Article published online: 2022-05-21

Original Article

Strategy for Bone Metastases Treatment in Patients with Impending Cord Compression or Vertebral Fractures: A Pilot Study

N. Rasulova, V. Lyubshin[1], F. Djalalov[2], K. H. Kim[3], L. Nazirova, N. Ormanov[4], D. Arybzhanov[4]

Nuclear Medicine Department of Republic Specialized Center of Surgery, [1]Private Clinic "Summit", [2]Department of Interventional Radiology, Republican Research Medical Centre of Emergency Medicine, Tashkent, Uzbekistan, [3]Department of Orthopedic Surgery, Hyundae General Hospital, Namyangju City, Gyungki-do, South Korea, [4]South Kazakhstan Oncology Clinic, Chimkent, Kazakhstan

Abstract

Impending spinal cord compression and vertebral fractures are considered contraindications for radionuclide bone pain palliation therapy. However, most of the patients with widespread bone metastases already have weakened vertebral segments that may be broken. Therefore, local field external-beam radiotherapy or percutaneous vertebroplasty (VP) should be considered to improve the patient's quality of life and to institute subsequent appropriate treatment, including radionuclide therapy for bone pain palliation. The objective of this study was to develop a strategy for an effective treatment of bone metastases in patients with widespread bone metastases and intolerable pain, associated with impending cord compression or vertebral fractures. Eleven patients (5 females and 6 males, aged 32–62 years; mean age 53.8 ± 2.7 years) with multiple skeletal metastases from carcinomas of prostate (n = 3), breast (n = 3) and lung (n = 5) were studied. Their mean pain score measured on a visual analogue scale of 10 was found to be 8.64 ± 0.15 (range 8–9) and the mean number of levels with impending cord compression or vertebral fracture was 2.64 ± 0.34 (range 1–4). All patients underwent vertebroplasty and after 3–7 days received Sm-153 ethylene diamine tetra methylene phosphonic acid (EDTMP) therapy. Sm-153 EDTMP was administered according to the recommended standard bone palliation dose of 37 MBq/kg body weight. Whole body (WB) bone scan, computed tomography and magnetic resonance imaging (MRI) were performed before and after treatment in all patients. Pain relief due to stabilization of vertebrae after VP occurred within the first 12 hours (mean 4.8 ± 1.2 hours; range 0.5–12 hours), and the mean pain score was reduced to 4.36 ± 0.39 (range 2–6). Subsequent to Sm-153 EDTMP treatment, further pain relief occurred after 3.91 ± 0.39 days (range 2–6 days) and the pain score decreased to 0.55 ± 0.21 (range 0–2). The responses to treatment were found to be statistically significant (P < 0.0001). Based on the results on this limited patient population, we conclude that spinal stabilization using VP in patients with widespread bone metastases and impending cord compression is an effective way to decrease disability with pain and to facilitate subsequent systemic palliation of painful skeletal metastases by Sm-153 EDTMP therapy.

Keywords: Bone pain palliation, Sm-153 EDTMP, vertebroplasty

Introduction

Bone metastasis remains a major cause of morbidity in patients with cancer and represents a common manifestation of the disease. It occurs in 65–75% of patients with cancers of the breast and prostate, 30–40% of patients with lung cancer, a and significant proportion of patients with cancers of the thyroid, bladder and kidney.[1] In patients with non-small cell lung cancer, 70% of patients with bone metastases have bone pain.[2,3] According to Varadhachary, 60–84% of all cases of metastatic disease invade bone and approximately 70% of patients with metastatic bone disease experience bone pain.[4]

The vertebral column is the most common site for bone metastases, with an incidence of 30–70% in patients with

Access this article online

Quick Response Code:

Website: www.wjnm.org

DOI: 10.4103/1450-1147.82114

Address for correspondence:
Dr. Nigora Rasulova, Nuclear Medicine Department, Republic Specialized Center of Surgery, Str. Farkhadskaya 10, Tashkent 100115, Uzbekistan.
E-mail: niga_r@yahoo.com

metastatic neoplasms.[5-7] Patients with metastatic cancer involving bone are also at increased risk of fractures, spinal cord compression (SCC), hypercalcemia, and immobility, resulting in substantial medical-associated morbidities. Jensen *et al*. reported high incidence of skeletal-related events (SREs) in Denmark's population among women with breast cancer. According to this data, SREs were the highest during the first year after the primary diagnosis of bone metastases and occurred in 47.6% of breast cancer's patients.[8]

Mechanical pain usually is associated with bone loss in lytic lesions; however, blastic lesions may weaken the bone sufficiently through the loss of structural integrity to cause functional pain. Progressive involvement of the bone cortex weakens the axial strength of the bone and gives rise to instability.[9] At this stage, more than 50% of patients with multiple skeletal metastases have ineffective chemotherapy.

Radiotherapy is often highly effective for individual bone metastatic lesions, but its use may be limited in patients with widely metastatic bone disease and disparate areas of pain.[10] Furthermore, even when one site of pain is being treated, other areas outside the radiation field may become symptomatic.[11] Moreover, external beam radiation remains the standard of care for patients with localized bone pain but no impending risk of fracture.[12] While it is effective at reducing tumor volume, it is not helpful to prevent pathologic fracture because it does not strengthen the anterior support of vertebral body.[13]

Role of vertebral metastases in worsening the quality of life is more and more emphasized, but the treatment is still controversial.[14]

Advantages of bone palliation by radionuclide therapy include the ability to simultaneously treat multiple sites of disease.[15] Unfortunately, impending cord compression and vertebral fractures are considered as contraindications for radionuclide bone therapy. However, most of the patients with widespread bone metastases already have weakened vertebral segments that may be broken. Therefore, stabilizing procedure, such as percutaneous vertebroplasty (VP), should be proceeded to enable radionuclide bone therapy.

VP is a minimal invasive technique consisting of percutaneous injection of polymethyl methacrylate (PMMA) into vertebral body to strengthen it and reduce the pain.[16]

Many authors consistently reported the advantage of percutaneous VP for the treatment of tumorous spinal lesion. However, there is no report presenting the clinical outcome of percutaneous VP as a procedure preceding radionuclide bone therapy. In addition, we could get a good clinical result from this type of treatment. Therefore, we report here the clinical results of these consecutive treatments.

Patients and Methods

Patients

During the period December 2007 to December 2010, we treated 11 patients (5 females and 6 males, aged 32–62 years, mean age 53.8 ± 2.7 years) with multiple skeletal metastases from prostatic carcinoma (n = 3), breast carcinoma (n = 3) or lung carcinoma (n = 5). All patients were referred by Tashkent's Oncology Centers and by South Kazakhstan Oncology Clinic (Chimkent, Kazakhstan). Pain assessment was based on a visual analogue scale (VAS); on this scale, 0 means no pain and 10 means intolerable pain. Their mean objective pain score before treatment was 8.64 ± 0.15 (range 8–9). Types and doses of the prescribed analgesics were recorded, and pain assessment was repeated after VP and after Sm-153 EDTMP treatment.

Computed tomography (CT) and magnetic resonance imaging (MRI) examinations confirmed the number and levels of vertebral bodies with impending cord compression or vertebral fracture as well as the anatomical features. Mean number of levels with impending cord compression or vertebral fracture was 2.64 ± 0.34 (range 1–4) [Figure 1].

Vertebroplasty

VP by percutaneous transpedicular injection of bone cement into the vertebral body was performed on Philips Allura Xper FD 20 by an orthopedic surgeon and an interventional radiologist. VP was performed in

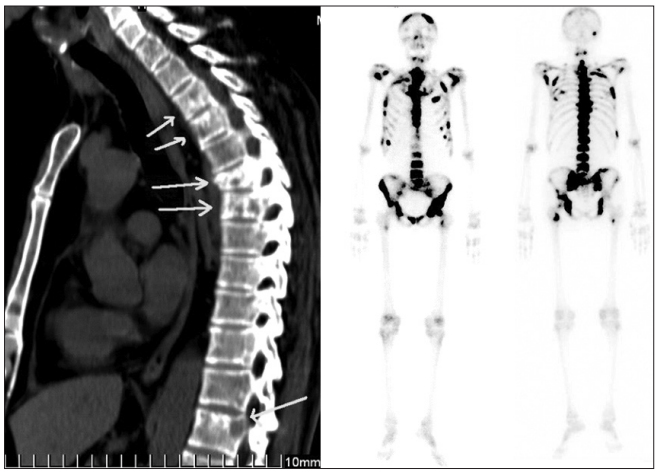

Figure 1: Patient with NSCLC with widespread bone metastases: multiple osteolytic and osteoblastic lesions and fracture in T-5, T6 and T-10 vertebare

all patients in prone position under local anesthesia. An anesthesiologist monitored the patient throughout the procedure. Skin entry points were made about 1 cm from the lateral edge of vertebrae under C-arm fluoroscopic guidance [Figure 2].

A VP needle was inserted through pinpoint skin incision. First, VP needles were inserted until the tips reached the pedicle base on the C-arm lateral view. Then, the VP needle tips were checked and after confirmation that the VP needle did not invade neural canal, VP needle tips were advanced into the anterior one-third of the vertebral body on C-arm lateral view. VP needle tips crossed the midline of vertebral body on C-arm AP view at the same time. Bone cement was injected to vertebral body VP needles with C-arm lateral guidance, until it was

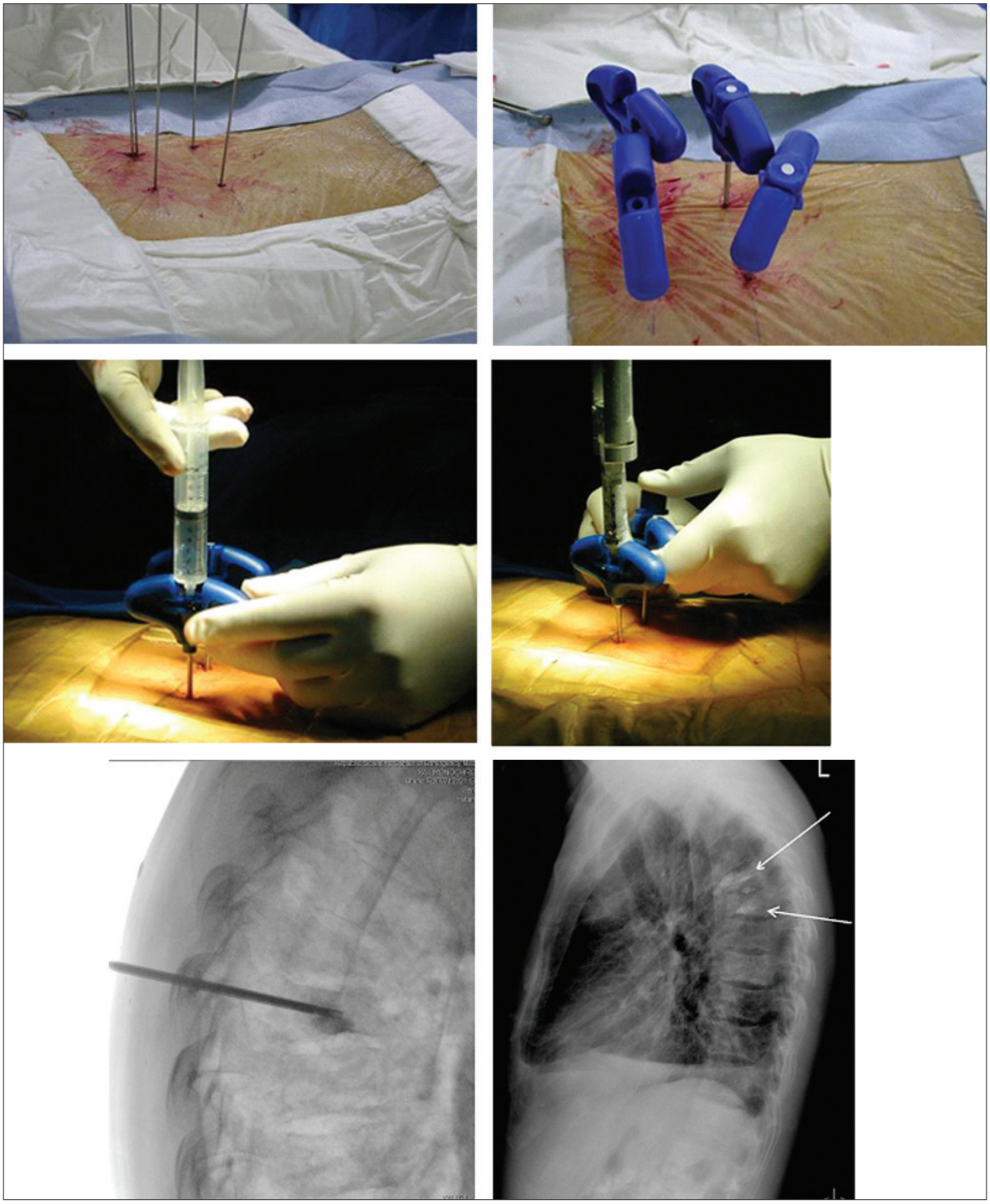

Figure 2: Percutaneous trans-pedicular injection of bone cement into the vertebral body

well distributed on both AP and lateral C-arm views. VP may be performed by unilateral or bilateral approach, depending on the surgeon's preference.

Sm-153 EDTMP therapy

Inclusion criteria for therapy were intense uptake around painful metastases on recent (2–4 weeks before treatment) Tc99m methylene diphosphonate (MDP) whole body (WB) bone scan, hemoglobin >90 g/L, white blood cell count >4 × 10^9/L and platelet count of >100 × 10^9/L. Prior to the administration of the radiopharmaceutical, the patients received information both orally and in a written pamphlet about the procedure, including an explanation of the therapeutic procedure; estimation as to when pain relief may be expected; a warning that a transient flare effect of pain may occur, and therefore, analgesic medication must be continued; radiation protection guidelines, for example, regarding contact with partner, and for pregnant women, children; hygienic measures (e.g. micturition while seated, how to deal with contamination). Also, they were advised that in case of hospitalization or other medical care within 30 days, the physician must be informed, as the therapy may influence other scintigraphic procedures and the patients should carry a medical declaration and radiation safety certificate when traveling shortly after therapy because of airport security checks.

All patients received Sm-153 EDTMP therapy 3–7 days after VP. Sm-153 EDTMP was administered at the standard bone palliation dose of 37 MBq/kg body weight of patient. Tc99m MDP WB bone scan, CT and MRI were repeated 3–8 months after treatment.

Statistical analysis

The acquired results were expressed as the mean ± SEM for each index. Comparison of data amongst various groups was performed with student's unpaired *t*-test for normal distributed values. *P* value of <0.05 was considered statistically significant.

Results

According to our data, pain relief due to stabilization of vertebrae after VP occurred within a relatively short time – during the first 12 hours (mean 4.8 ± 1.2; range 0.5–12 hours), and the mean objective pain score was reduced to 4.36 ± 0.39 (range 2–6) [Figures 3 and 4].

However, patients still had pain due to bone metastases. After subsequent Sm-153 EDTMP treatment, further pain relief occurred after 3.91 ± 0.39 days (range 2–6 days) and the objective pain score decreased further to 0.55 ± 0.21 (range 0–2). There was statistically significant difference between objective pain score before and after

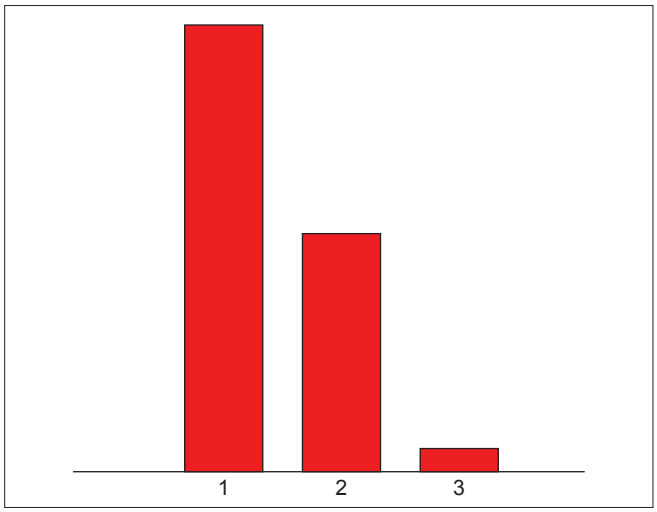

Figure 3: Mean objective pain score according VAS 0-10 system: (1) Before treatment: VAS=8.64±0.15; (2) After vertebroplasty: VAS= 4.6±0.39; (3) After Sm-153 EDTMP treatment: VAS= 0.55±0.21

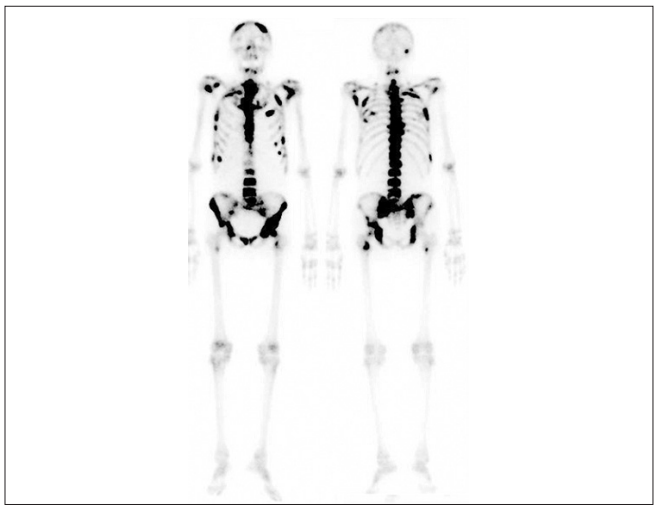

Figure 4a: Tc-99mWB bone scan before treatment showing extensive bone metastases

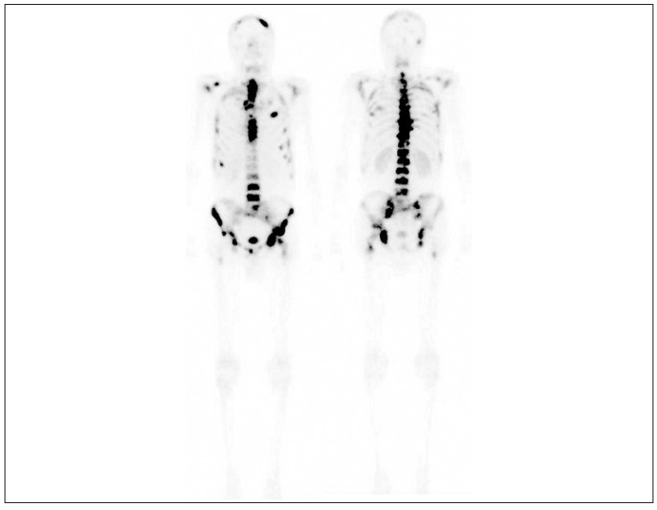

Figure 4b: 8 months after VP and Sm-153 EDTMP treatment, showing slight reduction in number of osteoblastic lesions

treatment ($P < 0.0001$). None of the patients needed to take analgesics afterward and none had SREs during the next 6–8 months of follow-up.

Moreover, according to Tc99m MDP WB bone scan, no patient developed new lesions of bone metastases. It may be noted that in addition to radionuclide treatment for bone pain palliation, all patients were allowed to continue their primary treatment of cancer with anti-cancer drugs.

Discussion

Development of bone metastases is common in many cancers. Bone lesions put these patients at high risk of skeletal complications, including pathologic fracture, SCC, debilitating bone pain, and hypercalcemia. Because of the high incidence of bone metastases in patients with solid tumors and the relatively long survival time after diagnosis of bone metastasis, therapies to reduce morbidity from skeletal complications in these patients are important.[17,18]

For prevention of SCC, Vidya Soerdjbalie-Maikoe and co-authors suggested the combination of bone-seeking radiopharmaceutical agent strontium-89 (Metastron) with the nitrogen-containing bisphosphonate Olpadronate in patients with hormone-refractory prostate cancer (HRPC). Their data show significant reduction in SCC in patients with symptomatic HRPC metastatic to the skeleton who received palliative therapies.[19]

However, in our group, the patients already had impending cord compression and vertebral fractures with severe and intolerable pain. Also, our first step in the treatment of these patients was to strengthen the vertebral body and reduce the pain.

The gold standard treatment of solitary metastatic spinal lesion is *en bloc* vertebrectomy; however, not all patients with spine metastases can be candidates for this extensive surgery and most patients present to the spinal surgeon with multiple metastases already at the time of diagnosis.[20]

Percutaneous VP has been performed to both primary and metastatic spinal tumor as one of the most useful treatment options and it has provided apparent improvement of axial mechanical pain for those patients via strengthening of vertebral body support.[21]

VP using PMMA bone cement is a mechanical stabilizer of fractures.[22] VP also has some benefit as a treatment option of metastatic spine lesion. It may have antitumor effect as a result of cytotoxicity and thermal effect.[23,24] In addition, vertebral biopsies can be readily performed during these procedures if the etiology of vertebral abnormality is unclear or to confirm a suspected pathology.[20] Many prospective[25-30] and retrospective[31-34] studies have reported apparent improvement of both pain score and functional outcome. We could also get statistically significant improvement after VP and consecutive radionuclide bone therapy.

Concerned about the possible complications of VP, some authors prefer to use balloon kyphoplasty. The reported range of radiologic extravasations in VP was 9.2–139% (multiple areas of extravasations occurred per level), whereas the range was 0–26.3% in kyphoplasty. The reported range of symptomatic extravasations in VP was 0–13.5%, while there were none in kyphoplasty.[25-30,35-40] Although cement leakage is more frequent in VP than in kyphoplasty in these reports, symptomatic cement leakage is rare in the clinical setting. In our series, VP did not cause symptomatic cement leakage or other systemic complications.

As for the prophylactic use of VP, there is some argument in case of osteoporosis.[41-43] However, prophylactic cement augmentation of vertebral body with metastatic lesion without fracture is worthwhile to relieve axial pain and improve the patient's quality of life.

Conclusion

According to our data, spinal stabilization using VP in patients with widespread bone metastases and impending cord compression is an effective way to decrease disability with pain and to facilitate subsequent systemic palliation of painful skeletal metastases by administration of Sm-153 EDTMP.

References

1. Coleman RE. Metastatic bone disease: Clinical features, pathophysiology and treatment strategies. Cancer Treat Rev 2001;27:165-76.
2. Kosteva J, Langer C. Skeletal metastases of non-small cell lung cancer: Advances in diagnosis and treatment. In: Carbone D, editor. Lung Cancer Principles and Practices. Philadelphia, PA: Lippincott Williams and Williams; 2003. p. 1-14.
3. Kanis JA. Bone and cancer: Pathophysiology and treatment of metastases. Bone 1995;17:101S-5S.
4. Varadhachary GR, Abbruzzese JL, Lenzi R. Diagnostic strategies for unknown primary cancer. Cancer.2004;100:1776-85.
5. Boland PJ, Lane JM, Sundaresan N. Metastatic disease of the spine. Clin Orthop Relat Res 1982;169:95-102.
6. Harrington KD. Metastatic disease of the spine. J Bone Joint Surg Am 1986;68:1110-5.
7. Wong DA, Fornasier VL, MacNab I. Spinal metastases: The obvious, the occult, and the impostors. Spine 1990;15:1-4.
8. Jensen A. Incidence of bone metastases and skeletal-related events in breast cancer patients: A population based cohort study in Denmark. BMC Cancer 2011;11:29.
9. Bunting R, Lamont-Havers W, Schweon D, Kliman A. Pathologic

fracture risk in rehabilitation of patients with bone metastases. Clin Orthop 1985;192:222-7.

10. Falkmer U, Järhult J, Wersäll P, Cavallin-Ståhl E. A systematic overview of radiation therapy effects in skeletal metastases. Acta Oncol 2003;42:620-33.
11. Deng H, Tan T, Luo S, Huo C, Liao Z, Hu Y, *et al*. Radiopharmaceutical (Sm-153-EDTMP) therapy of skeletal metastases: Clinical application in 350 patients. J Radiol 2002 www.jradiology.org
12. Biermann JS, Holt GE, Lewis VO, Schwartz HS, Yaszemski MJ. Metastatic bone disease: Diagnosis, evaluation and treatment. J Bone Joint Surg Am 2009;91:1518-30.
13. Bodei L, Lam M, Chiesa C, Flux G, Brans B, Chiti A, *et al*. EANM procedure guideline for treatment of refractory metastatic bone pain. Eur J Nucl Med Mol Imaging 2008;35:1934-40.
14. Langdon J, Bernard J, Molloy S. Prophylactic stabilization of vertebral body metastasis at risk of imminent fracture using balloon kyphoplasty. Spine 2009;34:E469-72.
15. Ryken TC, Eichholz KM, Gerszten PC, Welch WC, Gokaslan ZL, Resnick DK. Evidence-based review of the surgical management of vertebral column metastatic disease. Neurosurg Focus 2003;15:E11.
16. Bròdano GB, Cappuccio M, Gasbarrini A, Bandiera S, De Salvo F, Cosco F, *et al*. Vertebroplasty in the treatment of vertebral metastases: Clinical cases and review of the literature. Eur Rev Med Pharmacol Sci 2007;11:91-100.
17. Coleman RE. Skeletal complications of malignancy. Cancer 1997;80(suppl):1588-94.
18. Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2000: Cancer incidence, mortality and prevalence worldwide, version 1.0. IARC CancerBase No. 5. Lyon: IARC Press; 2001. Available from: http://www-dep.iarc.fr/globocan/cdrom.htm.
19. Soerdjbalie-Maikoe V, Pelger RC, Lycklama à Nijeholt GA, Arndt JW, Zwinderman AH, Papapoulos SE, *et al*. Strontium-89 (Metastron) and the bisphosphonate olpadronate reduce the incidence of spinal cord compression in patients with hormone-refractory prostate cancer metastatic to the skeleton. Eur J Nucl Med Mol Imaging 2002;29:494-8.
20. Tomita K, Kawahara N, Kobayashi T, Yoshida A, Murakami H, Akamaru T. Surgical strategy for spinal metastases. Spine 2001;26:298-306.
21. Mendel E, Bourekas E, Gerszten P, Golan JD. Percutaneous techniques in the treatment of spine tumors: What are the diagnostic and therapeutic indications and outcomes? Spine 2009;34(22 Suppl):S93-100.
22. Jensen ME, Kallmes DE. Percutaneous vertebroplasty in the treatment of malignant spine disease. Cancer J 2002;8:194-206.
23. Dahl OE, Garvik LJ, Lyberg T. Toxic effects of methylmethacrylate monomer on leukocytes and endothelial cells *in vitro*. Acta Orthop Scand 1994;65:147-53.
24. Deramond H, Wright NT, Belkoff SM. Temperature elevation caused by bone cement polymerization during vertebroplasty. Bone 1999;25:17S-21S.
25. Cahana A, Seium Y, Diby M, Martin JB, Ruefenacht D, Dietrich PY. Percutaneous vertebroplasty in octogenarians: Results and follow-up. Pain Pract 2005;5:316-23.
26. Cheung G, Chow E, Holden L, Vidmar M, Danjoux C, Yee AJ, *et al*. Percutaneous vertebroplasty in patients with intractable pain from osteoporotic or metastatic fractures: A prospective study using quality-of-life assessment. Can Assoc Radiol J 2006;57:13-21.
27. Ramos L, de Las Heras JA, Sánchez S, González-Porras JR, González R, Mateos MV, *et al*. Medium-term results of percutaneous vertebroplasty in multiple myeloma. Eur J Haematol 2006;77:7-13.
28. Cotten A, Dewatre F, Cortet B, Assaker R, Leblond D, Duquesnoy 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 1996;200:525-30.
29. Cortet B, Cotten A, Boutry N, Dewatre F, Flipo RM, Duquesnoy B, *et al*. Percutaneous vertebroplasty in patients with osteolytic metastases or multiple myeloma. Rev Rhum Engl Ed 1997;64:177-83.
30. Anselmetti GC, Zoarski G, Manca A, Masala S, Eminefendic H, Russo F, *et al*. Percutaneous vertebroplasty and bone cement leakage: Clinical experience with a new high-viscosity bone cement and delivery system for vertebral augmentation in benign and malignant compression fractures. Cardiovasc Intervent Radiol 2008;31:937-47.
31. McDonald RJ, Trout AT, Gray LA, Dispenzieri A, Thielen KR, Kallmes DF. Vertebroplasty in multiple myeloma: Outcomes in a large patient series. AJNR Am J Neuroradiol 2008;29:642-8.
32. Alvarez L, Pérez-Higueras A, Quiñones D, Calvo E, Rossi RE. Vertebroplasty in the treatment of vertebral tumors: Postprocedural outcome and quality of life. Eur Spine J 2003;12:356-60.
33. Shimony JS, Gilula LA, Zeller AJ, Brown DB. Percutaneous vertebroplasty for malignant compression fractures with epidural involvement. Radiology 2004;232:846-53.
34. Caudana R, Renzi Brivio L, Ventura L, Aitini E, Rozzanigo U, Barai G. CT-guided percutaneous vertebroplasty: Personal experience in the treatment of osteoporotic fractures and dorsolumbar metastases. Radiol Med 2008;113:114-33.
35. Khanna AJ, Reinhardt MK, Togawa D, Lieberman IH. Functional outcomes of kyphoplasty for the treatment of osteoporotic and osteolytic vertebral compression fractures. Osteoporos Int 2006;17:817-26.
36. Gerszten PC, Germanwala A, Burton SA, Welch WC, Ozhasoglu C, Vogel WJ. Combination kyphoplasty and spinal radiosurgery: A new treatment paradigm for pathological fractures. J Neurosurg Spine 2005;3:296-301.
37. Dudeney S, Lieberman IH, Reinhardt MK, Hussein M. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. J Clin Oncol 2002;20:2382-7.
38. Lane JM, Hong R, Koob J, Kiechle T, Niesvizky R, Pearse R, *et al*. Kyphoplasty enhances function and structural alignment in multiple myeloma. Clin Orthop Relat Res 2004;426:49-53.
39. Pflugmacher R, Kandziora F, Schroeder RJ, Melcher I, Haas NP, Klostermann CK. Percutaneous balloon kyphoplasty in the treatment of pathological vertebral body fracture and deformity in multiple myeloma: A one-year follow-up. Acta Radiol 2006;47:369-76.
40. Pflugmacher R, Beth P, Schroeder RJ, Schaser KD, Melcher I. Balloon kyphoplasty for the treatment of pathological fractures in the thoracic and lumbar spine caused by metastasis: One-year follow-up. Acta Radiol 2007;48:89-95.
41. Oakland RJ, Furtado NR, Timothy J, Hall RM. The biomechanics of vertebroplasty in multiple myeloma and metastatic bladder cancer: A preliminary cadaveric investigation. J Neurosurg Spine 2008;9:493-501.
42. Sun K, Liebschner MA. Biomechanics of prophylactic vertebral reinforcement. Spine 2004;29:1428-35.
43. Becker S, Garoscio M, Meissner J, Tuschel A, Ogon M. Is there an indication for prophylactic balloon kyphoplasty? A pilot study. Clin Orthop Relat Res 2007;458:83-9.

How to cite this article: Rasulova N, Lyubshin V, Djalalov F, Kim KH, Nazirova L, Ormanov N, Arybzhanov D. Strategy for bone metastases treatment in patients with impending cord compression or vertebral fractures: A pilot study. World J Nucl Med 2011;10:14-9.
Source of Support: Nil. **Conflict of Interest:** None declared.