Comparison of the postoperative pain change and spinal stenosis rate between percutaneous vertebroplasty combined with radiofrequency ablation and with $^{125}$I particle implantation in the treatment of metastatic spinal cord compression: A retrospective study

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ARTICLE INFO

Keywords:
Metastatic spinal cord compression
Pain management
Vertebroplasty
Radiofrequency ablation
$^{125}$I particle

ABSTRACT

Background context: Metastatic spinal cord compression (MSCC) seriously affects the survival rate.

Objective: The therapeutic effects of two treatment strategies for MSCC: percutaneous vertebroplasty (PVP) combined with radiofrequency ablation (RFA) and PVP combined with $^{125}$I particle implantation, were compared.

Study design: Retrospective study.

Patient sample: 40 patients with MSCC were divided into two groups: 19 cases in the RFA group and 21 cases in the $^{125}$I group.

Method: All patients were accessed to determine the differences in pain, which was evaluated using the visual analog scale (VAS) at 1 week, 1 month, and 3 months after the operation, and spinal stenosis rates (SSRs), which were measured at 1 and 3 months after the operation, between the two groups.

Results: The VAS scores and SSRs at baseline were comparable between the RFA group and the $^{125}$I group (7.19 ± 2.07 vs 7.42 ± 1.95, 37.7% ± 11.2% vs 41.1% ± 11.4%). The VAS scores and SSRs at 1 month and 3 months after the operation were significantly reduced in both groups, compared with those at baseline. The VAS scores and SSRs in the $^{125}$I group were lower than those in the RFA group at 3 months after the operation (1.09 ± 0.97 vs 1.75 ± 1.06 p = 0.048 and 12.3% ± 6.4% vs 18.1% ± 10.1% p = 0.034), while the VAS scores at 1 week after the operation in the RFA group were lower than those in the $^{125}$I group (4.39 ± 1.34 vs 5.05 ± 1.82 p = 0.049).

Conclusion: PVP combined with RFA has a slight advantage in relieving pain in the short term, while PVP combined with $^{125}$I particle implantation may have a better effect in the relieving pain and decreasing the SSRs at 3 months after the operation.

1. Introduction

Metastatic spinal cord compression (MSCC) is a type of nervous system damage caused by compression of the dural sac and its contents by an epidural or intradural mass in the late stage of malignancy. In most cases (85%), the causes of MSCC are hematogenous bone metastasis to the spine, resulting in bone collapse and destruction, and mass tumor compression of the spinal nerve. The incidence of MSCC is approximately 2%–10%, with most cases occurring in the thoracolumbar region. In MSCC, the most common primary tumors are prostate, breast, and lung cancers. The clinical manifestations of MSCC are local pain in the back and weakness and hypoesthesia of the limbs (>75% of cases), and the prognosis is often poor.

Percutaneous vertebroplasty (PVP) involves using polymethyl methacrylate, known for its analgesic effect, to strengthen the bone structure of the affected area. Radiofrequency ablation (RFA) and $^{125}$I particle implantation have also been reported to have positive effects on bone metastasis. PVP combined with RFA and PVP combined with $^{125}$I particle
implantation have been proven to be safe and effective in the treatment of vertebral metastasis.6,7 However, only few studies have compared these two approaches, especially in patients with MSCC. Therefore, to add to the limited existing literature, we aimed to compare the clinical outcomes and spinal stenosis rates (SSRs) in patients with MSCC treated with two therapeutic strategies, namely PVP combined with RFA and PVP combined with 125I particle implantation, to analyze their clinical differences to provide a reference for clinical treatment.

2. Methods

2.1. Study design and participants

This retrospective study included patients with MSCC who were admitted to the Department of Interventional Radiology from January 2017 to December 2019. All enrolled patients were diagnosed with MSCC on magnetic resonance imaging (MRI), with histological confirmation of malignancy of the primary tumor. The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Shanghai Sixth People's Hospital. All participants provided written informed consent for participation and publication.

The inclusion criteria were as follows: (1) a clear history and pathological diagnosis of malignant tumors; (2) improved computed tomography (CT) and enhanced MRI findings of the spine before the operation; (3) narrowing of the spinal canal and epidural compression in the local spinal cord visible on sagittal MRI scans before surgery; (4) osteolytic bone destruction of spinal metastasis; and (5) one or several clinical manifestations of the following secondary spinal cord injury: (a) local or radiation pain and progressive aggravation; (b) sensory function damage and progressive aggravation; (c) motor function damage and progressive aggravation; (d) sphincter function abnormality; and (e) involvement of ≤4 vertebral body segments in the tumors. The exclusion criteria were as follows: (1) predicted survival time of <3 months; (2) primary spinal tumors, such as multiple myeloma; (3) spinal infectious diseases, such as spinal tuberculosis and other bacterial infections; (4) severe cardiovascular and cerebrovascular diseases, respiratory failure, liver and kidney failure, and inability to tolerate surgery; (5) coagulation dysfunction; and (6) severe skin infection in the operation area.

All the selected patients had completed preoperative examinations, including routine blood tests, liver and kidney function tests, electrolyte tests, and coagulation function tests, CT and MRI. The patients were required to sign an informed consent form for the operation and medical device implantation. The selected patients were divided into two groups: the RFA group, which included patients treated with PVP combined with RFA, and the 125I particle group, which included patients treated with PVP combined with 125I particle implantation. All patients were randomly assigned to one of the two groups. In the 125I particle group, preoperative CT images were included in the radioactive particle treatment planning system to make treatment plans and determine the number of safe and effective radioactive particles.

2.2. Instruments and PVP preparation

The complete set of surgical instruments for PVP was obtained from Shandong Guanlong Medical Supplies Co., Ltd., China. The following materials and equipment were obtained: polymethyl methacrylate (PMMA) (Heraeus Medical GmbH, Germany), high-temperature disinfection barium sulfate (Qingdao Oriental Chemical Co., Ltd., China), three-dimensional treatment planning system (Beijing Feitianzhaow Industry Co., Ltd., China), 18G particle implant needle and device (Beijing Feitianzhaow Industry Co., Ltd., China), 125I particle (Shanghai Xinke Pharmaceutical Co., Ltd., China), digital subtraction angiography (DSA) system (GE, Innovia IGS 630, USA), 3.0T MRI (GE, USA), and 64-slice spiral CT (Toshiba, Japan).

DSA fluoroscopy was performed for all patients. After local disinfection and anesthesia, a 13G bone puncture needle was inserted into the diseased vertebral body using a transpedicular approach. After the puncture needle was in place, PVP combined with RFA or PVP combined with 125I particle implantation was performed. Both operations were performed by the same chief physician who specializes in spinal interventional surgery with 30 years of experience.

2.3. RFA procedure

After the 13G bone puncture needle was in place, the needle core was pulled out and placed into the radiofrequency needle. The target temperature was set at 85 °C, and RFA was performed for 10–15 min. The tumor tissue was damaged by rapid heating, after which, the radiofrequency needle was removed, and the point of the needle was placed at the front 1/3 of the vertebral body. Under X-ray monitoring, PMMA was slowly injected to strengthen the affected vertebral body (Fig. 1).

2.4. 125I particle procedure

Before implantation of the 125I particle, the prepared PMMA was slowly injected into the diseased vertebral body. After the PVP procedure, a CT scan of the spine was completed in all patients, and the location and range of residual lesions were confirmed. Then, according to the results of the treatment planning system (TPS), we outlined the gross tumor volume and measured and determined the prescription dose. In this study, the matching dose of 125I radioactive particles around the tumor was 120–160 Gy, and the dose to the spinal cord was <60 Gy. The radioactive activity of the 125I particles was 0.8 mCi. According to the TPS, we drew an isodose curve and then modified and improved the treatment plan to cover all residual lesions. During the operation, we used coaxial puncture technology. Using a 13G bone-piercing needle to create a passage in the target vertebral body, we inserted an 18G needle and then exchanged the angle and direction of the particle needle to place the 125I particle in the ideal position. The entire 125I particle implantation process was monitored by DSA to ensure the accurate placement of 125I particles (Fig. 2).

2.5. Data collection and follow-up

All patients completed preoperative examinations, including routine blood tests, and tests for liver and kidney function, electrolytes, and coagulation function. After the operation, all patients were required to remain in the supine position for 2 hours, during which, their vital signs were monitored, and symptomatic support treatments, such as dehydrating agents, anti-swelling drugs, steroids, and neurotrophic drugs, were provided. After the implantation of 125I particles, the operation area was covered with a lead coat to protect other individuals from ionizing radiation.

2.6. Outcome

All patients were assessed at baseline (1 week before the operation) and at 1 and 3 months after the operation. The outcome was to determine the difference in pain, which was evaluated using a visual analog scale (VAS) on a 10-point scale (1 = no pain and 10 = unbearable pain) between groups at 1 week, 1 month, and 3 months after the operation, and the SSR at 1 and 3 months after the operation. The amount of cement injected was 3.9 ± 1.8 ml for each vertebral body, and the number of implanted 125I particles was 33 ± 17.

Changes in the degree of compression of the spinal cord were evaluated by comparing the CT and MRI data for the spine before surgery and at 1 and 3 months after the operation. The stenosis rate of the spinal canal was determined by measuring the diameter of the spinal canal and the actual extent of the spinal canal at the site with the most severe compression. According to the results of preoperative spinal MRI, the degree of spinal stenosis was classified as mild (SSR <25%), moderate
(SSR <50% and SSR ≥25%), or severe (SSR ≥50%). The SSR was calculated using the following formula: $SSR = \frac{\text{maximum diameter of the spinal canal at the narrowest level} - \text{actual diameter at the narrowest level}}{\text{maximum diameter of the spinal canal at the narrowest level}}$. The SSR was measured by two experienced associate chief radiologists.

Adverse events were recorded, including local edema, increased pain, numbness of the lower extremities, transient aggravation of lower extremity function, decreased mobility in some patients after the operation, abnormal stool function and abnormal urine function after the operation.

2.7. Statistical analysis

Statistical analysis was performed using the SPSS statistical software ver. 17.0. Continuous and normally distributed variables are expressed as means and standard deviations, and non-normally distributed variables are expressed as medians and interquartile ranges. Before the operation and at 1 week, 1 month, and 3 months after the operation, the VAS scores of the two groups were analyzed using the paired t-test. Statistical analysis of the SSR before the operation, and 1 and 3 months after the operation in the two groups was also performed using the paired t-test. $P$-values $<0.05$ were considered to indicate significant differences.

3. Results

Forty patients with MSCC (21 men and 19 women; age range: 18–76 years, median age, 58 years) were enrolled in this retrospective study. The RFA group included 19 patients treated with PVP combined with RFA, and the $^{125}$I group included 21 patients treated with PVP combined with $^{125}$I particle implantation.

All patients in the two groups had multiple spinal metastases involving 90 vertebrae, including 3 cervical vertebrae, 54 thoracic vertebrae, 30 lumbar vertebrae, and 3 sacral vertebrae. The primary tumors outside the spine were confirmed by pathologic testing, and included 13 cases of lung cancer, 7 cases of thyroid cancer, 6 cases of liver cancer, 3 cases of colon cancer, 2 cases of kidney cancer, 2 cases of gastric cancer, 2 cases of cervical cancer, 2 cases of prostate cancer, and 3 cases of other cancers. The baseline demographic and tumor characteristics of the patients are presented in Table 1.

In imaging evaluations, the degree of preoperative spinal cord compression in the RFA group was mild in 4 cases, moderate in 10 cases, and severe in 5 cases after the operation. Spinal cord compression was mild in 9 cases, moderate in 3 cases, and severe in 0 cases, and 7 patients died during the follow-up period. The spinal canal stenosis rates were 37.7% ± 11.2%, 25.1% ± 10.2%, and 18.1% ± 10.0% before the operation, and 1 and 3 months after the operation, respectively. In

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**Fig. 1.** Imaging data for bone metastasis of thyroid cancer treated with PVP and RFA. (1A), (1B), and (1C) MIP images of preoperative lumbar MRI, sagittal T1WI, and transverse T2WI showing abnormal signals of the L1 vertebral body and right adnexa, accompanied by the formation of soft tissue at the right posterior margin of the vertebral body and the corresponding spinal stenosis; (1D), (1E), and (1F) images obtained 3 months after the operation, respectively. Reexamination of MIP images with enhanced lumbar MRI, sagittal T1WI, and transverse T2WI scans showed that the metastasis was significantly smaller than that before the operation, and the compression of the spinal cord was significantly reduced.
the $^{125}$I group, the degree of preoperative spinal cord compression was mild in 4 cases, moderate in 11 cases, and severe in 6 cases. After 3 months of follow-up, spinal cord compression was mild in 10 cases, moderate in 7 cases, severe in 1 case, and 3 patients died. The spinal canal stenosis rates were 41.1% /C6 11.4%, 27.5% /C6 8.6%, and 12.3% /C6 6.4%, respectively. There was no significant difference in the reduction of spinal stenosis rate between the two groups at 1 month after the operation ($P > 0.05$). Relief from spinal cord compression in the $^{125}$I group was better than that in the RFA group 3 months after the operation ($P < 0.05$).

A comparison of the incidence of adverse reactions within the group before and after the operation and between the groups after the operation showed that the incidence of severe pain and abnormal stool function was significantly reduced in both groups, at the end of the 3-month follow-up period. Moreover, the incidence of numbness in the lower limbs and abnormal urinary function in the $^{125}$I group was significantly lower (all $P < 0.05$; Table 3). In the RFA group, one patient died of gastrointestinal hemorrhage 1 month after the operation, and six patients died of multiple organ failure, brain metastasis, lung infection, and other causes 3 months after the operation. In the $^{125}$I group, one patient died of respiratory failure at 1 week after the operation, and two patients died of distant metastasis and multiple organ failure at 3 months after the operation.

4. Discussion

MSCC is a clinical manifestation of secondary spinal stenosis and spinal cord compression in the late stages of malignant tumor development, which seriously affects the quality of life and survival duration of patients. The PVP approach is widely used in the treatment of MSCC\(^5\) but has a disadvantage in that the tumor cells are not completely destroyed, resulting in a high tumor recurrence rate\(^6\); thus, various combined therapies have been proposed to solve this problem.\(^7\) In recent years, RFA and $^{125}$I particle implantation have yielded the most positive clinical results.\(^10\)-\(^13\) The aim of our study was to compare the clinical outcomes and spinal stenosis rates in patients with MSCC who were treated with two different therapeutic strategies: PVP combined with RFA and PVP combined with $^{125}$I particle implantation. We also sought to summarize and analyze the differences between the two groups to provide a reference for clinical treatment.

To the best of our knowledge, this retrospective observational study is the first to analyze the MSCC spinal stenosis rate, VAS pain score, and postoperative survival rate after PVP combined with RFA and PVP combined with $^{125}$I particle implantation. Although there was no significant difference in preoperative VAS score and spinal stenosis rate ($P > 0.05$), the postoperative results showed that the VAS score of the RFA group was lower than that of the $^{125}$I particle group at 1 week after the operation ($P < 0.05$), indicating that the short-term analgesic effect of RFA was better than that of $^{125}$I particle implantation. As the stimulation of the tumor area by RFA was relatively light and the influence of the swelling stage on the compression of the spinal cord was relatively small, the analgesic effect in these patients was better. There was no significant difference in VAS scores between the two groups at 1 month after the operation ($P > 0.05$); however, the VAS score in the $^{125}$I particle group was lower than that in the RFA group at 3 months after the operation ($P < 0.05$), indicating that the long-term analgesic effect in the $^{125}$I particle group was better.

The degree of spinal cord compression in the two groups was significantly lower at 1 and 3 months after the operation than at baseline. One month after the operation, there was no significant difference in the
and the tumor inhibition effect was longer, resulting in better clinical pain relief and a lower spinal stenosis rate 3 months after the operation. In addition, the reported median survival time of patients with MSCC is 3–6 months.11 Without treatment, the life expectancy of a patient with MSCC is approximately 1 month.22 The primary tumor histology affected not only the time between diagnosis and MSCC, but also the postoperative survival time of patients. According to Loblaw et al., lung cancer causes patients to have the shortest lifespan following their first MSCC episode (1.5 months).23 In our study, lung cancer accounted for the highest proportion (32.5%), and the 3-month survival rates were 63.2% and 85.7% in the RFA and 125I particle groups, respectively.

The clinical effect of PVP combined with RFA has been reported to be better than that of PVP alone,16 given that temperatures of >60 °C cause immediate protein coagulation, tissue necrosis, and irreversible cell damage.16 The thermal effects of RFA have been reported to destroy most tumor cells, and the secreted cytokines, reduce the distant spread caused by the injection of PMMA. These released cytokines also reduce the permeability of PMMA and the tumor activity due to tissue necrosis within the killing range and thrombosis in adjacent vessels.16 Our study also confirmed that the combination of PVP and RFA in the treatment of spinal metastases shows synergistic antitumor and analgesic effects and can control the tumor lesions to a certain extent. In the RFA group, the postoperative VAS scores were significantly lower than the preoperative score, and the spinal stenosis rates were 37.7% ± 11.2%, 25.1% ± 10.2%, and 18.1% ± 10.0% before the operation and at 1 and 3 months after the operation, respectively (P < 0.05). Furthermore, there was a significant difference between the preoperative and postoperative VAS scores and the spinal stenosis rate relief.

125I particle internal irradiation has also demonstrated the ability to kill tumor cells and tumor stem cells10, and inhibit the proliferative ability of tumor cells,17 thereby ensuring tumor control. Over the past 20 years,125I particle implantation has achieved notable clinical efficacy in solid tumors.18-20 This technique shows characteristics such as a short effective distance, continuous emission, low energy, failure with distance, and a general inability to cause loss to the surrounding normal structure, making it especially suitable for the treatment of spinal metastasis tumors with slow growth. In our study the VAS scores in the 125I particle group were 5.05 ± 1.82, 2.53 ± 1.39, and 1.09 ± 0.97 in the first week, first month, and third month after the operation, respectively. The spinal stenosis rates were 41.1% ± 11.4%, 27.5% ± 8.6%, and 12.3% ± 6.4% before the operation and at 1 and 3 months after the operation, respectively (P < 0.05). Moreover, the incidence of numbness in the lower limbs and abnormal urinary function in the 125I particle group was significantly lower, indicating that the spinal stenosis was effectively improved.

Although the principles underlying RFA are different from those underlying 125I particle implantation in the treatment of solid tumors, research shows that both of these techniques can inhibit tumor growth, delay tumor progression, and relieve pain to a certain extent.23 However, these minimally invasive operations alone cannot change the mechanical structure of the bone. However, in the treatment of bone metastases, in combination with PVP, they can control tumor focus from both physical and biological aspects, improve bone strength in the lesion area, and play a synergistic role in killing tumor cells and controlling tumor tissue.11 However, there are few reports on the clinical analgesic effect, spinal stenosis rate, and postoperative survival rate of these combined therapies, especially for patients with spinal metastasis accompanied by spinal cord compression syndromes.12

Our study has some limitations. First, the relatively small sample size does not allow for the full evaluation of the survival rate; thus, the difference in survival rate described in our study is likely to be related to other conditions and not to the surgical intervention itself. Second, the decision on the surgical approach was made partially by patients themselves, which allowed some bias in group formation; a blinded approach in this type of study is almost impossible to achieve, for ethical and economic reasons. Finally, the follow-up period was only 3 months, and the reduction of spinal stenosis rate between the two groups (P > 0.05), but at 3 months after the operation, relief from MSCC in the 125I particle group was better than that in the RFA group (P < 0.05). As the implantation of particles occurred after the injection of bone cement, 125I particles were mainly distributed at the posterior edge of the vertebral body. In the process of particle placement, physical stimulation of the tumor area leads to significant tissue edema and swelling, resulting in relatively obvious postoperative pain. Three months after the operation, the edema in the operation area had subsided, and the degree of spinal cord compression relief in the 125I particle group was better than that in the RFA group. As the half-life of 125I particles is 59.6 days,23 a sustained internal radiotherapy effect remained for some time after the operation.
because some clinical data are still missing, long-term follow-up data need to be analyzed in future studies.

5. Conclusion

To conclude, this study provides some experience and reference data for the minimally invasive interventional treatment of MSCC. The two combined therapies showed significant clinical effects. PVP combined with RFA has a slight advantage in relieving pain in the short term but may have a better effect in relieving pain and SSRs when combined with $^{125}$I particle implantation at 3 months after the operation.

Ethical approval

The study was approved by the ethics committee of Shanghai Sixth People's Hospital. All clinical practices and observations were conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each patient before the study was conducted.

Patient consent

Written informed consent was obtained from patients for publication of these case reports and any accompanying images.

Funding

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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