Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.5466-20
Intern Med 60: 1169-1174, 2021
http://internmed.jp

【 ORIGINAL ARTICLE 】

Efficacy and Safety of Balloon Kyphoplasty for Pathological Vertebral Fractures in Patients with Hematological Malignancies in Our Institution

Keigo Okada[1], Hiroki Fujiwara[1], Tomoyuki Arimatsu[1], Yotaro Motomura[1], Tsuyoshi Kato[2], Naoki Takezako[3] and Takashi Kumagai[1]

Abstract:

Objective Patients with hematological malignancies, particularly those with multiple myeloma, often suffer from pathological vertebral compression fractures (VCFs). Consequent and significant spinal pain and paralysis impair the activities of daily living and quality of life and delay subsequent chemotherapy. Balloon kyphoplasty (BKP), which is less invasive than conventional therapies, is a type of percutaneous vertebroplasty in which cement is injected into the broken vertebrae to stabilize the spinal column. The present study assessed the effect of BKP on hematological tumors.

Methods We retrospectively analyzed five myeloma patients and one lymphoma patient who underwent BKP for pathological VCFs in our institution.

Results The median age was 74 years old. The spinal operation level ranged from T2 to L4. BKP was performed at the diagnosis in two cases, after first-line chemotherapy in one case, and after subsequent chemotherapy in three cases. After approximately 1 month, the patients' average Eastern Cooperative Oncology Group performance status score rapidly improved from 3.2 to 1.3. The numeric rating scale score decreased from 8.8 to 2.0, and the Karnofsky Performance Status score increased from 35 to 75. No severe complications were observed. All patients became able to walk unassisted and underwent early subsequent chemotherapy.

Conclusion BKP can be a safe and effective treatment option for pathological VCFs in patients with hematological malignancies and allows for rapid induction with subsequent chemotherapy.

Key words: balloon kyphoplasty, vertebral compression fractures, multiple myeloma, cement

(Intern Med 60: 1169-1174, 2021)
(DOI: 10.2169/internalmedicine.5466-20)

Introduction

Multiple myeloma (MM) often causes osteolytic bone lesions, a myeloma-defining event, at the diagnosis or during the disease course (1). Bone destruction is induced by the activation of osteoclasts and the suppression of osteoblasts, which is caused by the interaction of myeloma cells and the bone marrow microenvironment through cytokines, such as receptor activator of nuclear factor kappa-B (RANK)/RANK ligand (RANKL) (2). Among the sites of bone lesions affected, vertebral compression fractures (VCFs) not only evoke robust back pain but also cause paralysis of the cauda equina or lower extremities. These severe complications impair the activities of daily living (ADLs) and quality of life (QOL), delay subsequent chemotherapy, and even increase mortality (3). Other hematological tumors, such as lymphoma, occasionally result in the development of VCFs via the invasion of tumor cells into the spinal column, which usually occurs in the advanced stage (4, 5).

To treat VCFs, nonsurgical and surgical options have typically been selected according to each case. Conservative

[1]Department of Hematology, Ome Municipal General Hospital, Japan, [2]Department of Orthopedics, Ome Municipal General Hospital, Japan and [3]Department of Hematology, National Disaster Medical Center, Japan
Received: May 28, 2020; Accepted: October 8, 2020; Advance Publication by J-STAGE: November 23, 2020
Correspondence to Dr. Keigo Okada, keig.hema@tmd.ac.jp

therapies, including resting, bracing, or analgesic drugs, have sometimes been adopted, but they frequently cause delayed bone union, nonunion, or pseudoarthrosis (6). Conventional surgical techniques, such as posterior vertebral fusion, are invasive and require months of healing before the patient can return to their normal activities, even if the procedure is successful. Furthermore, in patients with hematological malignancies, conventional therapies often result in a delay or discontinuation of subsequent chemotherapies, possibly leading to mortality. Therefore, less invasive methods to treat pathological VCFs for patients with hematological malignancy with rapid recovery are required.

Percutaneous vertebroplasty (PV) is an image-guided surgery in which cement is injected into a fractured vertebral body to relieve pain. This procedure is less invasive than the conventional operation, although it requires substantial cement extravasation (7). Balloon kyphoplasty (BKP) is a type of PV that has been developed in which a balloon is inflated in the broken vertebra to correct kyphosis, followed by cement injection to stabilize the spinal column (8). As BKP requires less cement injection and achieves more persistent pain relief than PV, it has been widely used for osteoporotic fractures that were not associated with malignancies (9-11).

Although its utility for osteoporotic VCFs has been reported (12-15), there have been few studies on pathological fractures. Indeed, only one prospective randomized trial, called CAFE study, compared the safety and efficacy of BKP to non-surgical management for patients with solid tumors and MM (16). In that study, the BKP group had a superior functional outcome, pain relief, improvement in the quality of life, and reduced number of pain medications compared with the control group, and few adverse events, such as back pain or symptomatic vertebral fractures, were observed.

In 2019, the International Myeloma Working Group (IMWG) published recommendations for PV or BKP for the treatment of VCFs in patients with MM (17). The IMWG proposed the consensus statement in which MM patients with significant pain due to vertebral fracture should be offered cement augmentation within four to eight weeks. However, BKP has not been widely performed for pathological VCFs associated with malignancies in Japan, where the technique was approved in 2011 and special training for orthopedists is needed.

Because BKP has not yet been widely applied for hematological malignancies, the accumulation of clinical data focused on the efficacy and safety of BKP in patients with hematological malignancies is required to clarify its clinical advantages and disadvantages. In our institution, we have successfully performed BKP in patients with hematological malignancies complicated with disease-associated VCFs in cooperation with orthopedics in six patients.

The present report will help hematologists understand BKP as a therapeutic option for pathological VCFs in patients with hematological malignancies.

Materials and Methods

Patients who were diagnosed with MM or lymphoma with pathological VCFs and who underwent BKP at our hospital from 2017 to 2019 were retrospectively analyzed. The clinical findings, Eastern Cooperative Oncology Group performance status (ECOG PS), and Karnofsky Performance Status (KPS) were assessed via a review of the medical records. The numeric rating scale (NRS) score, which indicates subjective pain on a scale from 0 (no pain) to 10 (the most severe pain), was obtained from a questionnaire before and approximately 1 month after BKP.

BKP was performed in our orthopedics department using Kyphon BKP devices (Medtronic Japan, Tokyo, Japan) as previously described (8). In brief, a surgeon first bilaterally inserted bone access needles into the fractured vertebra. Next, balloons were inserted and expanded, which raised the compressed vertebral body and corrected the kyphotic deformity. Finally, after the balloons were deflated and removed, the resulting cavity allowed the injection of bone cement under lower pressure than conventional PV.

Results

Patient characteristics are shown in Table 1. Five MM patients and one diffuse large B cell lymphoma (DLBCL) patient were included. The median age was 74 (range, 61 to 83) years old. The MM patients (cases 1-5) showed various subtypes of monoclonal proteins, international staging system (ISS) stages at the diagnosis, and previous chemotherapies. Supportive care, such as bracing, opioids, and bisphosphonates, was arbitrarily provided. The details of each patient are shown below.

Case 1

A 76-year-old woman with lumbar vertebral fractures was diagnosed with MM and IgA-kappa monoclonal protein. After two cycles of a bortezomib-containing regimen (bortezomib, cyclophosphamide, and dexamethasone; BCD) and zoledronate, new thoracic vertebral fractures emerged. The patient became unable to walk due to strong back pain and needed opioid medication. BKP was quickly performed for T2 and T4 on the same day, which promptly relieved the acute pain within 1 day, and subsequent BCD chemotherapy was resumed in the outpatient clinic just 13 days after the operation. Although the opioid dose did not change, the patient continued chemotherapy on foot. The representative X-ray and magnetic resonance images are shown in Fig. 1.

Case 2

A 61-year-old man with lower back pain was diagnosed with MM, IgG-kappa type. The patient suffered from nerve paralysis of the lower extremities caused by an L4 vertebral fracture. Although one cycle of BCD treatment and zoledronate was administered, the leg pain and paralysis did not

Table 1. Patient Characteristics.

No.	Age	Sex	Disease, monoclonal protein type for MM	Clinical Stage	Levels of VCFs	Previous treatment
1	76	F	MM, IgA-κ	IIIA (ISS)	T2, T4	BCD
2	61	M	MM, IgG-κ	IIIA (ISS)	L4	BCD
3	72	F	MM, BJP-κ	IIA (ISS)	L4	LD, BD
4	79	F	MM, IgG-λ	IIIA (ISS)	T12	none
5	66	F	MM, IgG-λ	IA (ISS)	L2, L4	aPBSCT BD, LD, PD
6	83	M	DLBCL	IV (Ann Arbor)	L3	Chemotherapy

MM: multiple myeloma, VCFs: vertebral compression fractures, DLBCL: diffuse large B cell lymphoma, ISS: international staging system, BCD: bortezomib, cyclophosphamide, and dexamethasone, LD: lenalidomide and dexamethasone, BD: bortezomib and dexamethasone, PD: pomalidomide and dexamethasone, aPBSCT: auto peripheral blood stem cell transplantation

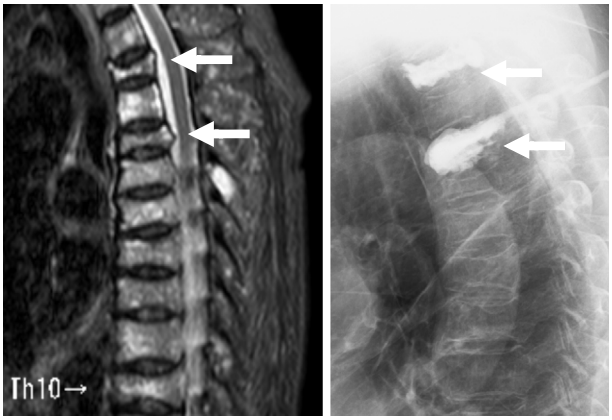

Figure 1. Vertebral compression fracture treated with balloon kyphoplasty (BKP) in case 1. Left: T2-weighted magnetic resonance imaging showing compression fractures of T2 and T4 (arrows). Right: X-ray after BKP indicating the cement-augmented vertebral bodies (high density areas with arrows).

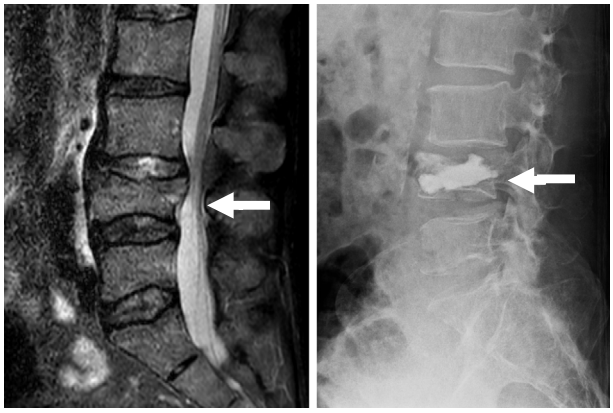

Figure 2. Vertebral compression fracture treated with balloon kyphoplasty (BKP) in case 2. Left: T2-weighted magnetic resonance imaging showing compression fractures of L4 (arrow). Right: X-ray after BKP indicating a cement-augmented vertebral body (high density area with an arrow).

improve, resulting in the patient being unable to walk without assistance. BKP was performed on day 21 of the diagnosis, which attenuated the paralysis in only a few days and enabled walking. The patient was transferred to another hospital to continue chemotherapy and finally received an autologous stem cell transplant for disease remission. The images of his bone lesions are shown in Fig. 2.

Case 3

A 72-year-old woman with lumbar pain was diagnosed with MM, BJP-kappa monoclonal protein. Osteolytic lesions in T6 and L4 were confirmed on computed tomography. Lenalidomide and dexamethasone (LD) treatment was introduced, and radiation therapy for L4 was performed. However, LD treatment was discontinued after three cycles because of neutropenia and anemia, and bortezomib and dexamethasone (BD) treatment started. The patient was still afflicted with constant lumbar pain despite opioid medication, bracing, and zoledronate. BKP for L4 was therefore performed between bortezomib injections, which relieved the pain and reduced the opioid dose. Carfilzomib and dexamethasone (Kd) treatment was subsequently initiated.

Case 4

A 79-year-old woman with anemia and lumbar pain was diagnosed with MM, IgG-lambda type. Pathological fractures of Th12 were found, causing significant pain. Because the serum IgG level was very high (more than 9 g/dL), dexamethasone monotherapy was initially performed to reduce the tumor burden. Immediately after the dexamethasone administration, BKP for T12 fracture was performed on day 14 of the diagnosis, followed by BCD treatment and rehabilitation.

Case 5

A 66-year-old woman had been diagnosed with asymptomatic MM, IgG-lambda type, 12 years ago. As the amount of serum IgG gradually increased and lumbar VCF occurred, the patient had received chemotherapy with auto peripheral blood stem cell transplantation (aPBSCT), BD, LD, and pomalidomide and dexamethasone (PD). Despite such chemotherapy, multiple fractures of lumbar vertebrae caused strong pain and impaired the ADL. BKP was performed for L2 and L4, which reduced the pain and enabled the continuation of

Table 2. Clinical Outcomes of BKP.

No.	ECOG PS		KPS		NRS		Postoperative treatment	Time to next treatment (days)	Opioid dose reduction
	pre	post	pre	post	pre	post			
1	3	1	30	80	9	2	BCD	13	No
2	3	1	30	80	10	3	BCD	49	No use
3	3	2	40	70	8	2	Kd	32	Yes
4	3	2	40	70	7	2	BCD	8	No use
5	4	1	30	70	10	3	Kd	7	No use
6	3	1	40	80	9	0	GCD	24	Yes
mean	3.2	1.3	35	75	8.8	2.0		22.1	

BKP: balloon kyphoplasty, ECOG PS: Eastern Cooperative Oncology Group performance status, KPS: Karnofsky Performance Status, NRS: numeric rating scale, BCD: bortezomib, cyclophosphamide, and dexamethasone, Kd: carfilzomib and dexamethasone, GCD: gemcitabine, carboplatin, and dexamethasone

new chemotherapy with carfilzomib and dexamethasone (Kd).

Case 6

An 83-year-old man with cervical lymphadenopathy had been diagnosed with DLBCL 2 years ago and received chemotherapy. When the second relapse occurred, tumor invasion for the L3 vertebra was detected on positron emission tomography. Strong lumbar pain was present, requiring opioids and bed rest. BKP was performed for L3 to relieve pain, followed by multi-agent chemotherapy in the outpatient clinic.

The outcomes of BKP are summarized in Table 2. After the operation, the mean ECOG PS score decreased from 3.2 to 1.3, the KPS score increased from 35 to 75, and the NRS score improved from 8.8 to 2.0. All of the patients who had spent most of their time in the bed and required bracing or opioids before BKP were able to walk independently within a few days after the operation. Most received subsequent chemotherapy within 1 month, and the mean time from BKP to subsequent chemotherapy was 22.1 (7 to 49) days. Two of the three patients who needed opioids were able to reduce their opioid dose. No severe complications were observed as of writing this paper.

Discussion

Patients with MM frequently suffer from osteolytic lesions and pathological bone fractures. Among the affected sites, VCFs are often associated with many complications, such as robust back pain, spinal cord compression, and pneumonia due to a deformed thoracic cavity, all of which delay sufficient administration of subsequent chemotherapy.

For patients with MM and osteolytic lesions, chemotherapy is the most important treatment, and proteasome inhibitors may be preferred in the treatment of bone disease. The bone remodeling effect of bortezomib was reported in the phase 3 VISTA trial and is now broadly acknowledged (18). Second-generation proteasome inhibitors, such as carfilzomib or ixazomib, have also shown beneficial effects on bone metabolism in preclinical and clinical studies (19-22). However, these novel agents may take time to achieve bone remodeling and not be suitable for acute pain.

PV is a method of cement augmentation with minimal surgical invasion to relieve the pain caused by VCFs. Developed from PV, BKP raises the crushed vertebrae with a balloon, corrects the kyphosis, and is less invasive than previous methods. In Japan, BKP was approved for VCFs in 2011. Both PV and BKP have been widely used for osteoporotic fractures by orthopedic surgeons, and a meta-analysis revealed that their beneficial effects were stable and similar, although cement leakage occurs less frequently in BKP (11). However, their effects on pathological fractures caused by malignant tumors have not been fully investigated. Only some retrospective (23-26) and prospective (27, 28) studies have reported its efficacy, and only one randomized trial, which compared BKP to nonsurgical options and enrolled patients with solid tumors and MM, showed the superiority of BKP (16). Although the IMWG recently presented recommendations for PV or BKP for the treatment of VCFs in patients with MM based on these reports (17), BKP has not been widely performed for pathological VCFs associated with malignancies in Japan, possibly due to the lack of orthopedic surgeons who have learned the technique and a lack of sharing information between orthopedic surgeons and oncologists, including hematologists. Therefore, it is important to increase the spread of BKP in patients with hematological malignancies by accumulating clinical cases and their real-world data.

In the present study, we focused on the effects of BKP, not including PV, in patients with hematological tumors. Thus far, five myeloma patients and one lymphoma patient have undergone BKP for pathological VCFs in our hospital. There was no trend regarding the ISS stage or monoclonal protein type. All cases presented significant acute pain and even paralysis in one case due to pathological VCFs, which met the absolute indication of cement augmentation from the IMWG. It was difficult to receive chemotherapy or radiotherapy unless the pain was improved, so BKP was considered to be a good technique for managing patients requiring quick pain relief. With respect to the timing of the operations, BKP was performed during any line of chemother-

apy, as shown in Table 1. Although it was difficult to precisely define the date of the onset of the fracture, the time from orthopedic consultation to operation was as short as 8 days in our institution (data not shown).

After the operation, the PS, KPS, and NRS scores of the patients dramatically improved. In practice, all patients who had been confined to a bed were able to walk independently within a few days and to continue subsequent chemotherapy. While we did not assess the vertebral body height or angle of kyphosis from an orthopedic perspective, consequent pain relief and improvement in the ADLs and QOL were clearly indicated. Our assessment was performed approximately one month after BKP. However, longer observation is required to assess the long-term prognosis of patients who undergo BKP.

In our cases, no minor or major adverse events were observed regarding the operation during the observation period. The incidence of cement leakage was reported to be less frequent in BKP than in PV in a recent meta-analysis that targeted osteoporotic fractures (29), but cement leakage remains a major complication of BKP. Cement leakage in cancer patients has been reported, and Mansour et al. noted that cement pulmonary embolism occurred in 12.7% of patients, although most of these emboli caused no clinical symptoms (30-32). For MM patients with frail bone density, close attention should be paid, and routine computed tomography after BKP may be recommended to detect cement leakage.

Adjacent vertebral fracture is another major problem of BKP, with a reported incidence ranging from 10% to 38% in osteoporosis (33). It is thought to be caused by the enforced pressure that results from the correction of kyphosis. As a result, the correction of kyphosis often returns to normal after long-term observation, while pain relief remains effective. Unfortunately, there is no standard for preventing or treating secondary fractures, but Tseng et al. reported the prophylactic effect of teriparatide (recombinant human parathyroid hormone) for adjacent VCFs (34).

Our study is limited by its retrospective nature and the fact that we analyzed only six cases in a single institution with short-term observation. Furthermore, the administration of bisphosphonates or opioids varied among cases, which may have influenced the assessment of the effects of BKP. It is necessary to collect more cases and analyze them in the long term in a prospective manner.

Despite those limitations, the improvement of PS, KPS, and NRS by BKP operation was remarkable and quick without major complications. We consider BKP to be a safe and effective treatment option for pathological VCFs. Further investigations concerning the efficacy and safety in patients with hematological malignancies will be necessary to increase the use of BKP, and the collaboration of hematologists with orthopedists is an important issue.

The authors state that they have no Conflict of Interest (COI).

References

1. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol **15**: e538-e548, 2014.
2. Terpos E, Ntanasis-Stathopoulos I, Gavriatopoulou M, Dimopoulos MA. Pathogenesis of bone disease in multiple myeloma: From bench to bedside. Blood Cancer J **8**: 7, 2018.
3. Eda H, Santo L, David Roodman G, Raje N. Bone disease in multiple myeloma. Cancer Treat Res **169**: 251-270, 2016.
4. Hashi S, Goodwin CR, Ahmed AK, Sciubba DM. Management of extranodal lymphoma of the spine: a study of 30 patients. CNS Oncol **7**: CNS11, 2018.
5. Uehara M, Takahashi J. Hirabayashi H et al. Hodgkin's disease of the thoracic vertebrae. Spine J **13**: e59-e63, 2013.
6. HoflerRC, SwongK, MartinB, WemhoffM, JonesGA. Risk of pseudoarthrosis after spinal fusion: analysis from the Healthcare Cost and Utilization Project. World Neurosurg **120**: e194-e202, 2018.
7. Cotten A, Dewatre F, Cortet B, et al. Percutaneous vertebroplasty for osteolytic metastases and myeloma: effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up. Radiology **200**: 525-530, 1996.
8. Garfin SR, Yuan HA, Reiley MA. New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures. Spine **26**: 1511-1515, 2001.
9. Wang H, Sribastav S, Sen Ye F, et al. Comparison of percutaneous vertebroplasty and balloon kyphoplasty for the treatment of single level vertebral compression fractures: a meta-analysis of the literature. Pain Physician **18**: 209-221, 2015.
10. Cheng J, Muheremu A, Zeng X, Liu L, Liu Y, Chen Y. Percutaneous vertebroplasty vs balloon kyphoplasty in the treatment of newly onset osteoporotic vertebral compression fractures: a retrospective cohort study. Medicine (Baltimore) **98**: e14793, 2019.
11. Wang B, Zhao CP, Song LX, Zhu L. Balloon kyphoplasty versus percutaneous vertebroplasty for osteoporotic vertebral compression fracture: a meta-analysis and systematic review. J Orthop Surg Res **13**: 1-8, 2018.
12. Wardlaw D, Cummings SR, Van Meirhaeghe, J et, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Lancet **373**: 1016-1024, 2009.
13. Van Meirhaeghe J, Bastian L, Boonen S, Ranstam J, Tillman JB, Wardlaw D. A randomized trial of balloon kyphoplasty and non-surgical management for treating acute vertebral compression fractures: vertebral body kyphosis correction and surgical parameters. Spine **38**: 971-983, 2013.
14. Zhu Y, Cheng J, Yin J, Zhang Z, Liu C, Hao D. Therapeutic effect of kyphoplasty and balloon vertebroplasty on osteoporotic vertebral compression fracture: a systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) **98**: e17810, 2019.
15. Beall DP, Chambers MR, Thomas S, et al. Prospective and multicenter evaluation of outcomes for quality of life and activities of daily living for balloon kyphoplasty in the treatment of vertebral compression fractures: the EVOLVE trial. Clin Neurosurg **84**: 169-178, 2019.
16. Berenson J, Pflugmacher R, Jarzem P, et al. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. Lancet Oncol **12**: 225-235, 2011.
17. Kyriakou C, Molloy S, Vrionis F, et al. The role of cement augmentation with percutaneous vertebroplasty and balloon kyphoplasty for the treatment of vertebral compression fractures in multiple myeloma: a consensus statement from the International

Myeloma Working Group (IMWG). Blood Cancer J **9**: 27, 2019.
18. Delforge M, Terpos E, Richardson PG, et al. Fewer bone disease events, improvement in bone remodeling, and evidence of bone healing with bortezomib plus melphalan-prednisone vs. melphalan-prednisone in the phase III VISTA trial in multiple myeloma. Eur J Haematol **86**: 372-384, 2011.
19. Hu B, Chen Y, Usmani SZ, et al. Characterization of the molecular mechanism of the bone-anabolic activity of carfilzomib in multiple myeloma. PLoS One **8**: 1-15, 2013.
20. Zangari M, Aujay M, Zhan F, et al. Alkaline phosphatase variation during carfilzomib treatment is associated with best response in multiple myeloma patients. Eur J Haematol **86**: 484-487, 2011.
21. Garcia-Gomez A, Quwaider D, Canavese M, et al. Preclinical activity of the oral proteasome inhibitor mln9708 in myeloma bone disease. Clin Cancer Res **20**: 1542-1554, 2014.
22. Zangari M, Suva LJ. The effects of proteasome inhibitors on bone remodeling in multiple myeloma. Bone **86**: 131-138, 2016.
23. Huber FX, McArthur N, Tanner M, et al. Kyphoplasty for patients with multiple myeloma is a safe surgical procedure: results from a large patient cohort. Clin Lymphoma Myeloma **9**: 375-380, 2009.
24. Dalbayrak S, Önen MR, Yilmaz M, Naderi S. Clinical and radiographic results of balloon kyphoplasty for treatment of vertebral body metastases and multiple myelomas. J Clin Neurosci **17**: 219-224, 2010.
25. LaMaida GA, Sala F, Callea G, Capitani D, Singh S. Efficacy of unipedicular baloon kyphoplasty for treatment of multiple myeloma vertebral lesions. Asian Spine J **5**: 162-168, 2011.
26. Ha KY, Min CK, Seo JY, et al. Bone cement augmentation procedures for spinal pathologic fractures by multiple myeloma. J Korean Med Sci **30**: 88-94, 2015.
27. Pflugmacher R, Schulz A, Schroeder RJ, Schaser KD, Klostermann K, Melcher I. A prospective two-year follow-up of thoracic and lumbar osteolytic vertebral fractures caused by multiple myeloma treated with balloon kyphoplasty. Z Orthop Unfall **145**: 39-47, 2007.
28. Pflugmacher R, Taylor R, Agarwal A, et al. Balloon kyphoplasty in the treatment of metastatic disease of the spine: a 2-year prospective evaluation.. Eur Spine J **17**: 1042-1048, 2008.
29. Wang P, Li J, Song Z, Peng Z, Wang G. Utilization of the directional balloon technique to improve the effectiveness of percutaneous kyphoplasty in the treatment of osteoporotic vertebral compression fractures and reduction of bone cement leakage. Medicine (Baltimore) **98**: e15272, 2019.
30. Rodrigues DM, Cunha Machado DP, Campainha Fernandes SA, Paixão Barroso AM. Pulmonary cement embolism following balloon kyphoplasty: The impact of a procedural complication in a new era for lung cancer management. Mol Clin Oncol **10**: 299-303, 2018.
31. Idiculla PS, Rajdev K, Pervaiz S, et al. Cement pulmonary embolism after balloon kyphoplasty. Respir Med Case Reports **28**: 100887, 2019.
32. Mansour A, Abdel-Razeq N, Abuali H. Cement pulmonary embolism as a complication of percutaneous vertebroplasty in cancer patients. Cancer Imaging **18**: 5, 2018.
33. Takahashi S, Hoshino M, Yasuda H, et al. Development of a scoring system for predicting adjacent vertebral fracture after balloon kyphoplasty. Spine J **19**: 1194-1201, 2019.
34. Tseng YY, Su CH, Lui TN, Yeh YS, Yeh SH. Prospective comparison of the therapeutic effect of teriparatide with that of combined vertebroplasty with antiresorptive agents for the treatment of new-onset adjacent vertebral compression fracture after percutaneous vertebroplasty. Osteoporos Int **23**: 1613-1622, 2012.