Risk Factors of Early Stage Residual Back Pain After Percutaneous Kyphoplasty or Vertebroplasty: A Retrospective Study of 853 Patients

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Abstract

**Background:** A small but significant proportion of patients experienced residual back pain after PVP or PKP treatment. The aim of the present study was to explore risk factors that may affect residual back pain after PKP or PVP. This study identified the risk factors of residual back pain after PKP or PVP, allowing proper intervention and improved clinical outcome.

**Methods:** From January 2010 to January 2017, a total of 853 patients were treated by PVP or PKP at The First Affiliated Hospital of Xi'an Jiaotong University. We recorded the Visual Analog Scale (VAS) scores. Patients with a VAS score > 3 post-operatively and at the 1 month follow-up evaluation were grouped into the “residual back pain” group. The others were grouped into the control group. The following possible risk factors were collected: age; gender; weight; bone mineral density (BMD); surgical approach; surgical type; cement distribution; anesthesia; hypertension; diabetes; smoking; alcohol consumption; vertebral fracture type, and vertebral fracture location. Risk factors associated with residual back pain were evaluated using logistic regression analysis.

**Results:** The incidence of residual back pain after PVP/PKP is 9.61%. Results showed that cement distribution, smoking, vertebral fracture type and vertebral fracture location were independently associated with residual back pain after PVP or PKP in the early post-operative stage.

**Conclusion:** Unsatisfactory cement distribution, smoking history, osteogenic vertebral tumors, osteolytic vertebral tumors, and thoracic fractures were independently associated with residual back pain after PVP or PKP at the early post-operative stage.

Background

Percutaneous vertebroplasty (PVP) or kyphoplasty (PKP) have been widely used over the last several decades for painful vertebral fractures. In 1987, Galibert and Deramond [1] first introduced the technique of PVP for the treatment of aggressive vertebral hemangiomas. Gradually, PVP was used to treat osteoporotic vertebral compression fractures (OVCFs), multiple myeloma, and metastases [2-4]. At the beginning of the 21st century, PKP was introduced to improve vertebral height [5]. A number of researchers showed that PKP and PVP can effectively treat vertebral fractures, alleviating pain and improving functional recovery compared with conservative treatment [6,7]; however, a small but significant proportion of patients experienced residual back pain after PVP or PKP treatment. The existing literature describes a number of possible risk factors, such as rib fractures, infections, new vertebral compression fractures, non-union bone cement interface, and transient thoracolumbar fascia injuries [8-10]; however, most studies have only focused on OVCFs and few studies have comprehensively analyzed these risk factors [9,10]. The aim of the present study was to explore risk factors that may affect residual back pain after PKP or PVP, including OVCFs, osteolytic vertebral tumors, and osteogenic vertebral tumors. This study identified the risk factors of residual back pain after PKP or PVP, allowing proper intervention and improved clinical outcome.
Methods

Study subjects

From January 2010 to January 2017, a total of 853 patients with OVCFs, osteolytic vertebral tumors, and osteogenic vertebral tumors were treated by PVP or PKP at The First Affiliated Hospital of Xi’an Jiaotong University. There were 502 female and 351 male patients. The inclusion criteria were as follows: (1) severe back pain (VAS score for back pain was > 6); and (2) magnetic resonance imaging (MRI) showing a vertebral fracture or a whole-body bone scan showing significant uptake at the abnormal level. The exclusion criteria were as follows: (1) previous spinal surgery; (2) other types of vertebral fractures (e.g., secondary to vertebral tuberculosis); (3) incomplete clinical data; (4) duration of follow-up <3 months.

Data Collection

Patients had follow-up evaluations at 1 day, 1 month, and 3 months post-operatively. Patients were recommended to follow a high-calcium diet, engage in moderate exercise, and have sun exposure for 2 h per day. In addition, calcium (600-1200 mg daily), calcitriol (0.25-0.5 ug daily), and alendronate (70 mg weekly) were prescribed. The researchers measured the BMD annually, and the medication was continued at least 3 y if no side effects occurred. The Visual Analog Scale (VAS) scores were recorded. Patients with a VAS score > 3 post-operatively and at the 1-month follow-up evaluation were grouped into the residual back pain group. The others were grouped into the control group. The following possible risk factors were recorded: age; gender; weight; BMD; surgical approach; surgical type; cement distribution; anesthesia; hypertension; diabetes; smoking; alcohol consumption; vertebral fracture type, and vertebral fracture location.

Surgical Technique

All PVP and PKP were performed by one surgeon (Y.M.Y.) through a unilateral transverse process-pedicle process or bilateral transpedicular approach. After local anesthesia was administered, the 11-G needle were advanced into the vertebral body under X-ray guidance. Polymethylmethacrylate (PMMA; Mendec Spine Resin, Italy) was used as the bone filler during PVP. Kyphon balloon tamps (KMC Kyphoplasty System; Shanghai Kinetic, Shanghai, China) were used in PKP. If leakage occurred when bone cement filling was not satisfactory, the following measures were taken to continue the surgical procedure. Secondary filling after solidifying bone cement to block the rupture was attempted, then the rupture was filled again. Alternatively, the position of the bone filler was adjusted or a side opening filler was used. Finally, the puncture direction was readjusted or a contralateral puncture filling was used. When a tumor is suspected, it may be appropriate to precede with PVP or PKP and a biopsy. After the cannula is placed for PVP or PKP, but before cement was injected, a coaxial biopsy specimen may easily be obtained. Patients were encouraged to ambulate 4 h after the procedure.
Statistical Analysis

Data were analyzed using SPSS 22.0 software. Continuous variables are shown as the mean ± standard deviation. Data are presented as percentages for categorical variables. Categorical variables were compared between groups using the chi-square test or Fisher exact test. Comparison of continuous variables between groups was done using a Student’s t-test or Wilcoxon rank sum test. Risk factors associated with residual back pain were evaluated using logistic regression analysis, and according to the inspection level, a P < 0.05 was defined as statistically significant.

Results

No major complications occurred after the PVP and PKP procedures. Among 853 patients who underwent PVP or PKP successfully, a total of 82 patients (35 males and 47 females; age range, 45-89 years; average age, 67.3±9.18 y) had residual back pain and were classified in the residual back pain group, which represented 9.61% of the patient population. Propensity score matching was used to select 82 patients without residual back pain, who were considered to be the control group. The VAS scores of both groups are reported in Table 1. Significant differences were observed at 1 day and 1 month post-operatively. With respect to OVCF patients, we suggested that the patients receive anti-osteoporosis treatment. Patients with malignant spinal lesions were recommended to undergo radiofrequency ablation, radiotherapy, or interstitial radiotherapy. After these methods, most patients with residual back pain recovered 3 months post-operatively and significant differences were not observed 3 months postoperatively.

| Group                        | Pre-op | Post-op 1 day | Post-op 1 month | Post-op 3 months |
|------------------------------|--------|---------------|-----------------|------------------|
| Residual back pain group     | 7.2 ± 0.6 | 4.8 ± 0.5*    | 4.1 ± 0.4*      | 2.8 ± 0.2        |
| Control group                | 7.4 ± 0.4 | 2.5 ± 0.4     | 2.1 ± 0.3       | 1.6 ± 0.2        |

*P < 0.05

There was no statistically significant difference in age, gender, weight, BMD, surgical approach, surgical type, anesthesia, hypertension, diabetes, and alcohol between the two groups. The presence of cement distribution, smoking, vertebral fracture type, and vertebral fracture location were significantly different between groups (P < 0.01; Table 2).
Table 2
Summary of variables between the control and residual back pain group following PVP or PKP

| Variable               | Control group (N = 82) | Residual back pain group (N = 82) | P    |
|------------------------|------------------------|-----------------------------------|------|
| Age (years)            | 70.0(9.63)             | 67.3(9.18)                        | 0.0637 |
| Gender                 |                        |                                   | 0.8750 |
| male                   | 37 (45.1%)             | 35 (42.7%)                        |      |
| female                 | 45 (54.9%)             | 47 (57.3%)                        |      |
| Weight (kg)            | 58.0(7.98)             | 59.2(9.17)                        | 0.3746 |
| BMD (SDs)              |                        |                                   | 0.4236 |
| ≤ 2.5                  | 35 (42.7%)             | 29 (35.4%)                        |      |
| ≥ 2.5                  | 47 (57.3%)             | 53 (64.6%)                        |      |
| Surgical approach      |                        |                                   | 0.6828 |
| unilateral             | 69 (84.1%)             | 66 (80.5%)                        |      |
| bilateral              | 13 (15.9%)             | 16 (19.5%)                        |      |
| Surgical type          |                        |                                   | 0.4545 |
| PVP                    | 11 (13.4%)             | 7 (8.5%)                          |      |
| PKP                    | 71 (86.6%)             | 75 (91.5%)                        |      |
| Cement distribution    |                        |                                   | < .0001 |
| satisfactory           | 60 (73.2%)             | 27 (32.9%)                        |      |
| unsatisfactory         | 22 (26.8%)             | 55 (67.1%)                        |      |
| Anesthesia             |                        |                                   | 0.5345 |
| local                  | 78 (95.1%)             | 75 (91.5%)                        |      |
| whole                  | 4 (4.9%)               | 7 (8.5%)                          |      |
| Hypertension           |                        |                                   | 0.5000 |
| yes                    | 59 (72.0%)             | 54 (65.9%)                        |      |
| no                     | 23 (28.0%)             | 28 (34.1%)                        |      |
| Diabetes               |                        |                                   | 0.7540 |
| yes                    | 46 (56.1%)             | 43 (52.4%)                        |      |
| no                     | 36 (43.9%)             | 39 (47.6%)                        |      |
| Smoking                |                        |                                   | < .0001 |
| Variable                          | Control group (N = 82) | Residual back pain group (N = 82) | P     |
|----------------------------------|------------------------|-----------------------------------|-------|
| yes                              | 31 (37.8%)             | 47 (57.3%)                        |       |
| no                               | 51 (62.2%)             | 35 (42.7%)                        |       |
| Alcohol consumption              |                        |                                   | 0.3060|
| yes                              | 54 (65.9%)             | 61 (74.4%)                        |       |
| no                               | 28 (34.1%)             | 21 (25.6%)                        |       |
| Vertebral fracture type          |                        |                                   | < .0001|
| OVCF                             | 37 (45.1%)             | 17 (20.7%)                        |       |
| osteogenic vertebral tumor       | 18 (22.0%)             | 30 (36.6%)                        |       |
| osteolytic vertebral tumor       | 27 (32.9%)             | 35 (42.7%)                        |       |
| Vertebral fracture location      |                        |                                   | < .0001|
| thoracic                         | 25 (30.5%)             | 53 (64.6%)                        |       |
| lumbar                           | 57 (69.5%)             | 29 (35.4%)                        |       |

A multivariate logistic analysis was used to test for factors associated with residual back pain. Results showed that cement distribution (odds ratio [OR], 5.84; 95% confidence interval [CI], 2.72-12.55; P < 0.0001), smoking (OR, 2.25; 95% CI, 1.07-4.77; P = 0.0332), vertebral fracture type (osteogenic vertebral tumor vs. OVCF: OR, 1.53; 95% CI, 1.73-12.30; P = 0.0022), vertebral fracture type (osteolytic vertebral tumor vs. OVCF: OR, 1.00; 95% CI, 1.09-6.73; P = 0.0316), and vertebral fracture location (lumbar vs. thoracic: OR, -1.28; 95% CI, 0.13-0.58; P = 0.0007) were independently associated with residual back pain after PVP or PKP in the early post-operative stage (Table 3).
**Table 3**
The multifactor logistic regression analysis for the factors associated with residual back pain after PVP or PKP.

| Variable                              | Estimated value | P     | OR   | 95%CI of OR |
|---------------------------------------|-----------------|-------|------|-------------|
| Cement distribution                   | 1.77            | < .0001 | 5.84 | 2.72,12.55  |
| (satisfactory vs. unsatisfactory)     |                 |       |      |             |
| Smoking (yes vs. no)                  | 0.81            | 0.0332 | 2.25 | 1.07,4.77   |
| Vertebral fracture type               | 1.53            | 0.0022 | 4.62 | 1.73,12.30  |
| (osteogenic vertebral tumor vs. OVCF) |                 |       |      |             |
| Vertebral fracture type               | 1.00            | 0.0316 | 2.71 | 1.09,6.73   |
| (osteolytic vertebral tumor vs. OVCF) |                 |       |      |             |
| Vertebral fracture location           | -1.28           | 0.0007 | 0.28 | 0.13,0.58   |
| (lumbar vs. thoracic)                |                 |       |      |             |

**Discussion**

PKP and PVP are widely used for the treatment of symptomatic OVCF and symptomatic vertebral fracture caused by malignant spinal lesions. The rate of significant back pain relief has been reported to be 78%-95.3% among patients with OVCFs and 73%-100% for patients with malignant spinal lesions [10,11]. Significant back pain relief was 90.39% (771/853) in the current study, which was consistent with the previously published literature [10,11]. Although the majority of patients achieved satisfactory results, some patients still had residual back pain. Residual back pain was defined as a VAS > 3, which can affect sleep. Significant differences in VAS scores were observed in the early stage post-operatively, including post-operative day 1 and month 1. The OVCF patients were placed on bed rest, wore a brace when walking, underwent regular anti-osteoporosis treatment, and were prescribed analgesics when necessary. Patients with malignant spinal lesions underwent radiofrequency ablation, radiotherapy, or interstitial radiotherapy. After these methods, most patients with residual back pain recovered at 3 months post-operatively and significant differences were not observed at 3 months post-operatively. In the current study, the results showed that unsatisfactory cement distribution, a smoking history, osteogenic vertebral tumors, osteolytic vertebral tumors, and thoracic fractures were independently associated with residual back pain after PVP or PKP at an early post-operative stage.

The best choice for the treatment of VCF between PKP and PVP is controversial. Cloft et al. [12] demonstrated that PKP has no significant advantages compared to PVP with respect to back pain relief and the cost of PKP is greater than PVP [12]. In contrast, Dohm et al. [13] reported that the PKP group had more complete back pain relief and a lower incidence of post-operative cement leakage compared with the PVP group. A meta-analysis published by Kaloostian et al. [11] showed that the percentage of back pain improvement was 91% (range, 73%-100%) in the PVP group and 93% (range, 80%-100%) in the PVP
group. Whether a PVP or PKP with the unilateral or bilateral approach provides similar efficacy is controversial. In a recent systematic review, no difference was found between the unilateral and bilateral approaches [14]. In the current study, there was no statistically significant difference in surgical approach and surgical type between the two groups. We think that the most important factor causing residual back pain is unsatisfactory cement distribution (OR, 5.84); unsatisfactory cement distribution did not induce a better effect to stabilize micromovements and fill the gap between microfractures. Yang et al. [10] showed that unsatisfactory cement distribution was a strong risk factor associated with residual back pain after PVP or PKP, which is in agreement with the current study. Accurate cement filling can completely occupy the fracture area and fractured vertebrae can be stabilized, and exert a good analgesic effect. The direction of the trocar cannot be uniformly specified from the back of the vertebra to the front, but should be based on the fracture location. As for different parts, individual selection of puncture points and the trocar make the cement pusher point to the fracture area. This is particularly important for fractures located at the anterior superior vertebra. Surgeons should not only attempt a unilateral puncture if the distribution of cement is unsatisfactory, and a bilateral puncture and filling should be added in time. The surgeon should not blindly pursue the amount of cement filling. As long as the cement is well-distributed, the excessive filling amount is not proportional to the back pain relief and will only increase the risk of leakage. Surgeons should reasonably use various techniques for cement filling, such as secondary filling, and the purpose is to achieve a satisfactory distribution.

Shi et al. [15] demonstrated that smoking is a risk factor for chronic pain. Ditre et al. [16] observed modest evidence to support the notions that smoking may be a risk factor in the multifactorial etiology of some chronically painful conditions. In the current study, the smoking history was a risk factor for residual back pain; the underlying mechanism may be as follows [15]. First, nicotine may produce central anti-nociceptive effects by agonizing nicotinic acetylcholine receptors in the brainstem, particularly the α4β2 subtype, resulting in activation of the spinal cord descending pain inhibitory pathways. Second, nicotine increases attentional resources and leads to attentional narrowing. Attentional narrowing is believed to restrict attention to a smaller number of the most salient environmental cues. Thus, smoking may result in greater awareness of painful stimuli when there is no alternative distractor to focus on.

Deramond et al. [17] and Chiras et al. [18] concluded that the complication rates of PKP and PVP were higher in patients with metastatic lesions (5%-10%) than in patients with osteoporotic fractures (1%-3%). The current study showed that compared with OVCF, residual back pain occurs more frequently in osteogenic vertebral tumors (OR, 4.62) and osteolytic vertebral tumors (OR, 2.71), which is in agreement with the existing literature. The higher incidence of residual back pain in malignant vertebral compression fractures compared to OVCFs is due not only to the fracture, but also the tumor. Compared to osteogenic vertebral tumors and osteolytic vertebral tumors, the vertebrae of osteogenic vertebral tumors are much harder, so the puncture is more difficult and the cement could not distribute satisfactorily.

Some patients who have vertebral fractures in the thoracic spine complained of midline and non-midline back pain areas, such as the rib, chest, hip, groin, and buttocks. Among the non-midline back pain, the ribs were the most common site, most of which are considered to be the result of stimulation of the
intercostal nerve at the affected vertebral segment [19]. The specific mechanism underlying the pain is not clear at present, the possible reasons may be the stimulation of the displaced fracture block, decreased vertebral height, and local inflammatory stimulation [19, 20]. Such patients after PKP or PVP achieve more rapid relief, but intercostal nerve pain of some patients still exist to different degrees and the residual time also varies. The residual back pain was also worsened by a change in posture and will lead to the treatment unsatisfaction; the protection still lacks effective measures in addition to the symptomatic treatment. By multifactor logistic regression analysis of the current study, when comparing the lumbar with thoracic vertebral compression fractures, the OR was 0.28. Therefore, it is necessary to know the location of the vertebral compression fracture before the operation and inform the patient of the possible outcome to obtain their understanding and face the issue correctly, cooperate with the follow-up auxiliary treatment, and improve the overall satisfaction rate.

There were several limitations to this study. Residual back pain in vertebral compression fractures is associated with multiple factors. Only the common factors associated with back pain were included in this analysis. This study included patients with residual back pain during the first month post-operatively; the long-term complications, such as non-union or secondary vertebral fractures were not included. A further prospective controlled study is needed to explore the risk factors associated with residual back pain.

Conclusion

Unsatisfactory cement distribution, smoking history, osteogenic vertebral tumors, osteolytic vertebral tumors, and thoracic fractures were independently associated with residual back pain after PVP or PKP at the early post-operative stage. All of those should be addressed during pre-operative communication and post-operative management.

Abbreviations

PVP: Percutaneous vertebroplasty; PKP: Percutaneous kyphoplasty; OVCF: Osteoporotic vertebral compression fracture

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committees of the First Affiliated Hospital of Xi’an Jiaotong University, and the requirement of informed consent was waived owing to the retrospective nature of the study.

Consent for publication
Availability of data and materials

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

Competing interests

No potential conflict of interest relevant to this article was reported.

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Authors’ contributions

All authors made substantive intellectual contributions in this study to qualify as authors. BB Z and YG Z designed this study. WZ Y and JT X participated in collecting and analyzing raw materials. An initial draft of the manuscript was written by BB Z. YG Z, ZW R and YM Y redrafted parts of the manuscript and provided helpful advice on the final revision. All authors were involved in writing the manuscript. All authors read and approved the final manuscript.

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