# Advances in the clinical research of the minimally invasive treatment for the posterior edge of vertebral-body defects by spinal metastases (Review)

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Abstract. Spinal metastasis is one of the commonly observed complications in the advanced stages of cancer patients, and is a serious threat to human life and health. Malignant tumor invasion usually leads to defects in the posterior margins of the vertebral body, which caused significant cancer pains to patients and increased the risk of surgery. Currently, minimally invasive treatments of vertebral defects caused by spinal metastases include percutaneous vertebroplasty (PVP) combined with radiofrequency ablation and PVP combined with <sup>125</sup>I seed implantation. These minimally invasive techniques have particular superiority to control pain in patients with spinal metastases, improve nerve function, reduce the incidence of fractures and surgical risk, and improve the quality of life. The present study reviewed the progress in clinical research on vertebral defects caused by spinal metastases, and the mechanisms and minimally invasive treatment.

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### 1. Introduction

Currently, malignant melanoma incidence rates have increased worldwide. Spinal metastasis is a commonly observed late complication in malignant tumor patients (1). Malignant tumor invasion usually leads to defects in the posterior margins of the vertebral body (2). Investigating the mechanisms of the posterior vertebral-body defects is important to aid the understanding of the minimally invasive treatment of spinal metastasis, which is helpful to control the pain of patients with spinal metastases, improve the neurological function, reduce the incidence of fractures and improve the quality of life.

# 2. Mechanism of the posterior vertebral-body defects with spinal metastases

Spinal metastasis is a common complication in patients with advanced malignancies. Scutellari et al (3) reported that spinal metastases were identified at autopsy in 30-70% of cancer patients. The majority of metastases are found in the thoracic spine (70%) followed by the lumbar spine (20%), cervical spine and sacral vertebrae (10%) (4). The majority of primary lesions are lung, breast and prostate cancers. Malignant tumor metastases to the spine are mostly dependent on blood-borne transmission. The middle and back of the vertebral body are the common metastatic site (5), which is possibly due to it being disseminated by vertebral venous plexus, and blood-borne transfection plays a major role in the process (6). Abdominal and thoracic venous plexus and pelvic venous plexus are connected with spine venous plexus, but there are no venous valves among it. Tumor emboli can directly transfer to and grow in the red marrow of the axial skeleton, not by the lungs, due to the muscle traction, the pressure of abdominal cavity or other factors, which easily form the damaged lesions that can be observed using the radiographic method (7). Computed tomography (CT) and magnetic resonance imaging can help to diagnose at an early time and accurately detect the spinal metastases with high sensitivity and specificity (8).

The most common form of the spinal metastases is osteolytic destruction (9). Local bone of the spine has the following characteristics: i) The bone mineral is generally lost in the vertebral body, including the vertebral body cortical and cancellous bone, which lead to a declined mechanical index of the vertebral body; and ii) metastatic foci induces posterior edge defects and the performances based on imaging mainly include sieve-like destruction, partial, flaky or missing lamellar, damaged posterior edge and tumor formation within the spinal canal (10).

## 3. Leakage of bone cement and the crowding effect in tumor regions

Mechanisms and consequences of bone cement leakage. The cancer foci invasively transfer and spread along the vertebral blood vessels. The irregular bone destruction 'crack' is formed, which is the anatomical basis for the migration of bone cement. The immature blood vessels within the tumor and the rich blood vessels in the tumor lesions of the vertebral body are connected to form a 'Straight Road', which can communicate with the peripheral vascular system of the vertebral body. Following bone cement injection, this is the main reason for the formation of branched seepage. Particularly when bone cement flows along the vascular access, thrombosis vital organs will be induced (11), oppressing the surrounding organs in the vertebral body. The tumors forming in the spinal canal and intervertebral foramen should be concerned with resulting in the compression and damage of the spinal cord and nerve root.

*Crowding-out effect in tumor lesions*. During the process of implantation, the metastatic lesions in the space of defects are easily moved from the defected part, and thus, planted metastases and spinal cord compression would be formed.

# 4. Traditional method for treating cancer metastasis of posterior vertebral-body defects

Spinal stability is decreased during bone damage in tumor lesions, which have manifested as local fractures, vertebral compression fractures and scoliosis, accompanied by varying degrees of bone-derived pain and compression symptoms of nerve root or spinal cord (12,13). Therefore, reconstructing the stability of the vertebral body or improving the mechanical index of the affected vertebra to effectively relieve bone-derived pain is the goal for therapy (14,15).

Traditional therapy methods of spinal metastases include radiotherapy, chemotherapy, isotopic therapy, bisphosphonate therapy, pain relief treatment and the palliative surgical treatment (16). Choice of treatment depends on histological type of the primary tumors, neurological function prior to treatment, number of the involved vertebrae, vertebral level, the location of osteolytic lesions within the vertebral body, intraspinal degree of diffusion, the patient's general condition and the severity of pain.

Although successful tumor treatment with radiation may provide effective pain relief, which showed >75% radiographic control rates, it generally shows the effect one to two weeks after the therapy. The most significant weakness is the lack of ability to resolve the spine instability caused by tumor destruction, and the increase of the vertebral collapse and nerve oppression risk (16,17). Chemotherapy and other conservative treatments are difficult to effectively achieve an analgesic effect and stabilize the spine. Bisphosphonates, biological immune therapy and radiation therapy are able to prolong the patient's life cycle and relieve the pain, but they cannot restore the vertebral biomechanical indicators of the spine (18,19).

The main purpose of surgery is to stabilize the spine and reduce pressure; however, due to the larger trauma and higher complications of the open surgery, a longer recovery time is required following the surgery. Therefore, the comprehensive treatment time is missed for primary tumors. For the patients with multiple segments of spinal damage, there is a significant difficulty for anterior and posterior surgery (20).

# **5.** Minimally invasive surgery on posterior edge defects of the spine for patients with metastatic carcinoma

*General*. Minimally invasive techniques are acceptable for the majority of patients with bone metastases, which has less trauma, effective results and fewer complications. Minimally invasive techniques have gradually become an important treatment for spinal metastases and are increasingly used in clinical application. The treatment methods commonly used in minimally invasive interventional therapy include percutaneous vertebroplasty (PVP), percutaneous kyphoplasty (PKP), percutaneous radiofrequency ablation (RFA), vascular embolization, a small incision in the spinal fixation surgery and radioactive seed implantation.

PVP. PVP is a percutaneous puncture injection of bone cement (polymethymethacrylate) into the vertebra guided by a digital subtraction angiography (DSA) machine, and can enhance the intensity of vertebrae and stability of the spine, prevent collapse, relieve waist and back pain and restore partial vertebral body height (21). In 1987, Galibert et al (22) first reported the successful treatment by PVP of one case of patients with chronic pain caused by C2 vertebral hemangioma. In 1989, Kaemmerlen et al (23) used the technology to treat the patients with metastatic carcinoma of the vertebral body. In recent years, the technology has been gradually extended to treat spinal metastases worldwide, and has been recognized and approved by clinicians and patients for the superior effect (24). Currently, posterior edge defect is considered as the PVP surgery contraindication by the majority of investigators, as vertebral defects are prone to induce bone cement leakage leading to the narrow spinal canal or intervertebral foramen stenosis, and even certain serious consequences, such as spinal cord or nerve root compression (25). Thus, there are a significant number of patients for whom it will be difficult to avoid the unbearable pain and paralysis.

Yang *et al* (26) believed that precautions in surgical procedures are as follows: i) It is recommended to complete with the beveled puncture needle, as it is conducive to accurately put the tip into the tumor lesion or the edge of tumor foci; ii) puncturing with the bevel needle, and the bevel back on the canal, making the injection pressure of the bone cement toward the tumor foci and back to the spinal vessle. iii) Target contrast should be finished prior to injection of bone cement and the comprehensive assessment of the distributions of the contrast agent in the region should be made; iv) bolus injection of bone cement solidification phase should be delayed and bone cement dispersion minimized to avoid the distribution of bone cement into the trailing edge cortex of the vertebral body; v) when necessary, a small amount of bone cement should be injected into the 'normal' cancellous bone in the periphery of the tumor foci, which played the anchor role, to avoid the bone cement moving into the spinal canal following surgery; and vi) limit the movement of the spine following surgery and make the regular radiographic observation. The patients with the posterior edge defects of spinal metastases can still implement PVP surgery.

PKP. PVP to kyphoplasty was another minimally invasive treatment of spinal metastases that was developed on the basis of PVP. The basic therapy methods and procedures were the same with PVP; it is expanded with a balloon to form a compartment in the target vertebral body, which can partially restore vertebral height. Subsequently, bone cement was injected into the vertebral body by needles (27). PKP requires a higher viscosity bone cement compared to PVP and the vertebral bone cement was slowly injected under fluoroscopic guidance, reaching the edge of the vertebral body, or two-thirds of the vertebral body. Due to the presence of lacuna formed by balloon dilatation, bone cement can be injected at the conditions of relatively low pressure and the incidence of bone cement leakage was reduced in theory (28). PKP indications include compressed fractures caused by osteoporosis of the vertebral body; more with vertebral compression fractures with kyphosis after 6 months; and pathological fractures and kyphotic deformities induced by metastases of the vertebral body. Although PVP can significantly alleviate severe pain induced by spinal metastases, it cannot restore kyphotic deformity and abnormal changes in spinal biomechanics, which may lead to a poorly analgesic effect at a long-term time. The pain remission rate of PKP is similar with that of PVP, but PKP has the role to increase the bone strength of the vertebral body, restore vertebral height, correct kyphosis and restore normal biological force lines of spinal body (29). As PKP can increase the vertebral defect area, it would not be recommended to the patients with vertebral defects caused by metastatic cancer of the spine (30).

Radiofrequency ablation combined with PVP technology. RFA technology uses the radiofrequency ablation device. Under the guidance of DSA, CT, B ultrasonic imaging equipment and percutaneous ablation needle (radiofrequency electrode) punctures to the inside of the tumor, the middle or high-frequency radio waves were excited by the electrode and the surrounding tissue is subjected to plasma and shocked to produce heat. An oval area is formed with high temperature. The central temperature can reach 90-100°C and the temperature is  $\leq$ 50°C, at which, coagulative necrosis of the cells arises. Thus, the tumor cells were inactivated. The blood vessels around the tumor lesions are coagulated to form a 'reaction zone' to interrupt the blood supply by the blood vessels within the tumor (31). Recently, RFA technology is being applied to treat bone tumor lesions. Clinical studies have shown that RFA can effectively alleviate the pain caused by bone tumors, such as osteoid osteoma, ossifying fibroma, vertebral hemangioma and vertebral metastases (32). Bone tumors are significantly different with substantive organs in organizational structure, biological and physicochemical properties, thus the range of radiofrequency ablation lesions, shape and distribution of the thermal field will be different from the parenchymal organs. The RFA diameters of the single electrode are 0.9-1.3 cm within the bone tissue, and cortical bone can effectively limit the heat conduction with a significant thermal insulation, which can protect the vital organs from thermal damage (33). The integrity of rear vertebral body bone cortex has important significance for the RFA ablation of spinal metastases. Theoretically, RFA induced the tumor tissue, paravertebral venous plexus or venous plexus within the vertebral body to coagulate to form a 'reactive zone', which can reduce the risk of bone cement leakage, making the bone cement more evenly distributed within the tumor tissues (34). The combination of RFA and PVP technology can largely overcome their own limitations and enhance the complementarity between them (35).

Vascular thrombosis combined with PVP surgery. The vascular thrombosis technique is another commonly used method for minimally invasive treatment of spinal tumors, and it can be carried out by arterial cannulation and also by percutaneous puncture. The main indications for vas embolism operation are the tumors with a rich blood supply. Prior to open surgery, tumor embolization is performed to reduce blood loss during surgery. For the patients with spinal metastases who cannot tolerate surgery, vascular embolization can also be used as a local control of the tumor to relieve pain symptoms in palliative treatment, which is particularly appropriate for the tumors with a sufficient blood supply, such as renal cell carcinoma and thyroid cancer. Polyvinyl alcohol is the most commonly used embolic material and other materials, such as gelatin and sponge, are also included. The vessels can be completely embolised in 80% of patients; however, the major complication of vascular thrombosis technology is nerve damage. Cervical tumor embolization may cause cerebellar or brainstem infarction, but they usually have no symptoms. The embolization therapy on thoracic spine may damage the spinal cord, leading to motor and sensory disorders of the limbs. Koike et al (36) evaluated the effect of transcatheter arterial chemoembolization/embolization for symptomatic bone metastases, particularly in palliation. The data demonstrated that 75% of targeted lesions underwent sufficient devascularization without any serious complication and there was a positive correlation between the blocking degree of the blood supply and pain relief. Thus, vas embolism operation is an effective treatment method that is palliative for symptomatic bone metastases. Truumees et al (37) believed that >60%of spinal metastases were hypervascular and preoperative embolization was considered to decrease the hemorrhage risk and improve outcomes. Vas embolism operation can suppress tumor growth, but is not able to restore the biomechanics of the affected vertebrae. Vas embolism in combination with PVP surgery can inhibit the tumor progress, and also restore the biomechanics of the affected vertebrae to prevent the affected vertebrae to collapse.

Spine internal fixation with small incision. Due to extensive destruction of the vertebral body in patients with spine metastases, spine instability severely occurred and spinal cord compression may be induced. When PVP surgery did not provide enough stability for the spine, spine internal fixation with a small incision has a unique therapeutic value. The commonly used open surgeries for vertebral metastases include removal and reconstruction surgery of the anterior tumor lesion and resection and reconstruction of the whole posterior spine. These types of surgery have large trauma, significant bleeding and a high incidence of complications. Generally, patients undergoing open surgery often require a longer postoperative rehabilitation phase. By palliative posterior spinal internal fixation, the upper and lower vertebral segments were fixed by pedicle screw, thus, the spine is rapidly stable and pain is relieved, the trauma by open surgery is avoided by the patient and they can recover in the short-term following surgery and receive further radiotherapy and chemotherapy as soon as possible to control the progression of the cancer. In the posterior approach surgery, if necessary, the vertebral plate can be decompressed to avoid or delay the damage to the spinal cord. For the thoracic spine metastasis, traditional anterior thoracic surgery has a serious impact on respiratory function. Previously, certain investigators have attempted an anterior approach for tumor removal surgery assisted by thoracoscopic surgery. Compared with undergoing thoracic surgery, internal fixation has a significantly shorter postoperative rehabilitation time and lower incidence of complications (38).

PVP combined with <sup>125</sup>I seed implantation. Radioactive seed implantation is a brachytherapy, which has become one of the important therapies for malignant tumors. The most commonly observed clinical radioactive particle is <sup>125</sup>I, which is mainly due to its characteristics. Radioactive seed implantation has unique advantages compared with external irradiation. The radiological area can get a more precise positioning. Particles are conformally distributed based on tumor size and shape. Particles are planted beyond the target range and the radiation dose decreased rapidly, which makes a high dose and long half-life of particles in the target area, and allows the spinal cord tissue to achieve a sufficient amount for the prescription (39). Yang et al (40-42) conducted a comparative study of the treatment method for spinal metastases: Simple PVP and PVP combined with 125I seed implantation. The analgesic effect and vertebral-body changes were observed 1 day, and 1, 3 and 6 months after surgery, respectively. The results demonstrated that the analgesic effect in the simple PVP group is relatively slow, and the combination group therapy has a rapid effect to inhibit the pain and the highest complete remission rate and remission rate. PVP in combination with <sup>125</sup>I seed implantation has a significant effect in the prevention of vertebral collapse or the occurrence of new compression fractures with no significant complications, suggesting that the combination therapy of <sup>125</sup>I PVP and spinal metastases is safe and effective (43).

## 6. Summary

With the continuous development of cancer treatment, the survival time of patients with spinal metastases will prolong, thus the number of the patients with spinal metastases increases. Treatment methods of vertebral bone metastases are diverse and the most appropriate treatment method should be selected based on the characteristics of the disease and systemic conditions of the patients. Among the types of treatment methods, minimally invasive treatment has received increasing attention for its less trauma, high efficacy and fewer complications, which has clear advantages compared to the traditional surgery. Internal fixation of minimally invasive surgery shortens the cycle time and saves time for the follow-up treatment, particularly for patients who require comprehensive treatment of radiotherapy and chemotherapy. The combined application of PVP, kyphoplasty, radiofrequency ablation and seed implantation in combination with drugs, radiotherapy and surgery can increase efficacy and reduce the complications. Minimally invasive techniques will play a greater role in the treatment of metastatic spinal tumors.

Compared to the cases with complete posterior edge, minimally invasive surgery has a high risk in patients with posterior edge defects caused by tumor metastases. The greater the defects, the higher the risk for implant migration. Therefore, the controllability of the implant following implantation is a key factor for successful minimally invasive surgery in patients with vertebral defect induced by spine metastases. Conducting minimally invasive surgery is feasible for metastatic cancer patients with posterior vertebral-body defects and it can achieve a good clinical effect to significantly relieve pain and improve the quality of life.

Minimally invasive treatment on the posterior edge defect of the spine in patients with metastatic cancer is an inevitable trend of future development. PVP is used to treat posterior vertebral-body defects and can serve to improve vertebral biomechanics, but also have a clear analgesic effect. PVP surgery combined with <sup>125</sup>I seed may effectively have antitumor effects and the patient's life cycle is prolonged. Therefore, we believe it should be widely used in China and worldwide.

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