Vertebroplasty and Kyphoplasty for the Palliation of Pain

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ABSTRACT

Vertebroplasty and kyphoplasty are percutaneous techniques developed over the past 20 years to treat vertebral hemangiomas, osteoporotic compression fractures, and osteolytic tumors of the spine. In carefully selected patients, these procedures have led to the cessation or significant reduction in pain in 80 to 90% of patients. In this article, we review the indications and contraindications of these procedures, appropriate patient selection and evaluation, the technique, outcomes, and the potential complications of this form of therapy when performed for the alleviation of pain for osteolytic tumors of the spine.

KEYWORDS: Vertebroplasty, kyphoplasty, spinal metastasis, multiple myeloma

Objectives: Upon completion of this article, the reader should understand the indications, contraindications, technique, outcomes, and complications of vertebroplasty and kyphoplasty as they relate to palliation of back pain from spinal metastasis and multiple myeloma.

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Vertebroplasty and kyphoplasty are percutaneous image-guided procedures used since the 1980s and 1990s to treat hemangiomas, osteoporotic vertebral compression fractures, and osteolytic tumors of the spine. Whereas vertebroplasty involves the direct injection of methylmethacrylate cement into compromised vertebral bodies, kyphoplasty involves the use of an inflatable balloon to raise the fractured endplate and create a void in the vertebral body to restore vertebral height followed by injection of cement. Both procedures restore the load-bearing capacity and stiffness of the vertebral segment, and more importantly, they provide significant pain relief. In this article we review the

indications, contraindications, technique, and reported outcomes of vertebroplasty and kyphoplasty, primarily as they relate to the palliation of pain in patients with osteolytic metastases and multiple myeloma. We also emphasize the potential complications of this form of therapy.

Cancer patients present with bone metastasis in 27% of cases, with the vertebral bodies the most common bone involved.^{1,2} Eighty percent of patients with prostate cancer, 50% with breast cancer, and 30% with lung, thyroid, or renal cell cancer develop metastatic spinal lesions.³ The lesions cause the destruction of portions of the vertebral body, often resulting in vertebral collapse

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and pain; however, the presence of a fracture is not necessary to cause the significant pain that can be associated with metastasis. Vertebral compression fractures are also present in 55 to 70% of patients with myeloma and are most often due to the diffuse osteoporosis caused by the disease and occasionally due to the focal osteolytic lesions characteristic of the disease.^{4,5}

INDICATIONS AND PATIENT SELECTION

The primary indication for percutaneous vertebroplasty and kyphoplasty in cancer patients is pain caused by a vertebral metastasis or compression fracture (pathological or osteoporotic). Proper patient selection is crucial because more than 80% of the population experiences back pain at some time in their life.⁶ To distinguish pain from other causes requires a careful correlation of the patient's history with clinical examination and available imaging. Patients may be referred for three main reasons: for known cancer and back pain related to a spinal metastasis, known cancer and a recently diagnosed but asymptomatic spinal lesion, or back pain and suspicious lesions but no known diagnosis.⁷ On clinical examination, focal pain should be present that correlates with the lesion being considered for treatment, pain should typically worsen with weightbearing and improve in the recumbent position, and it should lack the symptoms of nerve root or cord compression.⁶⁻⁸ In addition, the pain should be severe enough that it affects daily activities or requires substantial amounts of analgesics. It is also recommended that pain levels should be documented and quantified with questionnaires or the visual analogue scale.⁷

IMAGING AND LABORATORY STUDIES

The history of the pain and clinical examination findings are then compared with findings on plain radiographs, magnetic resonance imaging (MRI), and computed tomography (CT) and nuclear medicine scans. These images are used to assess for osteolysis, degree of collapse, extension of tumor into the epidural space, and compression of neural tissue.⁷ Because acute and chronic vertebral compression fractures cannot be adequately distinguished on plain radiographs or CT, MRI is used to identify the acute levels involved. Low signal on T1-weighted sequences and high signal on heavily T2-weighted sequences, such as sagittal short tau inversion recovery sequences, are manifestations of acute marrow edema. Healed vertebral compression fractures, however, may show normal signal.^{6,9} If MR cannot be performed, bone scintigraphy is considered the next best alternative and may provide enough information to decide if vertebroplasty is appropriate,⁶ especially when combined with CT. CT is best for detecting destruction of the posterior vertebral wall and

determining whether the lesion is osteoblastic or osteolytic.⁷

The patient should also undergo a preanesthetic evaluation, electrocardiogram, complete blood cell count, platelets, electrolytes, prothrombin time, partial thromboplastin time, blood urea nitrogen, and creatinine.

CONTRAINDICATIONS

Absolute contraindications to vertebroplasty and kyphoplasty include active local infection, such as osteomyelitis, discitis, or epidural abscess, or if fever or sepsis is present.⁶ Such patients should be postponed until these problems resolve. Patients with bleeding diatheses (platelets < 100,000, prothrombin time > 1.6, and partial thromboplastin time > 1.5 times normal) should have their coagulopathy controlled before the procedure. Other relative contraindications are vertebral fractures that have completely collapsed (25 to 30% of the original height is generally required), osteoblastic lesions (unless there is a mixed sclerotic or destruction lesion with focal pain and collapse), nonfocal or uncertain cause of back pain, complete destruction of the vertebra,⁷ patient unable to lie prone because of medical conditions, and lack of immediate availability of decompressive surgery. Also, if there is posterior wall destruction and tumor extends into the spinal canal, vertebroplasty and kyphoplasty should be avoided, even if asymptomatic, because there is a high risk for increasing neural compression with the injection of cement; that being said, vertebroplasty has been performed safely in these cases by skilled operators and is therefore not an absolute contraindication (Fig. 1).^{8,10} Anecdotally, in such cases vertebroplasty or kyphoplasty can be combined with other techniques such as radiofrequency ablation or, more recently, coblation, with the idea that the tumor/cell burden can be reduced before the injection of cement, thus decreasing the likelihood of pushing tumor cells into the epidural space (author experience).

Patient selection for kyphoplasty is largely similar to that of vertebroplasty in terms of history, physical examination, and imaging evaluation; there are, however, minor points worth mentioning. Acute fractures (1 to 3 weeks old) are much less likely to have healed significantly, and therefore kyphoplasty can better provide height restoration.¹¹ But severely compressed vertebrae may be more difficult to treat with kyphoplasty because the insertion of the balloon tamp requires more residual vertebral body height than the devices required for vertebroplasty. Exclusion criteria for kyphoplasty are similar to vertebroplasty in that the procedure should not be performed if there is a local or systemic infection, if the vertebral compression fracture is not painful, if there are retropulsed bone fragments, or if the tumor extends into the epidural space.¹¹

Figure 1 Painful renal cell carcinoma metastasis in a thoracic vertebra. (A–C) T1, short tau inversion recovery (STIR), and fat-saturated T1-weighted images demonstrating a holovertebral metastasis in the midthoracic spine. (D) Axial T1 postcontrast magnetic resonance (MR) image demonstrating extension of the tumor into the ventral epidural space (arrows). (E) Bipedicular approach with careful injection of polymethylmethacrylate (PMMA) under biplane fluoroscopic guidance. (F) Final anteroposterior view after removal of needles.

Figure 1 (Continued) (G,H) Sagittal T1 and STIR postprocedure MR demonstrating slight increase in the posterior protuberance of tumor into the vertebral epidural space due to the PMMA. Patient was asymptomatic.

PROCEDURE TECHNIQUE AND PERIOPERATIVE CARE

Preoperative Considerations

The image guidance equipment should be of optimal quality for proper visualization of the vertebral column and the region being worked on. Fluoroscopy is the optimal choice for procedural technique, preferably biplane, if available. Although more expensive and less mobile, biplane fluoroscopy allows visualization of the operative site in two planes; this helps with localization and monitoring of cement injection and leakage in real-time in two planes.⁸ Single-plane fluoroscopy with a C-arm is safe and feasible for vertebroplasty, but the duration of the procedure is prolonged. CT has been used alone but is more commonly an adjunctive form of imaging.^{12,13} Although it provides a better resolution than fluoroscopy, the use of CT alone implies the lack of real-time imaging, which is vital during cement injection. CT is especially helpful as an adjunctive imaging tool for localizing difficult-to-view regions,¹² such as the cervical region when approaching anterolaterally while avoiding the carotid-jugular complex.

Local anesthesia combined with conscious sedation is usually the most common method to ensure the patient is comfortable and relaxed during the procedure.⁸ If the patient is unable to tolerate or prefers not to receive intravenous sedation, local anesthetics may be used alone provided that the needle tract and periosteum at the bone entry site is thoroughly infiltrated.⁸ General anesthesia is not indicated unless the patient is in severe pain and unable to sustain the prone position. Patients with spinal metastasis or myeloma are often in tremendous pain and unable to lie prone; therefore, such patients may require larger amounts of intravenous analgesics and sedation or general anesthesia.¹⁴

The cement used is polymethylmethacrylate (PMMA), which may be modified by altering the ratio of liquid and powder or the addition of opacification agents and antibiotics. There is a very low infection rate, and few studies have shown any beneficial effect of mixing antibiotics with PMMA; therefore, unless treating immunocompromised patients, antibiotics are not routinely recommended.^{8,14}

Approaches

Four routes are used for needle introduction: transpedicular, parapedicular, posterolateral, and anterolateral.¹⁵ The most common approach is transpedicular because it provides the physician with a clear anatomical landmark that is easy to detect on intraoperative imaging and allows safe access to the vertebral body without causing injury to surrounding structures.^{8,14,16–19} It is also the technique employed for biopsying intracorporeal regions of the vertebra for various lesions.

The parapedicular (transcostovertebral) approach involves the needle passing along the lateral aspect of the pedicle rather than through it, allowing direction of the needle tip toward the center of the vertebral body. This angle may allow easier filling of the vertebra with a single injection. Indications for this route are if the pedicle is inaccessible, destroyed from neoplastic growth, or too small.¹⁴ The risks are a higher chance for paraspinal hematoma; as the needle enters the vertebral body in a lateral aspect, there is decreased ability to control postprocedural bleeding with local tamponade. There is also a greater risk for puncturing the lung and pneumothorax.⁸

The posterolateral and anterolateral approaches may also be indicated, especially in the patient with neoplastic spine disease.^{14,15} The posterolateral approach is similar to parapedicular and primarily employed for the subdiaphragmatic spine (lumbar spine) where the pedicle may be destroyed by neoplastic disease, making it difficult to use as an anatomical landmark.^{14,15} This approach involves entering the vertebral body inferiorly and at the lateral aspect,²⁰ increasing the risk for paraspinal hematoma, as mentioned earlier, and injury to a nerve root as it exits under the pedicle. An anterolateral approach can also be used, especially for neoplastic disease, but it is usually restricted to treating the cervical spine.^{8,14,15} Because important structures lie anteriorly, a CT scan used adjunctively may be an advantage, especially to avoid the carotid and jugular vasculature.^{8,14,15}

Technical Aspects

The patient is placed in prone, supine or lateral decubitus position on the operating bed, depending on the approach desired. The area of interest is first localized with fluoroscopy and/or CT. This region is marked and

Figure 2 A 40-year-old man with metastatic prostate cancer and severe neck pain. (A,B) Short tau inversion recovery and fat-saturated T1 sagittal magnetic resonance imaging showing diffuse metastatic involvement of the spine with superimposed fracture at C7 (arrows). (C) Anterolateral approach to C7 with injection of polymethylmethacrylate (PMMA). (D,E) Axial and sagittal postvertebroplasty computed tomography demonstrating filling of the fracture with PMMA.

prepared in the usual sterile fashion. The region should be reconfirmed after gowning to ensure the level is still correct (because the patient may have shifted, tenting of skin with draping, etc.).

The needle size is chosen after reviewing the patient's films preoperatively for evaluation of the pedicle size and planning the approach. A smaller size, usually a 15-gauge bone needle, can be used successfully for the cervical spine (Fig. 2); a larger size, 11 to 13 gauge, can be used for the thoracic and lumbar spines.^{8,14} In patients with underlying osteoporosis, a 15-gauge needle may work well even for thoracic and lumbar lesions (author experience). After infiltration with local anesthetics, carefully covering the entire route from skin to paraspinal and periosteal tissues, an 11-blade scalpel can be used to make a small stablike skin incision.⁸ The needle (trocar-cannula) is inserted via fluoroscopic guidance to the pedicle or the appropriate aspect of the vertebral body, depending on the approach. Care should be taken to make sure fluoroscopy allows both planes to be viewed, even if using the C-arm.¹⁵ When approaching a neoplastic spine, entering the bone cortex maybe more difficult than that of an osteoporotic spine, except in the case of tumor erosion, in which it may be soft.¹⁴ The tip of the needle should eventually be placed anterior to the middle portion of the vertebral body at the junction of the middle and anterior third.⁸ This should be verified, again, in both planes of view.

For vertebroplasty as well as kyphoplasty, a bilateral approach is advantageous. There is a greater risk for leakage of PMMA with a single needle, and although adequate filling can be achieved, a more uniform fill is more likely with a bilateral approach. After preparation of the PMMA, it is filled into syringes (usually 1 to 3 mL) or more usually dedicated injectors that can be affixed to the needle cannula after the trochar is taken out. In the case of kyphoplasty, the PMMA is placed in delivery cannulas holding 1 or 1.5 mL. For bilateral approaches one needle is used at a time during PMMA injection. The injection is performed under real-time fluoroscopic guidance because careful monitoring of extravasation is necessary. If any leakage is seen, the injection of PMMA is immediately stopped. It can be resumed after 1 to 2 minutes, to allow for the intracorporal cement to harden. If further cement is seen to leak out, then the injection from that needle should be terminated but may be resumed from the contralateral side.⁸ An external sample of the cement should be monitored and allowed to harden prior to moving the patient off the table. The amount to inject to obtain relief is variable and operator dependent, with a rough guideline of injecting ~50 to 70% of the vertebral body volume.⁸ In cases of vertebral body fracture, it is imperative to have the PMMA enter and "fixate" the fracture line/cavity to achieve pain relief.

For the termination of the procedure, the trochar can be reinserted after the syringe has been removed.

This allows for further PMMA in the cannula to be deposited in the bone and not in the paravertebral soft tissue on removal because this may cause local pain for the patient. Alternatively, and more frequently with vertebroplasty, negative pressure can be applied to the needle by withdrawing the plunger of the injector or syringe before removing the needle. On removal, it is also suggested to rotate the cannula in a few revolutions to break the needle away from the cement and to allow for the safe removal of the cannula.⁸

In kyphoplasty, larger trocars and a bilateral approach are usually used because two balloons are needed for height restoration. This creates a cavity in which PMMA would be injected (Fig. 3).¹⁵

After removal of all injectables, local pressure is applied for ~5 to 15 minutes, for achieving hemostasis. A sterile bandage is applied to the wound with or without antibiotic ointment.

Postoperative Care and Monitoring

The patient is taken to a recovery area and monitored for 2 to 3 hours. The patient should be kept in the supine position during that time. The PMMA cement usually hardens to 90% of its strength in 1 hour. The patient is monitored during this time for neurological and hemodynamic changes. If any such changes occur, especially neurological, prompt imaging, usually with CT, is warranted.⁸ Pain should also be assessed and managed postprocedurally with nonsteroidal anti-inflammatory drugs (NSAIDs) and other analgesics.⁸ Careful discharge instructions should be given to the patient, especially when to get incision wet and to report back urgently if pain levels significantly increase or neurological deterioration occurs.

OUTCOMES

Both vertebroplasty and kyphoplasty have been found to be highly effective in reducing pain from osteoporotic or pathological vertebral compression fractures and osteolytic tumors. Supporting data, however, have been based on individual experiences and published case series rather than prospective randomized trials. From the seven-case series published with patients receiving vertebroplasty for malignancies,^{13,17,21-26} (total 185 patients, 197 vertebral bodies), 86.2% of patients showed good to excellent pain response, with a mean reduction in pain of 6.30 points on the visual analogue scale.²⁷ Of the three series of kyphoplasty performed in patients with osteolytic tumors and multiple myeloma^{24,28,29} (total 38 patients, 99 vertebral bodies), 92.8% of patients showed a good to excellent pain response with reduction of 7 points on the visual analogue scale.²⁷ Fourny et al is the only study found in the literature to directly compare vertebroplasty and kyphoplasty in patients with cancer;

Figure 3 Multiple myeloma-induced fractures. (A,B) Sagittal short tau inversion recovery and T1 images demonstrating compression fractures in the midthoracic spine. (C–E) Sequential lateral fluoroscopic images demonstrating bipedicular placement of the needles and inflatable bone tamp and final injection of polymethylmethacrylate.

in 56 patients (21 with myeloma, 25 with metastatic spinal lesions) they reported equivalent results in relieving pain.²⁴

At 6-month follow-up, 65 to 76% of patients in all studies have experienced persistent pain relief.^{30,31} Both fractionated and unfractionated radiotherapy are associated with similar rates of pain relief after 6 months; however, pain relief after radiotherapy is delayed usually for 10 to 20 days and only minimal vertebral strengthening occurs.¹³ An important point to remember is that radiation therapy does not address the pain due to fracture in patients who have an underlying compression fracture (Fig. 1). But it should be emphasized that because vertebroplasty and kyphoplasty are palliative procedures, they do not prevent tumor growth; therefore, they should be used in conjunction with radiation and chemotherapy,⁷ if necessary.

Besides the effect of pain relief itself, the benefit of vertebroplasty on the restoration of mobility has also been well described. In a case series by Alvarez et al, 73%

of 11 wheelchair-bound patients with cancer resumed walking after treatment with vertebroplasty.²⁶ Also note that although the pain relief and the improvement in quality of life is substantial, it is less than what has been seen when these procedures have been done for osteoporotic vertebral compression fractures.⁷

The mechanisms of pain relief in patients with osteolytic tumors and myeloma are not fully understood. The main factors are likely the stabilization of microfractures and a reduction in mechanical forces.⁷ Others have postulated that the cement may have a chemical and thermal effect causing destruction of nerve endings as well as causing tumor ischemia.³²

COMPLICATIONS

The reported vertebroplasty- and kyphoplasty-related complication rate in cases of metastatic disease is ~10%,¹⁸ although the majority of such complications are minor or transient. This rate is higher than the rate

when these procedures are performed in patients with osteoporosis (1 to 3%) or vertebral hemangiomas (2 to 5%). The reason for the difference may be the destruction of the vertebral body or the medical condition of cancer patients.

Complications can be divided into four categories: medical- and anesthesia-related complications, instrument misplacement problems, cement leaks, and fractures of adjacent vertebrae. Medical- and anesthesia-related complications are fortunately uncommon because these percutaneous procedures have minimal systemic effects. However, patients with cardiac and pulmonary compromise may not be able to lie prone or tolerate general anesthesia, and cases of myocardial infarction during the procedure, worsening of congestive heart failure, and ileus can be found. These anesthesia-related complications are relatively more common after kyphoplasty because it is more typically performed under general anesthesia.

Technical problems involve misplacement of the instrumentation and can be explained by the inexperience of the operator, poor fluoroscopy systems, and severe spinal deformities. Kallmes et al described a fracture of the pedicle occurring after faulty placement of instruments in 1 patient in their series of 41.³³ Diamond et al reported fractures of the transverse process in 2 of their 55 patients receiving vertebroplasty.³⁴ Occasional rupture of the inflatable tamps has also been reported after balloon kyphoplasty; however, in these cases, the ruptured tamp was withdrawn without clinical complications.²⁹ Hemorrhage can also occur following cortical breaches, especially in patients with coagulopathies, and two cases of post-operative hematoma causing partial motor loss have been reported.³⁵

Few cases of infection following these procedures have also been published. Kallmes reported a case of *Staphylococcus epidermidis* infection,³³ and Yu et al described a case of osteomyelitis in a patient with a recent urinary tract infection.^{36,37} Sterility must therefore be strictly adhered to, and concurrent infection may be a contraindication to both vertebroplasty and kyphoplasty. Furthermore, in patients with an immunocompromised status, the prophylactic addition of antibiotics to the cement may be indicated.⁸

The most important complication of vertebroplasty is cement leak. Leaks can occur toward the epidural veins, the epidural space, and the neural foramina and, although they are usually well tolerated, they can be a source of pulmonary and neurological complications. Cement extravasation is more common when vertebroplasty is done in cases of metastasis and myeloma than osteoporosis³⁸ and is likely because of the cortical destruction associated with malignant lesions. One study by Vasconcelos et al, however, reported no such difference in over 200 procedures.³⁹

The most severe of cement leaks is the overflow of PMMA into the epidural space, causing spinal cord compression. Only one such case is reported of a patient with spinal metastasis, but anecdotal reports of this complication are rising as less experienced operators are performing vertebroplasties.³⁸ To minimize this risk, bone filling must be very carefully monitored with a high-quality fluoroscopy unit to ensure that the cement is sufficiently radio-opaque.

With neural foramina leaks, the major risk is radiculopathy. If such a complication occurs, that is, the patient develops intercostal neuralgia, local injections of steroid and anesthetics or oral NSAIDs can be used for treatment. In the rare refractory cases, surgical excision of the foraminal contents may be required, and, therefore, neurosurgical and orthopedic support should be available when these procedures are performed.

A leak into the paravertebral veins can cause pulmonary embolism that may or may not be symptomatic. By injecting slowly under fluoroscopic control during the pasty polymerization phase of the cement, one can avoid a possible major pulmonary infarction. If a leak into the paravertebral veins occurs, observed as paravertebral venous opacification, the injection should be immediately stopped. Because the risks of cement extravasation into the veins and epidural space increase with the volume used, authors have advised against injecting more than 5 mL in one vertebra⁴⁰ or treating more than three levels per session.⁴¹ It should also be mentioned that no correlation has been seen between the volume of cement injected and the clinical outcome¹⁷ (with the earlier caveat of the importance of placing the PMMA in the fracture line/cavity in cases of fracture).

Cement leaks into the paravertebral spaces often have no complications. Leaks toward the disk are also usually not clinically significant, but they increase the risk of vertebral body collapse of adjacent vertebra.^{42,43}

Pain is also considered a complication of the procedure, but it usually lasts < 24 hours. The incidence has been reported to be between 4 and 23% and is attributed to manipulation, injecting at a high pressure, osseous ischemia, or an inflammatory reaction to the cement.⁴⁴

CONCLUSION

To conclude, vertebroplasty and kyphoplasty are evolving techniques that have a beneficial role in alleviating the pain and improving the quality of life in patients with osteolytic tumors of the spine and multiple myeloma. Even though current data support these procedures as safe and effective in carefully selected patients, large prospective, randomized studies have yet to be performed. Several products are being investigated, including cements of various types with lesser viscosity

and longer polymerization time. Advancements in introducer systems and the increasing use of robotics and stereotactics ideally will make these techniques safer and more efficacious.

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