypertension, n (%)	230 (34.1)	19 (32.8)	211 (34.3)	0.818
History of diabetes, n (%)	132 (19.6)	9 (15.5)	123 (20.0)	0.414
Tobacco use, n (%)	52 (7.7)	8 (13.8)	44 (7.1)	0.119
Alcohol use, n (%)	6 (0.9)	1 (1.7)	5 (0.8)	1.000
Steroid medication, n (%)	23 (3.4)	4 (6.9)	19 (3.1)	0.250
Bisphosphonate therapy, n (%)	263 (39.0)	22 (37.9)	241 (39.1)	0.859
Previous history of OVCF, n (%)	115 (17.1)	20 (34.5)	95 (15.4)	**< 0.001***
Duration of follow-up, mon	18.85 ± 3.43	19.38 ± 3.42	18.80 ± 3.43	0.219
Fracture location, n (%)				0.569
TL junction	445 (66.0)	35 (60.4)	410 (66.6)	
Non-TL junction	139 (20.6)	13 (22.4)	126 (20.4)	
Non-TL + TL junction	90 (13.4)	10 (17.2)	80 (13.0)	
The number of fractured vertebrae, n (%)				0.177
1	509 (75.5)	38 (65.5)	471 (76.5)	
2	118 (17.5)	14 (24.1)	104 (16.9)	
≥ 3	47 (7.0)	6 (10.4)	41 (6.6)	
Operative method, n (%)				0.540
PVP	488 (72.4)	40 (69.0)	448 (72.7)	
PKP	186 (27.6)	18 (31.0)	168 (27.3)	
Cement volume, ml	4.37 ± 1.01	4.22 ± 0.80	4.38 ± 1.03	0.251
Cement distribution pattern, n (%)				0.481
Trabecular type	469 (69.6)	38 (65.5)	431 (70.0)	
Compact type	205 (30.4)	20 (34.5)	185 (30.0)	
Cement leakage, n (%)	129 (19.1)	13 (22.4)	116 (18.8)	0.507
Intradiscal cement leakage, n (%)	86 (12.8)	11 (19.0)	75 (12.2)	0.138
HU value	68.67 ± 28.36	49.86 ± 22.22	70.44 ± 28.25	**< 0.001***

Table 1. Baseline clinical characteristics and univariate analysis of the variables and AVF. *SVF* subsequent vertebral fracture, *BMI* body mass index, *TL* thoracolumbar, *PVP* percutaneous vertebroplasty, *PKP* percutaneous kyphoplasty, *HU* Hounsfield unit. *P < 0.05 was considered statistically significant.

Variables	B	SE	Wald	OR (95% CI)	*P* value
Age	0.026	0.018	2.188	1.027 (0.991–1.063)	0.139
BMI	− 0.148	0.050	8.563	0.863 (0.781–0.952)	**0.003***
Previous history of OVCF	0.658	0.314	4.397	1.931 (1.044–3.571)	**0.036***
HU value	− 0.022	0.006	13.618	0.979 (0.967–0.990)	**< 0.001***

Table 2. Multivariate logistic regression analysis of the risk factors and AVF. *SVF* subsequent vertebral fracture, *BMI* body mass index, *HU* Hounsfield unit, *B* unstandardized B coefficient, *S.E.* standard error, *OR* odds ratio, *CI* confidence interval. *P < 0.05 was considered statistically significant.

Variables	Cutoff	Sensitivity	Specificity	AUC (95% CI)	P value
BMI	21.425	0.534	0.747	0.662 (0.590–0.733)	**< 0.001***
HU value	65.150	0.776	0.597	0.712 (0.653–0.771)	**< 0.001***

Table 3. ROC curve analysis of BMI and HU value for predicting the occurrence of AVF. *BMI* body mass index, *HU* Hounsfield unit, *ROC* receiver operating characteristic, *AUC* area under curve, *CI* confidence interval. *P < 0.05 was considered statistically significant.

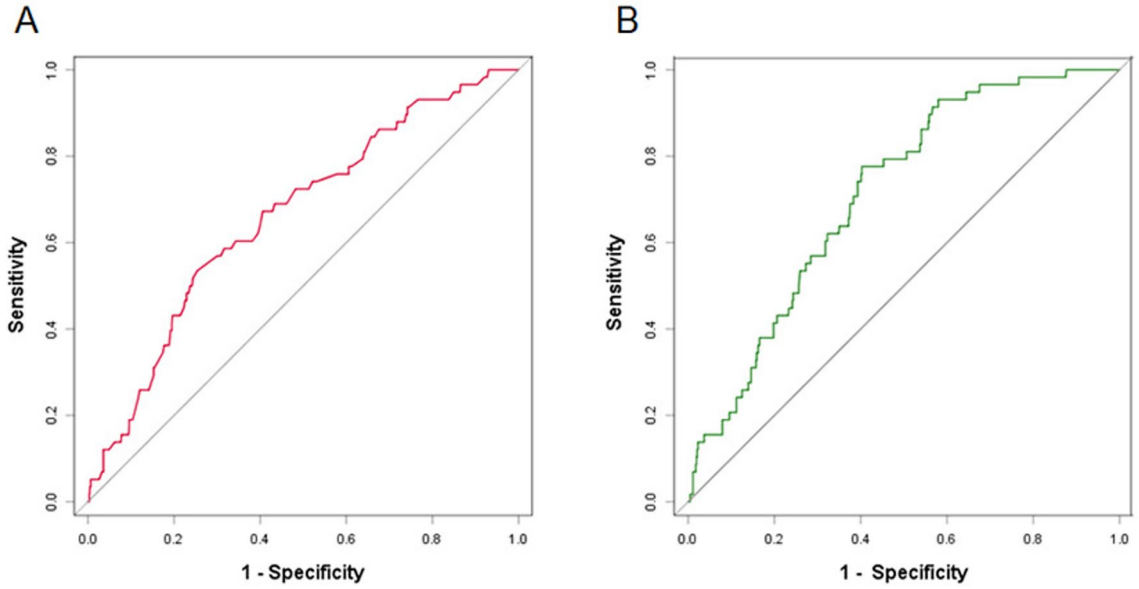

Figure 3. ROC curve of the risk factors (**A**,**B**). (**A**) ROC curve of BMI. (**B**) ROC curve of the HU value.

Reference	Country	Study type	Intervention	Sample size	Variables with significant difference
Qian et al. 2023[26]	China	Retrospective study	PVP	332	BMD, bone cement leakage, bone cement distribution
Chen et al. 2023[27]	China	Retrospective study	PVP	229	Bone cement volume, fat infiltration rate of multifidus, CSAA of multifidus and erector spinae
Mao et al. 2023[28]	China	Retrospective study	PKP	436	Gender, age, BMD, number of surgical vertebrae, cement volume, diabetes, hypertension, cement leakage, duration of anti-osteoporosis treatment, TL junction
Tao et al. 2022[14]	China	Retrospective study	PKP	445	BMD, kyphosis angle, cement distribution, disc degeneration
Matsumoto et al. 2021[29]	Japan	Retrospective study	PKP	65	Age, previous vertebral fracture, local kyphosis
Chen et al. 2020[30]	China	Retrospective study	PKP	102	Diabetic status, changed of Cobb angle
Ko et al. 2019[22]	Korea	Retrospective study	PKP	123	Cement leakage into the disc
Takahashi et al. 2019[21]	Japan	Prospective study	PKP	109	Wedge angle before surgery, correction degree of wedge angle, old OVCF presence, TL level
Li et al. 2017[15]	China	Retrospective study	PVP	390	BMD, duration of menopause, preoperative multi-level vertebral fractures
Takahara et al. 2016[18]	Japan	Retrospective study	PVP	61	Age, BMD
Yang et al. 2016[13]	China	Retrospective study	PKP	139	BMD, balloon volume, recovery rate of vertebral height, cement volume, cement leakage
Spross et al. 2014[11]	Switzerland	Retrospective study	PKP	375	Preoperative segmental kyphosis, rheumatoid arthritis, cardiovascular disease
Wang et al. 2014[19]	China	Retrospective study	PVP/PKP	358	Age, BMD, intravertebral cleft

Table 4. Summary of studies that investigated risk factors for AVF after PVP or PKP. *BMD* bone mineral density, *PVP* percutaneous vertebroplasty, *PKP* percutaneous kyphoplasty, *OVCF* osteoporotic vertebral compression fracture, *CSAA* cross-sectional area asymmetry, *TL* thoracolumbar.

445 patients who underwent PKP for OVCFs to explore the predictive factors for AVF, and the conclusion of this study was that BMI was not a predictive factor for AVF after PKP. Yang et al.[13] analyzed the risk of adjacent vertebral compression fracture following PKP and reported that there was no correlation between BMI and the occurrence of AVF. A retrospective analysis of 358 patients demonstrated that BMI was not a risk factor of symptomatic AVF following percutaneous vertebral augmentation[19]. In regard to postmenopausal women, only one study investigated the association between BMI and AVF. Takahara et al.[18] concluded that BMI was not strongly related to the risk of AVF after PVP. However, in the present study, BMI was likely to increase the odds of AVF after PVP or PKP in postmenopausal women.

A previous history of OVCF as a risk factor of AVF has aroused increasing concerns. Accumulating evidence has demonstrated that a history of previous vertebral fracture is strongly associated with increased odds of AVF after percutaneous vertebral augmentation. In a study of 421 patients, the results of this study demonstrated that preexisting old vertebral compression fracture was considered an independent risk factor of new AVF following PVP[20]. In a prospective multicenter cohort study, Takahashi et al.[21] identified several predictive factors of AVF following balloon kyphoplasty and found that the presence of old OVCF significantly correlated with the development of AVF. Consistent with previous studies, the findings of our study suggested that postmenopausal women with a previous history of OVCF had an increased risk of AVF after PVP or PKP.

There is controversy regarding whether cement leakage may contribute to the development of AVF after PVP or PKP. Several studies have shown that cement leakage is associated with an increased risk of AVF. Yang et al.[13] conducted a study of 139 patients who were treated with PKP and noted that bone cement leakage significantly increased the risk of adjacent vertebral collapse after PVP. With further research, intradiscal cement leakage has received increased amounts of attention. In a retrospective cohort study, Ko et al.[22] evaluated the association between cement leakage into the disc and AVF and concluded that intradiscal cement leakage significantly increased the risk of AVF following PKP. One reason was that intradiscal disc leakage disrupted the biomechanics of the intervertebral disc, thereby accelerating its degeneration. Consequently, intervertebral disc degeneration was a risk factor for increased risk of AVF after PKP[14]. Furthermore, cement leakage into the intervertebral space could increase the likelihood of subsequent vertebral fracture following PVP owing to a direct pillar effect[23]. However, in our study, cement leakage and intradiscal cement leakage were not found to be independent risk factors of AVF following PVP or PKP in postmenopausal women, seemingly due to the short follow-up time.

It is widely accepted that the BMD can significantly increase the risk of AVF following PVP or PKP. A retrospective study was conducted to investigate the risk factors of AVF following PVP in postmenopausal women and indicated that low BMD was associated with an elevated risk of AVF[18]. Wang et al.[19] retrospectively analyzed 358 patients who underwent percutaneous vertebral augmentation and reported that lower BMD was one of the risk factors for symptomatic AVF. Dual-energy X-ray absorptiometry (DEXA) is considered the gold standard for the measurement of BMD. However, to some extent, DEXA has several limitations, such as inaccessibility, especially in community hospitals, and inaccuracy in regard to spinal deformity, which restricts its application. In recent years, CT has attracted increasing attention as an alternative imaging method for evaluating BMD. Compared to DEXA, CT has the following advantages. As a routine medical examination, opportunistic CT scans such as thoracic CT and abdominal CT are available without additional medical burden. Moreover, CT scans have low medical costs and are easy to implement, especially in community hospitals. CT measures the BMD of the spine more accurately than does DEXA. The HU value measured by CT scan is an indicator of BMD and has been gradually used in evaluating the risk of new AVF. A low HU value was considered a risk factor of new osteoporotic vertebral fractures following PKP[24]. Moreover, a case–control study revealed that low HU value added the risk of new vertebral fracture after percutaneous vertebral augmentation[25]. In our study, a low HU value strongly correlated with a greater risk of AVF following PVP or PKP in postmenopausal women.

It should be noted that there were some limitations in this monocentric study. First, selection bias existed in this retrospective study. Additionally, causal relationships between risk factors and AVF has not been established. Third, only postmenopausal women who were treated with PVP or PKP were enrolled in this study; therefore, the findings cannot be generalized to male patients. Fourth, DEXA was not systematically performed to evaluate BMD in this study; thus, statistical analysis was not possible. Finally, only a part of patients received anti-osteoporosis treatment following surgery in the present study, which may impact the accuracy of the results. Therefore, a prospective randomized controlled trial will be conducted to identify the risk factors and determine the causal effect in postmenopausal women following PVP or PKP for the treatment of OVCFs.

Conclusion

AVF is a serious complication of PVP or PKP in postmenopausal women. In our study, the incidence of AVF was 8.61%. Additionally, BMI, previous history of OVCF and HU value were found to be independent risk factors of AVF in postmenopausal women following PVP or PKP for the treatment of OVCFs. Most importantly, women with these risk factors should be identified as early as possible, and some effective measures could be carried out in a timely manner to decrease the incidence of AVF.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Y.C. and H.W. conceived and designed the study. Y.C. and J.M. collected the data. Y.L. and X.C. analyzed the data. J.W. designed the figures. Y.C. wrote the manuscript. All authors reviewed and revised the manuscript.

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Competing interests

The authors declare no competing interests.

Additional information

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