An Evidence-Based Evaluation of Percutaneous Vertebroplasty

Costs are relatively low for this minimally invasive procedure, compared with open surgical interventions for vertebral compression fractures, such as internal fixation and spinal fusion.

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Abstract

Background Information: Percutaneous vertebroplasty is a therapeutic, interventional radiologic procedure that involves injection of bone cement into a cervical, thoracic, or lumbar vertebral body lesion for the relief of pain and the strengthening of bone. This procedure only recently has been introduced, and is being used for patients with lytic lesions due to bone metastases, aggressive hemangiomas, or multiple myeloma, and for patients who have medically intractable debilitating pain resulting from osteoporotic vertebral collapse.

Findings: Results from two uncontrolled prospective studies and several case series reports, including one with 187 patients, indicate that percutaneous vertebroplasty can produce significant pain relief and increase mobility in 70 percent to 80 percent of patients with osteolytic lesions in the vertebrae from hemangioma, metastases, or myeloma, or with osteoporotic compression fractures. In these reports, pain relief was apparent within one to two days after injection, and persisted for at least several months up to several years. While experimental studies and preliminary clinical results suggest that percutaneous vertebroplasty can also strengthen the vertebral bodies and increase mobility, it remains to be proven whether this procedure can prevent additional fractures in the injected vertebrae. In addition, the duration of effect is not known; there were no long-term follow-up data on most of these patients, and these data may be difficult to obtain and interpret in patients with an underlying malignant process, because disease progression may confound evaluation of the treatment effect. Complications were relatively rare, although some studies reported a high incidence of clinically insignificant leakage of bone cement into the paravertebral tissues. In a few cases, the leakage of polymer caused compression of spinal nerve roots or neuralgia. Several instances of pulmonary embolism were also reported.

Although patient selection criteria have not been definitively established, percutaneous vertebroplasty is considered appropriate treatment for patients with vertebral lesions resulting from osteolytic metastasis and myeloma, hemangioma, and painful osteoporotic compression fractures if the following criteria have been met:

- Severe debilitating pain or loss of mobility that cannot be relieved by correct medical therapy.
- Other causes of pain, such as herniated intervertebral disk, have been ruled out by computed tomography or magnetic resonance imaging.
- The affected vertebra has not been extensively destroyed and is at least one third of its original height.
- Radiation therapy or concurrent surgical interventions, such as laminectomy, may also be required in patients with compression of the spinal cord due to ingrowth of a tumor.

Conclusions: Percutaneous vetebroplasty has only recently been introduced as a treatment for osteolytic lesions and osteoporotic compression fractures of the vertebrae, but early results are promising. Up to 80 percent of patients with pain unresponsive to correct medical treatment experience a significant degree of pain relief, and few serious complications have been reported. However, relatively few patients have undergone this procedure, and there are no data from controlled clinical trials or from studies with long-term follow-up. At the present time this procedure is still in the investigational stages, but may be appropriate for patients with no other reasonable options for medical treatment.

Index terms: acrylic polymer, bone cement, compression fracture, hemangioma, interventional radiology, lytic lesions, methyl methacrylate, multiple myeloma, osteolytic metastasis, osteoporosis, spine, vertebral collapse, vertebral fragility, vertebroplasty.

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Introduction

Percutaneous vertebroplasty is a therapeutic, interventional radiologic procedure that involves injection of an acrylic polymer into a partially collapsed vertebral body in an effort to relieve pain and provide stability. This procedure was initially described by French radiologists for the treatment of painful vertebral hemangiomas, myeloma, and metastatic lesions, and is now also being used in patients with osteoporotic compression fractures. These vertebral fractures may cause persistent, often ex-

cruciating pain, which impairs mobility and reduces the patient's quality of life. Medical management of vertebral body fractures includes analgesics, bed rest, and external bracing; however, despite these types of management, progressive kyphosis, prolonged pain, and disability still occur in some patients. In these patients, percutaneous vertebroplasty can be used to prevent further collapse of fractured vertebrae, and to augment osteoporotic vertebral bodies at risk for fracture.[1,2]

If percutaneous vertebroplasty is being considered as a treatment option, radiography and computed tomography (CT) are performed to assess the extent of vertebral collapse, the location and extent of the 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 retropulsion.[1,2]

Percutaneous vertebroplasty is usually performed under local anesthesia combined with neuroleptanalgesia, and may be done as an outpatient procedure or may require a short hospital stay. For this procedure, the patient lies in the prone position, and a large bore (10- to 15-gauge) needle is placed into the vertebral body lesion under radiological guidance from CT scanning or fluoroscopy. An acrylic bone cement, usually methyl methacrylate, is then injected into the affected vertebra until resistance is met or until cement reaches the posterior wall of the vertebral body. This preparation is viscous to reduce leakage of the bone cement into adjacent structures or into the vasculature. Prior to injection, contrast material is added to increase its radiopacity, and in some cases antibiotics are also included. Some operators inject contrast material alone before injecting bone cement; this additional step may be useful in highly vascular lesions to avoid inadvertent injection of bone cement into a vessel, which could result in pulmonary embolism. The procedure generally takes one to two hours. CT may be used several hours after injection to assess vertebral body filling and to detect any leakage of the bone cement. Nonsteroidal or steroidal anti-inflammatory drugs can be used for two to four days after vertebroplasty to minimize the inflammatory reaction to the heat of polymerization of the acrylic compound. Pain relief is expected within 24 hours after the procedure. In patients with neural or nerve root compression from ingrowth of a tumor, vertebroplasty may be performed in conjunction with laminectomy or with radiation therapy.[1]

Health Care Financing Administration

As of November 1999, HCFA considers percutaneous poylmethacrylate vertebroplasty to be investigational, and not proven safe and effective, and therefore does not cover this procedure. However, local carriers may cover this procedure when it is deemed medically reasonable and necessary.[3]

Clinical research studies

Evidence evaluated for this report was obtained from a search of databases (Premedline, Medline, Embase and Healthstar), spanning 1996 to November 1999. Search terms included *vertebroplasty* as keyword, subject word, and title word. In addition, information was obtained from the Society of Cardiovascular and Interventional Radiology (SCVIR) and the American College of Radiology (ACR). Most of the initial studies were done in France, and included patients with either osteolytic lesions due to tumors or myeloma, and patients with osteoporotic compression fractures. Many of these studies were published in French-language journals and were not available for review. Of the reports published in English, there were five recent case series and two uncontrolled prospective studies. Only one case series study was from the United States, and involved patients with osteoporotic compression fractures; to date, this has been the primary use of percutaneous vertebroplasty in this country. Outcome measures were largely subjective, and included pain (assessed with the Visual Analogue Scale (VAS) or the McGill-Melzack classification), change in analgesic requirement or in degree of mobility, and adverse events. None of the studies provided long-term follow-up on most of the patients; this is a reflection of the very recent introduction of the technique, and also the fact that many of the patients with underlying malignancy either died or had progression of their disease. Findings from the English-language studies have been reviewed, and are summarized in the table "Studies Evaluating the Safety and Efficacy of Percutaneous Vertebroplasty," which begins on Page 58.

These case series reports and uncontrolled studies indicate that percutaneous vertebroplasty can produce significant pain relief and increase mobility in 70 percent to 80 percent of patients with osteolytic lesions from hemangiomas, metastases or myeloma, or with osteoporotic compression fractures. Pain relief was apparent within one to two days after injection, and persisted for at least several months up to several years. There is little long-term follow-up on these patients; long-term data may be difficult to obtain and interpret in patients with an underlying malignant process, because disease progression may confound evaluation of the treatment effect. While preliminary results suggest that percutaneous vertebroplasty can strengthen the vertebral bodies and increase mobility, it remains to be proven whether this procedure can prevent additional fractures in the injected vertebrae. Complications were relatively rare, although some studies reported a high incidence of clinically insignifi-

Studies Evaluating the Safety and Efficacy of Percutaneous Vertebroplasty

Key: PMMA, polymethyl methacrylate; VAS, visual analogue scale

Authors/ Study Design	Study Population	Procedures	Results	Conclusions/ Comments
Weill et al. (1996)[4] Groupe Hospitalier Pitie-Salpetriere, Paris, France Case series	Pts w/ pain or instability due to vertebral metastases (n=37; 20 men, 17 women; mean age 61 yrs, range 33-86) Indication for procedure: pain relief (29 procedures); stabilization of vertebral column (5 procedures); both indications (6 procedures) Exclusion criteria: less than one third of the vertebral height preserved; severe pulmonary insufficiency; coagulation disorder	Percutaneous vertebroplasty (52 vertebral bodies injected) Laminectomy and posterior fusion also performed in 3 pts; radiation therapy in 10 pts; surgery and radiation therapy in 2 pts	Mean f/u 7.1 mos; 6 pts lost to f/u after 1-3 mos 24/33 (73%) procedures resulted in good pain relief w/ at least 50% reduction in analgesic dose; 7 resulted in moderate pain relief; 2 did not work; results sustained at 6 mos No vertebral displacement in pts treated for instability; 1 pt had pain recurrence at 1 yr Complications: postoperative death due to pneumonia (1 pt) or pulmonary embolism (1 pt); transient radiculopathy due to cement extrusion (3 pts); transient difficulty in swallowing (2 pts)	Percutaneous vertebroplasty effective in reducing pain, stabilizing spine in pts w/ instability Limitations: case series study; heterogeneous pt population; limited long-term f/u
Cotten et al. (1996)[5] Hôpital B-CHRU de Lille, Lille, France Uncontrolled prospective study	Pts w/ pain due to osteolytic vertebral lesions (n=37; 14 men, 23 women; mean age 58 yrs, range 36-83) Lesions due to metastasis in 29 pts, multiple myeloma in 8 pts	Percutaneous vertebroplasty (40 vertebral bodies injected)	Mean f/u 4.2 mos (range, 6 d-6 mos) 36/37 (97%) pts obtained partial or complete relief of pain w/in mean of 36 hrs after injection No correlation between percentage of lesion filled and degree of pain reduction No further collapse of injected vertebral bodies in 16 pts available for 6-mo f/u Complications: femoral neuropathy (2 pts), sciatica (1 pt); bone cement leakage (29/40 injections; 2 pts had nerve root compression from this)	Percutaneous vertebroplasty effective in reducing pain in pts w/ malignant osteolytic lesions; degree of pain relief not related to amount of lesion filled; leakage occurred frequently, rarely symptomatic Limitations: uncontrolled study; long-term tx effect difficult to evaluate due to lack of f/u, also disease progression
Jensen et al. (1997)[6] University of Virginia Health Sciences Center, Charlottesville, VA Case series	Pts w/ pain due to osteoporotic vertebral compression fractures (n=29; 10 men, 19 women) 17 pts had fractures associated w/ age-related osteopenia, 12 pts had steroid-related osteopenia	Percutaneous vertebroplasty (47 vertebral bodies injected)	26/29 (90%) pts reported significant pain relief and improved mobility w/in 24 hrs after tx; 3 pts had no change in pain level Complications: rib fractures due to procedure (2 pts)	Percutaneous vertebroplasty effective in providing immediate pain relief in most pts; few complications Limitations: case series study; no long-term f/u
Martin et al. (1999)[7] University Hospital HUG, University of Geneva, Switzerland Case series	Pts w/ pain due to vertebral body lesions (40 pts; 20 men, 20 women; mean age 67 yrs, range 32-87) Pts w/ reduced vertebral body height and destruction of posterior vertebral wall were not excluded Lesions due to osteoporotic collapse (11 pts); hemangioma (7 pts); metastasis (19 pts); myeloma (2 pts); bone lymphoma (1 pt)	Percutaneous vertebroplasty (68 vertebral bodies injected)	Mean f/u 14 mos (range 2 wks-4 yrs), evaluation involved questionnaire for pain, analgesic use, mobility Complete pain relief and recovery of mobility in 24/34 (70%) evaluable pts; 6 pts lost to f/u or died of primary disease in early postop period Complications: deep vein thrombosis (1 pt); pneumonia (1 pt); pain increase (1 pt)	Percutaneous vertebroplasty effective in reducing pain, increasing mobility; tx failures related primarily to excessive volume of injection, insufficient pretx clinical evaluation; results not as good in pts w/ advanced metastatic disease Limitations: case series study, no long-term f/u for most pts

Table continued

Authors/ Study Design	Study Population	Procedures	Results	Conclusions/ Comments
Cortet et al. (1999)[8] University Hospital of Lille, France Uncontrolled prospective study	Pts w/ pain due to osteoporotic vertebral compression fractures (n=16; 7 men, 9 women) Inclusion criteria: 1-2 vertebral fractures responsible for severe pain; scores 3-5 on McGill-Melzack scoring system, evolving for more than 3 mos	Percutaneous vertebroplasty (20 vertebral bodies injected)	Evaluation at day 3, 30, 90, 180: significant decrease in VAS and McGill-Melzack pain scores ($p<0.005$); also improvement in health profile score ($p<0.05$) No additional vertebral fractures occurred; no complications	Percutaneous vertebroplasty effective in reducing pain, improving health status for 6 mos after procedure Limitations: very small pt population; uncontrolled study; no long-term f/u
Wenger and Markwalder (1999)[9] Kinik Beau-Site, Bern, Switzerland Case series	Pts w/ pain due to osteoporotic vertebral compression fractures (n=13; 4 men, 9 women; mean age 71 yrs, range 55-89)	Vertebroplasty (percutaneous approach in first 3 pts, open surgical approach under general anesthesia in next 10 pts) Internal fixation also used in 1 pt w/ multiple fractures and regional kyphosis	Evaluation at 6 and 12 wks: all pts free of pain; no additional vertebral fractures Complications: leakage of bone cement at fracture site in 1 pt using percutaneous approach	Vertebroplasty effective in reducing pain; authors expressed concerns regarding safety of percutaneous approach, potential for leakage of bone cement Limitations: case series study; very small pt population; no long-term f/u
Gangi et al. (1999)[10] University Hospital of Strasbourg, Strasbourg, France Case series	Pts w/ pain due to osteoporotic vertebral compression fractures (n=105), symptomatic hemangiomas (n=11), metastasis and myeloma (n=69), and postsurgical consolidation (n=2)	Percutaneous vertebroplasty (289 vertebral bodies injected) Laminectomy w/ partial excision of the tumor also performed in 3 pts w/ hemangioma	Mean f/u 2.7 yrs (maximum 7 yrs) Satisfactory outcome, defined as reduction in analgesic dose, reported in 78% pts w/ osteoporotic lesions, 83% pts w/ tumoral lesions, 73% pts w/ hemangioma Complications: leakage of bone cement into epidural space (11 asymptomatic pts; 3 w/ neuralgia); paravertebral leak (1 pt), asymptomatic pulmonary embolism (2 pts); asymptomatic leak into intercostal artery (1 pt)	Percutaneous vertebroplasty effective in reducing pain; complications related to leakage of bone cement Limitations: case series study; no long-term f/u on most pts; analgesic dose was only outcome measure

cant leakage of bone cement into the paravertebral tissues. In a few cases the leakage of polymer caused compression of spinal nerve roots or neuralgia, and several instances of pulmonary embolism were also reported. The degree of filling of the lytic lesion did not appear to correlate with the degree of pain relief, suggesting that complete filling of the lesion is not required.

Patient selection criteria

Percutaneous vertebroplasty is considered an appropriate treatment for patients with vertebral lesions resulting from osteolytic vertebral metastasis and myeloma, vertebral hemangioma, and osteoporotic compression fracture if the following criteria have been met:[1,2,10]

- Pain is severe and debilitating, and cannot be relieved by correct medical therapy.
- Other causes of pain, such as herniated intervertebral disk, have been ruled out by CT or magnetic resonance imaging.
- The affected vertebra has not been extensively destroyed and is at least one third of its original height.

Vertebroplasty is contraindicated in patients with infection in the area and in patients with coagulation disorders due to the large diameter of the needles used for injection. Some authors consider destruction of the posterior wall of the vertebral body to be a relative contraindication: extreme caution must be used in these patients during cement injection to prevent new or further neurologic compression that might result from leakage of the acrylic polymer into the epidural space. In some cases, radiation therapy or concurrent surgical intervention, such as laminectomy, may also be required in patients with compression of the spinal cord due to ingrowth of a tumor.[1,2,10]

Several experts in this field stress that the decision to perform vertebroplasty should be made by a multidisciplinary team because the choice between vertebroplasty, surgery, radiation therapy, medical treatment, or a combination of these therapies depends on a number of factors. These factors include the local and

general extent of the disease, the spinal level involved, and the pain experienced by the patient as well as his or her neurological condition, state of health, and life expectancy.[1,2]

Complications

While the overall risk is relatively low, potential complications associated with percutaneous vertebroplasty include bleeding at the puncture site, transitory worsening of pain and fever in the hours following injection due to the heat generated during polymerization, bone infection or fracture, damage to nerve roots or the spinal cord, with potential radiculopathy or paralysis, leakage of material into the epidural or paravertebral spaces, and passage of material into the venous system with embolization to the pulmonary vasculature or compression of neural tissue.[2] Padovani et al. (1999), reporting on a case of pulmonary infarction associated with embolism of acrylic material during a vertebroplasty procedure, hypothesizes that insufficient polymerization of the acrylic at the time of injection can allow migration into the inferior vena cava and the pulmonary arteries.[11] Gangi et al. (1999), in describing outcome of percutaneous vertebroplasty in a large series of patients, states that the following elements are necessary to avoid complications with the procedure and improve outcome: (1) appropriate patient selection; (2) adequate radiographic and fluoroscopic guidance to ensure correct needle placement; (3) injection of cement at the proper stage of polymerization to avoid leakage or embolism; and (4) sufficient operator training.[10]

Toxicity

There have been concerns related to the potential toxicity of the acrylic substances used as bone cement, both for the patient and for the medical personnel who are exposed to the vapor during a percutaneous vertebroplasty procedure. Cloft et al. (1999) addressed the issue of occupational exposure using air-sampling pumps during five vertebroplasty procedures. These samples yielded methyl methacrylate vapor levels of less than 5 ppm, well below the recommended maximum exposure of 100 ppm/day.[12]

Several in vitro studies have addressed the question of whether the heat generated by the exothermic reaction during polymerization of the acrylic bone cement could injure tissue surrounding the injection site. Deramond et al. (1999) measured the temperature in postmortem vertebrae during injection of two types of bone cement. While the temperature rose above 50°C within the vertebral bodies, the temperature within the spinal canal did not rise above 41°C, and the authors concluded that it is unlikely that any thermal damage to the spinal cord would occur during cement polymerization.[13] In a postmortem examination of the vertebrae of six patients who had undergone percutaneous vertebroplasty, San Millán Ruíz et al. (1999) found that the bone cement had a necrotizing effect on tumor tissue within and directly around the implant. This effect was particularly prominent with injection of polymethyl-methacrylate (PMMA) compared with N-buyl-cyano-acrylate (NBCA), which these authors hypothesize was due to the increased toxicity of PMMA, and the higher degree of exothermic reaction during polymerization.[14]

Mechanism of pain relief

The mechanism of pain relief experienced by patients who undergo vertebroplasty has not been well elucidated. While many investigators have concluded that the pain relief is due primarily to the mechanical support provided by the bone cement, some have hypothesized that other factors, such as nerve damage resulting from heat generated during the exothermic polymerization of PMMA or from toxicity caused by the unpolymerized monomer may also play a role in reducing pain perception.[15]

Technical issues

Clinicians who perform vertebroplasty commonly alter the monomer-to-powder ratio recommended by the manufacturer in an effort to decrease viscosity and increase the time before the mixture begins to harden. Jasper et al. (1999) demonstrated that this practice alters the compressive material properties of the cement, resulting in as much as a 24 percent decrease in strength. However, it is not known if this decrease in material strength could have clinically significant adverse effects on the outcome or durability of the treatment.[16]

There is no long-term clinical evidence to prove that injection of bone cement into lytic or osteoporotic lesions will prevent further compression and fracture. However, Tohmeh et al. (1999), in an postmortem study using 10 spines, demonstrated that injection of cement into osteoporotic vertebral bodies restored strength and stiffness, and that unipedicular injection was as effective as bipedicular injection. This study suggests that percutaneous vertebroplasty can increase the mechanical strength of osteoporotic vertebrae.[15]

Cost-effectiveness

There are no published studies that address the cost-effectiveness of percutaneous vertebroplasty. However, percutaneous vertebroplasty is a minimally invasive procedure, and generally does not require either general anesthesia or lengthy hospitalization, therefore the costs are relatively low compared with open surgical interventions for vertebral compression fractures, such as internal fixation and spinal fusion.

Future research

Although early evidence suggests that percutaneous vetebroplasty with acrylic polymers is a relatively suc-

cessful treatment, new biomaterials for bone augmentation are currently being developed to address complications associated with injection of these compounds and with the long-term presence of a synthetic material within the body. Several biodegradable materials are under investigation, including an injectable, nonexothermic, carbonated, apatitic bone mineral substitute intended to be chemically similar to the mineral composition of bone. Other products, such as a hydroxyapatite material that can serve as a matrix for new bone ingrowth, and a synthetic graft substitute made of bovine Type I collagen, hydroxyapatite, and tricalcium phosphate are also being tested as a way to augment the spine and induce new bone growth. While these compounds have not yet been tested clinically, results of a recent in vitro study indicate that a biodegradable calcium phosphate bone substitute can be as effective as acrylic bone cement in strengthening osteoporotic vertebral bodies.[17,18] These products would reduce the potential complications associated with acrylic bone cement, including thermal damage to the neural elements during polymerization of the acrylic compound and negative effects on bone remodeling. Ideally, these biodegradable materials would increase the strength of the vertebral body, degrade when the fracture repair is completed, and eventually be replaced by new bone growth.

Conclusions

Percutaneous vetebroplasty only recently has been introduced as a treatment for osteolytic lesions and osteoporotic compression fractures of the vertebrae, but early results are promising. Up to 80 percent of patients with pain unresponsive to correct medical treatment experience a significant degree of pain relief, and few serious complications have been reported. However, a limited number of patients have undergone this procedure, and there are no data from controlled clinical trials or from studies with long-term follow-up. At the present time percutaneous vertebroplasty is considered an investigational procedure, and is in the early stages of development, but may be appropriate for patients with no other reasonable options for medical treatment.

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