Joint Diseases and Related Surgery

Jt Dis Relat Surg
2025;36(3):535-542

ORIGINAL ARTICLE

Hidden blood loss of percutaneous vertebroplasty in the treatment of spinal metastases of breast cancer

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ABSTRACT

Objectives: The aim of this study was to evaluate hidden blood loss (HBL) and to identify its possible risk factors after percutaneous vertebroplasty (PVP) in patients with spinal metastases from breast cancer.

Patients and methods: Between January 2020 and January 2024, a total of 54 female patients (mean age: 65.3±7.9 years, range, 47 to 79 years) with breast cancer and vertebral metastases who underwent PVP were retrospectively analyzed. Patient data were collected including demographic characteristics, oncological profiles, laboratory parameters, particularly pre- and postoperative hematocrit (Hct) levels, and clinical variables. The Sehat equation was employed to quantify HBL based on Hct alterations. To identify significant predictors of HBL, a multiple linear regression analysis of potential risk factors was carried out.

Results: The mean surgical time was 32.0±8.5 min. Cement leakage occurred in 44.4% of cases. The mean hemoglobin (Hb) loss and Hct loss were 0.9±0.4 g/dL and 2.8±0.6%, respectively. The mean HBL was 287.2±57.4 mL. Multiple linear regression analysis showed that HBL was positively correlated with bone metastasis (p=0.010), surgical time (p=0.009), number of punctures (p=0.036), cement leakage (p=0.026), Hct loss (p=0.020), and TBL (p<0.001), while it was negatively correlated with postoperative Hct (p=0.024).

Conclusion: Bone metastasis, surgical time, number of punctures, cement leakage, Hct loss, and TBL are independent risk factors for HBL. Therefore, HBL warrants clinical attention in patients with spinal metastases from breast cancer undergoing PVP, particularly those with these risk factors.

Keywords: Breast cancer, hidden blood loss, pathological fracture, percutaneous vertebroplasty, risk factors, spinal metastases.

Breast cancer is the most prevalent malignant tumor worldwide and ranks first among the causes of cancer deaths in women.[1] Although there have been significant advances in the treatment of this disease, most patients are in advanced stages at the time of diagnosis. Data have shown that the median overall survival of patients with metastatic breast cancer (MBC) is about two to three years, with a five-year relative survival rate of only 27%.[2] Among the metastatic sites of MBC, bone metastasis is the most common.[3,4] Bone metastasis can lead to symptoms such as pain and weakness, and in severe cases, pathological fracture or spinal cord compression may occur, significantly reducing quality of life of patients.[5,6]

Currently, radiotherapy, chemotherapy and targeted drug therapy can partially relieve pain symptoms, but the effect is limited in some patients. Percutaneous vertebroplasty (PVP), which has been applied since the late 1980s, has now become the standard procedure for the treatment of spinal metastases in our hospital. Studies have shown that PVP can effectively reduce pain symptoms in patients with spinal metastases.[7] This technique has three main effects: analgesia, spine stabilization and anti-tumor.[8] Due to cytotoxic effects, thermal

Received: May 20, 2025
Accepted: June 10, 2025
Published online: July 21, 2025

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Citation: Chen LP, Peng YX. Hidden blood loss of percutaneous vertebroplasty in the treatment of spinal metastases of breast cancer. Jt Dis Relat Surg 2025;36(3):535-542. doi: 10.52312/jdrs.2025.2393.

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effects and ischemic mechanisms, PVP may also reduce the risk of local tumor recurrence.[8]

Although PVP is a minimally invasive procedure with significant advantages in short-term pain relief and functional improvement, a common clinical observation has been noted. Despite its brief duration and minimal intraoperative bleeding, a considerable proportion of patients still develop postoperative anemia. In the present study, we hypothesized that perioperative hidden blood loss (HBL) may account for this phenomenon. Since blood loss into tissues, residual dead space, or hemolysis remains invisible,[9] HBL is often overlooked by many spinal surgeons. Existing studies on PVP-related HBL confirm that it is not negligible but rather a substantial contributor to blood loss.[10-12] Ignoring this component may have significant consequences for patients,[13] particularly those with preexisting anemia or poor systemic conditions. Therefore, quantifying HBL enables more accurate estimation of perioperative total blood loss (TBL), enhancing clinical evaluation and ensuring patient safety during the perioperative period. In the literature, there is limited research on HBL in breast cancer patients with spinal metastases undergoing PVP. Additionally, it is not known whether HBL after PVP in this population differs from patients with osteoporotic vertebral compression fractures (OVCFs) alone. In this study, we, therefore, aimed to evaluate HBL in breast cancer patients with spinal metastases treated with PVP and to investigate its influencing factors, providing guidance for perioperative blood management.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at The Third People's Hospital of Chengdu, Department of Orthopaedics and Center of Breast and Thyroid Surgery between January 2020 and January 2024. Breast cancer patients with spinal metastases who underwent PVP treatment in our center were screened. Inclusion criteria were as follows: *(i)* age ≥18 years; *(ii)* confirmed diagnosis of breast cancer with spinal metastasis; *(iii)* persistent localized pain at the affected vertebral level refractory to conventional therapies (i.e., radiotherapy, chemotherapy, or targeted therapy), with magnetic resonance imaging (MRI)-confirmed pathological fracture; and *(iv)* single-level involvement. Exclusion criteria were as follows: *(i)* severe systemic comorbidities (cardiac, pulmonary, hepatic, or renal dysfunction); *(ii)* local infection of surgical site or active systemic infectious disease; *(iii)* coagulation disorders or significant bleeding tendency; and *(iv)* severe spinal canal stenosis or posterior vertebral wall fracture with epidural mass effect causing neurological compression. Finally, a total of 54 female patients (mean age: 65.3±7.9 years, range, 47 to 79 years) were included in the study. Written informed consent was obtained from each patient. This is an observational study. The ethics committee of The Third People's Hospital of Chengdu has confirmed that no ethical approval is required. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical procedure

All the operations were performed by the same surgeon under local anesthesia. The selected surgical approach was the unilateral transpedicular approach. The specific surgical operation approach was as follows: With the patient in prone position, fluoroscopic localization using a C-arm system was performed to identify the affected vertebral level and establish optimal puncture trajectories. The 10 o'clock position for left pedicle and 2 o'clock position for right pedicle were designated as bony landmarks, with skin entry points set approximately 5 mm lateral to these markers after careful surface mapping. Following standard antisepsis and local anesthetic administration, the introducer needle was advanced through the predetermined cutaneous access point. The needle trajectory was progressively adjusted with increasing caudal angulation from thoracic to lumbar segments.

Under continuous fluoroscopic monitoring

(i) Initial confirmation ensured proper needle positioning within the pedicle, when the tip reached its midportion (approximately 0.5 cm into vertebral body), confirming intact medial pedicle walls.

(ii) Subsequent advancement positioned the needle at the vertebral midline on anteroposterior view and near the anterior vertebral margin on lateral projection.

After removing the stylet, bone cement was slowly infused under real-time imaging until achieving a 5-mm safety margin from the posterior vertebral cortex. Injection was immediately halted upon detecting extravasation, with a 3 to 5 min pause allowing partial cement polymerization. The delivery system was then withdrawn, followed by manual compression for hemostasis.

Evaluation index

Demographic and clinical parameters were systematically documented including baseline

characteristics such as age, body height, weight, body mass index (BMI), underlying comorbidities, affected vertebral level, duration of segmental pain, and Visual Analog Scale (VAS) scores; oncological profiles such as immunohistochemical markers (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor-2 [HER-2]) and neoadjuvant therapies (radiotherapy, chemotherapy, or targeted therapy). Bone metastases are categorized into three subtypes as osteolytic, osteoblastic, or mixed patterns depending on radiographic findings of either bone resorption or new bone formation.[14] In addition, perioperative metrics such as the American Society of Anesthesiologists (ASA) classification, surgical time, intraoperative blood loss, intraoperative fluoroscopy frequency, number of punctures, amount of cement injected, cement leakage incidents, length of hospitalization, and follow-up time and laboratory indices such as hemoglobin (Hb), albumin (ALB), and hematocrit (Hct) levels obtained through complete blood count and liver function tests performed on Day 1 preoperatively and Day 3 postoperatively were noted. Anemia was defined as an Hb level of <120 g/L.[15] Notably, none of the enrolled patients received blood transfusions prior to surgery.

Calculation of HBL

Postoperative Day 3 complete blood count results were selected for analysis, as this timepoint allows for hemodynamic stabilization and completion of fluid compartment shifts.[9] The following standardized calculations were performed:

(i) Patient blood volume (PBV) determination:

Employing the Nadler equation:[16]

$PBV\ (L) = (k_1 \times height^3[m]) + (k_2 \times weight\ [kg]) + k_3$

with sex-specific coefficients:

Male: $k_1=0.3669$, $k_2=0.03219$, $k_3=0.6041$

Female: $k_1=0.3561$, $k_2=0.03308$, $k_3=0.1833$

(ii) TBL calculation:

Using the Gross method:[17]

$TBL\ (L) = PBV \times (Hct_{pre} - Hct_{post})/Hct_{ave}$

where:

Hct_{pre} = preoperative hematocrit

Hct_{post} = postoperative Day 3 hematocrit

Hct_{ave} = mean of pre- and postoperative values

(iii) HBL estimation:

Derived from the Sehat model:[9]

HBL= TBL - VBL

where:

VBL = clinically measurable blood loss; it was equivalent to intraoperative blood loss. It included the weight of blood in the gauze and gauze strips used during the procedure.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 27.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were presented in mean ± standard deviation (SD) or median (min-max), while categorical variables were presented in number and frequency. Continuous variables were compared using the independent samples t-tests. Categorical variables were analyzed using the Pearson chi-square tests. We initially performed univariate analysis on potential predictive variables. Variables demonstrating statistical significance ($p<0.05$) in the univariate analysis were subsequently entered into a multivariate logistic regression model to identify independent risk factors for HBL. A two-tailed *p* value of <0.5 was considered statistically significant.

RESULTS

Diabetes mellitus was present in nearly 30% of all patients. The mean VAS score significantly decreased from 6.9±1.0 preoperatively to 2.6±1.2 postoperatively. Mixed-type bone metastases represented the most common pathological pattern (Table I). The mean surgical time was 32.0±8.5 min, with a mean cement injection volume of 4.8±0.7 mL. Cement leakage occurred in 24 cases (44.4%). During a mean follow-up period of 12.1±1.6 months, laboratory analysis revealed mean Hb loss of 0.9±0.4 g/dL and Hct loss of 2.8±0.6%. Notably, the prevalence of anemia increased from 44.4% preoperatively to 85.2% postoperatively. The mean calculated HBL was 287.2±57.4 mL (Table II). We performed additional subgroup analyses using the original data to compare HBL between thoracic and lumbar vertebral metastases. There was no significant difference in HBL between thoracic and lumbar groups (p=0.269) (Table III).

Univariate analysis

Correlation analyses revealed significant associations between HBL and bone metastasis,

TABLE I
Demographic characteristics and oncological profiles

Variables	n	%	Mean±SD
Age (year)			65.3±7.9
Height (m)			1.62±0.05
Weight (kg)			57.0±5.3
Body mass index (kg/m^2)			21.8±2.5
Comorbidity			
Hypertension	7	13.0	
Diabetes mellitus	16	29.6	
Coronary heart disease	8	14.8	
Affected vertebral level			
Thoracic vertebrae	31	57.4	
Lumbar vertebra	23	42.6	
Duration of segmental pain (days)			44.6±16.1
Preoperative VAS			6.9±1.0
Postoperative VAS			2.6±1.2
Estrogen receptor			
Positive	25	46.3	
Negative	29	53.7	
Progesterone receptor			
Positive	31	57.4	
Negative	23	42.6	
HER-2			
Positive	28	51.9	
Negative	26	48.1	
Neoadjuvant therapies	22	40.7	
Bone metastases			
Osteolytic	18	33.3	
Osteoblastic	17	31.5	
Mixed	19	35.2	
Total	54	100	

SD: Standard deviation; VAS: Visual Analog Scale; HER-2: Human epidermal growth factor receptor-2.

TABLE II
Clinical variables and laboratory parameters

Variables	n	%	Mean±SD
ASA classification			
I	9	16.7	
II	32	59.2	
III	13	24.1	
Surgical time (min)			32.0±8.5
Intraoperative blood loss (mL)			7.6±2.1
Intraoperative fluoroscopy frequency			7.0±1.3
Number of puncture			
≤3	25	46.3	
>3	29	53.7	
Amount of cement injected (mL)			4.8±0.7
Cement leakage	24	44.4	
Length of hospitalization (days)			5.1±1.3
Follow-up time (months)			12.1±1.6
Preoperative Hb (gd/L)			11.5±1.5
Postoperative Hb (g/dL)			10.6±1.4
Hb loss (g/dL)			0.9±0.4
Preoperative Hct (%)			37.2±3.4
Postoperative Hct (%)			34.4±3.4
Hct loss (%)			2.8±0.6
Anemia			
Preoperative	24	44.4	
Postoperative	46	85.2	
Hidden blood loss (mL)			287.2±57.4
Visible blood loss (mL)			7.6±2.1
Total blood loss (mL)			294.8±56.9
Total	54	100	

SD: Standard deviation; ASA: American Society of Anesthesiologists; Hb: Hemoglobin; Hct: Hematocrit.

surgical time, number of punctures, cement leakage, postoperative Hct, Hct loss and TBL ($p<0.05$) (Table IV).

TABLE III
HBL between thoracic and lumbar vertebral metastases

		HBL (mL)	
Affected vertebral level	n	Mean±SD	*p*
Thoracic vertebrae	31	280.5±52.3	0.269
Lumbar vertebrae	23	295.8±63.1	

SD: Standard deviation; HBL: Hidden blood loss.

Multivariate logistic regression analysis

Multiple linear regression analysis showed that HBL was positively correlated with bone metastasis ($p=0.010$), surgical time ($p=0.009$), number of punctures ($p=0.036$), cement leakage ($p=0.026$), loss of Hct ($p=0.020$), and TBL ($p<0.001$), and negatively correlated with postoperative Hct ($p=0.024$) (Table V).

DISCUSSION

Percutaneous vertebroplasty indications encompass painful OVCFs, malignant vertebral lesions with

TABLE IV
Correlation analysis between related factors and HBL

Variables	*p*	Correlation
Age	0.759	0.043
Height	0.161	−0.194
Weight	0.318	0.138
Body mass index	0.098	0.228
Comorbidity	0.938	0.011
Affected vertebral level	0.269	−0.153
Duration of segmental pain, days	0.814	−0.033
Preoperative VAS	0.988	0.002
Postoperative VAS	0.729	0.048
Estrogen receptor	0.358	−0.127
Progesterone receptor	0.911	0.016
HER-2	0.083	−0.238
Neoadjuvant therapies	0.808	−0.034
Bone metastases	0.001	−0.427
ASA classification	0.856	−0.025
Surgical time (min)	<0.001	0.592
Intraoperative fluoroscopy frequency	0.743	−0.046
Number of puncture	0.003	0.402
Amount of cement injected	<0.001	0.762
Cement leakage	<0.001	0.493
Length of hospitalization	0.368	0.125
Follow-up time	0.190	0.181
Preoperative Hb	0.494	0.095
Postoperative Hb	0.531	0.087
Hb loss	0.721	0.050
Preoperative Hct	0.084	−0.238
Postoperative Hct	0.005	−0.377
Hct loss	<0.001	0.817
Preoperative anemia	0.513	−0.091
Postoperative anemia	0.810	0.033
Visible blood loss	0.076	−0.244
Total blood loss	<0.001	0.999

HBL: Hidden blood loss; VAS: Visual Analog Scale; HER-2: Human epidermal growth factor receptor-2; ASA: American Society of Anesthesiologists; Hb: Hemoglobin; Hct: Hematocrit; ALB: Albumin.

extensive osteolysis, and Kummell's disease.[18] Despite minimally invasive nature of PVP, HBL remains significantly underrecognized in clinical practice. Substantial HBL not only elevates complication risks, but also impedes recovery and extends hospitalization, adversely affecting patients' satisfaction.[19] Previous studies have reported considerable HBL following PVP. Yang and Peng[10] found that the HBL of OVCFs patients after PVP was 204.0±89.6 mL. Another systematic review showed that the HBL after PVP was as high as 276.12 mL.[11] Our results revealed even greater perioperative HBL (287.2±57.4 mL), with 22 initially non-anemic patients developing postoperative anemia. These findings substantially exceeded surgical team expectations. Particular concern arises for breast cancer patients with spinal metastases, who frequently present with preexisting anemia. The additional HBL burden exacerbates their condition and elevates complication risks. Consequently, orthopedic surgeons must maintain heightened awareness of clinical impact of HBL and implement rigorous perioperative monitoring protocols.

Our multivariate linear regression analysis revealed several clinically significant predictors of HBL following PVP, with important implications for surgical practice. The model demonstrated that HBL was a multifactorial phenomenon influenced by both procedural and patient-specific factors. The strongest association emerged with TBL, consistent with previous reports that HBL constituted a substantial portion of perioperative blood loss in spinal procedures.[20,21] This relationship underscores the importance of comprehensive blood loss monitoring beyond VBL, particularly in patients with preexisting anemia; i.e., a population where our study observed 22 cases (40.7%) of new-onset postoperative anemia despite normal preoperative hemoglobin levels.

Notably, bone metastasis characteristics showed significant predictive value, with osteoblastic/mixed lesions associated with greater HBL than osteolytic lesions. This finding aligned with the vascular disruption theory,[22] what documented increased vascular permeability in sclerotic metastases. Therefore, preoperative optimization should include anemia correction, particularly for patients with osteoblastic metastases. The negative correlation between postoperative Hct and HBL further emphasized the clinical impact of this blood loss, potentially explaining the higher transfusion requirements observed in metastatic spine surgery.[23]

In the current study, we found a positive correlation between surgical time and HBL. Prolonged surgical procedures may exacerbate cumulative tissue trauma, thereby contributing to elevated HBL. Implementing refined surgical protocols, such as preoperative imaging navigation and enhanced team coordination, could effectively

TABLE V
Multiple linear regression analysis of risk factors on HBL

Independent variables	Coefficient (B)	Standard error	Standardized β	t	*p*
Constant	-45.21	12.34		–3.66	<0.001
Bone metastases	8.56	3.21	0.18	2.67	0.010
Surgical time	1.23	0.45	0.15	2.73	0.009
Number of puncture	5.78	2.67	0.12	2.16	0.036
Amount of cement injected	3.45	1.89	0.10	1.82	0.075
Cement leakage	7.89	3.45	0.16	2.29	0.026
Postoperative Hct	–20.34	8.76	–0.22	–2.32	0.024
Hct loss	15.67	6.54	0.19	2.40	0.020
Total blood loss	0.45	0.12	0.25	3.75	<0.001

HBL: Hidden blood loss; Hct: Hematocrit; R2=0.42, adjusted R^2=0.38, F=9.87, p<0.001; In the qualitative variables, osteolytic, number of punctures ≤3 and no cement leakage were set as "1". Osteoblastic / Mixed, number of punctures >3 and cement leakage were set as "2".

reduce surgical time. Although vertebral level (thoracic vs. lumbar) did not significantly influence HBL in univariate or multivariate analyses, osteoblastic/mixed metastases and prolonged surgical time independently increased HBL. This implies that tumor biology and procedural complexity, not spinal location, govern HBL. Furthermore, HBL demonstrated significant associations with both number of punctures and cement leakage. Each additional puncture attempt increases soft tissue damage and potential vascular injury risk. The mechanisms underlying cement leakage-related HBL likely involve mechanical blood displacement and inflammatory effects induced by poly(methyl methacrylate) (PMMA).[24] These findings emphasize the necessity of adopting targeted strategies to mitigate these risk factors. Technical precision (C-arm guidance, first-pass accuracy) can minimize both puncture-related blood loss and cement leakage risks. Cement injection protocols should balance volume and safety, avoiding aggressive height restoration which may increase cavity formation.

The marginal significance of cement volume warrants further investigation with larger samples. Recent biomechanical studies have suggested that optimal cement volumes may be procedure-specific,[25] and our data indicate this variable may interact with leakage status. While PVP effectively stabilizes vertebrae and relieves pain, its role in oncological control remains adjunctive. Multidisciplinary planning (involving oncologists, radiologists, and spine surgeons) is critical to balance mechanical stabilization and long-term tumor control.

In our study, HBL was significantly higher in patients developing new-onset postoperative anemia versus those maintaining normal Hb levels. We recognize that anemia in MBC is multifactorial. Cytotoxic therapies, bone marrow infiltration, and chronic inflammation likely contributed to baseline anemia (44.4% preoperatively). However, the 40.7% incidence of new-onset postoperative anemia, strongly associated with HBL, implies that procedural blood loss is a clinically relevant additive stressor. Future studies should integrate transfusion metrics and detailed anemia workups to disentangle these contributions.

Nonetheless, this study has certain limitations that should be acknowledged. First, the retrospective design and limited sample size from a single institution may have affected parameter estimation precision. To address this and to confirm our results, further prospective multi-center trials with larger cohorts are needed. Additionally, the measurement of Hct levels and subsequent HBL calculations on postoperative Day 3 could potentially lead to underestimation due to incomplete hemodynamic stabilization. Further investigation is warranted to establish the optimal timing for accurate assessment of postoperative blood loss in relation to circulatory equilibrium.

In conclusion, HBL is substantially underestimated during PVP in patients with spinal metastases from breast cancer. In our study, several independent risk factors for HBL, including bone metastasis characteristics, surgical time, number of punctures, cement leakage, Hct loss, and TBL were identified. These findings underscore the need

for orthopedic surgeons to implement optimized perioperative strategies which address these risk factors, thereby mitigating the clinical impact of HBL.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conception and design, statistical expertise: L.C., Y.P.; Collection and assembly of data, critical revision of the article for important intellectual content: Y.P.; Analysis and interpretation of the data, drafting of the article: L.C. All authors read and approved the final manuscript.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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