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Review Article

Treatment of Painful Osteoporotic Vertebral Fractures with Percutaneous Vertebroplasty or Kyphoplasty

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Abstract. Vertebral fracture is the most common complication of osteoporosis. It results in significant mortality and morbidity, including prolonged and intractable pain in a minority of patients. Vertebroplasty and kyphoplasty, procedures that involve percutaneous injection of bone cement into a collapsed vertebra, have recently been introduced for treatment of osteoporotic patients who have prolonged pain (several weeks or longer) following vertebral fracture. To determine the details of the procedures and to gather information on their safety and efficacy, we performed a MEDLINE search using the terms 'vertebroplasty' and 'kyphoplasty.' We reviewed reports of these procedures in patients with osteoporosis. We supplemented the articles found with other papers known to the authors and with presentations at national meetings. Randomized trials of vertebroplasty and kyphoplasty have not been reported. Case reports suggest that these procedures are associated with pain relief in 67% to 100% of cases. Short-term complications, mainly the result of extravasation of cement, include increased pain and damage from heat or pressure to the spinal cord or nerve roots. Proper patient selection and good technique should minimize complications, but rarely, decompressive surgery is needed. Long-term benefits have not yet been shown, but potentially include prevention of recurrent pain at the treated level(s) with both procedures, and, with kyphoplasty, reversal of height loss and spinal deformity, an improved level of function, and avoidance of chronic pain and restriction of internal organs. Possible long-term complications, again not fully evaluated, include local acceleration of bone resorption caused by the treatment itself or by foreign-body reaction at the cement–bone interface, and increased risk of fracture in treated or adjacent vertebrae through changes in mechanical forces. Controlled trials are needed to determine both short-term and long-term safety and efficacy of vertebroplasty and kyphoplasty. Both procedures may be useful for osteoporotic patients who have prolonged pain following acute vertebral fracture. Until there is conclusive evidence for efficacy and long-term safety, these procedures should be done only in carefully selected patients, only by experienced operators with appropriate high-quality imaging equipment, and ideally at centers that are participating in controlled trials.

Keywords: Kyphoplasty; Osteoporosis; Vertebral fractures; Vertebroplasty

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Introduction

Vertebral fracture is the most common complication of osteoporosis. It is estimated that 750 000 new vertebral fractures occur in the United States each year. Although many vertebral fractures are not recognized as discrete clinical events, they can result in height loss, spinal deformity (kyphosis, scoliosis), acute and chronic pain, restriction of thoracic and abdominal contents, impaired mobility and disability. Patients with vertebral fractures have a significant increase in hospitalizations and all-cause mortality.

Between 20% and 30% of radiographically evident vertebral deformities are recognized as discrete clinical events characterized by the sudden onset of severe and

persistent pain in the region of the fracture. Pain from acute vertebral fracture appears to be due in part to instability (non-union or slow union) at the fracture site. Pain may be continuous, but typically is less when the patient is at rest and is worse when the patient is active.

Modalities for management of the acute fracture episode include rest, external support, analgesics and calcitonin, although none of these modalities have been studied in rigorously controlled trials. Sometimes, the pain cannot be controlled with oral analgesics and requires hospital admission for control. In 1996 there were approximately 120 000 hospital admissions in the USA for management of vertebral fractures with total costs of almost $1.5 billion.

For most patients who have acute, painful vertebral fractures, the pain gradually disappears within a few days to weeks, although it may last 8–12 weeks and sometimes longer. Many patients eventually become pain free; however, persistent vertebral deformity may lead to chronic pain because of paraspinal muscle spasm, degenerative arthritis in the region of the fracture, and changes in spinal alignment. Rarely, posterior or lateral displacement from a burst fracture may cause pain from pressure on nerve roots or the spinal cord.

Surgical decompression and instillation of polymethylmethacrylate (PMMA) has been used for some time to treat vertebral fractures due to metastatic malignancy or vertebral hemangiomas and fractures due to benign tumors of the long bones. The percutaneous approach to vertebroplasty was first reported from France in 1987 and in North America in 1997 in patients with malignant disease. Its use has subsequently been extended to patients with fractures due to osteoporosis resulting from advanced age, estrogen deficiency, and various secondary causes. Another procedure, kyphoplasty (Kyphoplasty^{TM}, Kyphon Corporation, Santa Clara, CA), involves inflation of a bone tamp within the vertebral body and re-expanding the fractured vertebra prior to injection of bone cement. Both procedures are intended to provide stability at the fracture site, thus reducing pain. Kyphoplasty also has the potential to correct the vertebral deformity, thus reversing or preventing height loss, spinal deformity, and compromise of internal organs. Vertebroplasty seems to be performed most frequently by interventional radiologists and kyphoplasty by orthopedic spine specialists.

Methods

At the request of the Professional Practice Committee of the American Society for Bone and Mineral Research (ASBMR), we performed a MEDLINE search for the terms ‘vertebroplasty’ and ‘kyphoplasty’ to determine the details of the procedures and their safety and efficacy in patients with osteoporosis. We included only reports of the use of these procedures in patients with fractures due to osteoporosis. We supplemented the search results with other papers and with presentations at major scientific meetings and discussions with people performing the procedures. We provide here a summary of technique, patient selection criteria and results.

Results

In the MEDLINE search on 16 February 2001, 39 papers were found using the search term ‘vertebroplasty.’ None were found using ‘kyphoplasty.’ Searching PREMEDLINE on the same date yielded 16 citations for vertebroplasty, one of which also came up under kyphoplasty. Preliminary results from a large trial of kyphoplasty were presented at a recent meeting. The articles found on MEDLINE and PREMEDLINE could be classified as: (1) individual case reports or series ($n = 10$), (2) overview or personal commentary ($n = 15$), (3) ex vivo investigation or technical notes ($n = 13$), and (4) other (e.g., vertebroplasty to treat malignancy or other non-osteoporotic cause of vertebral fracture, pathologic findings) ($n = 17$). In the series of case reports, efficacy and safety were assessed using different tools and different standards, making comparisons difficult.

Description of Technique

Vertebroplasty involves percutaneous injection of bone cement into the involved vertebra(e) using fluoroscopic and/or computed tomographic (CT) guidance. Depending on the nature of the fracture and the position of the needle relative to the midline, the injection is given into one or both sides of the affected vertebral body. Although the bone cement is injected under some pressure, it is usually not possible to correct the compression deformity. There is a potential for extravasation of cement with possible resultant neurologic damage.

Kyphoplasty differs from vertebroplasty by adding an initial step of expanding the vertebra with a bone tamp (balloon). Once the vertebra is re-expanded and a space is created, the bone tamp is withdrawn and cement is injected into the space. Insufficient data exist to compare the efficacy and safety of the two procedures in patients. Kyphoplasty appears to offer greater potential for reversal of vertebral deformity (Fig. 1) as well as a smaller risk of extravasation (because the bone cement is injected under lower pressure than vertebroplasty and can be more viscous when injected). On the other hand, the initial balloon expansion in kyphoplasty might increase the risk of further mechanical damage to the fractured vertebra or adjacent structures. Belkoff et al. [23] showed in cadaver vertebrae almost complete restoration (97% reversal) of vertebral height loss compared with vertebroplasty (30% reversal) and that vertebral stiffness was restored to normal with kyphoplasty but not with vertebroplasty.

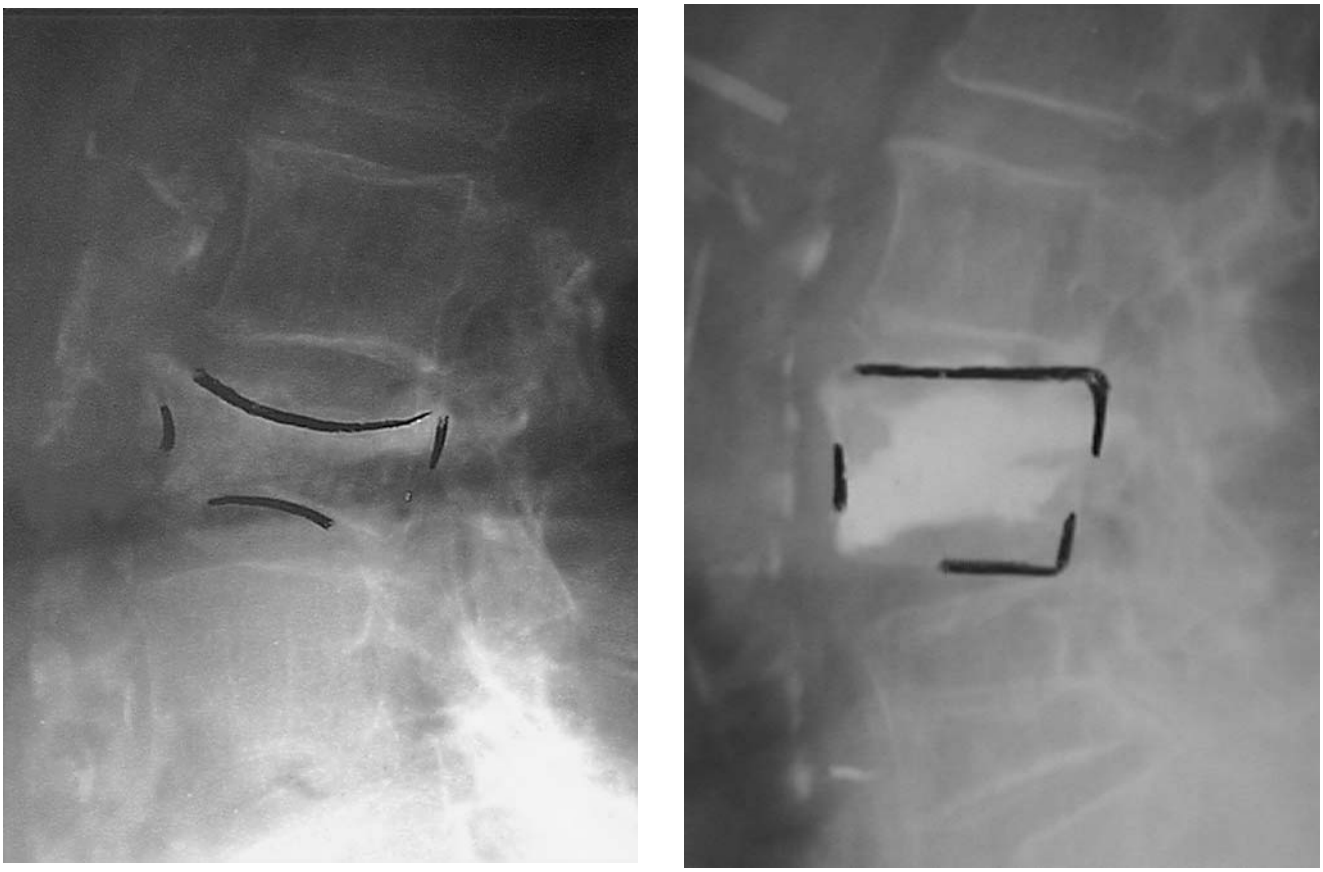

Fig. 1. Reversal of vertebral height loss after kyphoplasty. (Radiograph kindly provided by Frank Phillips MD, University of Chicago.)

Patient Selection

Patients who have vertebral fractures with pain that is unusually prolonged or severe have been treated with these procedures. It seems important to be as certain as possible about the origin of the pain and its relation to the observed vertebral lesion. This may be particularly problematic in patients who have multiple vertebral fractures. The best candidates appear to be patients who have focal, intense, deep pain with evidence of a new or progressive vertebral compression fracture by conventional radiography and magnetic resonance (MR) imaging confirmed by physical findings. The best time for intervention is not known. In most reported series, patients did not undergo the procedure unless their pain remained uncontrolled after several weeks or months of conventional medical management. In one series patients were treated a mean of 7 months after the onset of symptoms. However, in another series patients were selected for having pain of less than 1 month in duration. The likelihood of improvement probably decreases over time and appears to be low for remote fractures (i.e., >6 months in the past).

Contraindications

Relative contraindications to vertebroplasty and kyphoplasty include complete loss of vertebral body height (some success has been reported with compression up to 80%), fracture through or destruction of the posterior vertebral wall, pressure of bone fragments on the spinal cord, osteoblastic metastatic lesions, uncorrectable coagulation disorder, or medical conditions that would make the patient ineligible for emergency decompressive surgery should it be necessary to treat a complication of the procedure.

Pretreatment Evaluation

Most series have required conventional radiographs that show clear evidence of vertebral fracture. MR imaging appears to be helpful to document bone marrow edema (a sign of recent fracture) at the fracture site, particularly in patients who have multiple vertebral fractures, and may be sufficient to determine if a patient is a candidate for the procedure. Computed tomography (CT) may be useful to assess the extent of vertebral collapse, the location and extent of any lytic process, the visibility and degree of involvement of the pedicles, the presence of cortical destruction or fracture, and the presence of epidural or foraminal stenosis caused by tumor extension or bone fragment displacement. Prior to vertebroplasty, many recommend intraosseous vertebral phlebography to evaluate the venous filling pattern and to identify sites

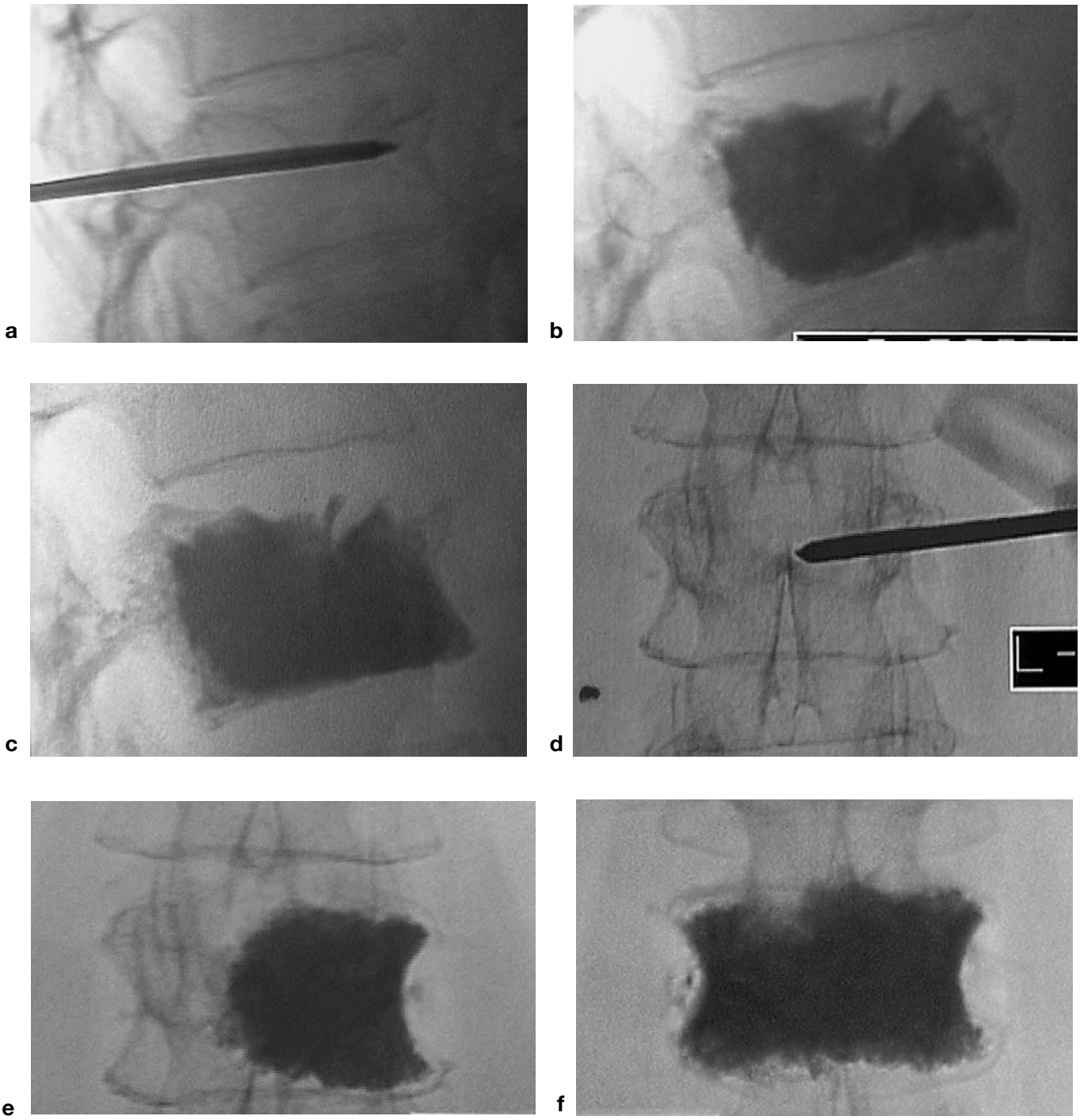

Fig. 2. Vertebroplasty requiring bipedicular injection, posterior–anterior and lateral views: needle inserted ready to inject the left side (A and D), left side injected (B and E), right side injected (C and F).

of potential cement leakage. In one series, nuclear bone scan showing increased uptake at the site to be treated predicted good relief of pain.

Approach

Both procedures are done with the patient in the prone position. Either general anesthesia or neuroleptic analgesics (e.g., fentanyl, midazolam) are used, with additional local anesthesia used with the latter. The transpedicular approach is preferred, while parapedicular and intercostopedicular approaches are also used. An open surgical approach has also been suggested. For vertebroplasty using a properly angulated needle and approach (needle tip ending anteriorly and in the midline), a unilateral injection results in adequate

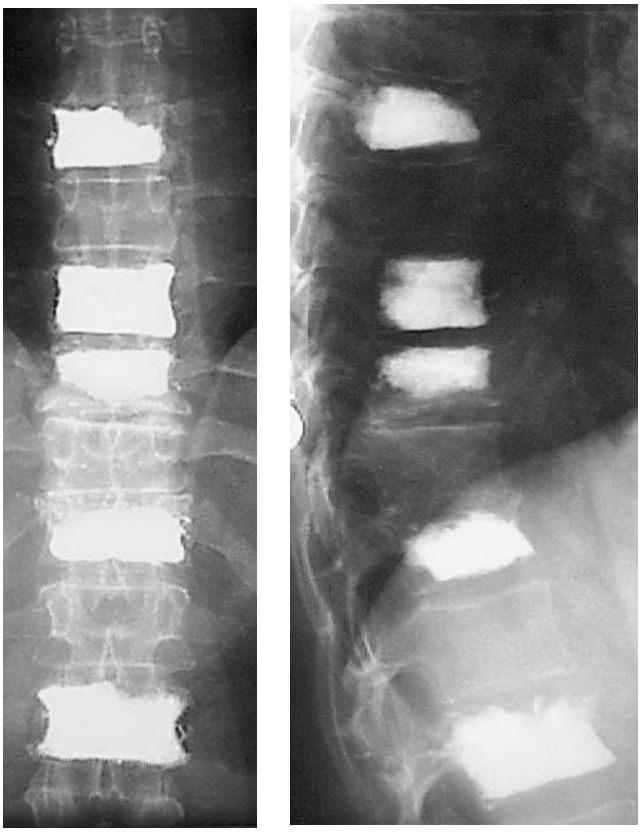

Fig. 3. Posterior–anterior (A) and lateral (B) radiographs of subject who has had vertebroplasty done at five levels.

instillation of cement in 80–90% of cases. Bilateral approach and injection is occasionally needed (Fig. 2). With kyphoplasty, a bipedicular approach is required. Needle guidance and control is maintained using biplane DSA fluoroscopy or single plane DSA and CT. A 10 or 11 gauge bone biopsy needle with a beveled or diamond tip obturator, 10–15 cm in length (e.g., Jamshidi), is inserted into the body of the vertebra. Cement is injected directly under continuous visual control to obtain adequate filling and avoid leakage. The injection is stopped when significant resistance is met, when the cement reaches the posterior quarter of the vertebral body, or when there is escape into extraosseous structures or veins (basivertebral plexus to epidural or paravertebral veins). Although one or two levels are usually treated in a session, as many as six levels have been treated in one session (Fig. 3). Throughout the procedure, blood pressure, heart rate, oxygen saturation and neurologic status should be monitored.

Cement

The most commonly used material is polymethylmethacrylate (PMMA), which cures with an exothermic reaction. There are several different forms of PMMA that seem to have similar strengthening properties. The average total volume injected is about 7 ml (range 1 to 11 ml), although the injection is usually given incrementally using 1-ml syringes (filled from above, via the barrel). Metallic powder (barium, tungsten, tantalum or a combination) is often added to the cement to optimize radio-opacity. The viscosity increases due to polymerization (time to set is 8–15 minutes, depending on the specific cement). The speed of the reaction depends on the ambient temperature and the quantity of the solvent, free contact with air, and the type of cement used. The viscosity at the time of the injection seems important; a paste consistency appears safer and should result in fewer leaks but might be more difficult to inject. Waiting a minute or so for the cement to become more viscous can reduce leakage that occurs during the procedure because of cement that is too liquid. Theoretically, local heat might damage adjacent tissues because of the exothermic reaction, but the surrounding vascularized tissues, particularly the dura, act to reduce local heat effects. Local tissue damage has been reported only anecdotally.

There is interest in the use of different bone cements including coral granules and a biodegradable calcium phosphate bone substitute. Advantages of these alternatives include lack of heat production during the procedure and the potential for eventual replacement of the cement by bone, which could result in less difference in strength between treated and untreated vertebrae and avoid the potential of foreign body reaction seen with PMMA.

Soon After the Procedure

During or soon after the procedure, CT imaging is done to evaluate the extent of vertebral filling and to exclude major compression of nerve roots and spinal cord. The patient remains supine for 1–2 hours to allow complete curing of the PMMA and can be discharged home as soon as 2 hours after the procedure is completed. Overnight hospital stay is required for patients with possible neurologic complications, uncontrolled pain, or who are otherwise unstable.

Short-term Efficacy

No controlled trials have been published with vertebroplasty or kyphoplasty, although a randomized trial of kyphoplasty is ongoing and preliminary results from open studies have been reported. Published series of vertebroplasty range from 1 to 80 patients and are shown in Table 1.

Grados et al. [43] reported systematic long-term follow-up (mean of 48 months, range 12–84 months) who were part of an earlier series. Pain score was reduced by approximately 50% 1 month after vertebroplasty and was similarly low at the long-term visit.

Table 1. Published series of vertebroplasty

Reference	Patient number	Levels treated	Duration of f/u	Pain improved	Complications
Debusche-Depriester 1991	15	?	1–>12 mos	93%	None
Gangi et al. 1994 [38]	4	8	4–15 mos	100%	None
Jensen et al. 1997 [20]	29	4.7	Up to 3 yrs	90%	Rib fractures in 2 of 29 patients
Mathis et al. 1998 [39]	1	7	9 mos	100%	None reported
Deramond et al. 1998 [40]	80	Not reported	Up to 10 yrs	90+%	Intercostal neuralgia in 1 of 80 patients
Martin et al. 1999 [41]	11	Not reported	Not reported	78%	None reported
Cortet et al. 1999 [24]	16	20	6 mos	88%	Leakage in 11 patients (13/20 vertebrae) of no clinical consequence
Cyteval et al. 1999 [25]	20	23	6 mos	90%	Painful cement leakage into the psoas muscle in 1 of 20 patients
Barr et al. 2000 [42]	38	70	2–42 mos	95%	Dermatome radicular neuritis in 1 of 38 patients
O'Brien et al. 2000 [26]	6[a]	6	3 months	67%	Leakage in 2 patients, not clinically significant
Heini 2000	17	45	12 months	76%	Leakage in 20% of interventions, none clinically significant

[a]Patients with 65% or greater compression

Short-term Complications

Short-term complications of vertebroplasty have been reported in less than 10% of patients and are mainly the result of epidural or foraminal leakage of cement. There appears to be a significant 'learning curve.' Reported complications include increased pain and damage to the spinal cord or nerve roots from pressure or heat (as the cement cures). Decompressive surgery has been required to relieve local pressure. Leakage of a small quantity of cement through the end plate into the disk space seems to be of no consequence. Rib fracture has resulted from osteoporosis and the prone position required for vertebroplasty while pressure is applied to the back during needle positioning. Post-procedure venous thromboembolism has been reported in cancer patients (but not in patients with osteoporosis), possibly related to the underlying malignancy. A foreign-body reaction to PMMA may cause fever and transient worsening of pain lasting a few days, which can be managed using non-steroidal anti-inflammatory drugs (NSAIDs) or corticosteroids. Complications seem to be more likely in highly vascular lesions (e.g., malignancy, hemangiomas), with liquid consistency of cement, and if there is destruction or fracture of the cortex. Infection would be particularly hard to eradicate given its location in bone but has been reported (personal communication, Jacques Dion MD); prophylactic antibiotics can either be added to the cement (e.g., tobramycin) or given systemically (e.g., cefazolin) just before the procedure. Reported complications of kyphoplasty include epidural bleeding, transient spinal cord injury, and transient acute respiratory distress syndrome (ARDS).

Long-term Follow-up

Both vertebroplasty and kyphoplasty substantially strengthen treated vertebra as assessed on post-mortem specimens. Treated vertebrae may then be stronger and stiffer than untreated vertebrae. Marked increases in density occur in treated vertebrae assessed by dual-energy X-ray absorptiometry (DXA) studies, with a characteristic appearance on DXA imaging (Fig. 4); treated vertebrae should be deleted from DXA analysis.

It is possible that the risk of future fracture in treated or untreated vertebrae will be increased, either directly or indirectly (through changes in biomechanical properties). There may also be negative effects on bone remodeling as a result of foreign-body reaction at the cement–bone interface. Spinal radiographs have been advised after 6 months and should be repeated periodically to evaluate the treated vertebra(e) and to look for fractures in untreated vertebrae. Patients should receive appropriate medical treatment and follow-up for their underlying osteoporosis.

In the series of Grados et al. [43] with a mean followup of 48 months, 13 patients (52%) developed a total of 34 new vertebral fractures in the follow-up period. The odds ratio for a fracture in the vicinity of a cemented vertebra was 2.3 (95% CI 1.1–4.6) compared with 1.4 (95% CI 0.8–2.6) for a fracture adjacent to a non-cemented fractured vertebra.

Conclusions

It should be noted that treatment of painful vertebral fractures is empirical. There have been no clinical trials of the modalities currently in use. Vertebroplasty and kyphoplasty may be effective for pain relief in vertebral fracture patients who have pain that is refractory to conventional management. However, these procedures have not been evaluated in controlled trials. These procedures have not been explored in patients in the early stages of acute painful vertebral compression fracture or in patients with remote fractures who have significant long-term sequelae. Serious short-term complications are uncommon but do occur. Long-term benefits (e.g., reversal of kyphosis and height loss,

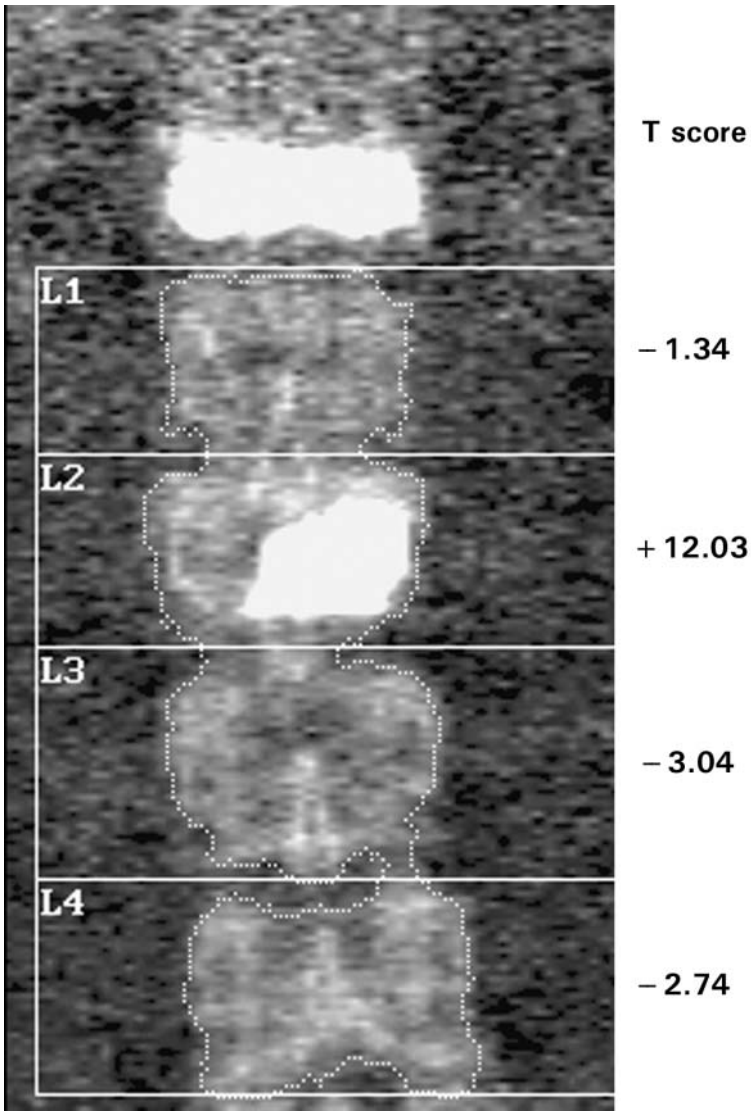

Fig. 4. Dual-energy X-ray scan showing very high density in L2 following vertebroplasty. Also visible is vertebroplasty in T12.

improved functional capacity) and risks (e.g., increased risk of fracture) are not known.

Recommendations

Vertebroplasty and kyphoplasty should be offered only to carefully selected patients whose pain is not controlled by outpatient measures, when severe pain persists for more than several weeks, or if there is significant height loss with negative consequences (e.g., reduction of vital capacity in patients who have pulmonary disease). When symptoms have persisted more than 6–12 months, the efficacy of these procedures appears to drop significantly. At the present time, vertebroplasty and kyphoplasty are not indicated for asymptomatic patients or acute fracture patients (within a week or two of the event). Because of the potential for serious complications, only experienced operators who have appropriate high-quality imaging equipment should perform these procedures.

The risk of future vertebral fracture is particularly high following the first fracture; one in five patients who have a vertebral fracture will have another in the year that follows. Evaluation for secondary causes of osteoporosis and treatment with appropriate pharmacologic agents for osteoporosis, if not already done by the time of vertebroplasty or kyphoplasty, is particularly important for these patients.

Controlled trials should be done. Complex issues are involved in clinical trials, particularly trials that involve invasive procedures. Any trial design needs to be carefully considered by investigators and their Institutional Review Boards.

A definitive way to determine the safety and efficacy of these procedures would be a trial in which eligible subjects were randomized into three groups: a ‘control’ group to be managed medically, a ‘sham’ group to

undergo a sham procedure, and an active intervention group. A relatively small study could address short-term efficacy; a large trial would be needed to determine the effect of these procedures on fracture rates.

Practical issues may make it difficult to do a classical randomized trial of these procedures. Having a group assigned to sham procedures, with attendant risks, raises important ethical considerations. Patients who have severe or prolonged pain may be reluctant to enter a study that might deny them a procedure for relief of pain, particularly if that procedure is available outside the setting of a trial.

An alternative to a classic randomized, sham-controlled trial would be to randomize appropriate subjects into two groups: one to undergo the procedure immediately after evaluation (i.e., when it is first considered) and the other (control) group that is accepted for the procedure but waits 2 to 4 weeks before having it. To compare the results of vertebroplasty with kyphoplasty, patients could undergo one or the other procedure in random order (either immediate treatment or delayed [control]). Data could be collected on short-term and long-term efficacy including pain, functional status, change in spinal contours, loss of height, and change in pulmonary function. All patients in the trial should receive medical treatment (e.g., bisphosphonates, calcitonin, raloxifene) for their underlying osteoporosis.

Evaluation of the long-term effect of these procedures on fracture risk is more problematic. Although it may not be possible to have a true control group in a long-term trial, vertebral fracture incidence (both clinical fractures and radiographic vertebral deformities) should be assessed for at least a year or two following the procedure.

Summary

Percutaneous vertebroplasty and kyphoplasty are being performed for patients with acute painful vertebral fractures, particularly patients whose pain cannot be controlled outside the hospital, those with severe persistent pain, and when height loss or spinal deformity result in clinically-apparent consequences. Complete or substantial pain relief is seen in at least two-thirds of cases. Serious complications are uncommon. Controlled trials are needed to fully determine the short-term and long-term benefits and risks.

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