Published in final edited form as:

J Pain. 2012 June ; 13(6): 564–570. doi:10.1016/j.jpain.2012.03.003.

Changes in pain and other symptoms in patients with painful multiple myeloma-related vertebral fracture treated with kyphoplasty or vertebroplasty

Tito R. Mendoza, PhD¹, Dhanalakshmi Koyyalagunta, MD², Allen W. Burton, MD³, Sheeba K. Thomas, MD⁴, My-Hanh V. Phan, BBA⁵, Sergio A. Giralt, MD⁶, Jatin J. Shah, MD⁴, and Charles S. Cleeland, PhD¹

¹Department of Symptom Research, The University of Texas MD Anderson Cancer Center, Houston, Texas

²Department of Pain Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

³Houston Pain Associates, Houston, TX

⁴Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, Texas

⁵Department of Anesthesiology and Critical Care, The University of Texas MD Anderson Cancer Center, Houston, Texas

⁶Adult Bone Marrow Transplant Service, Memorial Sloan-Kettering Cancer Center, New York, New York

Abstract

Patients with painful vertebral compression fractures produced by multiple myeloma (MM) often experience reduction in pain after spinal augmentation with kyphoplasty or vertebroplasty. Previous studies have shown pain reduction and improvement in functional status after augmentation, but no studies have examined the effect of augmentation on other cancer-related symptoms. We hypothesized that reduction in pain severity would be significantly associated with improvement in other reported symptoms. We retrospectively studied 79 patients who rated pain and symptom severity both before and after kyphoplasty or vertebroplasty. Pain was significantly reduced after spinal augmentation (1.3 on a 0 to 10 scale; effect size [ES] = .59; $P < .001$), as were anxiety (1.3; ES = .47), drowsiness (1.3; ES = .39), fatigue (1.1; ES = .32), depression (0.7; ES = .

© 2012 The American Pain Society. Published by Elsevier Inc. All rights reserved.

Corresponding author: Tito R. Mendoza, PhD, MEd, The University of Texas MD Anderson Cancer Center, Department of Symptom Research, 1515 Holcombe Boulevard, Unit 1450, Houston, Texas 77030, Phone: 713-745-3486; Fax: 713-745-3475; tmendoza@mdanderson.org, URL: www.mdanderson.org/symptom-research.

Institution where work was done: The University of Texas MD Anderson Cancer Center, Houston, Texas

Disclosures

Research funding: Grant support for this study was provided by National Cancer Institute grant P01 CA124787 to Charles S. Cleeland, by an AstraZeneca Center of Excellence grant to Charles S. Cleeland, and by an unrestricted grant from Medtronic, Inc, to Allen W. Burton. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Cancer Institute or the National Institutes of Health.

Conflict of interest statement: No conflicts of interest are associated with this study.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

28), and difficulty thinking clearly (0.7; ES = .26) (all $P < .05$). Greater reduction in pain was associated with a greater number of symptoms being reduced. Interestingly, insomnia worsened regardless of any amount of improvement in pain. Because appropriate symptom control contributes to the overall well-being of cancer patients, future studies of pain reduction procedures should include measures of other symptoms to fully characterize the potential benefit of treating pain.

Keywords

spine; augmentation; vertebroplasty; kyphoplasty; symptoms; Brief Pain Inventory

Introduction

The American Cancer Society estimates that in 2010 there were more than 20,000 newly diagnosed cases of multiple myeloma (MM) in the United States and more than 10,000 deaths.¹ MM is currently incurable; as of 2005, its 5-year survival rate was 37%,¹ with age and disease stage as major determinants of overall survival. Spinal fractures secondary to osteolytic metastasis are a common source of severe pain, morbidity, and profoundly impaired quality of life for patients with MM.^{15,16} Bone pain is a predominant symptom: one study reported that approximately two-thirds of MM patients had bone pain at the time of diagnosis.¹⁸

Percutaneous vertebral cement procedures—kyphoplasty, vertebroplasty, or a combination of both—are often used for spinal stabilization during the course of MM, as augmentation to radiation therapy. Kyphoplasty and vertebroplasty are effective, minimally invasive methods for restoring the original height of the vertebrae in vertebral compression fractures and vertebral metastases and for controlling associated pain.¹⁹ These procedures have an acceptably low complication rate.²⁰ A recent systematic review and meta-analysis of patients treated with kyphoplasty for malignant spinal fractures secondary to osteolytic metastasis and MM found a 30% to 41% reduction in reported pain and improved functional outcomes after the procedure.⁴ Sandri et al.²² reported mean pain scores of 1.8 (range 0 to 3) and 1.9 (range 1 to 3) 72 hours and 6 weeks, respectively, after a combined radiofrequency and kyphoplasty procedure, compared with a mean baseline score of 8 (range 7 to 10). In another study of 30 patients with MM, kyphoplasty resulted in pain improvement from an average preoperative score of 8.65 to 2.84 at 1 month and to 2.35 at 3 months.²

Cancer pain is frequently associated with and may increase the severity of other symptoms, such as fatigue, sleep disruption, and emotional distress,^{11,12} which may be induced by cancer, its treatment, or other factors such as high serum calcium.²¹ We therefore conducted a retrospective study of patients with MM who received augmentation therapy for vertebral compression fractures, hypothesizing that pain reduction associated with augmentation procedures would be associated with improvement in other symptoms, particularly fatigue, disturbed sleep, depression, and anxiety.

Materials and Methods

Patients

The sample for this retrospective study was obtained from a larger study of patients with any cancer diagnosis who presented with vertebral compression fractures in the Pain Clinic at The University of Texas MD Anderson Cancer Center in Houston, Texas.⁶ Patients were treated with kyphoplasty, vertebroplasty, or a combination of both between January 2001 and May 2008 by pain physicians from the Department of Pain Medicine working

collaboratively with clinicians from the Departments of Radiation Oncology, Neurosurgery, and Neuroradiology at MD Anderson. Patients provided symptom ratings before and after augmentation procedures.

For this study, the inclusion criteria were (1) a diagnosis of MM and (2) a posttreatment assessment that occurred within 60 days of the baseline symptom assessment. We believed that extending the study period beyond 60 days would introduce too much variability in the pain reports. Symptom ratings and other demographic and clinical data were collected from the institutional electronic medical record and other institutional databases.

This study was approved by the MD Anderson Institutional Review Board. Because the study was a retrospective analysis of previously collected data that did not require additional patient contact and did not influence medical care, a waiver of informed consent was granted.

Measures

Before undergoing kyphoplasty or vertebroplasty (baseline), patients had rated their pain using the Brief Pain Inventory (BPI) and had reported the severity of other symptoms using the Edmonton Symptom Assessment Scale (ESAS). These symptoms were reassessed no more than 60 days after the procedure (posttreatment assessment).

Pain Severity Items of the Brief Pain Inventory—The BPI^{8–10,14} used in this study asked patients to rate the severity of their pain at its worst and its least in the past week, on average in the past week, and right now (at the time the questionnaire was administered). The items are rated on a 0 to 10 scale, where 0 = “no pain” and 10 = “pain as bad as you can imagine.”

Edmonton Symptom Assessment Scale—The ESAS^{5,7} is a validated measure of 9 common patient-rated symptoms. For this study, we modified the ESAS to assess fatigue, nausea, depression, anxiety, drowsiness, difficulty thinking clearly, shortness of breath, poor appetite, insomnia, and feeling of well-being. Each symptom is rated on an 11-point scale, with 0 = “none/best” and 10 = “worst.” Because pain ratings were obtained on the Brief Pain Inventory, the pain item of the ESAS was not included.

Statistical Analysis

Summary statistics were used to describe the patient sample. Means, medians, standard deviation (SD), and range of scores were computed for pain and other symptoms at baseline and at the posttreatment assessment. Change scores, defined to be the difference between baseline and posttreatment values, were calculated. We used paired sample t-tests and Wilcoxon signed rank tests to determine if the mean or median change scores were significantly different from zero. Effect sizes (ES) were calculated to provide an estimate of the magnitude of the change scores. An effect size greater than about one-half standard deviation may be considered clinically meaningful.²⁴

We calculated changes in pain between baseline and the posttreatment assessment using the BPI item “your pain on the average.” We formed three binary groups of patients according to the magnitude of this pain reduction: patients with a 1-point reduction versus patients whose symptoms got worse; patients with a 2-point reduction versus patients whose symptoms got worse; and patients with a 3-point reduction versus patients whose symptoms got worse. Patients who reported no improvement were included with those patients whose symptoms got worse. Independent sample t-tests were used to compare each group having a

reduction in pain with the group of patients having either no improvement or worsening of pain.

Pearson correlations were used to compute two sets of correlations among symptom ratings, at baseline and at the posttreatment assessment. A linear mixed model with autoregressive covariance structure was fitted to determine the effect of age, gender (male vs. female), assessment time point (baseline vs. posttreatment), chemotherapy before treatment (yes vs. no), radiation therapy before treatment (yes vs. no), and the type of augmentation procedure (kyphoplasty, vertebroplasty, or both) on each of the symptoms that showed significant reduction.

Statistical analysis was conducted using Statistical Package of the Social Sciences (SPSS) version 17.0.²⁵ The criterion for statistical significance was set at $\alpha = .05$. Because this is a retrospective analysis, any generalizations we have made are correlative and exploratory. This type of study informs future studies and we have been liberal in reporting our findings.

Results

Patient Characteristics

Of the 407 patients with any cancer diagnosis in the parent study, 175 had MM; 79 of the 175 patients with MM also had posttreatment assessments that occurred within 60 days of the baseline assessment. These 79 patients were included in the study (Fig 1). Table 1 summarizes the demographic and clinical characteristics of the patient sample. The sample was predominantly non-Hispanic white (70%) and male (60%), with a mean age of 60 years.

Almost half (47%) of the patients were treated with vertebroplasty alone; the remainder were almost evenly split between kyphoplasty alone (28%) and a combination of both procedures (25%). Most patients (62%) underwent 1 procedure during the 60-day follow-up period, although one third (33%) had 2 procedures and a few (5%) underwent 3 or more procedures. Before undergoing kyphoplasty or vertebroplasty, 89% of patients had received chemotherapy and 34% had been treated with radiation therapy. On average, patients' postoperative return visits occurred 26 days after the baseline assessment (range 2 to 59 days; $SD = 14.4$). In the case of patients who underwent more than one procedure, the posttreatment assessment occurred at a mean of 29.2 days ($SD=12.9$), ranging from 11 to 56 days.

Changes in Pain and Other Symptoms

Table 2 shows that mean and median ratings of pain severity (at its worst, at its least, right now, and on average) showed statistically significant reduction from baseline to the posttreatment assessment. The mean of ratings for "pain on the average" before any augmentation procedure was 5.2 on a 0 to 10 scale. The mean score for "pain on the average" after the procedure was 3.9, a statistically significant and clinically meaningful reduction of 1.3 ($ES = .59$, $P < .001$).

Anxiety and well-being showed highly significant improvement ($P < .001$). In addition, fatigue, depression, drowsiness, and difficulty thinking clearly were significantly lower at the posttreatment assessment ($P < .05$). The magnitude of the effect sizes for the difference scores for pain, anxiety, well-being, and drowsiness ranged from .39 to .70.

Magnitude of Pain Reduction and Improvement in Symptoms

We were interested in examining the effect of incremental reduction in pain on others symptoms. Using patient ratings of BPI "pain on the average" (available for 70 patients; see

Table 2), we found that 14% of patients ($n = 10$) had a 1-point reduction in pain, 17% ($n = 12$) had a 2-point reduction, and 9% ($n = 6$) had a 3-point reduction; 16% ($n = 11$) had pain reduction of 4 points or greater, and 27% ($n = 19$) reported neither increase nor decrease in pain. Approximately 17% ($n = 12$) had at least a 1-point increase in pain, including 1 patient who had a 3-point increase in pain. Thus, for our comparisons, 56% ($n = 39$), 41% ($n = 29$), and 24% ($n = 17$) of patients had pain reductions of at least 1 point, 2 points, and 3 points, respectively.

Fig 2 shows the changes in each symptom for a 1-point reduction in pain; bars projecting downward (i.e., below 0) indicate improvement in that symptom. Fatigue and well-being improved regardless of whether or not there was a reduction in pain. Compared with the group of patients whose pain either did not improve or worsened, the group with a 1-point improvement showed statistically and clinically significant reduction in depression ($ES = .46$, $P < .02$), anxiety ($ES = .74$, $P < .005$) and drowsiness ($ES = .65$, $P < .03$).

For the group with a 2-point reduction (not shown in the figure), significant reductions were associated with nausea ($ES = .85$, $P < .008$), anxiety ($ES = .74$, $P < .006$), difficulty thinking clearly ($ES = .68$, $P < .02$), and poor appetite ($ES = .78$, $P < .01$). For the group with a 3-point reduction, significant reductions were observed for nausea ($ES = .77$, $P < .01$), anxiety ($ES = .97$, $P < .002$), drowsiness ($ES = 1.2$, $P < .02$), difficulty thinking clearly ($ES = .65$, $P < .04$), shortness of breath, ($ES = .74$, $P < .05$), and poor appetite ($ES = .55$, $P < .03$).

Relationships Among Symptom Ratings Before Treatment

Table 3 (lower diagonal) shows the correlations among symptom ratings before the augmentation procedure. "Pain on the average" was significantly related to all symptoms except shortness of breath, whereas fatigue was correlated with depression, anxiety, drowsiness, difficulty thinking clearly, shortness of breath, and well-being. Nausea was correlated with depression, anxiety, drowsiness, shortness of breath, poor appetite, and well-being. Depression and anxiety were correlated with all symptoms. Drowsiness was correlated with all symptoms except shortness of breath. Difficulty thinking clearly was not related to nausea. Shortness of breath was not related to pain, drowsiness, or poor appetite. Finally, well-being was correlated with all symptoms (i.e., worst well being was associated with more-severe symptoms).

Relationships Among Symptom Ratings After Treatment

Table 3 (upper diagonal) also shows the correlations among symptom ratings at the posttreatment assessment. At this time point, average pain was significantly correlated with all symptoms except insomnia. Fatigue was significantly related to all symptoms except nausea and insomnia. Nausea was significantly related to all symptoms except fatigue, poor appetite, insomnia, and well-being. Depression was significantly correlated with all symptoms except shortness of breath.

Posttreatment, anxiety was significantly related to all symptoms except poor appetite and insomnia. Drowsiness was significantly related to all other symptoms except poor appetite. Difficulty thinking clearly was significantly related to all symptoms. Shortness of breath was related to pain, fatigue, nausea, anxiety, drowsiness, and difficulty thinking clearly. Finally, well-being was correlated with all symptoms except nausea, shortness of breath, and insomnia.

Predictors of Pain Reduction

Our linear mixed model showed that the assessment time point (before or after treatment) and age were significant predictors of pain (Table 4). In the model, patients reported higher

pain severity at the baseline assessment, whereas pain report at the posttreatment assessment was significantly lower. As age increased, pain severity also increased. The hypothesis test for the changes in pain scores in Table 2 is consistent with this result.

Even adjusting for the effect of other important covariates, no significant differences in pain severity were found according to the type of augmentation procedure (kyphoplasty, vertebroplasty, or a combination of both). These covariates included age, gender, assessment time point, having had radiation therapy before treatment, and having had chemotherapy before treatment. Previous chemotherapy or radiation therapy did not have an effect on the reduction in pain severity.

Discussion

Patients with MM commonly experience severe pain as a result of spinal fractures. Spinal augmentation procedures such as kyphoplasty and vertebroplasty are often used in this patient population to restore weakened or fractured vertebrae and to control pain, typically with good effect. In the present study, we hypothesized that pain reduction associated with augmentation procedures would also be associated with improvement in other symptoms, particularly fatigue, disturbed sleep, depression, and anxiety. Symptom severities rated by patients before (baseline) and approximately 1 month after treatment were compared.

Pain was assessed at its worst, at its least, now, and on average (Table 2). We chose to focus on the BPI item "pain on the average" to examine reduction in pain instead of "pain at its worst," because of the restricted range of pain for "pain at its worst" ratings prior to the augmentation procedure: the mean worst-pain rating before treatment was 8.1 (SD = 2.0), whereas the average-pain item had a mean rating of 5.2 (SD = 2.2) at baseline. The magnitude of these preoperative pain ratings was similar to those in other augmentation procedure studies.^{2,22} The mean pretreatment severity for 3 measures of pain (pain at its worst, its average, and now) for all patients was severe enough to affect patient functioning. Studies in cancer patients have shown that pain ratings of 5 or greater on a 0 to 10 numeric rating scale are enough to cause significant interference in activity-related and mood related functioning.^{10,23} Pain, fatigue, drowsiness, and anxiety were the most severe symptoms before the augmentation procedure.

Effect sizes were calculated to provide an estimate of the magnitude of the change scores, which we computed to characterize the difference between baseline and posttreatment values. Sloan and Dueck²⁴ suggest that an effect size greater than about half a standard deviation is clinically meaningful. By this standard, the reduction in ratings of "pain on the average" represents a significant and clinically meaningful reduction (estimate = 1.3, ES = .59, $P < .001$).

Compared with baseline levels, postaugmentation pain was significantly reduced on all 4 pain severity ratings (Table 2). The improvement in ratings of average pain was as much as 8 points, although one patient reported pain that worsened as much as 3 points. Severity levels for fatigue, depression, anxiety, drowsiness, and difficulty thinking were also statistically significantly lower after treatment; well-being also improved significantly. The effect scores for anxiety and well-being (ES = .47, $P < .001$) were very near to clinical importance. Overall, changes in other symptoms, such as anxiety (ES=.47), drowsiness (ES=.39), fatigue (ES=.32), depression (ES=.28) and difficulty thinking clearly (ES=.26), were not as large as the change in pain (ES=.59).

We found that 56% of patients reported at least a 1-point reduction in pain over the time of the study. For this group, anxiety was the most improved symptom on the basis of effect size, followed by drowsiness and depression. As expected, a smaller proportion of patients

(41%) had a 2-point reduction in pain. The most-improved symptoms for these patients included nausea, poor appetite, anxiety, and difficulty thinking clearly. Even fewer patients (24%) achieved a 3-point reduction in pain. On the basis of effect size, the most improved symptom for this group was drowsiness, followed by anxiety, nausea, shortness of breath, difficulty thinking clearly, and poor appetite. As might be expected, these results suggest that the greater the magnitude of pain reduction, the greater the magnitude of improvement in other symptoms and in the number of improved symptoms.

Results obtained from this retrospective study agree with previous studies of spinal augmentation procedures in cancer patients who reported improvement in functional status associated with pain improvement. For example, the Cancer Patient Fracture Evaluation (CAFÉ) study showed that, compared with nonsurgical pain management, kyphoplasty reduced pain and improved function as measured by the Roland-Morris disability questionnaire³. In a study of patients who underwent kyphoplasty for metastatic spinal disease, improvement in pain and function was evidenced via the Oswestry Disability Index.¹⁷ Zou et al.²⁸ reported that, in addition to pain reduction and better functioning as measured by the Oswestry Disability Index, 6 of the 8 subscales of the Short Form 36 Health Survey (bodily pain, mental health, vitality, physical functioning, role functioning, and role emotional) showed improvement for patients treated with kyphoplasty.

To our knowledge, no published studies have documented improvement in nonpain symptoms associated with these augmentation procedures. The current study is the first to examine patient report of other symptoms when there is a large observable reduction in pain. Although some studies outside of the augmentation literature report on patients who rated their symptoms longitudinally,^{13,26,27} none have documented dramatic reductions in pain where 1-point, 2-point, and 3-point pain reduction comparisons can be made with respect to other symptoms.

Our study has limitations. First, the changes in pain and other symptoms may have been the result of factors other than kyphoplasty or vertebroplasty, such as cancer therapy, use of bisphosphonates, or disease status. Importantly, reduction in such symptoms as fatigue, drowsiness, and difficulty thinking clearly may have been associated with a reduction in opioid analgesics made possible by augmentation-produced improvement in pain. The study did not collect pain medication data, hence we were unable to account for the effect of opioid use in this analysis. If opioids were reduced following the procedure, improvement in some symptoms, such as fatigue and drowsiness might have been due to this change. Because our study was retrospective, we could not control for these factors. A prospective, randomized study would address such issues. Second, the measures used in this study are modified versions of the validated instruments. For example, we administered only the BPI pain severity items, and the ESAS did not include pain as one of the symptoms. However, internal consistency reliability coefficients for the BPI pain severity items and the ESAS in this study were at least .70. Third, the BPI pain items measure pain in general terms. Spinal pain was not specifically asked about during the clinic visit, and it is possible that patients experienced pain associated with myeloma and other painful confounding factors. However, in most of these patients the pain was caused by the vertebral fracture.

We conclude that for patients with high levels of pain, such as this subset of patients with MM, other symptoms should also improve when pain is reduced. Because appropriate symptom control contributes to the overall well-being of patients with cancer, future studies of pain reduction procedures should include measures of other symptoms to fully characterize the potential benefit of treating pain.

Acknowledgments

The authors acknowledge the editorial assistance of Jeanie F. Woodruff, ELS.

References

1. American Cancer Society. [accessed June 16, 2011] Cancer facts and figures. 2010. Available at <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-026238.pdf>
2. Astolfi S, Scaramuzzo L, Logroscino CA. A minimally invasive surgical treatment possibility of osteolytic vertebral collapse in multiple myeloma. *Eur Spine J*. 2009; 18 (Suppl 1):115–121. [PubMed: 19437045]
3. Berenson J, Pflugmacher R, Jarzem P, Zonder J, Schechtman K, Tillman JB, Bastian L, Ashraf T, Vrionis F. 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*. 2011; 12:225–235. [PubMed: 21333599]
4. Bouza C, López-Cuadrado T, Cediñ P, Saz-Parkinson Z, Amate JM. Balloon kyphoplasty in malignant spinal fractures: a systematic review and meta-analysis. *BMC Palliat Care*. 2009; 8:12. [PubMed: 19740423]
5. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care*. 1991; 7:6–9. [PubMed: 1714502]
6. Burton AW, Mendoza T, Gebhardt R, Hamid B, Nouri K, Perez-Toro M, Ting J, Koyyalagunta D. Vertebral compression fracture treatment with vertebroplasty and kyphoplasty: experience in 407 patients with 1,156 fractures in a tertiary cancer center. *Pain Med*. 2011 Nov 28. [Epub ahead of print].
7. Chang VT, Hwang SS, Feuerman M. Validation of the Edmonton Symptom Assessment Scale. *Cancer*. 2000; 88:2164–2171. [PubMed: 10813730]
8. Cleeland, CS. Measurement of pain by subjective report. In: Chapman, CR.; Loeser, JD., editors. *Issues in Pain Measurement*. New York: Raven Press; 1989. p. 391–403.
9. Cleeland, CS. Assessment of pain in cancer: measurement issues. In: Foley, KM.; Bonica, JJ.; Ventafridda, V., editors. *Proceedings of the Second International Congress on Cancer Pain*. New York: Raven Press; 1990. p. 47–55.
10. Cleeland, CS. Pain assessment in cancer. In: Osoba, D., editor. *Effect of Cancer on Quality of Life*. Boca Raton: CRC Press, Inc; 1991. p. 293–305.
11. Cleeland CS. Symptom burden: multiple symptoms and their impact as patient-reported outcomes. *J Natl Cancer Inst Monogr*. 2007; 37:16–21. [PubMed: 17951226]
12. Cleeland CS, Mendoza TR, Wang XS, Chou C, Harle MT, Morrissey M, Engstrom MC. Assessing symptom distress in cancer patients: the M. D. Anderson Symptom Inventory. *Cancer*. 2000; 89:1634–1646. [PubMed: 11013380]
13. Cleeland CS, Mendoza TR, Wang XS, Woodruff JF, Palos GR, Richman SP, Nazario A, Lynch GR, Liao KP, Mobley GM, Lu C. Levels of symptom burden during chemotherapy for advanced lung cancer: differences between public hospitals and a tertiary cancer center. *J Clin Oncol*. 2011; 29:2859–2865. [PubMed: 21690477]
14. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore*. 1994; 23:129–138. [PubMed: 8080219]
15. Coleman RE. Management of bone metastases. *Oncologist*. 2000; 5:463–470. [PubMed: 11110597]
16. Costa L, Badia X, Chow E, Lipton A, Wardley A. Impact of skeletal complications on patients' quality of life, mobility, and functional independence. *Support Care Cancer*. 2008; 16:879–889. [PubMed: 18392862]
17. Eleraky M, Papanastassiou I, Setzer M, Baaj AA, Tran ND, Vrionis FD. Balloon kyphoplasty in the treatment of metastatic tumors of the upper thoracic spine. *J Neurosurg Spine*. 2011; 14:372–376. [PubMed: 21250808]

18. Kyle RA. Multiple myeloma: review of 869 cases. *Mayo Clin Proc.* 1975; 50:29–40. [PubMed: 1110582]
19. Ludwig H, Zojer N. Supportive care in multiple myeloma. *Best Pract Res Clin Haematol.* 2007; 20:817–835. [PubMed: 18070721]
20. Nairn RJ, Binkhamis S, Sheikh A. Current perspectives on percutaneous vertebroplasty: current evidence/controversies, patient selection and assessment, and technique and complications. *Radiol Res Pract.* 2011; 2011:175079. [PubMed: 22091375]
21. Raab MS, Podar K, Breitkreutz I, Richardson PG, Anderson KC. Multiple myeloma. *The Lancet.* 2009; 374:324–339.
22. Sandri A, Carbognin G, Regis D, Gaspari D, Calciolari C, Girardi V, Mansueto G, Bartolozzi P. Combined radiofrequency and kyphoplasty in painful osteolytic metastases to vertebral bodies. *Radiol Med.* 2010; 115:261–271. [PubMed: 19662341]
23. Serlin RC, Mendoza TR, Nakamura Y, Edwards KR, Cleeland CS. When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. *Pain.* 1995; 61:277–284. [PubMed: 7659438]
24. Sloan JA, Dueck A. Issues for statisticians in conducting analyses and translating results for quality of life end points in clinical trials. *J Biopharm Stat.* 2004; 14:73–96. [PubMed: 15027501]
25. SPSS. Statistical Package for the Social Sciences [computer program]. Version 15.0. Chicago, IL: SPSS, Inc; 2006.
26. Wang XS, Shi Q, Lu C, Basch EM, Johnson VE, Mendoza TR, Mobley GM, Cleeland CS. Prognostic value of symptom burden for overall survival in patients receiving chemotherapy for advanced nonsmall cell lung cancer. *Cancer.* 2010; 116:137–145. [PubMed: 19852033]
27. Wang XS, Shi Q, Williams LA, Mao L, Cleeland CS, Komaki RR, Mobley GM, Liao Z. Inflammatory cytokines are associated with the development of symptom burden in patients with NSCLC undergoing concurrent chemoradiation therapy. *Brain Behav Immun.* 2010; 24:968–974. [PubMed: 20353817]
28. Zou J, Mei X, Gan M, Yang H. Kyphoplasty for spinal fractures from multiple myeloma. *J Surg Oncol.* 2010; 102:43–47. [PubMed: 20578077]

Perspective

Appropriate symptom control contributes to overall well-being for cancer patients. This study demonstrated that pain reduction after spinal augmentation with vertebroplasty or kyphoplasty was positively associated with reduction in other patient-reported cancer-related symptoms. Future studies of these augmentation procedures should measure multiple symptoms, in addition to pain and functional status.

Figure 1.
Inclusion of patients in the study.

Figure 2.
Changes in symptoms associated with a 1-point reduction in severity.

Table 1

Demographic and clinical characteristics (N = 79)

Variable	Mean (SD)
Age	60.1 (9.8)
Variable	n (Percent)
Gender	
Men	47 (60)
Women	32 (40)
Race/ethnicity	
Minority – black non-Hispanic and Hispanic	24 (30)
Nonminority – white non-Hispanic	55 (70)
Procedure	
Vertebroplasty	37 (47)
Kyphoplasty	22 (28)
Kyphoplasty and vertebroplasty	20 (25)
Number of procedures	
1	49 (62)
2	26 (33)
3 or more	4 (5)
Patients who received chemotherapy prior to augmentation therapy	70 (89)
Patients who received radiation therapy prior to augmentation therapy	27 (34)

Table 2
Mean Reduction in Scores and Their Effect Sizes for Pain and Other Symptoms Rated on a 0 to 10 Scale Before and After Treatment

	n	Mean, median scores (SD), baseline assessment	Mean, median scores (SD), posttreatment assessment	Mean reduction	SD of the difference score	Effect size	P*
Pain:							
Least	75	3.8, 3 (2.3)	2.3, 2 (2.0)	1.6	2.2	.70	< .001
Worst	79	8.1, 8 (2.0)	6.3, 7 (2.9)	1.9	2.7	.68	< .001
Now	73	5.6, 6 (2.4)	3.9, 4 (2.5)	1.7	2.5	.66	< .001
On average	70	5.2, 5 (2.2)	3.9, 4 (2.4)	1.3	2.1	.59	< .001
Other symptoms:							
Fatigue	64	5.0, 5 (3.0)	3.9, 4 (2.8)	1.1	3.4	.32	.01
Nausea	56	1.6, 0 (2.4)	1.3, 0 (2.4)	0.3	2.8	.10	.44 (.40)
Depression	60	2.8, 2 (2.6)	2.1, 1 (2.6)	0.7	2.5	.28	.03
Anxiety	61	3.3, 3 (2.8)	2.0, 1 (2.5)	1.3	2.8	.47	< .001
Drowsiness	58	3.2, 2 (3.2)	2.0, 0 (2.7)	1.3	3.3	.39	.004 (.006)
Difficulty thinking clearly	61	2.7, 1 (3.1)	2.0, 1 (2.4)	0.7	2.5	.26	.04
Shortness of breath	60	2.3, 0 (2.9)	1.8, 0 (2.4)	0.5	2.6	.20	.12 (.15)
Poor appetite	61	2.8, 2 (2.8)	2.6, 2 (3.1)	0.2	3.0	.05	.70 (.59)
Insomnia	58	2.4, 1 (2.9)	2.3, 1 (2.8)	0.1	3.3	.04	.75 (.85)
Well-being	52	4.0, 4 (3.1)	2.6, 2 (2.8)	1.4	2.9	.47	< .001

* *P* values were based on paired sample *t*-tests. *P* values in parentheses were based on the Wilcoxon signed rank tests. Only the *P* values that differed between tests are shown.

Table 3
Correlations Between Pain and Other Symptoms Before Treatment (Lower Diagonal) and After Treatment (Upper Diagonal)

	Pain	Fatigue	Nausea	Depression	Anxiety	Drowsiness	Difficulty thinking clearly	Shortness of breath	poor appetite	Insomnia	Well-being
Pain		.42 *	.32 *	.34 *	.28 *	.30 *	.41 *	.29 *	.44 *	.06	.36 *
Fatigue	.28 *		.14	.37 *	.28 *	.45 *	.33 *	.46 *	.43 *	.01	.37 *
Nausea	.45 *	-.03		.36 *	.25 *	.49 *	.37 *	.27 *	.17	.21	.12
Depression	.29 *	.55 *	.33 *		.80 *	.48 *	.59 *	.16	.35 *	.31 *	.37 *
Anxiety	.46 *	.53 *	.36 *	.84 *		.42 *	.55 *	.28 *	.16	.18	.35 *
Drowsiness	.30 *	.32 *	.30 *	.62 *	.62 *		.48 *	.41 *	.23	.35 *	.32 *
Difficulty thinking clearly	.25 *	.36 *	.15	.64 *	.54 *	.72 *		.30 *	.36 *	.30 *	.39 *
Shortness of breath	.22	.37 *	.29 *	.35 *	.35 *	.15	.33 *		.15	.00	.23
Poor appetite	.49 *	.14	.48 *	.31 *	.36 *	.36 *	.35 *	.22		.26 *	.39 *
Insomnia	.28 *	.16	.19	.31 *	.33 *	.33 *	.30 *	.39 *	.44 *		.24
Well-being	.47 *	.48 *	.43 *	.46 *	.62 *	.62 *	.43 *	.39 *	.58 *	.35 *	

* Significant association, $P < .05$.

Table 4

Predictors of Reduction in Pain Severity

Variable	Estimated means	Estimate	95% Confidence Interval	P
Radiation before treatment	Had radiation: 3.8 No radiation: 4.4	0.6	−0.4, 1.6	.23
Chemotherapy before treatment	Had chemotherapy: 4.4 No chemotherapy: 3.7	−0.7	−2.5, 1.2	.47
Augmentation procedure	Both (kyphoplasty and vertebroplasty): 3.9 Kyphoplasty: 3.8 Vertebroplasty: 4.5	−0.7	−1.7, 0.4	.20
Vertebroplasty vs. kyphoplasty		−0.6	−1.6, 0.5	.26
Vertebroplasty vs. both (kyphoplasty and vertebroplasty)				
Age		0.1	0.03, 0.1	< .001
Gender	Male: 3.6 Female: 4.5	−0.9	−1.8, 0.004	.051
Assessment time point	Baseline: 4.7 Posttreatment: 3.4	1.3	0.8, 1.8	< .001