

doi:10.3969/j.issn.2095-4344.2013.34.003 [http://www.crter.org]

Yang J, Yu B, Guo XH, Yang P, Zhang KR, Zhang S, Cai WB, Ku JB, Tian LY. Combination therapy of bone cement filling and plate internal fixation with limb salvage is used for metastatic malignant bone tumors. *Zhongguo Zuzhi Gongcheng Yanjiu*. 2013;17(34): 6073-6082.

Combination of bone cement filling and plate internal fixation with limb salvage is used for metastatic malignant bone tumors[☆]

Yang Jun^{1,2}, Yu Bin¹, Guo Xin-hui², Yang Peng³, Zhang Kai-rui¹, Zhang Sheng¹, Cai Wei-bin², Ku Jian-bin², Tian Ling-yan²

1 Department of Traumatic Orthopedics, Nanfang Hospital of Southern Medical University, Guangzhou 510515, Guangdong Province, China

2 Department of Orthopedics, the 421 Hospital of Chinese PLA, Guangzhou 510318, Guangdong Province, China

3 Second Affiliated Hospital of Inner Mongolia Medical University, Hohhot 010030, Inner Mongolia Autonomous Region, China

Abstract

BACKGROUND: Currently, limb salvage therapy has become the standard treatment of malignant bone tumors way, but improper treatments will result in tumor recurrence, secondary infection, internal fixation or prosthesis loosening.

OBJECTIVE: Based on the traditional surgical principle for metastatic bone tumors of the limbs, this study designed a user-friendly, individualized, simplistic palliative treatment regimen from the actual conditions of patients to observe the reasonability, clinical efficacy and prognosis of bone cement filling combined with internal fixation in the treatment of metastatic malignant bone tumors.

METHODS: Thirty-one patients with metastatic malignant bone tumors who required salvage treatment were screened from the Department of Orthopedics, the 421 Hospital of Chinese PLA, and their clinical data were retrospectively analyzed. All the 31 patients were divided into two groups: tumor removal+internal fixation group (non-chemoradiotherapy group, $n=11$) treated with bone cement filling plus plate internal fixation (palliative treatment); tumor removal+internal fixation+chemoradiotherapy group (chemoradiotherapy group, $n=20$), treated with radiotherapy before internal fixation plus plate internal fixation with limb salvage. The follow-up period was 4–38 months, averagely 18 months.

RESULTS AND CONCLUSION: The follow-up results showed that in the non-chemoradiotherapy group, all the 11 patients survived, who could live independently and have good motor functions; in the chemoradiotherapy group, 17 of the 20 patients survived and the rest three patients died of tumor metastasis, their poor conditions and complications at 9 and 13 months after internal fixation. In patients undergoing tumor removal+plate internal fixation with limb salvage, the integrated scores for nerve and motor functions were increased by more than level 1. These findings confirm that a simple palliative therapy of bone cement filling and internal fixation without chemoradiotherapy is better for metastatic malignant bone tumors patients who require limb salvage.

Key Words: biomaterials; tissue-engineered bone materials; bone tumor; bone cement; internal fixation; metastasis; malignant tumor; limb salvage treatment; radiotherapy; chemotherapy; pathological fracture; retrospective analysis

Yang Jun[☆], Studying for doctorate, Attending physician, Department of Traumatic Orthopedics, Nanfang Hospital of Southern Medical University, Guangzhou 510515, Guangdong Province, China; Department of Orthopedics, the 421 Hospital of Chinese PLA, Guangzhou 510318, Guangdong Province, China yangjun1267@sina.com

Corresponding author: Guo Xin-hui, M.D., Associate chief physician, Department of Orthopedics, the 421 Hospital of Chinese PLA, Guangzhou 510318, Guangdong Province, China guoxh421@163.com

Received: 2013-03-08
Accepted: 2013-04-19
(20120726009/WJ · W)

INTRODUCTION

Metastatic bone tumors account for 15%–20% of systemic metastatic tumors, resulting in a high clinical mortality^[1-7]. Traditional chemotherapy+amputation therapy is mostly used for metastatic malignant bone tumors of the extremities, leading to a poor quality of life and a short survival of 5–10 years. However,

amputation-caused disabilities are more unfortunate for young patients. During the follow-up, the amputation patients feel down and are unable to participate in the rehabilitation care in the interactive mode; some patients are even in despair, pessimism, depression and mental state. Therefore, it is even more important for clinicians to understand the pathogenesis and treatment optimization of metastatic malignant bone tumors.

Recent studies have shown that there is a similar survival rate between the salvage treatment and amputation in patients with metastatic malignant bone tumor, and the local recurrence rates of both the two kinds of surgical treatments are 4%–6%^[8]. Currently, limb salvage therapy has become the standard treatment of malignant bone tumors manner^[9], but improper treatments can cause tumor recurrence, secondary infection, internal fixation or prosthesis loosening^[10-12], thereby resulting in the failure of limb salvage treatment. With the development of new medical treatment techniques, indications for limb salvage therapy of malignant bone tumors continue to expand, and the limb salvage rate and survival rate are both significantly increased^[13].

In this study, we designed a user-friendly, individualized, simplistic palliative treatment regimen from the actual conditions of patients on the basis of the traditional surgical principle for metastatic bone tumors of the limbs, and then observed the reasonability, clinical efficacy and prognosis of bone cement filling combined with internal fixation in the treatment of metastatic malignant bone tumors.

SUBJECTS AND METHODS

Design

Retrospective case control analysis.

Time and setting

The study was completed at the Department of Orthopedics, the 421 Hospital of Chinese PLA, from January 2008 to June 2009.

Subjects

Thirty-one patients with metastatic malignant bone tumors who required salvage treatment were selected from the Department of Orthopedics, the 421 Hospital of Chinese PLA, China from January 2009 to June 2010. The involved 31 patients included 19 males and 12 females, with a mean age of 42.5 years (range, 22–57 years). According to different treatments, all the patients were divided into two groups: non-chemioradiotherapy group ($n=11$) and chemoradiotherapy group ($n=20$).

Patients in the non-chemoradiotherapy group received bone cement filling and plate internal fixation with limb salvage, including eight males and three females at a mean age of 32 years. Of the 11 cases, there were two cases of upper limb treatment and nine cases of lower limb treatment; five cases of lung cancer, two of

prostate cancer, one of esophageal cancer, two of breast cancer, and one of cervical cancer. All the 11 patients were confirmed as having metastatic malignant bone tumors by preoperative CT, MRI and pathological biopsy. Laboratory tests showed that there were two cases of mild anemia and four cases of alanine and aspartate aminotransferase increased slightly; other cases were normal in blood, urine, stool routine, liver and kidney function, blood coagulation test, erythrocyte sedimentation rate, C-reactive protein.

Patients in the chemioradiotherapy group received 1–2 course of radiotherapy, chemotherapy or their combination before salvage treatment, including 11 males and nine females at a mean age of 46 years. Of the 20 cases, four cases underwent upper limb treatment and 16 cases underwent lower limb treatment; there were nine cases of lung cancer, three of prostate cancer, four of breast cancer, three of cervical cancer and one of liver cancer. All the 20 patients were confirmed as having metastatic malignant bone tumors by preoperative CT, MRI and pathological biopsy. Laboratory tests showed that there were six cases of mild anemia and 11 cases in which alanine and aspartate aminotransferase was increased in the controllable range, and 15 cases in which carcinoembryonic antigen was significantly increased, and erythrocyte sedimentation rate and C-reactive protein were both increased.

Diagnostic criteria

Patients with bone metastases were all confirmed by using histology and/or cytology examinations. Clinical examination, routine laboratory, tumor markers, isotopes, endoscopy, imaging and other tests were performed to find the primary lesions. Before internal fixation, the routine examination and isotope bone scan were done; metastatic bone tumor lesions were subjected to X-ray, CT and MRI and confirmed as metastatic malignant bone tumors.

Inclusion criteria

(1) II A or II B patients who had good correspondence to chemotherapy before fixation. (2) No major neurovascular involvement. (3) No pathological fracture, local infection and diffuse skin infiltration. (4) Patients who were expected to survive more than 6 weeks could receive surgical treatment. (5) Patients who were expected to keep the limb function better than prostheses. (6) Pre-fracture functional score was more than 65 points by clinical, radiologic and pathologic diagnosis and assessment of systemic conditions. (7) Patients with no heart, lung, liver and

kidney dysfunction or who can tolerate surgery. (8) Patients and their families had a strong desire to save the limb^[14].

Exclusion criteria

(1) A wide range of tumors that could not be removed widespreadly or marginally at least (patients sensitive to chemotherapy). (2) No important nerves and blood vessels were violated. (3) Active infections still existed in local tumors or other parts. (4) Advanced cancer had widely metastasized. (5) Because of poor local skin, soft tissue and blood supply due to radiotherapy or repeated surgeries, it was predicted that the incision was hard to heal or prone to cause skin and soft tissue necrosis and infection.

Retrospective analysis of the screening data

At admission, related examinations showed that the primary tumor cells were in a more active state for patients in the chemoradiotherapy group. The average age of the chemoradiotherapy group was slightly higher than that of the non-chemoradiotherapy group. The patients in the chemoradiotherapy group were psychologically easier to accept chemoradiotherapy technology than those in the non-chemoradiotherapy group. In addition, appropriate chemoradiotherapy was also a conventional choice for patients whose tumor cells were in an active state. However, in the non-chemoradiotherapy, the five patients who were too younger and their families refused to take chemo radiotherapy, and patient's tumor cells were also in a relatively stable state. The other six patients in the non-chemoradiotherapy group were considered to directly receive salvage treatment without chemoradiotherapy because their primary tumors were isolated with no significant progress in the local lesion and patients' vital signs and laboratory tests were in a stable state. All the 31 patients had limb pain that severely declined daily life and limb function. Routine laboratory tests showed that all the patients were able to tolerate surgery. Correction of anemia was performed in individual patients prior to internal fixation. Based on long-term quality of life, Dutch grading system was used to decide whether fixation treatment was done or not^[15]. Mirels scoring system was used to decide whether internal fixation techniques were adopted or not^[16].

The Dutch grading system shows that scores 0–3 refer to the median survival of 3 months; 4–5 refer to the median survival of 9 months; 6 refer to the median survival of 18.7 months. Some researchers suggested that if the expected survival is more than 6 weeks,

surgical methods can be used^[17]. To improve the quality of life of patients, it is generally recommended that patients with expected survival of more than 3 months can receive surgical treatment when the physical condition is suitable for surgery. However, some scholars believe that the surgical treatment is suitable for breast cancer patients with bone metastases who had the expected survival time of greater than 4 weeks, or patients with metastatic femoral lesions of more than 2.5 cm in diameter and bone metastasis to the femoral neck^[18]. Patients with more than 50% cortical destruction are suitable for surgery. For patients with thyroid cancer or kidney cancer, some single bone metastases can be cured after resection, and patients should strive for early surgery^[19]. In this study, we suggested that the surgical treatment was recommended for patients with bone metastasis to weight-bearing long bones who had the expected survival of greater than 6 weeks, and those with bone metastasis to non-weight-bearing long bones (such as the humerus, ulna) who had the expected survival of more than 3 months. Bone cement filling and internal fixation were performed in all the 31 patients from our study who were expected to survive more than 6 weeks.

Materials and instruments

Materials and instruments	Source
Acrylic bone cement	Tianjin Institute of Synthetic Materials Industry (110706)
Titanium plates, titanium screws	Beijing Best Bio-technical Co., Ltd. (1159-2008)
Continuous passive motion machine	Hangzhou Zhengda Medical Co., Ltd.

Methods

Pre-fixation preparation

In the non-chemoradiotherapy group, the 11 patients did not receive chemoradiotherapy before fixation. Surgical risk assessment, determination of the scope of tumor resection, and assessment for prevention of complications after fixation were conducted prior to salvage treatment consisting of tumor removal+ internal fixation+bone cement filling. In the chemoradiotherapy group, the 20 patients underwent 1–2 courses of radiotherapy, chemotherapy or the combination before internal fixation. Preoperative routine examination was done in the two groups to exclude major surgical contraindications, including no significant heart and lung dysfunction and respiratory abnormalities; no liver dysfunction; no abnormal coagulation tests. Then, patients were scheduled for

surgery. For metastatic tumors, the surgical approach should be selected based on the primary tumor treatment; for single metastasis patients whose primary tumors are cured, the surgical approach is similar to that for primary malignant bone tumors; while marginal excision is often used for patients whose primary tumors are not cured or patients with multiple lesions^[21-22].

Incision, tumor curettage and internal fixation

A long incision was made longitudinally along the outer of the limbs, which was centered at the tumor surface projection, to bluntly dissect muscle tissue bewareing of bleeding and completely expose tumor tissues layer by layer, then removing proliferated bone tissue and tissue with strong periosteal reaction around the tumors^[22-24].

It was important to maintain the longitudinal integrity of the backbone, and to avoid excessive removal causing fractures. After incomplete or complete resection of the tumor tissue, hydrogen peroxide, normal saline, and iodine were used to soak the marrow cavity and peritumoral tissue 3–5 times, once for 5–8 minutes.

Finally, the long-segment titanium locking plate with screws were implanted into the two ends of tumor resection *via* drilling after rinsing with normal saline and drying as much as possible. After fixing, bone cement was filled into the two cut ends at a length of about 3 cm. Until the bone cement hardened, the incision was washed with normal saline and a drainage tube was placed for adequate drainage. After that, the incision was sutured layer by layer. After fixation the patients were subjected to treatment against infections, nutritional therapy, and symptomatic and supportive treatment. One to two weeks later, the patients were subjected to continuous passive motion machine-assisted passive exercise of affected limbs to prevent deep vein thrombosis. Meanwhile, a psychological comfort and counseling is also necessary.

Post-fixation efficacy evaluation

The function assessment of affected limbs was performed before and after fixation as follows^[25].

Main outcome measures

Follow-up results after fixation and functional assessment results of the limbs.

Statistical analysis

Count data were expressed as percentage. SPSS 13.0 software was used for data analysis. Count data was

analyzed using the chi-square test. A value of $P < 0.05$ was considered statistically significant.

Grade	Muscle recovery	Grade	Nerve function recovery
M ₀	Absolutely no muscle contraction	S ₀	Loss of sensation in the innervated zone
M ₁	Proximal muscle contractile function recovers	S ₁	Deep pain recovery in the innervated zone
M ₂	Proximal and distal muscle contractile function recovers	S ₂	Deep pain restores in the innervated zone
M ₃	Anti-resistance activities recover in all the important muscles	S ₂ ⁺	Pain and tactile recover in the innervated zone, but there is hypersensitivity
M ₄	Muscle synergies begin to recover	S ₃	Pain and tactile full recover
M ₅	Muscle movements fully recover discrimination	S ₃ ⁺	Besides the fully recovery of pain and tactile, there is a certain two-point
		S ₄	Feeling is completely normal

RESULTS

Quantitative analysis of participants

Except three cases in the chemoradiotherapy group died of tumor metastasis, their poor conditions and complications at 9 and 13 months after internal fixation, the 28 patients were included in the follow-up and result analysis.

Baseline analysis of participants

In the present study, the mean age of the 31 patients was 42.5 years. There was no difference in the mean age between the non-chemoradiotherapy group (averagely 37.5 years) and chemoradiotherapy group (averagely 43.5 years; $P > 0.05$).

Therapeutic efficacy of bone cement filling plus internal fixation with limb salvage on metastatic malignant bone tumors (Tables 1–4)

Before fixation	After fixation					
	M ₀	M ₁	M ₂	M ₃	M ₄	M ₅
M ₀						
M ₁						
M ₂					2	1
M ₃					4	2
M ₄						2
M ₅						

100% patients in the non-chemoradiotherapy group recovered to at least M₄ stage.

Table 2 Motor function of the limbs in the patients of the chemoradiotherapy before and after fixation (n)

Before fixation	After fixation					
	M ₀	M ₁	M ₂	M ₃	M ₄	M ₅
M ₀						
M ₁				1	1	1
M ₂				1	2	2
M ₃				2	1	3
M ₄					2	1
M ₅						

82.3% patients in the chemoradiotherapy group recovered to M₄ stage.

The 28 patients were followed 9–12 months after internal fixation, with a mean period of 10.4 months. Most of the patients had significant improvement in the quality of life with the help of nutrition and symptomatic and supportive therapies: digestive ability and appetite were strengthened, limb pain and other symptoms were relieved or disappeared, the patient's psychological qualities were improved significantly, personal living skills were greatly improved, and patients felt more confident in life.

The grading of limb muscles and nerve function in the non-chemoradiotherapy was slightly better than that in the chemoradiotherapy after treatment. The percentage of patients whose motor function recovered to M₄ stage at least was higher in the non-chemoradiotherapy group than the chemoradiotherapy group ($\chi^2=1.45, P < 0.05$; Tables 1, 2).

The percentage of patients whose nerve function recovered to S₃⁺ stage at least was higher in the non-chemoradiotherapy group than the chemoradiotherapy group ($\chi^2= 1.02, P < 0.05$; Tables 3, 4).

Table 3 Nerve function of the patients in the non-chemoradiotherapy before and after fixation (n)

Before fixation	After fixation						
	S ₀	S ₁	S ₂	S ₂ ⁺	S ₃	S ₃ ⁺	S ₄
S ₀							
S ₁							
S ₂					1	2	1
S ₂ ⁺					1	1	1
S ₃						3	1
S ₃ ⁺							
S ₄							

81.8% patients in the non-chemoradiotherapy group recovered to S₃⁺ stage.


Table 4 Nerve function of the patients in the chemoradiotherapy before and after fixation (n)

Before fixation	After fixation						
	S ₀	S ₁	S ₂	S ₂ ⁺	S ₃	S ₃ ⁺	S ₄
S ₀							
S ₁							
S ₂					1	1	1
S ₂ ⁺				2	2	2	3
S ₃					1	1	2
S ₃ ⁺					2	1	


876.5% patients in the chemoradiotherapy group recovered to S₃⁺ stage.

Typical cases


Figures 1–3 show the imaging and pathological characteristics of a typical case of malignant bone metastases who received tumor removal+plate internal fixation.




A: Chest X-ray showed primary lung lesion in the left hilar and left lower lobe



B: Femoral X-ray showed bone metastases to the distal femur occupied the entire distal femur

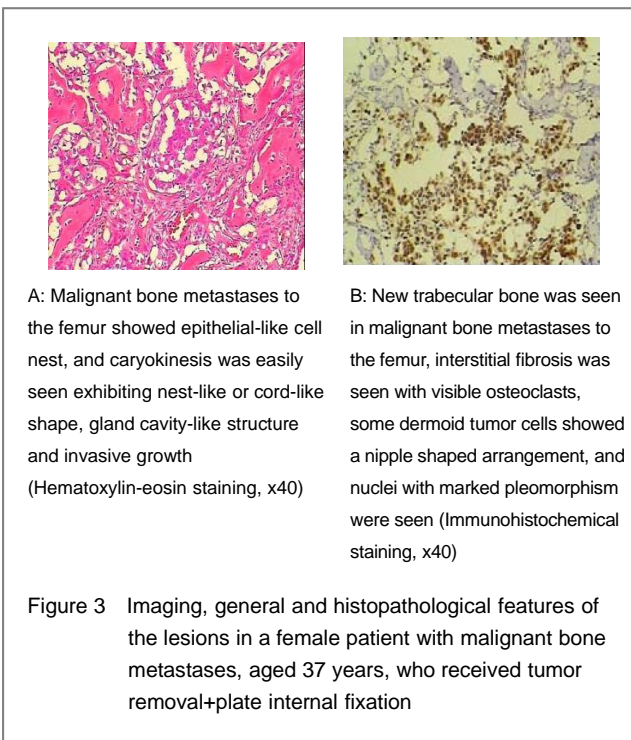
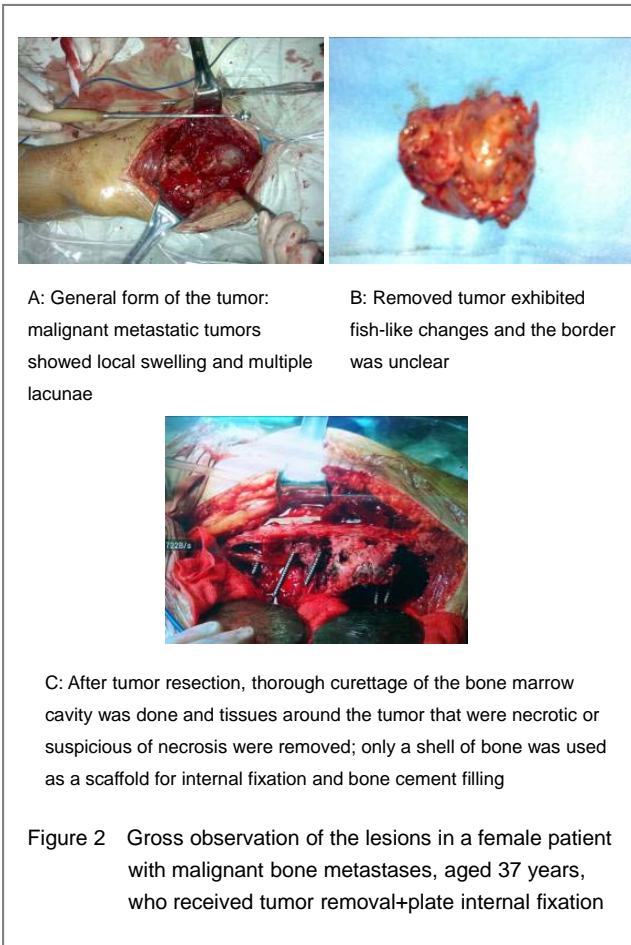


C: Lower extremity MRI showed bone metastases were full of the bone marrow cavity and diffused to the surrounding tissue



D: Lower extremity X-ray which was performed at 3 d after fixation showed tumor lesions had been scraped, the bone marrow cavity was filled with bone cement, and the plate was in good position

Figure 1 Imaging features of a female patient with malignant bone metastases, aged 37 years, who received tumor removal+plate internal fixation



tumor, and its mechanism and therapeutic mechanism mainly involves three aspects: (1) intrinsic characteristics of tumor cells, that is, tumor cells can migrate from the primary lesions to the distant bone tissue; (2) specific parts of the skeletal system have the special anatomical characteristics that allow tumor cells to spread in these specific parts; (3) involved bone tissues produce a variety of biological responses to metastatic tumor cells which make the tumor cells are able to grow and reproduce in the host bone, thereby destroying normal tissue morphology and structure^[26-31]. Although the origin and property of metastatic bone tumors are varied, the body's performance is the same, that is, even if no obvious symptoms, bone metastases means the terminal stage of tumors. Thus, the vast majority of metastatic bone tumors are treated with radiotherapy, and bisphosphonate drugs for conservative treatment^[17]. However, the tumors have always existed in the body and continued to produce bone destruction and release substances to invade the surrounding tissues. In some patients with pathological fractures, there are worsening wounds difficult to repair, which not only reduce the quality of life of patients, and even further shorten the survival time of patients. Therefore, in this paper, it is envisaged whether we can remove the tumors in the body with limb salvage, and then perform the appropriate preventive internal fixation to strengthen the local structural stability, thereby providing a new stable and strong support for the involved bone tissue that is contribute to better functional exercise and walking, as well as to improve the quality of life and extend the lifetime of the patients.

We screened 31 patients with metastatic malignant bone tumors from our hospital between January 2008 and June 2009 to retrospectively analyze and compare the clinical data in the non-chemoradiotherapy group ($n=11$) and chemoradiotherapy group ($n=20$; three of 20 patients were withdrawn because of death). Then, we drew the following conclusions:

(1) To give full consideration to the survival time of patients with metastatic bone tumors. In this study, patients who can survive more than 12 months are considered to be suitable for fixation treatment. Besides the survival time, we should determine whether patients can be tolerant to the anesthesia, surgery and rehabilitation after fixation based on the patient's own physiological status, including vital signs, clinical blood biochemistry, multiple-organ functions, blood coagulation test, diet and nutritional status. Tumor treatment need to be more humane, personalized, diversified. In the present study, we found that the motor and nerve

DISCUSSION

Metastatic bone tumor is the most common malignant

functions had a better tendency in the 11 patients given tumor removal+internal fixation+bone cement filling than the other 17 ones receiving chemoradiotherapy before tumor removal+internal fixation+bone cement filling. Three cases of death in the chemoradiotherapy group might be associated with further deterioration of the primary tumors related, but we could not rule out that the persistence of tumors in the limbs further aggravate the patient's condition. Therefore, we considered whether salvage treatment after complete tumor resection was more conducive to the control of metastatic malignant bone tumors?

(2) Is internal fixation is used to prevent pathological fractures in patients with metastatic bone tumors? Foreign scholars think when Mirels score is > 8, the measures to prevent pathological fractures are recommended. But we believe that when Mirels score is less than 8 points, even if the diameter of metastatic bone tumors is 1/3 as long as that of the backbone, and the tumors are located in weight-bearing bones, the internal fixation is recommended for prevention of pathological fractures. Therefore, there were no pathological fractures, no fixation fracture or loosening in the 11 patients of the non-chemoradiotherapy group. After follow-up, the sensory and motor function in the non-chemoradiotherapy group was improved at least by one level, including seven patients whose sensory and motor function recovered normal. In the chemoradiotherapy group, motor function was normal in five cases and sensory function was normal in three patients, including patients whose motor and sensory function became both normal. Are simple tumor resection+internal fixation treatment conducive to the recovery of sensory and motor function in patients with metastatic bone tumors? For elderly patients with osteoporosis, it is important to minimize nail application. In the past, Chinese scholars selected prosthesis replacement *via* internal fixation+bone cement or external fixation+bone cement to achieve good clinical results according to the disease, reconstruction and fixation approach^[31-35].

In the present study, the combination therapy of tumor removal, internal fixation and bone cement filling led to a strong fixation. On the one hand, bone cement filling is suitable for patients with osteoporosis; on the other hand, a long-segment fixation plate prevents cancer tumors too large to maintain the connection with the longitudinal axis of normal bone. On this basis, the study also noted to prevent deep vein thrombosis in patients after internal fixation, and meanwhile monitored blood coagulation and protected the liver and kidney function.

(3) Some Chinese scholars still have disputed over the treatment of solitary bone metastases without pathological fractures as well as whether surgical treatments are recommended for different sources of metastatic bone tumors^[15]. For example, generally, lung cancer patients with bone metastasis have poor prognosis, who are not advocated to receive tumor resection even if there are solitary bone metastases; while either surgical treatments or other treatments can be used to control breast cancer, prostate cancer, lymphoma, and multiple myeloma; while there is a high failure rate of local tumor resection up to 30%–40% for kidney cancer patients with bone metastases^[5], and therefore, large-segment tumor resection and reconstruction are recommended when the kidney is removed so as to obtain a better quality of life^[36]. But the present study showed that in the non-chemoradiotherapy group, lung cancer, breast cancer, prostate cancer, and liver cancer patients with bone metastases were all subjected to tumor resection+internal fixation+bone cement filling; and the follow-up results showed a better outcomes of limb sensory-motor function recovery. In the chemoradiotherapy group, only chemoradiotherapy was done for limb salvage.

In addition, if the follow-up is extended in both groups, will the risk for pathological fractures be increased gradually with time in the patients receiving tumor removal+plate internal fixation+chemoradiotherapy? Will the persistent appearance of local tumors invade or further destroy the surrounding bone, muscle, skin and other tissues in patients undergoing chemoradiotherapy? These issues are required to be considered. Therefore, we believe that simple tumor resection+internal fixation+bone cement filling exert a more important role in the rehabilitation of such diseases. Whether this approach can completely replace the chemoradiotherapy for metastatic bone tumors can be determined comprehensively according to the patient's own body, the nature of the tumor and its distribution range.

Raffi *et al*^[37] treated malignant bone tumors of the proximal tibia using bone cement treatment, with an average follow-up of 25 months, and they found that none of the patients had local recurrence or metastasis, indicating bone cement filling is suitable for well-differentiated tumors. Therefore, our regimen of local tumor resection+internal fixation+bone cement filling follows a certain surgical principle. We believe it is important when removing tumors locally to minimize damage to the surrounding bone tissue and avoid secondary damage induced by cancer cachexia. More attentions should be paid on the thorough curettage of

tumors in the femoral medullary cavity, while repeatedly rinsing with a lot of hydrogen peroxide and normal saline for future implantation of bone cement, which is not be ignored for efficacy improvement. To minimize the application of intramedullary nails, plate internal fixation was mostly used in the present study, which can make full use of benefits of bone cement filling, that is, bone cement cannot only fill the tumor cavity, but also kill residual tumor cells using the heat of polymerization (up to 80–90 °C)^[38]. When the bone cement become hardened gradually, it can close the lesioned bone marrow cavity immediately, break the survival of tumor microenvironment, and also block the tumor cells in close contact. In this study, we do not advocate enlarged resection of metastatic bone tumor, which is different from the opinions of other health care workers^[39]. We only removed the visible tumor tissue or necrotic tissue around the tumors, ligated arteries with adequate blood supply, tried to reserve the subcutaneous muscle and soft tissue, avoided limb necrosis due to tumor curettage and limb edema at the incision closed after bone cement filling. In addition, it is necessary to indwell a drainage tube for 3–5 days continuous rinsing under negative pressure at the site of tumor resection and bone cement filling. Continuous washing can remove exudates from the surgical field and metabolites produced by the residual tumor, and reduce infections after fixation. One the other hand, the continuous washing under negative pressure can promote the growth of new granulation tissue to quickly cover the curettage region, providing a better internal environment for the recovery of sensory and motor function of the affected limbs.

We do not deny that cancer chemoradiotherapy is very important in the treatment of malignant metastatic bone tumors. In the control of tumor development or worsening further, trying to give salvage treatment is a humanized choice based on thinking of patient's own conditions. But at all, chemoradiotherapy has a destructive effect on the immune system. If we can reduce the application of such treatments, salvage treatment with simple tumor resection may be a good choice for patients whose malignant tumors have no apparent progress.

Thus, the chemoradiotherapy cannot be abandoned in the treatment of malignant tumors, though this paper shows a good achievement in some patients. We are committed to develop patient-oriented therapies which can obtain the longest survival, best quality of life and best surgical mode. In a word, the comprehensive evaluation of patient's survival period is necessary in the treatment of malignant metastatic bone tumors; the choice of chemoradiotherapy should be based on the

actual situation; reducing the enlarged tumor resection, strictly grasping the indications for surgery, actively correcting cachexia before fixation, improving the body's own immune functions, and better use of bone cement filling and internal fixation will support a more humanized, personalized, idealized treatment modality for salvage treatment in patients with metastatic malignant bone tumors.

REFERENCES

- [1] Xu ST, Ge BF, Xu YK. *Shiyong Gukexue*, 3rd. Beijing: People's Military Publishing House. 2006.
- [2] Rougraff BT, Kneisel JS, Simon MA, et al. Skeletal metastases of unknown origin: a prospective study of a diagnostic strategy. *Bone Joint Surg Am*. 1993;75(9):1276-1281.
- [3] Mankin HJ, Lange TA, Spanier SS, et al. The hazards of biopsy in patients with malignant primary bone and soft tissue tumors. *J Bone Joint Surg Am*. 1982;64(8):1121-1127.
- [4] Coleman RE. Skeletal complications of malignancy. *Cancer*. 1997;80(8 Suppl):1588-1594.
- [5] Wedin R, Bauer HC, Wersall P. Failures after operation for skeletal metastatic lesions of long bones. *Clin Orthop Relat Res*. 1999;(358):128-139.
- [6] Deng ZC, Chen ZG, Zahng TH, et al. Clinical analysis of the pathological fracture in femur. *Zhongguo Zonghe Linchuang*. 2000;16(11):828-829.
- [7] Salmon JM, Kilpatrick SE. Pathology of skeletal metastases. *Orthop Clin North Am*. 2000;31(4):537-544.
- [8] Sampo M, Koivikko M, Taskinen M, et al. Incidence, epidemiology and treatment results of osteosarcoma in Finland—a nationwide populationbased study. *Acta Oncol*. 2011;50(8):1206-1214.
- [9] Kabukcuoglu Y, Grimer RJ, Tillman RM, et al. Endoprosthetic replacement for primary malignant tumor of the proximal femur. *Clin Orthop Relat Res*. 1999;(358):8-14.
- [10] Dedkov AG. Treatment outcome of patients with bone tumors after limb salvage surgery. *Lik Sprava*. 2010;(3-4):46-56.
- [11] Graci C, Maccauro G, Muratori F, et al. Infection following bone tumor resection and reconstruction with tumoral prostheses: a literature review. *Int J Immunopathol Pharmacol*. 2010;23(4):1005-1013.
- [12] Jeys LM, Grimer RJ, Carter SR, et al. Risk of amputation following limb salvage surgery with endoprosthetic replacement, in a consecutive series of 1261 patients. *Int Orthop*. 2003;27(3):160-163.
- [13] Chandrasekar CR, Grimer RJ, Carter SR, et al. Modular endoprosthetic replacement for tumours of the proximal femur. *J Bone Joint Surg (Br)*. 2009;91(1):108-112.
- [14] State Council of the People's Republic of China. Administrative Regulations on Medical Institution. 1994-09-01.

- [15] Wan R, Zhang WB. Treatment of metastatic bone tumor limb surgical principles. *Shiyong Zhongliu Zazhi*. 2008;23(4):297-300.
- [16] Mirels H, Metastatic disease in long bones: a proposed scoring system for diagnosing impending pathologic fractures. *Clin Orthop*. 1989;(249):256-264.
- [17] Ye CM, Yang DS. Operation treatment of metastatic bone tumor. *Shiyong Zhongliu Zazhi*. 2006;21(1):12-14.
- [18] Ruxianai Guzhuanyi and Guxianguan Jibing Linchuangzhenliao Zhuanjiazhu. Consensus and bone metastasis of breast cancer related diseases clinical diagnosis and treatment expert. *Zhonghua Zhongliu Zazhi*. 2009;31(2):156-159.
- [19] Liu YC, Hu YC, Xia Q, et al. Management of tumorous long bone pathological fractures: Allogeneic bone reconstruction, graft reconstruction or prosthesis replacement? *Zhongguo Zuzhi Gongcheng Yanjiu yu Linchuang Kangfu*. 2010;(14-22):4139-4133.
- [20] Bacci G, Ferrari S, Mercuri M, et al. Predictive factors for local recurrence in osteosarcoma: 540 patients with extremity tumors followed for minimum 2.5 years after neoadjuvant chemotherapy. *Acta Orthop Scand*. 1998; 69(3):230-236.
- [21] Scully SP, Ghert MA, Zurakowski D, et al. Pathologic fracture in osteosarcoma: prognostic importance and treatment implications. *J Bone Joint Surg (Am)*. 2002; 84-A(1):49-57.
- [22] Gupta GR, Yasko AW, Lewis VO, et al. Risk of local recurrence after deltoid-sparing resection for osteosarcoma of the proximal humerus. *Cancer*. 2009;115(16):3767-3773.
- [23] Kim HJ, Chalmers PN, Morris CD. Pediatric osteogenic sarcoma. *Curr Opin Pediatr*. 2010;22(1):61-66.
- [24] Poffyn B, Sys G, Van Maele G, et al. Radiographic analysis of extracorporeally irradiated autografts. *Skeletal radiology*. 2010;39(10):999-1008.
- [25] Zhu B. Limb salvage operation treatment of malignant bone tumor. *Shiyong Gukexue*. 2007;8(3):1553-1535.
- [26] Jing X, Wu HS, Zhou WJ. Progress in the study of pathogenesis of metastatic tumor of bone. *Zhonghua Guke Zazhi*. 2002;22(6):377-379.
- [27] Guo W, Guo Y, Feng CH. Therapeutic mechanism of bisphosphonates for metastatic tumor of bone. *Zhonghua Guke Zazhi*. 2003;23(1):36-38.
- [28] Mundy GR. Mechanisms of bone metastasis. *Cancer*. 1997;80(8 Suppl):1546-1556.
- [29] Frassica FJ, McCarthy EF. Metastatic carcinoma in bone. In *pathology of bone and joint disorders*. Philadelphia: WB Saunders. 1998.
- [30] Basset P, Bellocq JP, Wolf C, et al. A novel metalloproteinase gene specifically expressed in stromal cells of breast carcinomas. *Nature*. 1990;348(6303): 699-704.
- [31] Yang RL, Xu WP, Guo W, et al. Surgery of metastases in limbs of 61 patients. *Zhongguo Guzhongliu Gubing*. 2004; (6):3330-3341.
- [32] Tang XD, Guo W, Yang RL, et al. Segmental allograft reconstruction in skeletal defect after limb tumor resection. *Zhongguo Xiufu Chongjian Waikexue Zazhi*. 2006;(10): 985-988.
- [33] Li DS, Zhang ZY, Huang MY, et al. Methods and opportunity of operation for the malignant tumor intercurrent fracture of extremity. *Zhongguo Jiaoxing Waikexue Zazhi*. 2006;(5): 331-333.
- [34] Gao ST, Li DS, Zhang ZY, et al. Operation modes for proximal femur tumor with pathological fracture. *Zhongguo Jiaoxing Waikexue Zazhi*. 2009;(7):488-490.
- [35] Sun Q, Zhao DW. Treatment of metastatic carcinoma of extremities with pathological fracture by combination of percutaneous cementation and external fixation. *Zhongguo Guzhongliu Gubing*. 2005;(3):133-134.
- [36] Durr HR, Maier M, Pfaler M, et al. Surgical treatment of osseous metastases in patients with renal cell carcinoma. *Clin Orthop*. 1999;(367):283-290.
- [37] Raffi S, Avedian, Rex C, et al. Peabody Multiplanar osteotomy with limited wide margins: a tissue preserving surgical technique for high-grade bone sarcomas. *Clin Orthop Relat Res*. 2010;468(10):2754-2764.
- [38] Fraquet N, Faizon G, Rosset P, et al. Long bones giant cells tumors: treatment by curettage and cavity filling cementation. *Orthop Traumatol Surg Res*. 2009;95(6): 402-406.
- [39] Liu J, Yang S, Li L. *Department of Orthopedics Diagnosis Classification And Function Evaluation*, 1st. Beijing: People's Military Publishing House. 2012.

骨水泥填充法与钢板内固定保肢治疗转移性恶性骨肿瘤☆

杨俊^{1,2}, 余斌¹, 郭新辉², 杨鹏³, 张凯瑞¹, 张晟¹, 蔡伟斌², 库建斌², 田凌彦² (¹南方医科大学附属南方医院创伤骨科, 广东省广州市 510515; ²解放军第四二一医院骨科, 广东省广州市 510318; ³内蒙古医科大学第二附属医院, 内蒙古自治区呼和浩特市 010030)

杨俊☆, 男, 1977年生, 辽宁省辽阳市人, 南方医科大学在读博士, 主治医师。

通讯作者: 郭新辉, 博士, 副主任医师。解放军第四二一医院骨科, 广东省广州市 510318

文章亮点:

1 文章以传统的肢体转移性骨肿瘤外科治疗原则为基础, 从四肢恶性转移性骨肿瘤患者的实际情况出发, 制定人性化、个体化、简单化的姑息性治疗方案, 观察骨水泥填充法结合内固定治疗转移性恶性骨肿瘤的合理性、临床疗效及预后情况。

2 结果证实, 对于转移性恶性骨肿瘤的保肢治疗可以不采用化疗技术, 简单的骨水泥填充法结合内固定姑息性治疗也可为患者提供良好的生活质量和提高治疗空间。

3 文章样本量较少尚需积累, 继续延长随访时间, 关注固定后患者康复情况; 进一步关注恶性肿瘤复发情况, 积累相关信息与临床资料。

关键词:

生物材料; 组织工程骨材料; 骨肿瘤; 骨水泥; 内固定; 转移性; 恶性肿瘤; 保肢治疗; 放疗; 化疗; 病理性骨折; 回顾性分析

摘要

背景: 目前保肢治疗已成为四肢恶性骨肿瘤的规范治疗方式, 但若治疗处理不当, 则会造成肿瘤复发、继发性感染、内固定或重建假体松脱等并发症。

目的: 文章以传统的肢体转移性骨肿瘤外科治疗原则为基础, 从四肢恶性转移性骨肿瘤患者的实际情况出发, 制定人性化、个体化、简单化的姑息性治疗方案, 观察骨水泥填充法结合内固定治疗转移性恶

性骨肿瘤的合理性、临床疗效及预后情况。

方法: 回顾分析解放军第四二一医院骨科2008年1月至2009年6月收治的恶性转移性骨肿瘤患者中筛选的31例患者, 均要求保肢治疗。将31例患者按治疗方式分为2组: 肿瘤清除+钢板内固定组11例, 采用骨水泥填充法结合钢板内固定内固定姑息性治疗; 肿瘤清除+钢板内固定+固定前化疗组20例, 采用固定前化疗结合钢板内固定保肢治疗。全部患者固定后获4-38个月随访, 平均18个月。

结果与结论: 随访结果显示, 肿瘤清除+钢板内固定组11例均存活、生活能自理, 肢体运动功能良好; 肿瘤清除+钢板内固定+固定前化疗组20例患者中17例存活, 3例分别于固定后第9, 13个月因原发肿瘤的多脏器转移和自身条件较差、并发其他并发症而死亡。肿瘤清除+钢板内固定组保肢治疗后肢体神经及运动功能综合评分均较固定前提高至少1个级别以上。结果证实, 对于转移性恶性骨肿瘤的保肢治疗可不采用化疗技术, 简单的骨水泥填充法结合内固定姑息性治疗的方法也有较好的效果。

致谢: 南方医科大学临床解剖学研究所, 广东省组织构建与检测重点实验室秦建强教授, 余磊老师; 南方医院消化病研究所白杨副教授; 南方医科大学公共卫生与热带医学学院流行病学系聂军教授, 李建栋老师; 解放军第四二一医院刘新梅主任、凌龙副主任、张卫民主任、郝健主任。感谢他们为本次试验提供的帮助!

作者贡献: 杨俊收集、整理临床资料、撰写论文; 杨俊、郭新辉、杨双石设计临床治疗方案; 宋飞、张凯瑞、张晟、蔡伟斌、叶汉深、陈大军、田凌彦

参与流行病学调查和影像学处理、病理学鉴定和统计学处理。余斌负责论文审校。

利益冲突: 课题未涉及任何厂家及相关雇主或其他经济组织直接或间接的经济或利益的赞助。

伦理要求: 根据中华人民共和国国务院颁发的《医疗机构管理条例》, 在实验前将实验方案和风险告知对方, 并签署知情同意书。

学术术语: 转移性骨肿瘤-原发于身体其他部位的肿瘤, 主要是恶性肿瘤通过各种途径转移至骨骼并在骨内继续生长, 形成子肿瘤。原发肿瘤诊断明确并经治疗后转移至骨骼一般较易发现但原发肿瘤部位和症状隐匿以转移性骨肿瘤作为主要就诊主诉时, 诊断上往往容易混淆甚至将转移性的骨肿瘤当做骨原发的肿瘤进行诊断和治疗。骨是肿瘤最常见的3个转移部位之一, 因此转移性骨肿瘤在癌症患者中有一定的发病率。

作者声明: 文章为原创作品, 数据准确, 内容不涉及泄密, 无一稿两投, 无抄袭, 无内容剽窃, 无作者署名争议, 无与他人课题以及专利技术的争执, 内容真实, 文责自负。

中图分类号: R318 文献标识码: A

文章编号: 2095-4344(2013)34-06073-10

杨俊, 余斌, 郭新辉, 杨鹏, 张凯瑞, 张晟, 蔡伟斌, 库建斌, 田凌彦. 骨水泥填充法与钢板内固定保肢治疗转移性恶性骨肿瘤[J]. 中国组织工程研究, 2013, 17(34): 6073-6082.

(Edited by Zhang XY, Zhang HJ/Wang L)