Review Article

A narrative review of the application of radiofrequency ablation in the surgery of spinal metastases

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Abstract: Spinal metastasis is one of the common complications in the late stage of cancer, which seriously threatens human life and health. The invasion of malignant tumor often leads to pathological fracture of vertebral body, compression of spinal cord and nerve, etc., which leads to cancer pain and nerve injury symptoms. At present, radiofrequency ablation (RFA) combined with vertebroplasty is a safe and effective minimally invasive method for the treatment of spinal metastases, which has unique advantages in relieving pain, improving neurological function, reducing incidence of fracture and the risk of surgery, and improving life quality in spinal metastases patients. This article reviews the state of art of RFA in the surgical treatment of spinal metastases.

Keywords: Spinal metastases; radiofrequency ablation (RFA); vertebroplasty; minimally invasive

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Introduction

Spinal metastasis is the most common spinal tumor, about 40% of cancer patients will have spinal metastasis (1). About 5% of cancer patients develop spinal metastasis every year. The most common primary lesions are breast (21%), lung (14%), prostate (8%) and kidney (5%) (2-4).

The most common symptom of spinal metastasis is pain, which has a significant impact on the quality of life. Nearly 80% of patients have severe pain symptoms (2,3). In addition, other complications include spinal fractures, nerve root and spinal cord compression. As high as 10–20% of the patients will suffer the tumor growing to the rear and protruding into the spinal canal, leading to never injury symptoms (1,3,4). Therefore, the main treatment goals for spinal metastases are to relieve pain, preserve neurological function, improve quality of life and improve overall survival.

Because the patients with spinal metastases are usually accompanied by weight loss, fatigue, poor general condition and other symptoms, the treatment is difficult. Conventional conservative therapies usually include analgesics, bisphosphonates and radiotherapy (2,3,5). Although bisphosphonates treatment can benefit patients with spinal metastases in alleviating metastatic bone pain and reducing complications related to metastases, it is also easy to cause gastrointestinal, renal and hematopoietic system damage, such as esophagitis and mandibular necrosis. Generally, narcotic analgesics are used as the first-line analgesic treatment options. However, these drugs are usually not enough to completely control the pain, accompanied by a large number of side effects, such as drowsiness, fatigue and gastrointestinal reactions, thus limiting the long-term use of such drugs. It is reported that the effective pain relief rate of palliative radiotherapy for spinal metastasis is 50–90% (6), but usually the effect of radiotherapy may be delayed by 10–14 days. In addition, pain relief after radiotherapy is usually temporary, and up to 57% of patients have pain

recurrence in an average time of about 15 weeks after the completion of radiotherapy (7). For patients with painful spinal metastases, the second radiotherapy usually does not make them benefit again. Although the reason is unknown, it is generally considered that the second radiotherapy may be insensitive. Besides, too large dose of radiotherapy is easy to cause complications such as osteonecrosis, gastrointestinal discomfort (nausea or diarrhea), radiation-induced spinal cord injury and progressive nerve paralysis (8).

Surgical treatment can significantly improve metastatic pain and stabilize pathological fractures, but usually most of the patients with spinal metastases should not be operated with extensive surgery. Surgical intervention is usually needed in the treatment of spinal metastases with unstable pathological fractures or severe neurological damage. Usually, tumor curettage, laminectomy and/or vertebrectomy, decompression and reconstruction with pedicle screws and titanium cages are needed according to the condition (1,4). The operation is generally suitable for patients with a life expectancy of more than 6 months, often accompanied by a high incidence of surgical complications and mortality. The average incidence of complications reported in the literature is about 20–40%. Common complications such as surgical incision infection, pneumonia and urinary tract infection (1,9).

Radiofrequency ablation (RFA) and vertebroplasty are minimally invasive methods for the treatment of spinal metastases under the guidance of images. The combination of the two methods has a significant effect on the treatment of spinal metastases pain and pathological fracture (10-12). This review summarizes the current status and progress of RFA in the treatment of painful spinal metastases.

We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx.doi.org/10.21037/aoj-20-103).

Methods

The present study reviewed the progress in clinical research and application of RFA in the surgery of spinal metastases. A systematic literature research was performed in PubMed for English-language studies and summarized as follows.

RFA

The principle of tumor RFA is to introduce high-frequency alternating current into tumor focus tissue through needle electrode, resulting in heat, coagulation and necrosis of the focus tissue (3). This technique was first used as a target therapy in the treatment of liver and lung tumors. In 1992, Rosenthal *et al.* successfully used RFA to treat osteoid osteoma with effective pain relieving result (4). Since then, RFA had been widely used in the management of osseous lesions, including bony metastases, but not used on vertebral lesions because of the potential risk of spinal cord or never root heating injury by RFA. In 2000, Dupuy *et al.* reported for the first time that RFA can effectively relieve pain symptoms in metastatic hemangioendothelioma and osteoid osteoma in the spine. This study demonstrated that RFA can be safely performed in the vertebral body and the temperature levels in the spinal canal do not reach cytotoxic levels (5). According to the report, with the help of real-time CT image guidance, the radiofrequency electrode can be precisely placed in the spinal lesions for RFA treatment, and it can be applied to patients with poor general conditions, and can be operated under local anesthesia in patients with awake state. Since then, a number of studies have shown that RFA for the treatment of spinal metastases has a good pain relief effect, can significantly reduce the intensity and duration of bone metastases pain, reduce VAS score and improve the quality of life of patients (6-12). In 2002, Grönemeyer *et al.* reported 21 spinal lesions with an average relative pain reduction of 74% after RFA treatment in a single center retrospective study (6). Anchala *et al.* published the retrospective results of 92 patients with 128 lesions who received RFA, reporting significantly decreased average VAS pain scores from 7.51 per-operative to 1.73 at 1 week, 2.25 at 1 month, and 1.75 at 6 months post-operative in 2014 (8). In unresectable spinal metastases, 90% of the patients could effectively reduce the pain symptoms within 3–11 months after the RFA. The pain intensity decreased by 74% on average, and the treatment effect was significant (7).

The mechanism of RFA in the treatment of metastatic tumor pain is as follows (13): (I) RFA produces thermal damage to pain sensitive fibers, thereby reducing the transmission of pain signals to periosteum; (II) after RFA, the lesions are damaged and regain mechanical stability; (III) the death of tumor cells caused by RFA can reduce the production and release of a large number of cytokines, such as TNF-α, substance P and interleukin, which can be produced to stimulate sensitive nerves; (IV) RFA can kill osteoclasts.

Clinical study of vertebroplasty combined with RFA

Vertebroplasty is also used for palliative treatment of spinal

metastases. It is often used in the treatment of painful metastases with poor effect of conservative treatment. Under the guidance of CT or X-ray, PMMA is injected into the vertebra to fill the diseased vertebra evenly (2,3). The mechanism of vertebroplasty for pain relief is as follows: (I) injection of bone cement to reconstruct the stability of trabecula in the vertebral body, so as to reduce the sensitivity of pain nerves. (II) Bone cement is injected to support the vertebral body structure, so as to prevent further compression fracture of the vertebral body. (III) Through the exothermic reaction of bone cement, the chemical toxicity and thermal coagulation necrosis of pain nerve endings were directly caused (14).

In view of the independent mechanism of vertebroplasty and RFA in the treatment of spinal metastases, some researchers advocate the combination of the two in the treatment of spinal metastases. RFA alone can effectively relieve the pain of spinal metastasis, but it cannot achieve the effect of vertebral body strengthening and reconstruction stability brought by vertebroplasty. Similarly, when there are more soft tissue lesions in the lesions, the use of vertebroplasty alone may lead to uneven distribution of bone cement injection and reduce the therapeutic effect. RFA can effectively ablate tumor soft tissue lesions and make tumor blood vessels hot coagulate and occlude, create space for injected bone cement and reduce injection pressure, so as to improve the distribution of vertebroplasty bone cement, reduce the incidence of leakage of bone cement (15), increase the stability of vertebral body, and reduce the risk of distant metastasis of tumor through paravertebral and vertebral vein. In view of the above theoretical analysis, it is generally considered that the combined application of the two has certain synergistic effect. The results show that RFA combined with vertebroplasty is a safe and effective treatment for the pain symptoms and local control of spinal metastases, which is commonly used in the treatment of spinal metastasis pain and vertebral stability, especially for the patients with better general conditions, life expectancy greater than 6 months and no definite metastasis of important organs, accompanied by the following symptoms: (I) asymptomatic spinal metastasis, (II) simple metastasis pain or (III) stable vertebral pathological fracture (16). A large number of studies have reported that RFA combined with vertebroplasty has achieved satisfactory results in the treatment of spinal metastases. Reyes and others (17) reported the results of a multicenter case study. A total of 49 patients with spinal metastases, a total of 72 diseased vertebrae, were treated with RFA combined with vertebroplasty. The VAS score of this group of patients decreased from 7.9 before operation to 3.5 within 2–4 weeks after operation. Oswestry Disability Index (ODI) scores decreased from 34.9 to 21.6. Lane *et al.* (18) reported that 34 cases of spinal metastases were treated by RFA combined with vertebroplasty. The pain of all the patients was significantly improved within 24 hours after the operation. The VAS score decreased from 7.2 before the operation to 3.4 after the operation, without significant complications. However, there are also studies that suggest that combined vertebroplasty does not benefit patients with bone metastases who have been treated with RFA in pain relief. Clarençon *et al.* (13) reported 24 cases of painful bone metastases, of which 12 patients received RFA combined with vertebroplasty, and the other 12 patients only received RFA, the results showed that RFA can effectively alleviate the pain of bone metastases and promote the functional recovery, and the patients combined with vertebroplasty did not show a better pain relief effect. There is no direct evidence shows better treatment effect of the combination treatment as compared with RFA or vertebroplasty alone. A comparative analysis of multicenter with large sample study is essential.

Indications and contraindications

Generally, patients with spinal metastasis need to be evaluated comprehensively before operation. The patient's history of primary tumor, general condition, life expectancy and prognosis, tumor medication control, neurological injury, mental state and treatment objectives need to be comprehensively considered. If necessary, multi-disciplinary team can be organized for evaluation. Detailed medical history inquiry and physical examination to determine the responsible vertebrae for surgery and whether it is combined with nerve function injury. If there is nerve injury, the severity of the injury (Asia or Frankel classification) needs to be further evaluated. Appropriate imaging examination should be selected before operation. CT can evaluate the osteoanatomical structure and the degree of bone destruction of the vertebral body. MRI can evaluate the cumulative bone marrow signal, spinal cord compression, paravertebral and spinal canal soft tissue masses and the blood supply of the tumor. PET-CT can evaluate the suspicious metastasis of the whole body. A complete set of biochemical examination and cardiopulmonary function evaluation are necessary to evaluate the safety of anesthesia.

In general, RFA combined with vertebroplasty is

recommended for patients with pain of spinal metastases accompanied by surrounding soft tissue masses and the risk of pathological fractures. The indications include:

(I) The effect of routine analgesic treatment is not good, which seriously affects daily life;
(II) Palliative treatment for painful spinal metastases patients with moderate pain;
(III) The source of pain can be found clearly, and the clinical symptoms are consistent with the imaging findings.

Absolute contraindications include:

(I) Local or systemic infection;
(II) Severe coagulation dysfunction;
(III) Tumor compression of spinal cord or spinal instability;
(IV) Allergic to bone cement;
(V) Patients with severe cardiopulmonary disease.

Technical points of RFA and vertebroplasty

According to the location and size of the tumor, CT or fluoroscopy guidance should be used as appropriate. According to the actual situation, the operation can be performed under local anesthesia, epidural/spinal anesthesia, or general anesthesia. During the operation, pay attention to monitor the vital signs of patients. Strictly aseptic operation, use antibiotics to prevent infection when necessary.

After anesthesia, under the guidance of real-time image, bone biopsy needle was placed in the center of the focus. Then the RFA electrode was inserted into the pinhole, and the probe was implanted into the center of the target focus. Adjust the length of electrode head according to the size of lesion. The temperature of the tip can be between 60 and 100 ℃, with an average heating time of 5 minutes (range, 3–7 minutes) (13,14). After RFA, the radiofrequency probe was replaced with a vertebroplasty cannula. Depending on the location of spinal lesions, the route of puncture may be different. Anterior lateral or posterior transpedicular approach is recommended for cervical lesions. One side transpedicular approach is the first choice for thoracolumbar lesions. After the puncture reaches the predetermined position, prepare the bone cement injection. The process of bone cement injection needs to be carried out under continuous X-ray fluoroscopy to observe whether there is leakage in spinal canal and the distribution of bone cement. The risk of cement leakage is higher at the initial stage of the injection because the cement is more fluid at the initial stage. When leakage of cement is detected, injection should be stopped.

RFA complications

RFA of spinal metastases has been reported in the literature. The incidence of surgical complications is about 5.4–6.5% (19,20). The common complications were hematoma at the puncture site and transient pain aggravation caused by local high temperature (2,13). Serious complications include severe burn of skin and soft tissue and neurovascular injury, which may lead to foot ptosis, incontinence and neuropathic pain (21). The residual cancellous bone or cortical bone structure in the focus area can play a role in isolating heat conduction, thus blocking the damage of nerve caused by RFA. Keeping a safe distance of at least 1cm from the ablation center of the focus area to important structural tissues, and ensuring that the temperature in the spinal canal cannot be too high to reach the cytotoxic level during the operation, can reduce the risk of neurovascular and soft tissue damage during the RFA of spinal metastasis (22,23).

Summary

RFA can be used for palliative treatment of painful spinal metastases, which can effectively alleviate the pain symptoms of spinal metastases and improve the quality of life of patients. Vertebroplasty combined with RFA is considered to have a theoretical synergistic effect, which is commonly used in the treatment of spinal metastasis and vertebral stability. A comparative analysis of multicenter with large sample study is essential to confirm this synergistic effect. Strictly grasp the indications and contraindications, operate correctly under the guidance of real-time image, can avoid the occurrence of surgical complications. RFA combined with vertebroplasty is a safe and effective treatment for the pain symptoms and local control of spinal metastases.

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