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Risk Factors of Secondary Vertebral Compression Fracture After Percutaneous Vertebroplasty or Kyphoplasty: A Retrospective Study of 650 Patients

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Background: In this study, we aimed to investigate the risk factors contributing to secondary vertebral compression fractures (SVCF) in patients undergoing percutaneous vertebroplasty (PVP) or kyphoplasty (PKP) due to osteoporotic vertebral compression fracture (OVCF).


Material/Methods: Between January 2010 and December 2017, 650 patients with regular follow-up were identified and retrospectively analyzed in this study. Of these patients, 410 patients underwent PVP and 240 patients underwent PKP surgery. Patients were followed for 24 months on average, ranging from 6 months to 36 months follow-up. Possible risk factors screened for were age, gender, regional distribution, outdoor activity (ODA), bone mineral density (BMD), surgical methods (unilateral or bilateral), bone cement dose, bone cement leakage, chronic disease history, postoperative anti-osteoporosis treatment, and level of preoperative OVCF. Logistic regression analysis was applied to determine potential risk factors.

Results: As a result, 102 patients (15.7%) suffered SVCF after PVP/PKP surgery at the last follow-up. Binary logistic regression model showed that older age increased the risk of developing SVCF [odds ratio (OR)=2.48, $P=0.031$] while high-level BMD (OR=0.31, $P<0.001$) and ODA (OR=0.38, $P=0.001$) decreased the risk. Binary logistic regression model showed the following: $\text{Logit}(P)=1.03+0.91X_1-1.18X_2-0.97X_3$ (X_1 =age, OR=2.48, $P=0.031$; X_2 =BMD, OR=0.31, $P<0.001$; X_3 =ODA, OR=0.38, $P=0.001$).

Conclusions: In conclusion, older age and lower BMD were identified as risk factors of SVCF for OVCF patients following PVP/PKP surgery, whereas more ODA played a protective role in SVCF development.

MeSH Keywords: **Fractures, Compression • Kyphoplasty • Osteoporosis • Risk Factors • Vertebroplasty**

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Background

Nowadays, we have to pay more attention to osteoporotic vertebral compression fracture (OVCF) which has become a severe medical issue as the global population has increasingly aged [1]. To our knowledge, OVCF is a common disorder which particularly affects elderly patients. Usually, OVCF can reduce life quality of the aged patients by causing long-time back pain, impairing their mobility, and thus influencing their daily activities [2]. Hence, research is urgently needed to seek methods to prevent osteoporosis, as well as OVCF [3,4].

Over the past years, we have frequently applied percutaneous vertebroplasty (PVP) and kyphoplasty (PKP) in clinical situation and have cured many patients who suffered from OVCF [5–9]. However, secondary vertebral compression fractures (SVCF) have been linked to PVP/PKP surgery for patients with OVCF [7,10–17]. It has been reported that long-time menopause and preoperative multi-level vertebral fractures were likely to increase the risk that the patients would suffer from SVCF after PVP surgery, while high bone mineral density (BMD) likely decreased that risk [7]. Bae et al. [16] indicated that SVCF that followed PVP surgery was associated with poor bone mineral content and poor distribution of bone cement. Besides, a higher incidence of SVCF may be caused by bone cement leakage into the disc, as compared to non-leakage. Similarly, another study [15] showed that the SVCF group had higher cement leakage, obviously when the cement volume fraction increased during the PKP surgery. However, others have indicated that PVP might reduce the incidence of SVCF [18]. Farrokhi et al. [10] reported that PVP group had statistically significant improvement in visual analogue scale and life quality scores, and fewer adjacent-level fractures compared with the optimal medical therapy group. Hence, it still remains elusive regarding the relation between the incidence of postoperative SVCF and PVP/PKP surgery.

Herein, we focused on the occurrence of SVCF that followed PVP/PKP surgery. In addition, we tried to investigate and identify the risk contributors which may be relevant to SVCF after PVP/PKP surgery in OVCF patients.

Material and Methods

Ethics statement

This study was approved by Ethics Committee of Orthopaedic Hospital of Xingtai. The approval number is K2018-03-001. And all informed consents of the patients were obtained.

Patients

Between January 2010 and December 2017, 650 OVCF patients underwent PVP surgery (410 patients) or PKP surgery (240 patients) and all had regular follow-up thereafter. All of their medical records were collected, including medical radiographic images, and were retrospectively analyzed in this study. Inclusion criteria were: OVCF patients who underwent PVP or PKP surgery and no trauma or systematic diseases occurred during the follow-up period. All patients returned to our hospital for regular follow-up every 6 months after surgery. Based on the occurrence of SVCF, patients were divided into the following group: the SVCF group and the non-SVCF group.

Evaluation of risk factors

We screened for the following possible risk factors: age, gender, regional distribution (RD), outdoor activity (ODA), surgical methods (unilateral or bilateral), bone cement dose, bone cement leakage (BCL), chronic disease history [including hypertension, heart disease (HD), diabetes mellitus (DM), and chronic obstructive pulmonary disease (COPD)], and postoperative anti-osteoporosis treatment (AOT), bone mineral density (BMD), and QCT measurement $<80 \text{ mg/cm}^3$ for osteoporosis [19].

Statistical analyses

Statistical analyses were performed using SPSS for Windows, version 18.0 (SPSS IBM, Chicago, IL, USA). Data are presented as the median (interquartile range, IQR) where appropriate. Chi-square tests were used for data analysis. Potential risk factors with $P < 0.10$ were included in binary logistic regression analysis. Statistical significance was identified where P value was less than 0.05 with a 2-tailed test.

Results

Distribution of vertebral fractures

In this study, 650 OVCF patients underwent PVP surgery (410 patients) or PKP surgery (240 patients). There were 526 females and 124 males. The medium age was 73 (from 56 to 85 years). All patients were followed for 24 months on average (range, 6 months to 36 months). Totally, 701 fractured vertebrae were identified in 650 OVCF patients. Figure 1A shows OVCF distribution. In addition, Figure 1B shows that 122 fractured vertebrae were found in 102 patients (15.7%) who sustained SVCF after PVP/PKP. Notably, most fractures were located in L1 and T12 vertebrae, no matter OVCF or SVCF.

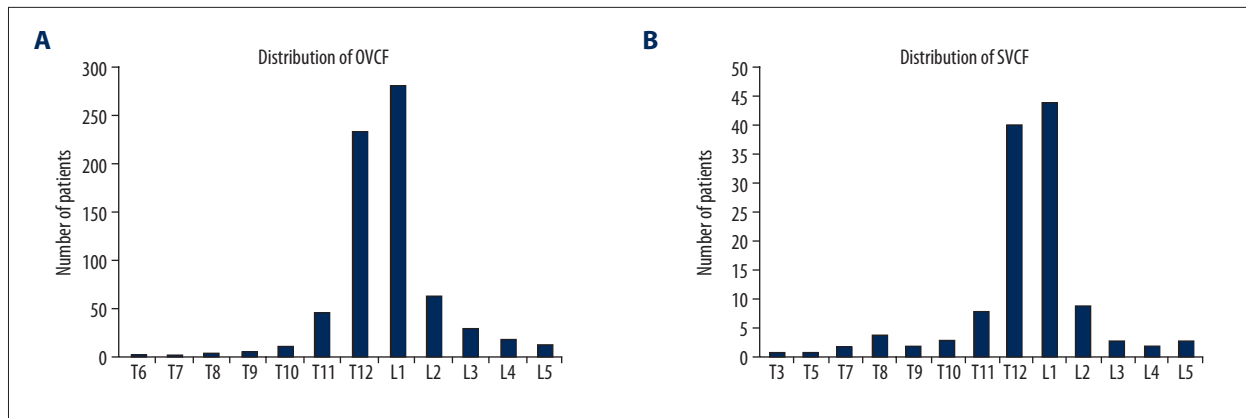


Figure 1. The distribution of OVCF/SVCF in vertebral bodies. (A) OVCFs before PVP/ PKP surgery are shown. (B) SVCFs after surgery are shown. OVCF – osteoporotic vertebral compression fracture; SVCF – secondary vertebral compression fracture; PVP – percutaneous vertebroplasty; PKP – percutaneous kyphoplasty.

Table 1. Comparison regarding age.

	Age <60	60 ≤ age <70	70 ≤ age <80	Age ≥80
SVCF* (n=102)	2	31	63	6
Non-SVCF (n=548)	15	266	254	13

* $P=0.003$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture.

Table 2. Comparison regarding gender.

	Female	Male
SVCF* (n=102)	84	18
Non-SVCF (n=548)	442	106

* $P=0.689$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture.

Table 4. Comparison regarding regional distribution.

	Rural area	Urban area
SVCF* (n=102)	50	52
Non-SVCF (n=548)	322	226

* $P=0.068$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture.

Table 3. Comparison regarding BMD.

BMD (mg/cm ³)	60 ≤ BMD <80	40 ≤ BMD <60	20 ≤ BMD <40	<20
SVCF* (n=102)	50	38	11	3
Non-SVCF (n=548)	364	145	34	5

* $P=0.004$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture; BMD – bone mineral density.

Comparison regarding age and gender

As shown in Table 1, the medium age of the SVCF patients (n=102, 15.7%) was 75 years, and age in the non-SVCF group (n=548, 84.3%) was 69 years. It was apparent that more aged patients existed in the SVCF group ($P=0.003$). As Table 2 is displaying, no statistical difference was found regarding gender comparison between the two groups ($P=0.689$).

Comparisons of BMD and regional distribution

As Table 3 shows, BMD in the SVCF group was lower than BMD in the non-SVCF group ($P=0.004$). Over half of SVCF patients suffered low BMD level with less than 60 mg/cm³, while only one-third of patients in the non-SVCF group did. As Table 4 shows, comparison of regional distribution found no difference between the SVCF group and the non-SVCF group ($P=0.068$).

Table 5. Comparison regarding outdoor activity (ODA).

ODA level	SVCF patients* (n=102)	Non-SVCF (n=548)
High	15	133
Modetare	23	280
Low	64	135

* $P < 0.001$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture; low level, ODA < 0.5 hour/day; medium level, $0.5 \leq$ ODA < 2 hour/day; high level, ODA ≥ 2 hour/day.

Table 6. Comparison regarding bone cement leakage.

Bone cement leakage	Yes	No
SVCF* (n=102)	8	94
Non-SVCF (n=548)	19	529

* $P = 0.042$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture.

Comparisons of outdoor activity and bone cement leakage

In this study, the patients were asked to give feedback regarding their outdoor activity (ODA) time. Outdoor activity was scored as 3 levels: low level (ODA < 0.5 hour per day), medium level ($0.5 \leq$ ODA < 2 hours per day), and high level (ODA ≥ 2 hours per day). As shown in Table 5, outdoor activity between the SVCF group and the non-SVCF group showed a significant difference ($P < 0.001$). Most SVCF patients were observed with

Table 8. Comparison regarding chronic disease history.

	SVCF patients (n=102)	Non-SVCF (n=548)	χ^2 -Value	p-Value
HBD	24	98	1.798	0.18
DM	16	72	0.477	0.49
HD	22	106	0.269	0.604
COPD	9	34	0.955	0.328

SVCF – secondary vertebral compression fracture; HBD – high blood pressure; DM – diabetes mellitus; HD – heart disease; COPD – chronic obstructive pulmonary disease.

Table 9. Comparison regarding the level of preoperative OVCF between SVCF group and non-SVCF group.

Level of OVCF	1	2	3
SVCF* (n=102)	93	8	1
Non-SVCF (n=548)	510	35	3

* $P = 0.752$, compared with non-SVCF group, by chi-squared test. OVCF – osteoporotic vertebral compression fracture; SVCF – secondary vertebral compression fracture.

Table 7. Comparison regarding postoperative anti-osteoporosis treatment.

AOT	Yes	No
SVCF* (n=102)	55	47
Non-SVCF (n=548)	347	201

* $P = 0.073$, compared with non-SVCF group, by chi-squared test. SVCF – secondary vertebral compression fracture; AOT – anti-osteoporosis treatment.

low-level outdoor activity, compared with the non-SVCF group. As shown in Table 6, there was a significant difference regarding bone cement leakage between the SVCF group and the non-SVCF group ($P = 0.042$). The SVCF patients showed a higher percent of bone cement leakage than the non-SVCF patients.

Comparisons of other parameters

As shown in Tables 7 and 8, there was no significant difference regarding anti-osteoporosis treatment or chronic disease history between the SVCF group and the non-SVCF group respectively (both $P > 0.05$). As shown in Table 9, there was no significant difference regarding the level of preoperative OVCF ($P = 0.752$). In addition, no significance was identified regarding surgical methods or bone cement dose (all $P > 0.05$).

Logistic regression analysis

The conditions of regression were set as follows: backward (LR), probability for stepwise (Entry 0.10, Removal 0.15). As Table 10 shows, the binary logistic regression analysis used the following

Table 10. Binary logistic regression analysis for SVCF.

No.	Items	B	Exp(B)	P-value	95% CI for Exp(B)
X1	Age	0.91	2.48	0.031	(1.16, 3.80)
X2	BMD	-1.18	0.31	<0.001	(0.06, 0.56)
X3	ODA	-0.97	0.38	0.001	(0.11, 0.65)
X4	RD	0.15	1.16	0.241	(0.14, 2.18)
X5	BCL	0.22	1.25	0.506	(0.31, 2.19)
X6	AOT	-0.43	0.65	0.147	(0.13, 1.17)
X0	Constant	1.03	2.80	0.000	-

SVCF – secondary vertebral compression fracture; BMD – bone mineral density; ODA – outdoor activity; RD – regional distribution; BCL – bone cement leakage; AOT – anti-osteoporosis treatment. $\text{Logit}(P)=1.03+0.91X_1-1.18X_2-0.97X_3$ [X_1 =age: age <60 (value: 0), 60≤ age <70 (value: 1), 70≤ age <80 (value: 2), age ≥80 (value: 3); X_2 =BMD: <20 (value: 0), 20≤ BMD <40 (value: 1), 40≤ BMD <60 (value: 2), 60≤ BMD <80 (value: 3); X_3 =ODA: low level, <0.5 hour/day (value: 0), medium level, 0.5≤ ODA <2 hour/day (value: 1), high level, ODA ≥2 hour/day (value: 2)].

model: $\text{Logit}(P)=1.03+0.91X_1-1.18X_2-0.97X_3$ [X_1 =age: age <60 (value: 0), 60≤ age <70 (value: 1), 70≤ age <80 (value: 2), age ≥80 (value: 3); X_2 =BMD: <20 (value: 0), 20≤ BMD <40 (value: 1), 40≤ BMD <60 (value: 2), 60≤ BMD <80 (value: 3); X_3 =ODA: low level, ODA <0.5 hour/day (value: 0), medium level, 0.5≤ ODA <2 hour/day (value: 1), high level, ODA ≥2 hour/day (value: 2)]. Pearson chi-square test showed that the equation above was statistically significant ($P<0.001$).

Discussion

As we know, lower BMD is a general character of osteoporosis, which may result in a high fracture risk [20,21]. Clinically, OVCF of the vertebrae is usually caused by osteoporosis, leading to low back pain, and even disability in the elderly [22]. Thus, how to treat such patients is very important. Conservative treatment, such as staying in bed and taking pain-killers, has proven to be effective for the relief of low back pain, but it may work for only a few weeks. Invasive surgery can be an option although may not be the best therapeutic option, because the body status of the elderly patients is usually always poor [23]. For the past few years, the minimally invasive methods of PVP and PKP have been widely used to treat OVCF in order to relieve low back pain and correct spinal deformity [1,24–26]. Both PVP and PKP are believed effective and safe to treat OVCF clinically. However, SVCF might occur after PVP and PKP [10–13,27], and it tends to form postoperatively, within 1 month, next to the surgically treated segment [28]. By contrast, some findings have reported the opposite conclusion [1,6,29]; others even have indicated that PVP can reduce the risk of new fractures [18]. To date, there has been a debate on whether PVP/PKP likely increases the incidence of postoperative SVCF, or whether it is only caused by the natural progression of osteoporosis.

In a recent retrospective study of 193 OVCF patients, Bae et al. [16] found that 14.6% OVCF patients sustained SVCF after PVP procedures. Compared with the patients who did not experience SVCF, SVCF patients were identified as having poorer bone mineral content and worse bone cement distribution, which can be predictive factors of SVCF. In our current study, univariable analysis showed that bone cement leakage was a likely risk factor in development of postoperative SVCF following PVP/PKP procedures ($P<0.05$), but not a risk factor in the logistic regression model ($P>0.05$). Thus, our findings showed that bone cement leakage was not a risk factor in development of postoperative SVCF following PVP/PKP procedures.

Older age and lower BMD were identified as significant risk factors of OVCF [30], as well as SVCF for patients following PVP/PKP surgery in some previous studies [7,28]. In our study, as independent risk factors, age and BMD were first analyzed (both $P<0.05$), and then they were analyzed by binary logistic regression. Both older age and BMD were identified as risk factors of postoperative SVCF after PVP/PKP surgery, and formed a logistic regression equation. It was obvious that advanced age patients usually have lower BMD, so that would be the reason why older age and lower BMD seemed to be bound together as a whole in the development of SVCF after PVP/PKP surgery.

Another study [30] indicated that the prevalence of vertebral fractures in postmenopausal women would increase from 13% for women younger than age 60 to over 50% for women by age 80 years. A model with 7 clinical risk factors with or without BMD is considered better than simple models and might guide the use of spine x-rays to identify women with vertebral fractures. Notably, it was found that more than half an hour of outdoor activity might correlate with lower risk of vertebral fracture in this population. The aforementioned study divided

outdoor activity (ODA) into 3 levels: <0.5 hours per day, <1.0 (including <0.5 hours per day), <2.0 (including <1.0 hour per day). Having less than half an hour outdoor activities was significantly associated with the probability of having a vertebral fracture: the risk increased by 1.73 times for < 0.5 hours per day compared with ≥ 0.5 hours per day. In contrast, ODA was scored in 3 levels in our study: low level (ODA <0.5 hours per day), medium level ($0.5 \leq$ ODA <2 hours per day), and high level (ODA ≥ 2 hours per day). As our result showed, ODA between the SVCF group and the non-SVCF group showed a significant difference ($P < 0.001$); most SVCF patients were observed with low-level outdoor activity, compared with the non-SVCF group. Therefore, appropriate ODA level would be more beneficial to less fracture events caused by osteoporosis. The reason could be that high-level ODA was more helpful to higher BMD level, which was a protective factor in postoperative SVCF development after PVP/PKP surgery.

This study has indicated some clinically significant findings. However, some study limitations still exist. To start with,

the current study design may lack extensive representativeness due to the retrospective single-center study design. In addition, we did not apply blind methods in assessment of this study. Hence, future researches should overcome those study limitations and provide more reliable clinical research data. We believe it would be best to conduct a large-sample, prospective, multicenter, randomized, controlled study with blind methodology applied.

Conclusions

In summary, this study indicated that older age and lower BMD were likely risk factors of SVCF for OVCF patients following PVP/PKP surgery, whereas more outdoor activity played a protective role in SVCF development.

Conflict of interest

None.

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