Original Article

Vertebral Augmentation for Compression Fractures Caused by Malignant Disease

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Key Words

Vertebroplasty, kyphoplasty, vertebral augmentation, spinal neoplasms, spinal compression fractures

Abstract

Vertebral compression fractures are common in malignant disease and frequently cause severe back pain. However, management of that pain with conventional medical, radiotherapy, or surgical modalities is often inadequate. Vertebral augmentation techniques, such as vertebroplasty and kyphoplasty, are minimally invasive techniques in which methylmethacrylate bone cement is percutaneously injected into compressed vertebral bodies. Vertebral augmentation often improves mechanical stability of compressed vertebrae, provides pain relief, and may prevent progression of vertebral collapse. Kyphoplasty may provide increased chance for vertebral body height restoration, but the clinical importance of slight change in vertebral body height is unclear. Vertebral augmentation can be used in conjunction with other treatment modalities, and associated pain relief may improve patient tolerance of needed antitumor therapies, such as radiation therapy. Vertebral augmentation is generally very well tolerated, and complications associated with bone cement extravasation beyond the vertebral body have rarely been reported. Because it often provides good to excellent relief of otherwise intractable pain and is generally well tolerated, vertebral augmentation is becoming a first-line agent for management of painful vertebral compression fractures, especially in the setting of malignant disease. (*JNCCN* 2010;8:1095–1102)

Vertebral compression fractures are a major source of morbidity in patients with primary or metastatic bony malignancy, resulting in back pain, neurologic complications, kyphotic deformities, and reduction in quality of life. Vertebrae are the most common site of bony metastasis, and 40% to 80% of patients with cancer have vertebral metastases during the course of their disease.[1] Vertebral metastases most frequently have osteolytic (vs. sclerotic) morphology, and almost 30% of these lesions result in vertebral compression fractures. Pain, the most common presentation for bony spinal tumors,[2] may be related to periosteal deformation, tumor release of neuroinflammatory mediators, and mechanical instability from pathologic fracture. Tumor mass effect on neural structures may also result in pain, and also cause altered sensation or motor deficit. Kyphoscoliosis from vertebral fractures can greatly reduce pulmonary function, lead to early satiety and malnutrition, and have psychosocial implications. The degree of kyphosis caused by pathologic vertebral fracture shows a strong correlation with impairment of both general physical capacity and pulmonary function.[3] A single thoracic vertebral compression fracture can cause sagittal kyphosis, resulting in up to a 9% loss of forced vital capacity.[3,4] Kyphotic deformity from thoracic vertebral fractures changes spinal biomechanics such that altered vertebral load transfer increases the risk of adjacent vertebral fracture.

In recent years, improved cancer treatments have significantly increased cancer survival, requiring that the perspective of management strategies for cancer pain syndromes, including management of spinal tumors, change from end-of-life palliation to chronic disease management. The primary treatment of spinal malignancy is often radiation therapy, which may provide pain relief and local tumor control. However, remaining spinal instability may result in persistent pain. Symptomatic management of pain with analgesics, bedrest, and spinal orthotics may be helpful, but protracted

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bedrest is undesirable and increases the risk for other complications. Systemic analgesics, even optimally adjusted, often fail to adequately control the severe, fluctuating pain from a pathologic bony fracture.[5,6] Surgical stabilization may be invaluable if spinal cord or neural compression is causing neurologic deficit, but spine fusion surgery is a major undertaking that may be contraindicated by a chronically ill patient's weakened physical condition or poor bone quality (which can lead to spine fusion hardware failure).[7]

Percutaneous vertebral augmentation has been shown to be a useful, minimally invasive tool in the stabilization and management of pathologic vertebral compression fractures. Vertebroplasty was first reported by Galibert et al.[8] in 1987 for management of a pathologic C2 vertebral fracture caused by aggressive hemangioma. Methylmethacrylate cement was injected into the vertebral body, resulting in marked improvement in pain. Subsequently, vertebroplasty has been widely used in the management of pathologic vertebral compression fractures related to benign and malignant tumors, and osteoporosis.[9]

Kyphoplasty was introduced in 1998 in an effort to limit vertebroplasty-associated complications; reduce cement extravasation, which causes neurologic complications; and prevent embolization of cement through venous channels, which causes pulmonary emboli. With kyphoplasty, an inflatable balloon catheter is placed through percutaneous needles into the vertebral body. Subsequent balloon inflation may result in some vertebral body height restoration and creates a void into which bone cement can be subsequently injected. Although kyphoplasty is an intriguing technique for vertebral augmentation, vertebral body height restoration is not consistently achieved and cement extravasation can still result in complications.[10] No prospective trial has compared the techniques in terms of safety or efficacy, but review of available data suggests that vertebroplasty and kyphoplasty have a similar analgesic effect.[11]

The pain relief from vertebral augmentation is most likely related to increased mechanical stability after cement injection,[12] although experts have also proposed that heat produced from the exothermic polymerization of methylmethacrylate cement, or direct chemical neurotoxic effect of methylmethacrylate on nociceptors, may contribute to the analgesic effect. Biomechanical studies of human cadaveric vertebral bodies have shown that vertebroplasty improves vertebral body mechanical strength or stiffness after compression fracture. Experts hypothesize that improved strength and stiffness reduce micromovements at vertebral body fractures, thereby alleviating pain.

Vertebral augmentation (vertebroplasty, kyphoplasty) is an important tool for managing pathologic vertebral fracture. These treatments can be used concomitantly with antitumor therapies and other disease management strategies.

Vertebral Fracture: Clinical Presentation and Diagnostic Evaluation

Pain is the principal symptom of vertebral malignancy, especially when associated with compression fractures.[2] Axial back pain in the region of the vertebral fracture, and particularly pain incident to movement, such as moving from sitting to standing, is the most common presentation of vertebral pathologic compression fracture. Patients may also have persistent localized back or radicular pain. It is especially common for thoracic compression fractures to be associated with radiating, belt-like chest wall pain, in addition to axial back pain. Physical examination may show marked tenderness, especially on firm palpation of the spinous processes of fractured vertebrae and nearby paravertebral musculature.

Vertebral compression fractures are readily identified through loss of vertebral body height on lateral radiographs, but, at least with osteoporotic compression fractures, acute or subacute fractures are more likely associated with good reduction in pain relief from vertebral augmentation. Back pain in persons with older, chronic osteoporotic compression fractures, which have had many months or years to stabilize, is often related to facet arthropathy or other musculoskeletal causes of back pain rather than persistent instability along fracture lines. Acuity of the fracture can be identified through review of older radiographs, if available. If the patient's radiographic history is inconclusive, MRI or bone scan can be used to indentify acute or subacute vertebral fractures.

MRI with short tau inversion recovery (MRI-STIR) sequence is considered the most effective imaging to identify the increased water content (bone marrow edema) associated with acute bony fracture. Bone marrow edema of vertebral bodies with acute and subacute compression fractures results in hy-

pointense signal on T1-weighted images and hyperintense signal on T2-weighted images.[13] If MRI is not feasible, technetium-99 methyl diphosphonate bone scan with SPECT (single photon emission computer-assisted tomography) imaging may show increased uptake secondary to increased osteoblastic activity in acute fractures, although lack of osteoblastic activity in multiple myeloma may give false-negative results.[13] However, bone scan may be too sensitive to detect acute and subacute vertebral fractures because increased uptake of tracer may occur long after substantial stabilization of the vertebral body.

Because some vertebral compression fractures (osteoporotic or malignant) may result in severe spinal canal stenosis (which is a relative contraindication for vertebral augmentation), axial imaging (CT or MRI) is indicated before undertaking vertebral augmentation. Axial imaging also provides details of vertebral bony anatomy, which are helpful in planning the vertebral augmentation procedure. In summary, radiographic evaluation should include some indication of fracture acuity (review of serial radiographs, spine MRI, or bone scan) and axial imaging to evaluate for possible spinal stenosis (CT or MRI); therefore, spine MRI is the single most useful imaging technique for evaluating vertebral compression fractures for possible vertebral augmentation. Routine screening for coagulopathy is optional before vertebral augmentation, but the coagulation status of patients suspected of having coagulopathy should be evaluated through laboratory testing (platelet count, prothrombin time, and partial thromboplastin time).

Vertebral Augmentation

Evidence Supporting Use

Vertebral augmentation (including both vertebroplasty and kyphoplasty) has been widely used for the management of pathologic vertebral compression fracture.[9] Although a growing body of evidence supports the use of vertebral augmentation, there is a paucity of randomized control trials and a lack of comparative trials of available techniques (vertebroplasty vs. kyphoplasty), leaving the selection of technique to the practitioner's discretion. Published case series reporting effectiveness of vertebral augmentation often include both osteoporotic and malignant fractures, with few studies specifically reporting efficacy of vertebral augmentation in malignant disease. Nonetheless, case data indicate that vertebral augmentation often provides significant benefit, with rapid onset of pain relief, in vertebral compression fractures caused by malignant disease.[3,14–19]

Vertebroplasty or kyphoplasty can be used as the principal palliative treatment for painful compression fractures caused by malignant disease or, if antitumor therapies are appropriate, can be performed along with either chemotherapy or radiation therapy. Because the pain relief associated with these vertebral augmentation techniques has rapid onset (most commonly within a day), these techniques may be used to provide rapid pain relief and thereby facilitate patient access to needed antitumor therapies (which may be effective over many days to several weeks).

Both vertebroplasty[18,20,21] and kyphoplasty[22] provide improvements in function and quality of life. Vertebral augmentation improves vertebral body strength and stiffness to stabilize fractured vertebrae, thereby providing pain relief and potentially preventing further vertebral body collapse.[16,20] Although vertebral height restoration is cited as a potential benefit of kyphoplasty, it may not be statistically significant.[11,23–25] Even if short-term improvement in vertebral body height occurs, this improvement may not persist over time.[22] The clinical significance of slight vertebral body height restoration is also unclear because it seems that pain relief and improvements in quality of life are independent from vertebral augmentation-derived improvements in vertebral body height or reduction in kyphotic angle.[20,26] Improvement in respiratory function occurs after both vertebroplasty and kyphoplasty, which is especially important with thoracic compression fractures associated with respiratory compromise caused by painful respiration.

Although the clinical significance of the vertebral body height restoration sometimes associated with kyphoplasty is uncertain, even partial vertebral body height restoration may be helpful in patients with multiple, simultaneous thoracic compression fractures. For example, multiple myeloma may present acutely with several levels of vertebral fracture.[27] In these patients, even modest height restoration, if achieved with each of several adjacent fractures, may result in improved spinal alignment, perhaps with long-term biomechanical benefits. Data are currently insufficient to clarify the potential significance of selecting kyphoplasty over vertebroplasty in various clinical settings.

Recently, 2 randomized controlled trials were published comparing vertebroplasty with conservative therapy[28,29] in ambulatory patients with osteoporotic compression fracture. The authors found no advantage of vertebroplasty over a sham (control) procedure. Before extrapolating results of this study, the particular patient population reported must be understood. In each of the studies, most of the screened patients were excluded from the trial, including a large proportion that chose not to participate in the trial. In both of these studies, for each person enrolled, approximately 2 screened, eligible persons declined participation. No explanation is provided as to why patients declined participation, but patients with severe pain may have opted out because of concern that they would be randomized to the control group and not receive vertebroplasty. As a result, selection could have been biased toward patients with more modest pain. Furthermore, the authors in each study included patients who had compression fractures up to 1 year before enrollment. During the course of 1 year, many osteoporotic fractures will stabilize, casting doubt on the benefit of vertebroplasty in these patients. Although the authors identified a highly selected group of ambulatory outpatients with osteoporotic fractures up to 1 year old, their conclusion that vertebroplasty is of no benefit should not be extrapolated to patients with acute compression fractures and severe pain, and especially not to those with vertebral compression fractures from malignant disease. Additional controlled data are needed to clarify the role of vertebral augmentation in various clinical settings; however, available data (including case series and clinical experience) show that vertebral augmentation techniques are useful in managing severe pain from vertebral compression fractures.

Indications and Contraindications

The indications and contraindications for vertebral augmentation are presented in Table 1.[30,31]

Complications and Adverse Effects

In general, the very low complication rates associated with vertebral augmentation techniques[32] have supported their use for management of pathologic verte-

Table 1 Vertebral Augmentation: Indications and Contraindications

Indications		Acute or subacute vertebral body compression fractures producing pain not controlled with analgesics or bracing (acuity based on history, including review of prior radiographic images, abnormal STIR signal on spine MRI, or increased radionuclide uptake on bone scan/single photon emission computer-assisted tomography)
		Reproducible midline spine pain in the region of the fracture
Contraindications	Absolute	Asymptomatic fracture
		Symptomatic spinal cord compression
		Local or systemic infection
		Uncorrectable coagulopathy
		Allergy to bone cement or radiopaque contrast media
	Relative	Posterior vertebral body wall disruption
		Posterior retropulsed bony fragment with greater than one third spinal canal compromise
		Intraspinal tumor extension with > one third spinal canal compromise
		Significant non–cancer-related spinal stenosis
		Burst fractures
		Extension of lesion in pedicle (at the fracture level)
		Greater than two thirds loss of vertebral body height
		Severe cardiopulmonary disease
		No abnormal STIR signal on MRI, normal bone scan
		Radicular or musculoskeletal pain or pain off midline
		Inability to lie prone for the duration of procedure
		Lack of spine surgical backup to assist with management of complications, if needed

Abbreviation: STIR, short tau inversion recovery.

bral compression fractures. The most common complication of vertebral augmentation is extravasation of methylmethacrylate cement beyond the borders of the compressed vertebral body. Vertebroplasty is associated with more frequent cement extravasation compared with kyphoplasty,[33] but most instances are asymptomatic and clinically insignificant.[15,21] Bone cement extravasations resulting in severe complications such as paralysis have been reported for both vertebroplasty and kyphoplasty.[10] Several case reports have also described venous embolization of methylmethacrylate cement, resulting in pulmonary embolism.[32,34,35] Although the extent to which the compressed vertebral body is filled with methylmethacrylate cement has not been shown to correlate with treatment efficacy, high cement volume has been associated with increased risk of extravasation.[36]

Various technical modifications to vertebral augmentation have been described that might favorably impact the risk of procedural complications. Experts have suggested that using more viscous cement might decrease complications related to cement extravasation or venous embolization.[37] A modification of vertebral augmentation, potentially used with either vertebroplasty[38] or kyphoplasty,[39] has been described in which a radiofrequency wand is placed through the vertebral augmentation needle to destroy tumor within the vertebral body, leaving a void in the vertebral body into which bone cement is placed, potentially reducing cement extravasation. Although these are intriguing technical developments, broader investigation is needed to determine efficacy.

Although patients undergoing vertebral augmentation are at risk for subsequent vertebral fracture,[40] whether this is an incremental risk from the vertebral augmentation or simply a reflection of the natural history of underlying bone disease is unknown.[41] At least in osteoporotic compression fractures, the risk of new fracture from vertebral augmentation does not seem to be significantly increased.[11,42]

Both vertebroplasty and kyphoplasty are technically demanding interventions that require use of intermittent fluoroscopic imaging throughout the procedures. Because of the additional steps involved with kyphoplasty (e.g., inflation of balloon), it is generally associated with significantly greater radiation exposure to both patients and practitioners. The skill levels of the clinician and radiation technologist have been shown to impact the total radiation dose associated with these procedures.[43]

Because of concern for potential toxic effects of injecting larger volumes of methylmethacrylate cement, vertebral augmentation is generally limited to no more than 3 vertebral levels in one procedure.[44] Patients requiring more than 3 levels of vertebral augmentation are generally managed in staged procedures over subsequent days.

Cost Considerations

The overall cost effectiveness of vertebral augmentation is unclear, because a specific value is difficult (perhaps impossible) to assign to improved pain control. Vertebroplasty and kyphoplasty generally have similar analgesic efficacy. Kyphoplasty is substantially more expensive than vertebroplasty because of the cost of additional (disposable) equipment and required procedural time.[45]

Clinical Case

A 63-year-old woman with transitional cell carcinoma had intractable pain from spinal metastases asso-

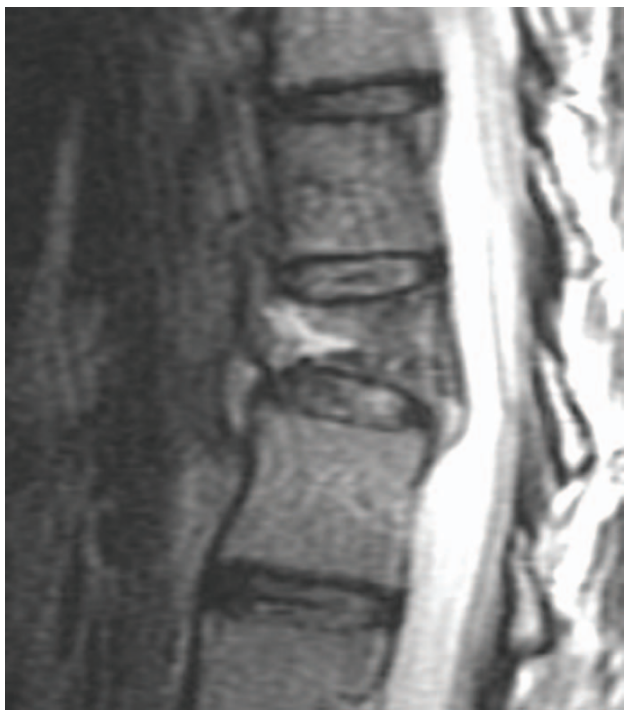

Figure 1 Sagittal thoracolumbar MRI T2 image showing T12 vertebral compression fracture. The area of increased intensity (lighter shade of gray) within the anterior portion of the compressed vertebral body indicates increased water content consistent with an acute or subacute compression fracture. Epidural spread of tumor extends inferiorly behind the T12-L1 disc, causing mild spinal canal narrowing.

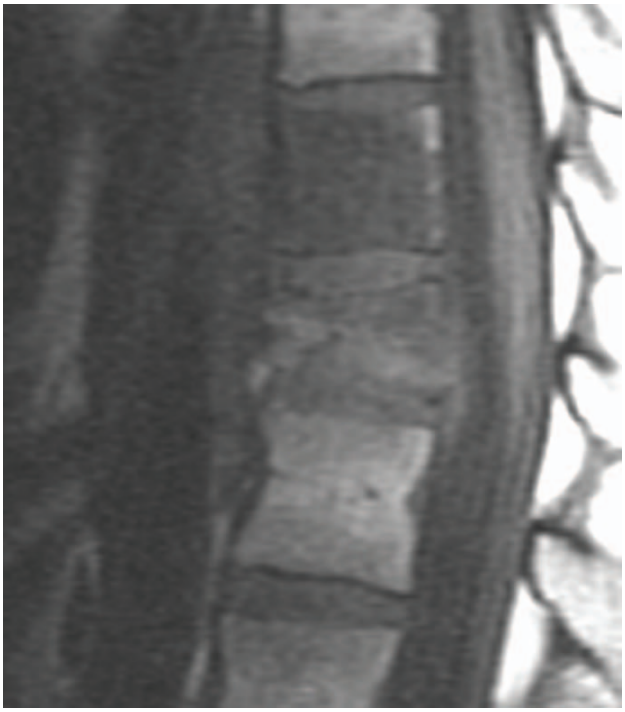

Figure 2 Sagittal thoracolumbar MRI T1 image showing T12 vertebral compression fracture. Decreased signal (darker shade of gray) seen in the fractured T12 vertebral body and the adjacent T11 vertebral body indicates increased water content. The T11 abnormality, based on additional MRI images, was thought to be from diffuse tumor infiltration.

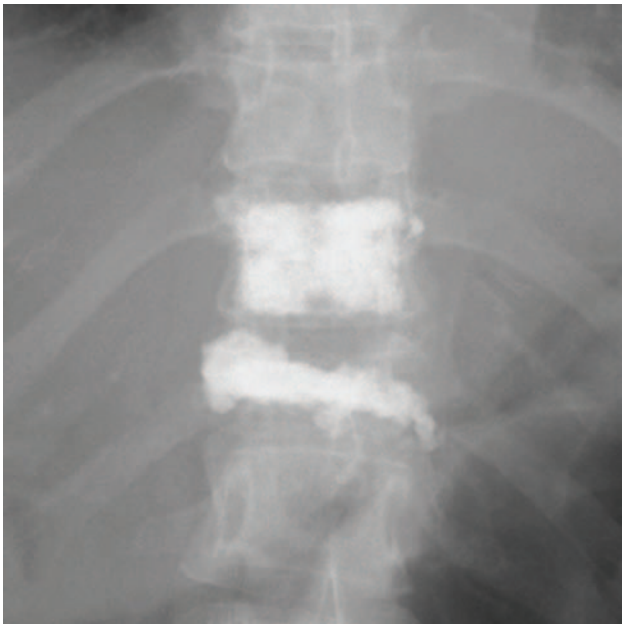

Figure 3 Spine radiograph after vertebroplasty at T11 and T12.

ciated with pathologic compression fracture at T12. MRI imaging showed the compressed vertebral body of T12, with increased signal intensity in T2 images (Figure 1) and decreased signal in T1 images (Figure 2), indicating bone marrow edema consistent with acute or subacute compression fracture. At T12, evidence was seen of some spinal canal narrowing from epidural tumor. Investigators thought the diffuse, decreased signal in the T11 vertebral body was likely caused by diffuse infiltration with tumor, based on additional MRI images. The patient had intractable back pain despite efforts to optimize systemic analgesics, including home palliative care support and hydromorphone intravenous patient-controlled analgesia (IV PCA) device (5.5 mg/h basal infusion, 0.5-mg bolus dose with 15-minute lockout interval). Attempts at increasing the opioid dose led to increases in nausea and myoclonus but no improvement in pain control. A trial of morphine also resulted in increased myoclonus (and increased pain), and she was switched back to hydromorphone. Gabapentin was associated with worsened sedation but no improvement in pain control.

Outpatient vertebroplasty was performed at T12 and T11 (Figure 3) to stabilize the T12 fracture and prevent fracture of the T11 vertebral body. Although "prophylactic" vertebroplasty to prevent compression fracture is generally not indicated (especially for osteoporosis), it was performed in this patient as a palliative supplement to the vertebroplasty at T12 in view of the extreme pain and debility that she experienced from the T12 fracture and because of concern that she was at significantly increased risk for subsequent T11 fracture. After vertebroplasty, she had rapid onset of marked pain relief, and therefore IV PCA could be tapered and discontinued. Residual back pain was well controlled with oxycodone extended-release, 40 mg, twice daily with hydromorphone 2 to 4 mg by mouth, as needed for pain.

Conclusions

Vertebral augmentation techniques may often provide marked reduction in pain and improvement in quality of life associated with pathologic vertebral compression fractures. As a result, these techniques are rapidly becoming first-line tools for managing pathologic fractures, especially those associated with malignant disease. The principal advantage of percutaneous vertebral augmentation is achievement of rapid-onset, significant pain relief with improved stability of the fractured vertebrae. Vertebral aug-

mentation techniques can be used in conjunction with other symptom-control treatments (e.g., analgesics, bracing, physical therapy) and disease-specific therapies (e.g., chemotherapy, radiation therapy).

Vertebroplasty and balloon kyphoplasty are equally efficacious in providing pain relief, functional improvement, and vertebral stability. Height restoration, reduction of kyphotic angle, radiation exposure, cement extravasation, and cost are areas in which the techniques have been suggested to differ, but the lack of prospective comparative trials precludes definitive conclusions. Recently described modifications include radioisotope vertebroplasty[46] (in which methylmethacrylate cement is combined with radioisotopes for destruction of tumor and prevention of local tumor recurrence/progression) and the percutaneous injection of bone graft material into vertebral compression fractures for bone repair and regeneration.[47] Fortunately, vertebral augmentation is often effective in managing vertebral compression fractures resulting from malignant disease.

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