Perioperative Hidden Blood Loss in Elderly Osteoporotic Vertebral Compression Fracture Patients With Percutaneous Vertebroplasty and Influencing Factors

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Abstract

Introduction: To analyze perioperative hidden blood loss (HBL) and its influencing factors in elderly patients with osteoporotic vertebral compression fracture (OVCF) treated with percutaneous vertebroplasty (PVP). Materials and Methods: From January 2016 to December 2018, 103 elderly patients with OVCF (age > 85 years) treated with PVP were selected. The patient's height, weight, duration of symptoms, previous medical history and other basic information were recorded. The hemoglobin (Hb) and hematocrit (Hct) immediately after admission and the next day postoperative were recorded. The operation time, surgical bleeding, Kummell's disease, vertebral height preoperative and postoperative, and bone cement leakage was recorded. The total blood loss (TBL) was calculated according to Gross's formula, and HBL was calculated based on the TBL and surgical bleeding. The influential factors were analyzed by multivariate linear regression analysis and single factor correlation analysis. Results: The mean surgical bleeding was 11.83 + 5.37 mL, and HBL was 306.19 + 185.92 mL, with a statistically significant difference (P = 0.000). According to the multiple linear regression analysis, the duration of symptoms (P = 0.030), number of fracture segments (P = 0.016), operation time (P = 0.004), loss of vertebral height (P = 0.026), recovery of vertebral height (P = 0.004), Kummell's disease (P = 0.040) and cement leakage (P = 0.004) were correlated with an increased amount of HBL. Sex (P = 0.077), body mass index (BMI) (P = 0.486), hypertension (P = 0.734), diabetes (P = 0.769), fracture level (P = 0.518) and surgical bleeding (P = 0.821) had no correlation with the amount of HBL. **Conclusions:** There was obvious HBL during the perioperative period of PVP in elderly patients with OVCF. A fresh fracture, multi-segment vertebral fracture, longer operation time, presence of Kummell's disease, loss of vertebral height, recovery of vertebral height and cement leakage the increased perioperative HBL during PVP.

Keywords

osteoporosis, osteoporotic vertebral compression fractures, percutaneous vertebroplasty, hidden blood loss, elderly patients

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Introduction

With the development of society and the aging of the population, the incidence of osteoporosis is increasing.¹ Osteoporotic vertebral compression fracture (OVCF) which occurs mostly in the thoracolumbar region is one of the most common complications of osteoporosis.² The main symptoms of OVCF are back pain and limited mobility which seriously affect the quality of life and result in a substantial social and economic burden.³ Older people (>85 years old) have a higher incidence of OVCF, and most of these patients are in poor physical

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condition, have other chronic diseases, and a poor tolerance of blood loss. Conservative treatment methods such as bed rest can easily lead to a vicious cycle of worsening osteoporosis. Long-term bed rest can also lead to pneumonia, bedsores, thrombosis and other serious complications. Traditional open surgery with its higher risks cannot be performed due to these patients' poor general condition. Percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) have become the first choice for the treatment of OVCF after failure of conservative treatment.⁴

In 2000, Sehat et al found that visible blood loss and the amount of blood loss calculated according to the results of the auxiliary examination before and after surgery were significantly different during total knee arthroplasty (TKA).⁵ Thus, they defined blood loss due to diffusion into the tissue, residue in the dead space or loss by hemolysis as hidden blood loss (HBL). HBL accounted for 49% of the total blood loss (TBL) during the perioperative period after TKA surgery.⁵ Many other studies have reported that HBL accounted for a higher proportion of total blood loss due to spine surgery.⁶⁻⁸ Ren et al found that the HBL was 501.1 + 216.9 mL (nearly 58% of the TBL) in posterior lumbar fusion surgery.⁶ Chen and Ogura also found a large volume of HBL in the perioperative period of thoracolumbar fracture surgery and multilevel posterior lumbar fusion surgery.^{7,8} Therefore, the discovery of HBL provides the possibility of better assessing the actual blood loss in surgery.

Owning to the almost "zero" surgical blood loss, most spine surgeons are not aware of the actual blood loss from a PVP or PKP procedure. However, previous studies found that there was significant HBL during the perioperative period of PKP.^{9,10} It is commonly believed that the PVP procedure is simpler and it is more economical than PKP, and thus PVP is used more often in the treatment of OVCF.¹¹ Clarifying that perioperative HBL can more accurately evaluate the total blood loss due to PVP is of great importance, especially for the perioperative safety of elderly patients. However, there is no previous published study evaluating the HBL in elderly OVCF patients treated with PVP.

In this study, we retrospectively analyzed the perioperative HBL during the perioperative period of PVP in elderly patients with OVCF and identified influencing factors causing HBL.

Materials and Methods

Patient Selection

This study was approved by the Ethics Committee of the Clinical Medical College of XX University and all patients signed informed consent forms. A total of 103 elderly OVCF patients (29 men and 74 women) treated with PVP under general anesthesia from January 2016 to December 2018 were retrospectively reviewed.

The inclusion criteria were as follows: (1) age over 85 years; (2) local back pain unresponsive to at least 8 weeks of conservative treatment; (3) back pain related to the location of the OVCF on spinal radiographs; and (4) decreased bone mineral density (T-score < -1). We excluded patients with (1) the use of anticoagulants, hemostatics, antiplatelet drugs, thrombolytic drugs and blood circulation and stasis drugs within 7 days before surgery; (2) coagulopathy and a history of venous thromboembolism; (3) severe liver dysfunction (any liver function index the exceeds the upper limit of the normal value by 2 times) or the creatinine clearance rate is less than 15 mL/min; (4) a preoperative hemoglobin less than 100 g/L; (5) chronic hemorrhagic diseases; (6) breastfeeding or pregnant; (7) other chronic diseases (metastatic tumors, autoimmune diseases, systemic blood diseases); and (8) other fractures or multiple injuries.

All patients' general data including sex, weight, height, hypertension, diabetes, duration of symptoms, hematocrit (Hct) and hemoglobin (Hb) preoperative and postoperative, fracture level, number of fracture segments, Kummell's disease, vertebral height before and after surgery, and bone cement leakage were recorded. The presence of cement leakage in this study was assessed by an independent radiologist on radiographs taken on the first day after surgery. All data were collected, assessed and analyzed by the same person to reduce bias caused by different observers.

Surgical Procedure

The PVP procedure was performed under general anesthesia in prone hyperextension and the symptomatic vertebra were localized through fluoroscopy. A small skin puncture was made approximately 2.5 cm from the mid-line. The introducer was directed to the junction of the middle and anterior 1/3 of the affected vertebral body under C-arm fluoroscopic guidance. Once the needle position was confirmed, bone cement (polymethylmethacrylate, PMMA) was injected slowly and cautiously under continuous fluoroscopic guidance. The injection was stopped when satisfactory filling was completed, cement leakage (epidural or paravertebral) was observed or the cement reached the dorsal quarter of the vertebral body. All patients were mobilized 12-24 hours after surgery and were given anti-osteoporosis treatment (calcium, vitamin D supplements and antiresorptive agents).¹²

Moreover, because of the short duration of the surgery and limited visible blood loss, the patients included in this study received only a small amount of fluids intravenously to replace perioperative fluid loss. At the same time, all patients received oral or limited intravenous injections for pain relief and related treatments. To reduce the bias caused by infusion during the perioperative period, all patients received a similar volume of fluid. Therefore, the dilution effect of intravenous infusion cannot affect the results of the study as the intravenous infusion volume was the almost the same and very small in all patients.

Calculation of HBL

According to the patients' sex, height, weight and other data, their blood volume was calculated using the method reported by

Index	Total		
Number of patients(n)	103		
Height (m)	1.611 ± 0.084		
Weight (kg)	61.917 ± 9.493		
BMI (kg/m2)	23.688 ± 2.867		
Duration of symptoms (days)	19.322 + 29.826		
Loss rate of vertebral height (%)	36.708 <u>+</u> 9.745		
Recovery rate of vertebral height (%)	25.853 ± 9.855		
Operation time (minutes)	42.439 + 16.436		
Surgical bleeding (mL)	.83 + 5.374		

Data are expressed as mean \pm SD. BMI, Body Mass Index.

Index	Total
Preoperative Hct (%)	38.821 <u>+</u> 3.139
Postoperative Hct (%)	35.838 ± 3.014
Preoperative Hb (g/L)	131.835 ± 13.614
Postoperative Hb (g/L)	121.102 ± 12.477
Loss rate of Hct (%)	7.614 + 4.272
Loss rate of Hb (%)	7.947 ± 5.803
Loss of Hb (g/L)	10.743 ± 8.202

Data are expressed as mean \pm SD. Hb, hemoglobin; Hct, hematocrit.

 Table 3. Comparison of HBL in Patients With Different Number of

 Fracture Segments.

Fracture segments	Number of Patients(n)	HBL (ml)	P- value	
Single segment	61	229.182 <u>+</u> 148.089	0.000	
Double segment	33	390.788 <u>+</u> 146.689		
Multi-segment	9	535.895 ± 238.968		

Nadler et al.¹³ The formula was as follows: Blood volume = $k1 \times height (m)^3 + k2 \times weight (kg) + k3$. For male patients: k1 = 0.3669, k2 = 0.03219 and k3 = 0.6041; for female patients: k1 = 0.3561, k2 = 0.03308 and k3 = 0.1833. Total blood loss was calculated according to the formula reported by Gross as follows¹⁴: Total blood loss = blood volume × (preoperative Hct – postoperative Hct)/average (preoperative Hct + postoperative Hct).

The formula used to estimate hidden HBL was as follows: HBL = total blood loss + blood infused - surgical bleeding - the volume of drainage. Since no patient received a blood transfusion throughout the assessment period and no drainage was placed, HBL was calculated as total blood loss - surgical bleeding in the present study.

Loss and Restoration Percentage of Vertebral Height

The average height of the 2 adjacent vertebrae to the fractured vertebrae was calculated as the normal vertebral body height. Then, the loss rate of vertebral body height and the recovery rate of vertebral body height were calculated as follows:

 $H_{ave} = (adjacent vertebral height H_1 + adjacent vertebral height H_2)/2; Loss rate of vertebral body height = (H_{ave}-H_{pre})/H_{ave} \times 100\%; Recovery rate of vertebral body height = (H_{post}-H_{pre})/H_{ave} \times 100\%. H_{ave}$ is the predicted normal vertebral body height. H₁ is the height of the vertebral body above the fractured vertebrae. H₂ is the height of the vertebral body below the fractured vertebrae. H_{post} is the prostoperative anterior vertebral body height. H_{pre} is the preoperative anterior vertebral body height.

Statistical Analysis

All data analysis was performed using the SPSS 21.0 software package (SPSS, Chicago, IL) and the statistical significance level was set at P < 0.05. The difference between surgical bleeding and HBL was evaluated by a paired-sample t-test, and the independent sample t-test was used to test the differences between the sexes.

All variables that may be related to HBL were screened by single factor correlation analysis, including 8 quantitative variables (BMI, duration of symptoms, loss rate of vertebral body height, recovery rate of vertebral body height, number of fracture segments, surgical bleeding and operation time) and 5 qualitative variables (sex, hypertension, diabetes, Kummell's disease, fracture level and cement leakage). Then, multiple linear regression analysis was used to select the variables with a high correlation and to determine the independent factors related to HBL.

A positive coefficient indicated a positive effect on the dependent variable (HBL), and a negative coefficient indicated a negative effect on the dependent variable.

Results

Among the 103 patients, 29 were men and 74 were women, with an average age of 88.14 ± 3.09 years. Sixty-one patients had a single-segment fracture, 33 a double-segment fracture, and 9 a multisegment fracture. As showed in Table 1, the average height was 1.61 ± 0.08 meters, weight was 61.91 ± 9.49 kg and BMI was 23.68 ± 2.86 kg/m2. The duration of symptoms was 19.32 ± 29.82 days. The loss rate of vertebral height was $36.70 \pm 9.74\%$ and the recovery rate of vertebral height was $25.85 \pm 9.85\%$. The operation time was 42.43 ± 16.43 minutes and surgical bleeding was 11.83 ± 5.37 mL.

All patients exhibited an obvious and sustained pain reduction immediately after surgery. As shown in Table 2, according to the results of Hct and Hb before and after the operation, the loss rate of Hct and Hb was 7.61 \pm 4.27% and 7.94 \pm 5.8% respectively, and the loss of Hb was 10.74 \pm 8.2 g/L. The perioperative HBL was 229.18 \pm 148.09 mL for single-segment fractures, 390.79 \pm 146.69 mL for double-segment and 535.89 \pm 238.97 mL for multiple-segment fractures. There were significant differences in HBL among the different segment fracture (P < 0.05, Table 3).

Index	Groups	n	HBL	t/F	Р
Gender Male Female	Male	29	372.331 <u>+</u> 184.005	2.247	0.027
	Female	74	282.454 <u>+</u> 181.977		
Hypertension	With	38	244.352 <u>+</u> 149.547	-2.725	0.008
	Without	65	344.828 <u>+</u> 196.222		
Diabetes	With	33	396.824 <u>+</u> 196.591	2.376	0.019
	Without	70	278.500 <u>+</u> 174.870		
Fracture level	Thoracic	34	290.766 ± 168.526	-0.649	0.518
	Lumbar	69	3 6. 33 <u>+</u> 94.856		
Cement leakage	With	68	383.185 <u>+</u> 162.017	6.929	0.000
	Without	35	161.217 <u>+</u> 136.833		
Number of fracture segments	Single	61	229.182 <u>+</u> 148.089	21.789	0.000
	Double	33	390.788 ± 146.689		
	Multi	9	535.895 <u>+</u> 238.968		
	With	51	395.456 <u>+</u> 179.100	5.335	0.000
	Without	52	221.748 ± 150.360		
Index			r	Р	
BMI			0.069	0.486	
Surgical bleeding			0.023	0.821	
Duration of symptoms			-0.433	0.000	
Operation time			0.479	0.000	
Loss rate of vertebral height			0.766	0.000	
Recovery rate of vertebral height			0.787	0.000	

Table 4. Single Factor Correlation Analysis of HBL.

Data are expressed as mean \pm SD.

Table 5. Results of Multiple Line Regression Analysis for HBL Coefficients.

	Unstandardized				
	β	SE	Standardized β	т	P- value
Gender (male: female)	-38.813	21.671	-0.092	-1.791	0.077
Kummell's disease	42.817	20.561	0.118	2.083	0.040
Hypertension	-7.056	20.703	-0.022	-0.347	0.734
Diabetes	6.125	20.751	0.015	0.302	0.769
Number of fracture segments	44.325	18.032	0.164	2.464	0.016
Duration of symptoms (days)	-0.851	0.386	-0.145	-2.206	0.030
Operation time (minutes)	2.129	0.720	0.193	2.972	0.004
Loss rate of vertebral height (%)	4.344	1.906	0.232	2.277	0.026
Recovery rate of vertebral height (%)	5.985	2.003	0.325	2.993	0.004
Cement leakage	70.104	23.784	0.189	2.952	0.004

Data are expressed as mean \pm SD. HBL: Hidden Blood Loss.

As shown in Table 4, sex (P = 0.027), hypertension (P = 0.008), diabetes (P = 0.019), duration of symptoms (P = 0.000), Kummell's disease (P = 0.000), number of fracture segments (P = 0.000), operation time (P = 0.000), cement leakage (P = 0.000), loss rate of vertebral height (P = 0.000) and recovery rate of vertebral height (P = 0.000) were significantly correlated with HBL through the single factor correlation analysis. However, the fracture level (P = 0.518) and BMI (P = 0.486) were not correlated with HBL. There was a significant difference between surgical bleeding and HBL (P = 0.000), but the surgical bleeding was not correlated with HBL.

As shown in Table 5, the duration of symptoms (P = 0.030), Kummell's disease (P = 0.000), the number of fracture segments (P = 0.016), operation time (P = 0.004), loss rate of vertebral height (P = 0.026), recovery rate of vertebral height (P = 0.004) and cement leakage (P = 0.004) were positively associated with HBL. However, sex (P = 0.077), hypertension (P = 0.734) and diabetes (P = 0.769) were not associated with HBL.

Discussion

As one of the most common complications of osteoporosis, the incidence of OVCF is increasing with social development.¹ As the first choice for OVCF that fails to respond to conservative treatment, PVP and PKP have a short operation time, less

surgical bleeding, rapid pain relief and a quick postoperative recovery.⁴ Considering the surgical bleeding is almost zero, blood loss is often ignored during PVP and PKP treatment. However, Wu et al. found 19.5% (26/133) and Cao et al. found 39.3% (48/122) of patients developed anemia, whose Hb was normal preoperatively, after PKP treatment for OVCF.9,10 Elderly patients are generally in poor physical condition, are more obviously affected by surgical trauma, and have less tolerance for blood loss.^{15,16} Even a small amount of blood loss may also cause an imbalance of body homeostasis in elderly patients, resulting in serious postoperative complications. These may include surgical wound infections, delayed healing of surgical incisions, severe anemia requiring allogeneic blood transfusion leading to adverse reactions, and severe anemia leading to major organ dysfunction.^{17,18} The present study first found that the average HBL during the perioperative period of PVP was 293.82 mL which was significantly higher than the surgical bleeding (11.89 mL). Although none of the patients in this study experienced any serious complications, hidden blood loss secondary to the initial PVP or PKP procedure and the potential adverse effects of anemia may increase the postoperative mortality and morbidity, especially for older patients. Therefore, the HBL should be valued carefully, especially in elderly patients, and patients should be closely monitored after surgery.

It is commonly believed that HBL is caused by perioperative bleeding spreading into tissues, remaining in the dead space and blood hemolysis.⁵ The duration of symptoms, number of fracture segments, loss and recovery rate of vertebral body height, operation time and cement leakage were reported as risk factors for increased HBL during PKP.⁹ Although the procedure of PVP is similar to PKP, a lower recovery rate of vertebral height, a shorter operation time and higher cement leakage rate are reported for PVP compared with PKP.^{11,19} However, PVP is more widely used due to its lower cost and equivalent clinical effect compared with PKP. Therefore, it is particularly important to study the risk factors of perioperative HBL during PVP in elderly patients.

The results of the present study indicated that a shorter duration of symptoms, more fracture segments, a longer operation time, a greater loss of vertebral height, better recovery of vertebral height, the presence of Kummell's disease and cement leakage are risk factors of perioperative HBL in the PVP procedure. Therefore, these factors (operation time, vertebral height recovery and cement leakage) should be controlled as much as possible to reduce HBL. At the same time, surgeons should increase their awareness of the existence of HBL and strengthen monitoring during the perioperative period in elderly patients with less controllable risk factors (more fracture segments, a longer duration of symptoms, a greater loss rate of vertebral height and Kummell's disease).

The results of the statistical analysis showed that patients with a longer operation time suffered from more HBL. The operation time is commonly believed to be directly related to the number of fracture levels. There was also a significant correlation between HBL and the number of fracture levels in the present study and Wu's study.¹⁰ However, these result contradicted that of Cao's.⁹ A possible reason may be that there were 14 mid-thoracic vertebrae in Cao's study.

At present, there is no research to describe the time difference between thoracic and lumbar PVP surgery in detail. However, the mid-thoracic PVP has the following features: (1) The pedicle of thoracic vertebra is smaller, and the fluoroscopy is often not clear in C-arm during operation. Thus it may take more time for fluoroscopy during operation; (2) The thoracic vertebral canal is smaller and the result of bone cement leakage is more dangerous, so the injection speed of bone cement is slower and the fluoroscopy times are more; (3) In order to make the cement sufficiently dispersed, we used bilateral puncture in almost all mid-thoracic PVP surgery. Therefore, based on our experiences and communication with other experts, we believe that the operation time of 1 mid-thoracic vertebra significantly longer then that of lumbar vertebra.

In the present study, HBL was directly related to the loss rate of vertebral height and the recovery rate of vertebral height. A reduction of the fractured segment may cause an "empty shell phenomenon" in the vertebral body.²⁰ The more loss of vertebral height and the better recovery of vertebral height, the greater the volume of the "cavity."²⁰ It is believed that restoring the vertebral body height might cause a secondary injury to the fractured vertebral body as a fracture gap may occur around the vertebral wall.¹⁰ The fracture gap may cause more blood diffusion into the tissue or it may flow into the dead space. However, patients with Kummell's disease usually have severe vertebral compression, which leads to greater vertebral height loss and a better recovery rate than ordinary OVCF. In addition, patients with Kummell's disease also have intervertebral vacuum clefts caused by osteonecrosis. These factors can further increased the blood loss in patients with Kummell's disease. Therefore, there is no need to achieve a complete reduction of the vertebral body height especially for patients with significant loss of vertebral body height and Kummell's disease.

The results of the present study also found that HBL in patients with cement leakage was significantly greater than that of patients with nonleakage. The main reason for this may be a pre-existing defect of cortical bone, which will cause persistent bleeding of the vertebra. Another important reason may be thermal necrosis caused by the PMMA, which can increase blood hemolysis during injection.²¹ However, our results differed from that of Cao's study, and the possible reason may be the higher cement leakage rate (31.9%) and greater volume of injected cement (6.6 mL).⁹ Thus, it is important to decrease cement leakage as much as possible.

The results of the present study showed that HBL is not related to sex, age, BMI, hypertension, diabetes, fracture level or surgical bleeding. However, the results of other surgeries such as TKA, total hip arthroplasty (THA) and anterior cervical discectomy and fusion (ACDF) were different.²²⁻²⁵ For example, sex had an important impact on perioperative HBL in TKA and ACDF surgery, and patients with a lower BMI had more HBL in THA surgery. The cause of the different results may be attributed to the less surgical trauma and shorter operation time in PVP surgery compared with other surgeries which are often accompanied by huge trauma and a longer operation time.

This study also has several limitations. First, we conducted a retrospective study and the enrolled number of patients was small, so a large-scale prospective study should be conducted to verify the results in the future. Second, routine blood tests were performed before and at the second day after surgery to obtain Hct and Hb values, and there was no long-term follow-up of postoperative anemia. Finally, repeated percutaneous insertion of the guide needle during location may cause paraspinal muscle bleeding and the cortical defect may be increased during repositioning once the pedicle wall is pierced.¹⁰ Therefore, the impact of the operation details during PVP on HBL needs to be further refined.

Conclusion

In conclusion, there is obvious HBL in the perioperative period of PVP in elderly patients with OVCF. A greater number of fracture segments, a fresh fracture, a longer operation time, the presence of Kummell's disease, severe loss of vertebral height, better recovery of vertebral height and cement leakage are risk factors for increased perioperative HBL during PVP. More attention should be paid to the existence of HBL to ensure the safety of elderly patients with risk factors.

Declaration of Conflicting Interests

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