Clinical Report

Less PMMA Injection as an Independent Predictor of Poor Neurologic Recovery Following Percutaneous Vertebroplasty in Patients with Malignant Vertebral Compression Fractures

Hongkai Cui1,2, Xianliang Zhang3, Ruifang Yan2 and Jingliang Cheng1

1 Department of Radiology, The First Affiliated Hospital, Zhengzhou University, Zhengzhou, China
2 Department of Interventional Radiology, The First Affiliated Hospital of Xinxiang Medical University, Weihui, China
3 Department of Interventional Radiology, The Center Hospital of Zhoukou, Zhoukou, China

Abstract: To evaluate the efficacy of percutaneous vertebroplasty (PVP) for malignant vertebral compression fractures with symptoms of neurological compression and the predictive factors for poor neurologic outcomes following PVP. Forty-three patients with malignant vertebral compression fracture symptoms and symptoms of neurological compression were treated with PVP, and were classified into two groups according to the American Spinal Injury Association (ASIA) impairment scale at the last follow-up. Data were collected, and the patients were followed up for more than three months after the procedure. Univariate and multivariate analyses were performed to evaluate predictive factors of poor neurological recovery. PVP was successful in all patients. Full recovery from (n = 2) or improvement of (n = 16) neurological compression symptoms was achieved in 18 patients (Group A), and no improvement of neurological compression symptoms in 25 patients (Group B). Univariate analysis showed more PMMA leakage (p = 0.038) and less PMMA volume injection (p < 0.001) was associated with the poor neurological recovery, and multivariate analysis showed that less PMMA volume injection (p = 0.004) was an independent predictor of poor neurologic recovery. PVP should not be served as an effective treatment for malignant compression fractures with symptoms of neurological compression, and less PMMA volume injection was an independent predictor of a poor neurologic recovery.

Key words: Neurological compression, Pain, Percutaneous vertebroplasty, Predictor, Vertebral compression fracture

Introduction

The skeletal system is the third most common site of metastasis, and metastatic spinal tumors develop in an estimated 5–10% of all cancer patients. The conventional treatment of spinal metastasis is an open surgery, which often results in complications, and delays treatment of the primary disease owing to prolonged hospitalization. To overcome these problems, a minimally invasive procedure, percutaneous vertebroplasty (PVP), has been developed. It involves the percutaneous injection of polymethylmethacrylate bone cement (PMMA) into the collapsed vertebral bone, which has proven to have a rapid implementation, and to be associated with complications rarely. This procedure has been highly effective in reducing axial spinal pain in osteoporotic vertebral compression fractures as well as vertebral metastatic diseases. But little is known about PVP for malignant spinal lesions with epidural involvement in patients with neurologic deficit.

Although several reports have demonstrated that severe spinal canal compromise and even spinal cord compression should not preclude performance of PVP, the increased risk may still be caused by breakdown of the posterior cortex of the vertebral body, with an increased likelihood of leakage of PMMA into the epidural space or paravertebral space and impingement on nerves. The authors surmised the cases of the malignant vertebral compression fractures with symptoms of neurological compression following PVP and aimed to evaluate the efficacy of PVP for malignant vertebral compression fractures with symptoms of neurologic compression and to identify the predictive factors of poor neurologic outcomes following PVP.

Materials and Methods

Patients

Forty-three patients with malignant vertebral compression fractures and symptoms of neurological compression were treated with PVP from October 2009 to December 2012. The presence of malignant vertebral compression fracture symptoms and symptoms of neurological compression was confirmed by reviewing the patients’ history and findings on computer tomography (CT) and magnetic resonance imaging (MRI). The etiological parameters of the spinal diseases were determined by means of histological examination of biopsy specimens obtained before or during the procedure.

This study was approved by the university committee for the protection of human subjects, and informed consent was obtained from each patient. All patients who were referred for the treatment were asked to complete a short questionnaire about presence, severity, and duration of pain (spinal and radicular pain), etiology of the spinal disease, and the presence of neurologic compression symptoms by a practitioner. Patients were eligible for enrollment if they met the following criteria: (1) definite malignant vertebral compression fractures, either primary or metastatic, confirmed by CT or MRI examinations; (2) symptoms of neurologic compression, confirmed by physical examinations; (3) the percentage of height reduction in vertebral body less than 50%; and (4) the patients had one clinical follow-up ≥ 3 months after the initial treatment. Patients were excluded if any of the followings was present: (1) Patients who underwent PVP for a malignant vertebral lesion without symptoms of neurologic deficit.
compression; (2) severe cardiopulmonary comorbidity; (3) untreated coagulopathy; (4) inability of the patient to undergo general anesthesia; or (5) contraindication to MRI.

**Interventions**

All PVP procedures were performed using a single plane angiography system under fluoroscopic guidance by two orthopedists who had more than 10 years experience in orthopedics. Blood pressure, heart rate, SPO2 and other vital signs were monitored by electrocardiography during the procedure.

The patient was placed in a prone position on an operating table. After local anesthesia, a small incision was made with a scalpel blade. Thereafter, a 13G bone puncture needle (Cook, Bloomington, IN) was placed transpedicularly in the fractured vertebra. After removal of the inner needle, commercially available polymethyl methacrylate (PMMA) (Osteo-Firm, COOK Medical, Bloomington, IN, USA) was carefully injected into the fractured vertebra under continuous fluoroscopic monitoring via lateral and anteroposterior projections in order to ensure adequate lesion filling and to avoid PMMA leakage or migration into the venous system towards the lungs. The injection was ceased when substantial resistance was met or when the cement reached the cortical edge of the fractured vertebral body; injection was also stopped if cement leaked into extraosseous structures or veins. In general, a total of 3-5 ml PMMA was injected into the fractured vertebral body. The post-procedural fluoroscopic evaluation was also obtained to show optimal filling of the lesion with no evidence of PMMA extravasation. In addition, PVP was also performed in both groups with one or more procedures on other malignant vertebral metastasis without compression fractures on MRI at other levels above and below the compression fractures. After the procedure, a CT scan of the treated vertebral bodies 3 days after PVP was done with 2 mm slices to identify the distribution of cement in the lesion, cement leakage outside the vertebral body or other possible local complications.

**Data collection and definitions**

Patients were clinically examined by two of the authors, who gathered the data before the procedure and at 1, 3, 6 and 12 months afterward. Imaging follow-up comprised anteroposterior and lateral spinal radiography at 1 month, 6 months and 1 year after the procedure. CT and/or MRI were performed in the same manner as before the procedure at 3 months and every 6 months after the procedure in all patients.

Data regarding (a) technical success, (b) primary clinical success, (c) secondary clinical success and (d) complications were evaluated at the time of the report or patient death. All data were obtained prospectively by completion of clinical surveys by the authors. Technical success was defined as successful PVP performance without major complications. The severity of the neurological compression was assessed using the American Spinal Injury Association (ASIA) impairment scale: A (complete impairment), no motor or sensory function is preserved in segments S4 through S5; B (incomplete impairment), sensory but not motor function is preserved below the neurological level and includes segments S4 through S5; C (incomplete impairment), motor function...
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selection was planned for finding independent predictive factors associated with patients without improvement of ASIA impairment scale. Only variables with p < 0.2 at univariate analysis (Mann-Whitney U-test or Fisher’s exact test) were entered into the multivariate logistic regression model. Statistical analyses were performed using SPSS statistical software (version 13.0 for Windows, SPSS Inc., Chicago, IL, USA). The P-value was considered statistically significant if lower than, or equal to 0.05.

Results

Baseline characteristics of the patients

Forty-three patients (26 men and 17 women, mean age 60.70 ± 11.69, range 39-75 years) were included in this study. Their baseline characteristics are summarized in Table 1. Among these patients, one presented with complete paraplegia (no motor function, ASIA scale A or B) and forty-two presented with incomplete paraplegia (ASIA scale C or D) (Table 1). Levels of complete paraplegia were at T5 (n = 1). Levels of incomplete paraplegia were at T2 (n = 1), T3 (n = 4), T5 (n = 3), T6 (n = 5), T10 (n = 3), T11 (n = 5), T12 (n = 3), L1 (n = 7), L2 (n = 5), L3 (n = 3), and L4 (n = 3).

Technical and initial clinical results

PVP were technically successful in all patients. Twenty-three patients had improved neurological compression symptoms, and twenty had no change at the time of discharge. None of the patients reported worsening at the date of discharge. There were no complications including infection, bleeding, pulmonary embolism, stroke or cardiac arrest. A single-level PVP was performed in the fractured vertebral body in all patients, and PVP at other levels without compression fracture underwent in 19 patients. CT showed cement leakage in 35 (59%) of the 59 treated vertebral bodies. Leaks were leaked into the intervertebral disk (n = 8), puncture site (n = 3), paravertebral space (n = 10) or veins (n = 13); cement leaked into the spinal canal in one patient which resulted in complete paraplegia of the patient. No other complications were observed in the two groups. The mean postoperative hospital stay for the procedure was 6.09 ± 1.02 days (range, 4–9 days), and the thirty-day mortality rate was zero.

Follow-up clinical results

Clinical follow-ups were obtained for 43 patients in group B (mean: 14 ± 6 months; 95% CI: 12, 16 months; range: 4-35 months), and outcome measures were completed preoperatively and at the last follow-up visit. All patients were followed-up and assessed at 1 month and 3 months, 40 at 6 months and 25 at 1 year. Two were evaluated for more than 2 years prospectively. Clinical assessment at the final follow-up found complete resolution of pain (n = 15) or decreased pain (n = 13) in 28 patients, a primary clinical success rate of 65% (95% CI: 50%, 80%). Full recovery from (n = 2) or improvement of (n = 16, Fig. 1) neurological compression symptoms were achieved in 18 patients (Group A), a secondary clinical success rate of 42% (95% CI: 26%, 57%). 16 patients continued with follow-up health care after the procedures and were alive with the improvement of pain and symptoms of neurologic compression at the time of this report; 27 patients died of the underlying diseases unrelated to the procedures. The mean and median survival periods were 22 ± 2 months (95% CI: 16-24) and 19 ± 2 months (95% CI: 16-22), respectively (Kaplan-Meier analysis).

Univariate and multivariate logistic regression analysis

Thirteen variables were considered for the univariate analysis. The results were provided in Table 2. The univariate analysis showed the poor neurological recovery was associated with more PMMA leakage (25% vs. 50%, p = 0.038, Table 2) and less PMMA volume (3.63 ml vs. 5.22 ml, p < 0.001, Table 2). No other variables including age, sex, duration of the symptoms, preprocedural VAS and ODI score, location (thoracic or lumbar), type of primary tumor, the number of levels treated per patient, duration of follow-ups, prior chemotherapy or radiotherapy showed no significant difference between the two groups respect to. The multivariate analysis revealed that less PMMA volume (odds ratio [OR], 11.90; 95% CI, 2.293–63.524; p = 0.004) was an independent predictor of a poor neurologic recovery (Table 3).

Discussion

In this present study, we found that PVP had several advantages, such as a high technical success rate, moderately improved pain and neurological compression symptoms. Multiple logistic regression analysis revealed that less PMMA volume (odds ratio, p = 0.004) was an independent predictor of a poor neurologic recovery. But all the following displayed negative associations: age, sex, duration of the symptoms, pre-procedural VAS and ODI score, location (thoracic or lumbar), type of primary tumor, the number of levels treated per patient, duration of follow-ups, prior chemotherapy or radiotherapy. To date, this is the first report to evaluate the predictive factors for malignant vertebral compression fractures with symptoms of neurological compression.

Metastatic spinal cord compression (MSCC) is a serious complication of metastatic cancer that requires immediate diagnosis and treatment. In most MCSS patients, the treatment is largely palliative, aiming to achieve relief of pain and to regain function and to improve the quality of the life of the patient as quickly as possible. Because of their immunocompromised status from ongoing chemotherapy, poor nutrition, and comorbid medical conditions, surgery is often not an option in these patients with limited life expectancy. In addition, radiotherapy, however, requires 2–4 weeks to take effect and does not achieve complete pain relief in most cases. Furthermore, it does not maintain the stability of the vertebral compression fractures19,20).

Recently, more and more minimally invasive spinal interventions, such as PVP is reasonable alternatives to treat metastatic spinal disease. These procedures can result in less soft tissue trauma, lower blood loss, and shorter hospitalization time. Moreover, the overall morbidity is considerably lower in comparison to conventional spine surgery. Therefore, PVP may be a promising option and are beginning to be used in these patients for relief of pain and stabilization of the spine13-16).

Several reports have demonstrated that severe spinal canal compromise and even spinal cord compression should not preclude PVP13-16). In the opinion of these authors, with an experienced operator, the risk of procedure-related symptomatic complications is small, even in clinical situations that have been cited in the literature as contraindications or relative contraindications to PVP. However, for patients with MSCC, it is tough to obtain satisfactory pain relief and neurologic function recovery due to the destruction of the posterior cortex and massive PMMA leakage caused by the metastatic tumors21,22). Therefore, a reasonable concern is that small volume of cement may not be enough
to produce a long-term analgesic effect and prevent further vertebral body collapse. Another concern is that the likelihood of leakage of PMMA leak into the epidural space or paravertebral space and nerve impingement\(^{1,3,5}\).

In this study, we aimed to evaluate its clinical results in the management of malignant vertebral compression fractures with symptoms of neurological compression and to answer the question of whether the difference in neurological compression symptoms recovery between the two groups could be specifically attributed to the difference in PMMA volume. The univariate analysis found no differences but the incidence of PMMA leakage and PMMA volume between the two groups. Using multivariate analysis, we were easy to demonstrate the PMMA volume was the only risk factor for neurological compression symptoms recovery, which correspondence with our speculation. That is to say, more PMMA volume injection into the targeted vertebral body may result in good neurological compression symptoms recovery, whereas, less PMMA volume injection may lead to poor recovery.

In this study, we confirmed that PMMA volume played a major role in neurological compression symptoms recovery. It ensured the effectiveness of the procedure and gave us some important guidance for the further performance of the procedure. Without enough cement into the targeted vertebral body, it’s hard to ensure long-term analgesic effect and prevent further vertebral body collapse. For patients with malignant vertebral compression fractures, it is tough to inject enough cement into the targeted vertebral body due to the breakdown of the vertebral cortex and massive leakage. Therefore, the multivariate analysis was consistent with the results we obtained from the study.

The recent literature on spinal metastases treated with PVP revealed that complete or partial pain relief in 73–100% of the treated patients\(^ {4,5,6,10,14,20-27}\). For example, Cotten et al.\(^ {5}\) reported a decrease in pain level in 75% of patients at 6-month follow-up in a series of 37 patients with osteolytic metastases and myeloma. Weill et al.\(^ {20}\) reported a decrease in pain level in 73% of patients at 6 months in a series of 37 patients with spinal metastases. Our results of 65% pain relief or pain improvement during follow-ups were lower than the reported range of 73–100% pain relief in patients with spinal metastases\(^ {5,10,14,20-27}\). The result indicated that PVP alone were a moderately effective approach for malignant vertebral compression fractures and symptoms of neurological compression. Our results of 42% full recovery or improved from neurologic compression symptoms in the final follow-up was in line with those of Shimony et al.\(^ {10}\) in patients with symptoms of neurologic compression. The results suggested that PVP alone was not an effective approach for malignant vertebral compression fractures and symptoms of neurological compression.

Some limitations should be known in this study. One was the lack of a control group who underwent laminectomy and internal fixation. A comparison of laminectomy and internal fixation with PVP would have been enlightening, particularly with respect to the improvement of symptoms of neurological compression. Another limitation was that the number of patients treated was relatively small, their life span was short, and death due to rapid progression of the disease might have masked both benefits and risks of the procedure; thus, expanded clinical trials are required to determine mid-term outcomes.

In conclusion, our results indicated PVP alone seemed to be a safe procedure but can not be served as an effective treatment for malignant compression fractures with symptoms of neurological compression. Less PMMA volume injection was an independent predictor of poor neurologic compression recovery.

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**Competing Interests**

The authors have declared that no Competing interest exists.

**References**