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Original Article

Cortical bone destruction-the major factor causing bone cement leakage after kyphoplasty in multiple myeloma

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Abstract: Purpose: To compare the bone cement leakage (BCL) rates after percutaneous kyphoplasty (PKP) treatment of vertebral compression fractures (VCFs) caused by multiple myeloma (MM) and osteoporosis (OP) and to analyze their risk factors. Methods: Data from 58 vertebraes of 33 VCF patients caused by MM and 53 vertebraes of 48 VCF patients caused by OP were retrospectively analyzed. All patients underwent PKP in our hospital between Sept. 2011 and Sept. 2016. The extent of the preoperative damage in the vertebral cortical bone and the postoperative BCL rate in the two groups of patients were evaluated by 3-D CT reconstruction. Results: The operation success rate was 100% in both groups. The average intraoperative balloon dilatation pressure in the MM and OP groups was 170.77 PSI and 168.49 PSI, respectively (P>0.05). The average amount of bone cement injected in the MM and OP groups was 3.538 mL and 3.528 mL, respectively (P>0.05). The BCL rate of the MM group was 37.9%, and that of the OP group was 11.3% (P<0.05). The average cortical bone destruction ratesin the MM and OP groups were 2.9% and 0.8%, respectively (P<0.05). Conclusions: Compared with OP, PKP treatment of VCFs caused by MM is more prone to lead to BCL; the main reasons for this may be the more severe damage to cortical bone and the decreased integrity of the peripheral edge of the vertebrae in MM.

Keywords: Percutaneous kyphoplasty, multiple myeloma, osteoporosis, bone cement leakage, cortical bone destruction rate

Introduction

Multiple myeloma (MM), a malignant tumor of plasma cells, frequently occurs in the spine, skull, ribs and other locations and primarily manifests as osteolytic bone destruction, often causing vertebral compression fractures (VCFs) [1]. Percutaneous kyphoplasty (PKP) has been widely used in the treatment of VCFs caused by osteoporosis (OP) and MM [2-9]. In particular, the treatment efficacy of PKP for VCFs caused by OP has been confirmed, and the associated complications have also attracted clinical attention [10, 11]. Of these complications, bone cement leakage (BCL) after PKP is the most common. We have clinically observed that BCL is more common in MM than in OP; however, the cause of this is unclear, and there is no literature addressing whether risk factors for BCL are the same after PKP for VCF caused by MM compared with VCF caused by OP. In this paper, we investigate this issue to provide information for clinical treatment.

Materials and methods

General information

Between September 2011 and September 2016, our hospital admitted and treated MM and OP patients with PKP. All patients were admitted to the hospital the day prior totheprocedure. The MM group included a total of 33 patients (14 females; 19 males); all of these patients met the diagnostic criteria recommended by the International Myeloma Working Group (IMWG) [1] and had received regular chemotherapy in the Department of Hematology prior to surgery. All the patients had obvious back pain without neurological symptoms, and imaging examinations found VCFs. The OP group comprised a total of 48 patients (34 females; 14 males); the diagnoses of these patients were consistent with OP [12]. All the patients in the OP group had obvious back pain without neurological symptoms, and imaging

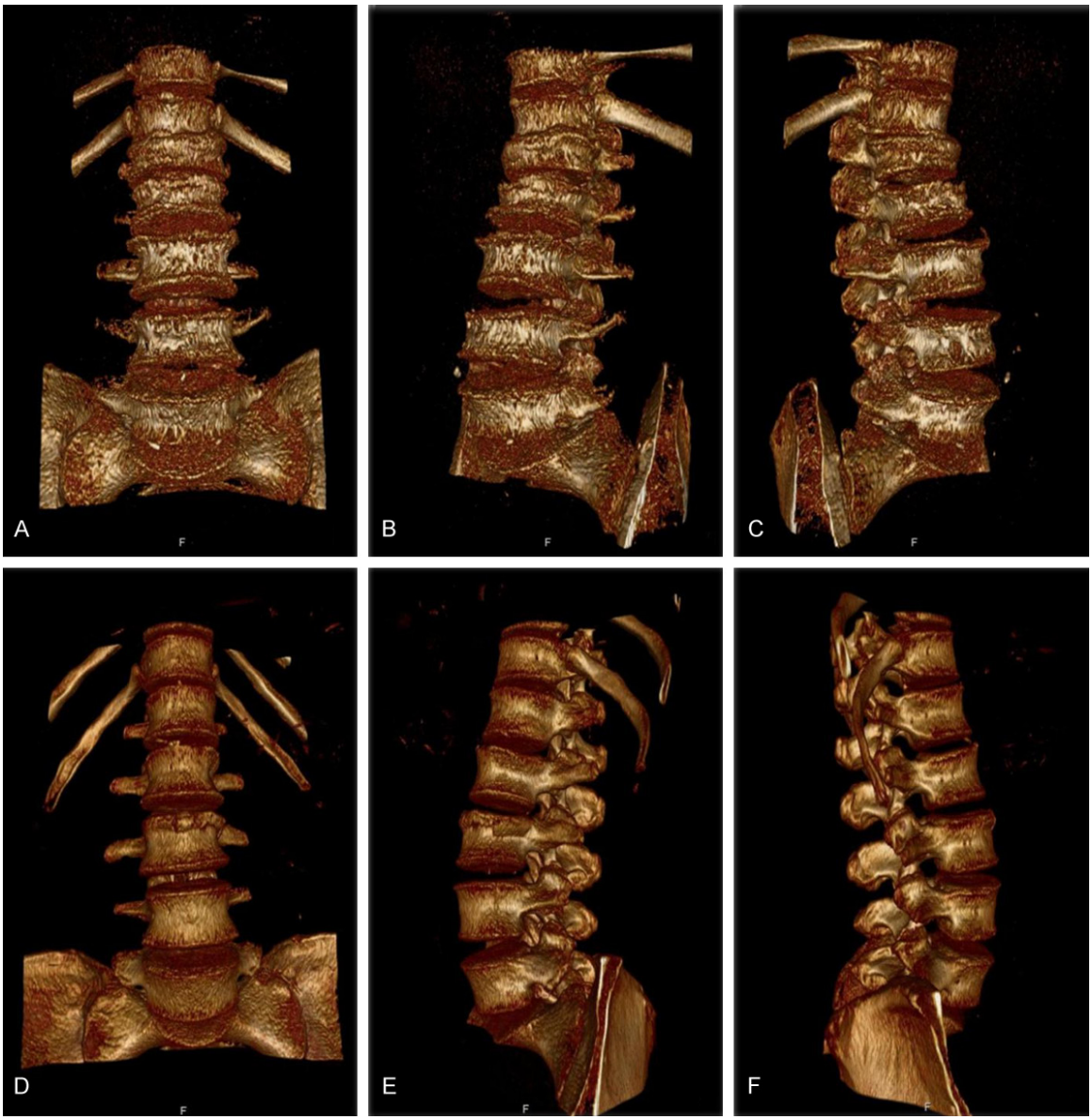

Figure 1. A-C: 3-D CT reconstruction images of MM patient. D-F: 3-D CT reconstruction images of OP patient. comparison of the condition of the cortical bone damage on the surface of the vertebra in MM patient and OP patient.

examinations found VCFs, all of which were initial VCFs.

The locations of the diseased vertebrae were determined by preoperative MRI, CT and X-ray examination. The MM group involved a total of 58 vertebraes, of which 28 were thoracic vertebrae and 30 were lumbar vertebrae. The OP group involved a total of 53 vertebraes, of which 26 were thoracic vertebrae and 27 were lumbar vertebrae. All patients underwent unilateral PKP.

Surgical methods

The patients were placed in the prone position, and the location of the lesion was determined by X-ray using a C-arm and marked. Conventional disinfected drapes were used, and 1% lidocaine was used for topical infiltration anesthesia. A longitudinal incision approximately 0.5 cm in length was made on the skin corresponding to the puncture site. A puncture needle was inserted into the vertebral body through the pedicle under X-ray observation, and

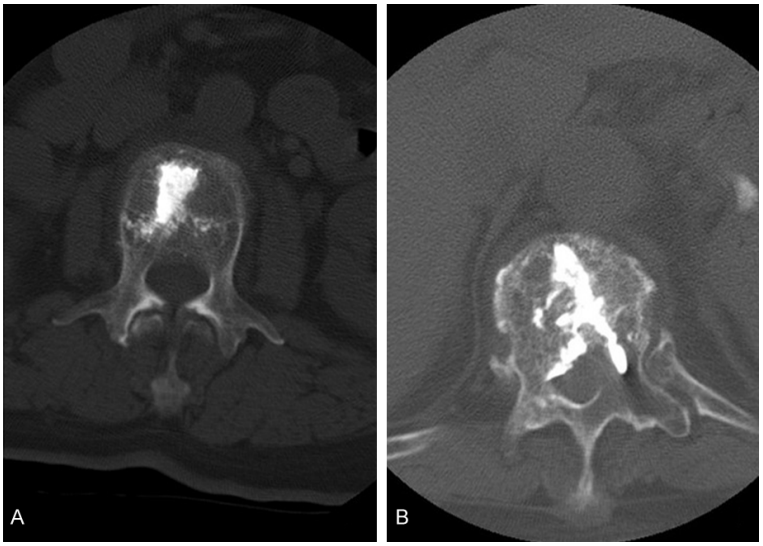

Figure 2. The contrast of postoperative bone cement leakage. A: Image (axial CT scan) after kyphoplasty of OP patient. it shows that bone cement disperses very well and no leakage occurs. B: Image (axial CT scan) after kyphoplasty of MM patient, from the figure we can see that the bone destruction of vertebral body is more serious and bone cement has leaked into the spinal canal. Fortunately the patient has no neurological symptoms.

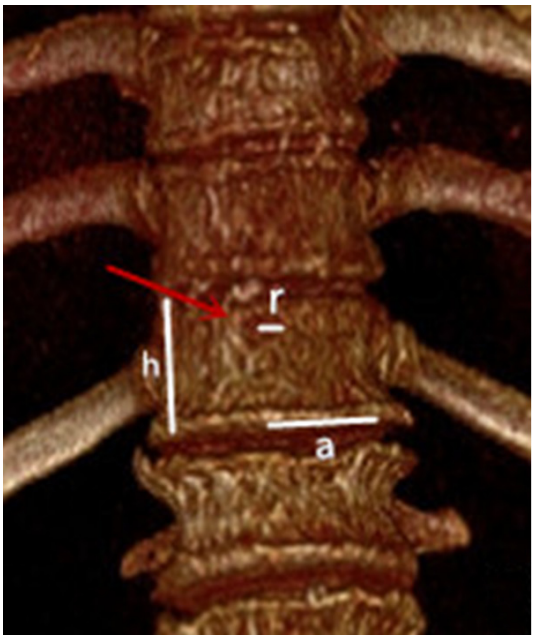

Figure 3. SCHEMES: A 3-D CT reconstruction image of MM patient. The image signs cortical bone destruction by t he red arrow. The h is vertebral height. The r is on behalf of radius to the area of cortical bone destruction. Each segment of the vertebral body was simulated as a cylinder so the a indicates the radius of cylindrical bottom surface.

the needle was held stationary after it had passed 2-3 mm beyond the posterior edge of the vertebral body. The inner core of the puncture needle was removed, a cannula was inserted, and the balloon was placed in an appropriate location. The balloon was inflated under X-ray observation, and balloon dilation and recovery of the vertebral height were monitored. The balloon was removed, and the working phase (polymethyl methacrylate (PMMA) bone cement) was slowly injected into the vertebral body under X-ray observation. The filling of the vertebral body with bone cement was monitored; simultaneously, the patient's reaction and the sensation and movement of both lower limbs were closely monitored. The surgical devices were removed after the injection was finished and before the bone cement hardened. Local compression was applied to stop bleeding. After suturing, a sterile dressing was used to wrap the wound. All patients were able to get out of bed one day after the surgery and were discharged three days after the operation. Waist support was worn for one month as protection.

Observation indicators

All patients had a complete preoperative imaging examination, including X-ray, three-dimensional CT reconstruction and MRI, to determine the segment and number of diseased vertebrae and to evaluate the integrity of the posterior edge of the diseased vertebra, the condition of the cortical bone damage on the surface of the vertebra (**Figure 1**), and the oppression of the spinal canal and the nerves. The intraoperative balloon pressure and the amount of injected bone cement were recorded. Three days after the operation, X-ray examination and three-dimensional CT reconstruction were performed again to evaluate the BCL condition (**Figure 2**).

Measurement of cortical bone destruction

Based on the raw CT data in the preoperative PACS system, a Sectra Table was used to reconstruct a three-dimensional spine model. Each

Table 1. Comparison of complications between the 2 groups

Complications	Multiply Myeloma n (%)	Osteoporosis	x^2 (*P*-value)
Cement Leakage	22 (37.9%)	6 (11.3%)	0.001

segment of the vertebral body was simulated as a cylinder, and the shape of the area of cortical bone destruction was simulated as a circle under the same magnification factor. Various vertebral body and cortical bone destruction parameters were directly measured (**Figure 3**); the formula B = 2πa * h was used to calculate the surface area of the vertebral body B, and the formula A = πr^2 was used to calculate the cortical bone destruction area A. Bone DestructionRate (R) = Cortical Bone Destruction Area (A)/Vertebral Body Surface Area (B) was used as the formula to calculate the cortical bone destruction rate (R).

Statistical methods

SPSS 23.0 statistical software was used to analyze the data. The measurement data of each group are expressed as ($\bar{X}$ ± S). A t-test was used for the analysis of various preoperative and postoperative data of patients in both groups, and the chi-squared test was used for the analysis of the cortical bone destruction and postoperative BCL rate of both groups. P<0.05 was considered statistically significant.

Results

Eighty-one patients (48 females; 33 males) who underwent 111 vertebroplasty procedures were included in the study. The patients were divided into two groups. The mean age was 65.4 years (standard deviation (SD) = 9.9, standard error (SE) = 2.8) in the MM group and 69.6 years (SD = 6.5, SE = 0.9) in the OP group (p = 0.073). The MM group included a total of 58 vertebrae, 22 of which showed BCL, yielding a postoperative BCL incidence of 37.9%. The OP group included a total of 53 vertebrae, six of which showed BCL, for a postoperative BCL incidence of 11.3% (**Table 1**). There was a significant difference between the two groups in BCL incidence (P<0.05). In the MM group, sixteen vertebraes showed intraspinal leakage, and six vertebraes showed leakage around the vertebrae; in the OP group, four vertebraes showed leakage around the vertebrae, one vertebra showed intervertebral disc leakage, and one vertebra showed intraspinal leakage. None of the patients showed neurological symptoms. In the MM group, the intraoperative balloon dilation pressure was 120-200 PSI, with an average of 170.77 PSI; in the OP group, the balloon dilation pressure was 110-350 PSI, with an average of 168.49 PSI; there was no significant difference between the two groups in intraoperative balloon dilation pressure (P>0.05). In the MM group, the amount of injected bone cement was 1.5 to 6.5 mL, with an average of 3.538 mL; in the OP group, the amount of injected bone cement was 1.5-5.5 mL, with an average of 3.528 mL; there was no significant difference between the two groups in this parameter (P>0.05). In the MM group, the average peripheral cortical bone destruction rate (R) of non-fractured vertebrae was 2.9%, and in the OP group, the average peripheral cortical bone destruction rate (R) of non-fractured vertebrae was 0.8%; there was a significant difference in this parameter between the two groups (P<0.05) (**Table 2**).

In the MM group, the average balloon dilation pressure of the vertebrae with BCL was 175.46 PSI, and the average balloon dilation pressure of the vertebrae without BCL was 167.33 PSI; there was no significant difference in this parameter between the two groups (P>0.05). In the MM group, the average amount of bone cement injected into vertebrae with BCL was 3.909 mL, and the average amount of bone cement injected into vertebrae without BCL was 3.267 mL; there was no significant difference between the two groups in the amount of bone cement injected (P>0.05) (**Table 3**).

Discussion

The treatment of VCFs by PKP can effectively relieve pain and restore anterior vertebral height, and PKP has become the preferred method for the treatment of spinal fractures caused by OP [8]. MM is a common malignant tumor of the blood. With disease progression, various degrees of myeloma bone disease (MBD) often occur [13], and severe cases may experience pathological fractures. For patients with pathological fractures of the spine who have no significant tumor mass in the spinal canal and no neurological symptoms and in

Table 2. The comparison of surgery outcomes between the 2 groups ($\bar{X} \pm S$)

Surgery outcomes	Multiply Myeloma	Osteoporosis	*P*-value
Cement volume (ml)	3.538±1.385	3.528±1.067	0.971
Balloon pressure (PSI)	170.769±29.519	168.491±36.077	0.781
Totle Vertebral body periphery destruction	0.029±0.021	0.008±0.007	0.000

Table 3. The comparison of surgery outcomes between leakage and non-leakage in MM group ($\bar{X} \pm S$)

Surgery outcomes	Leakage	Non-leakage	*P*-value
Cement volume (ml)	3.909±1.514	3.267±1.266	0.251
Balloon pressure (PSI)	175.455±29.787	167.333±29.873	0.499

Table 4. The comparison of cortical bone destruction between 2 groups in thoracic and lumber ($\bar{X} \pm S$)

Cortical bone destruction	Multiply Myeloma	Osteoporosis	*P*-value
Thoracic	0.028±0.024	0.009±0.007	0.003
Lumber	0.030±0.018	0.008±0.006	0.000

whom the posterior vertebral edge is integral, PKP treatment can be performed to achieve a better therapeutic outcome [2, 13, 14].

BCL is the most common complication of PKP surgery. Some cases of BCL show no clinical symptoms, some produce neurological symptoms, and severe cases can lead to lower limb paralysis. The existing literature [15, 16] reports that the balloon dilation pressure, the amount of injected bone cement and the integrity of the vertebral edge are the major relevant risk factors for BCL after PKP surgery. The present study found that compared with OP patients, MM patients are more prone to BCL after receiving PKP surgical treatment and that the leakage mainly occurs inside the spinal canal. We compared the balloon dilation pressure and the amount of injected bone cement used in the two groups and found no significant difference between the groups in these parameters (P>0.05). We compared the relevant risk factors for BCL in patients with and without BCL in the MM group and found that neither the balloon dilation pressure nor the amount of injected bone cement had a significant effect (P>0.05). By means of preoperative three-dimensional CT reconstruction, we directly measured the vertebral peripheral area (except for the upper and lower endplates and the posterior edge of the vertebral body) of 20 vertebrae, including each of the non-surgical thoracic and lumbar vertebrae of the two groups and the area of cortical bone destruction on the surfaces of these vertebrae. After comparing the extent of cortical bone destruction of non-fractured vertebrae in patients in the two groups, we found that both the thoracic vertebrae and the lumbar vertebrae of the MM group patients were more severely damaged than those of the OP group (P<0.05) (**Table 4**). When an MM patient has MBD, it manifests as increased osteoclastic bone resorption and osteoblast inhibition, which lead to osteolytic bone destruction. Initially, osteolytic destruction occurs primarily at the interface of the bone and bone marrow, and the lesion does not involve the cortical bone, so the trabeculae do not show significant changes. With disease progression, cortical bone involvement gradually occurs, the number of trabeculae decreases, and the cortical bone becomes thinner; this is followed by reduced bone density. X-rays usually show honeycomb-like, worm-erosion-like, or chiseled bone destruction [17, 18]. This characteristic of MM is one of the factors that causes more severe damage to the peripheral edge of the vertebra.

The present study suggests that cortical bone destruction of the vertebral periphery is the major factor causing high BCL rates after PKP surgery in MM patients, with 90% of MM patients having intraspinal leakage. We speculate that the cause of the increased BCL rates in MM patients may be the greater potential for severe damage to the posterior vertebral edge in these patients, which increases the intraspinal leakage risk for MM patients to a certain extent. Therefore, in patients with VCF caused by MM, routine three-dimensional CT reconstruction and MRI examination should be performed to evaluate the extent of damage to the vertebral periphery, especially the integrity of the vertebral posterior edge, before perform-

ing a PKP operation. For patients with severe damage of the vertebral periphery, the surgical method should be modified appropriately. For patients who cannot tolerate open surgery and patients with VCFs in multiple segments, we suggest using high-viscosity cement and attempting to avoid high balloon dilation pressures so as to extend the bone cement injection time as much as possible, limit the amount of injected bone cement, and reduce the postoperative occurrence of BCL. In addition, MM is a systemic disease that requires a multi-disciplinary treatment approach. Regular pre- and postoperative chemotherapy can significantly reduce the risk associated with surgery [19].

Because the number of cases in the MM group in this study was relatively small, we did not evaluate other intraoperative risk factors that could lead to BCL, such as the recovery of the anterior height of the operated vertebrae, the operative time, or the location of the operated vertebrae. Therefore, the results of the study have certain limitations. Moreover, due to the limitations of current three-dimensional CT reconstruction techniques, the cortical bone conditions at the upper, lower, and posterior edges of the vertebrae were difficult to visualize, and the measurements were thus limited. Therefore, we hope to develop a better measurement method and measurement parameters that can be used to more accurately evaluate the peripheral integrity of the vertebrae. In addition, based on the risk factors described in this study, PKP surgery for MM patients can be appropriately improved, and specific suggestions can be provided to surgeons to reduce the incidence of postoperative BCL and achieve better outcomes for PKP treatment of VCFs caused by MM.

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Disclosure of conflict of interest

None.

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