Percutaneous Vertebroplasty and Sacroplasty

Description

Percutaneous vertebroplasty is an interventional technique involving the fluoroscopically guided injection of polymethylmethacrylate (PMMA) through a needle inserted into a weakened vertebral body. The technique has been investigated as an option to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture or in those with osteolytic lesions of the spine, ie, multiple myeloma or metastatic malignancies. Percutaneous vertebroplasty has also been investigated as an adjunct to surgery for aggressive vertebral body hemangiomas, as a technique to limit blood loss related to surgery. Injection of PMMA is also being investigated for the treatment of sacral insufficiency fracture.

Background

Percutaneous Vertebroplasty

It has been proposed that vertebroplasty may provide an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body. However, other possible mechanisms of effect have been postulated, including thermal damage to intraosseous nerve fibers.

Percutaneous Sacroplasty

Sacroplasty evolved from the treatment of insufficiency fractures in the thoracic and lumbar vertebrae with vertebroplasty. The procedure, essentially identical, entails guided injection of PMMA through a needle inserted into the fracture zone. While first described in 2000 as a treatment for symptomatic sacral metastatic lesions, (1,2) it is most often described as a minimally invasive procedure employed as an alternative to conservative management (3-5) for sacral insufficiency fractures (SIFs). SIFs are the consequence of excessive stress on weakened bone and are often the cause of low back pain among the elderly. Osteoporosis is the most common risk factor for SIF.

Osteoporotic Vertebral Compression Fracture

Osteoporotic compression fractures are a common problem, and it is estimated that up to one half of women and approximately one quarter of men will have a vertebral fracture at some point in their lives. However, only about one third of vertebral fractures actually reach clinical diagnosis, and most symptomatic fractures will heal within a few weeks or 1 month. However, a minority of patients will exhibit chronic pain following osteoporotic compression fracture that presents
challenges for medical management. Chronic symptoms do not tend to respond to the management strategies for acute pain such as bed rest, immobilization/bracing device, and analgesic medication, sometimes including narcotic analgesics. The source of chronic pain after vertebral compression fracture may not be from the vertebra itself but may be predominantly related to strain on muscles and ligaments secondary to kyphosis. This type of pain frequently is not improved with analgesics and may be better addressed through exercise.

Sacral Insufficiency Fractures
Spontaneous fracture of the sacrum in patients with osteoporosis was described by Lourie in 1982 and presents as lower back and buttock pain with or without referred pain in the legs. (6, 7) Although common, SIFs can escape detection due to low provider suspicion and poor sensitivity on plain radiographs, slowing the application of appropriate intervention. Similar interventions are used for sacral and vertebral fractures including bed rest, bracing and analgesics. Initial clinical improvements may occur quickly; however, the resolution of all symptoms may not occur for 9 to 12 months. (6, 8)

Vertebral/Sacral Body Metastasis
Metastatic malignant disease involving the spine generally involves the vertebrae/sacrum, with pain being the most frequent complaint. While radiation and chemotherapy are frequently effective in reducing tumor burden and associated symptoms, pain relief may be delayed days to weeks, depending on tumor response. Further, these approaches rely on bone remodeling to regain strength in the vertebrae/sacrum, which may necessitate supportive bracing to minimize the risk of vertebral/sacral collapse during healing.

Vertebral Hemangiomas
Vertebral hemangiomas are relatively common lesions noted in up to 12% of the population based on autopsy series; however, only rarely do these lesions display aggressive features and produce neurologic compromise and/or pain. Treatment of aggressive vertebral hemangiomas has evolved from radiation therapy to surgical approaches using anterior spinal surgery for resection and decompression. There is the potential for large blood loss during surgical resection, and vascular embolization techniques have been used as adjuncts to treatment to reduce blood loss. Percutaneous vertebroplasty has been proposed as a way to treat and stabilize some hemangioma to limit the extent of surgical resection and as an adjunct to reduce associated blood loss from the surgery.

Regulatory Status
Vertebroplasty is a surgical procedure and, as such, is not subject to U.S. Food and Drug Administration (FDA) approval. PMMA bone cement was available as a drug product prior to enactment of the FDA’s device regulation and was at first considered what the FDA terms a “transitional device.” It was transitioned to a class III device requiring premarketing applications. Several orthopedic companies have received approval of their bone cement products since 1976. In October 1999, PMMA was reclassified from class III to class II, which requires future 510(k) submissions to meet “special controls” instead of “general controls” to assure safety and effectiveness. Thus, use of PMMA in vertebroplasty represented an off-label use of an FDA-regulated product before 2005. In 2005, PMMA bone cements such as Spine-Fix® Biomimetic Bone Cement
and Osteopal® V were issued 510(k) marketing clearance for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures.

The use of PMMA in sacroplasty represents an off-label use of an FDA-regulated product (bone cements such as Spine-Fix® Biomimetic Bone Cement and Osteopal® V), as the 510(k) marketing clearance was for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures. Sacroplasty was not included. FDA product code: NDN

ArthroCare received FDA clearance for the Parallax® Contour® Vertebral Augmentation Device in 2010. The device creates a void in cancellous bone that can then be filled with bone cement. FDA product code: HXG

Vesselplasty using Vessel-X®, (MAXXSPINE) and a similar procedure from A-Spine, are variations of vertebroplasty that are reported to eliminate leakage of bone cement by containing the filler in an inflatable vessel. These devices do not have clearance for marketing by the FDA.

Related Policies

6.01.23    Diagnosis and Treatment of Sacroiliac Joint Pain
6.01.38  Percutaneous Balloon Kyphoplasty and Mechanical Vertebral Augmentation

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Percutaneous vertebroplasty may be considered medically necessary for the treatment of symptomatic osteoporotic vertebral fractures that have failed to respond to conservative treatment (e.g., analgesics, physical therapy and rest).

Percutaneous vertebroplasty may be considered medically necessary for the treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies.

Percutaneous vertebroplasty is considered investigational for all other indications.

Percutaneous sacroplasty is considered investigational for all indications, including use in sacral insufficiency fractures due to osteoporosis and spinal lesions due to metastatic malignancies or multiple myeloma.

Policy Guideline

If this is a non-traumatic vertebral fracture it should be evaluated for osteoporosis.

Rationale

For treatment of osteoporosis and malignancy with percutaneous vertebroplasty or sacroplasty, the primary beneficial outcomes of interest are relief of pain and improvement in ability to function.
Ex vivo cadaver studies reporting bone strength as a surrogate outcome measure have been reported but are not included in this evaluation of health outcomes. In treatment of aggressive hemangioma, the primary benefits of percutaneous vertebroplasty include relief of pain and reduction of blood loss associated with surgical treatment.

Pain and functional ability are subjective outcomes and, thus, may be susceptible to placebo effects. Furthermore, the natural history of pain and disability associated with these conditions may be variable. Therefore, controlled comparison studies would be valuable to demonstrate the clinical effectiveness of vertebroplasty and sacroplasty over and above any associated nonspecific or placebo effects and to demonstrate the effect of treatment compared to alternatives such as continued medical management.

In all clinical situations, adverse effects related to complications from vertebroplasty and sacroplasty are the primary harms to be considered. Principal safety concerns relate to the incidence and consequences of leakage of the injected PMMA.

**Percutaneous Vertebroplasty**

The evidence on this question consists of a number of randomized clinical trials (RCTs), 2 of which included a sham control, and many case series. The Blue Cross and Blue Shield Association (BCBSA) Technology Evaluation Center (TEC) Assessments from 2000 through 2010 (9-14) relied on available data that was observational. The largest of the case series reported results from a prospectively collected database with 552 patients from a large academic department. (15) Evidence from observational studies were generally consistent in showing significant decreases in pain from an initial preoperative level of 8 to 9 on a visual analog scale (VAS, or similar score proportionate to the highest possible score) to 2 to 4, typically within 1 day of receiving the procedure. Such pain relief appeared to be lasting in the limited studies that reported long-term outcomes. In terms of adverse outcomes, leakage of the cement outside of the vertebral body was a common event, occurring in between 19% and 72% in studies that reported its occurrence.

Beginning in 2007, data from RCTs began appearing in the literature. This policy is focused on RCT data.

**RCTs of Vertebroplasty versus Medical Management with Sham Controls**

In 2009, 2 RCTs compared vertebroplasty with a medical management using a sham procedure (that included local anesthetic) that mimicked the vertebroplasty procedure up to the point of cement injection. (16, 17) Buchbinder et al reported results of a 4-center, randomized, double-blind, sham-controlled trial that was designed to determine short-term efficacy and safety of vertebroplasty for alleviating pain and improving physical functioning in persons with painful osteoporotic vertebral fractures. A total of 78 participants with 1 or 2 painful osteoporotic vertebral fractures of duration less than 1 year were assigned to undergo vertebroplasty or sham procedure (ie, injection of local anesthetic into the facet capsule and/or periosteum). (16) Ninety-one percent of participants completed 6-month follow-up. The participants, investigators (other than the radiologists performing the procedure), and outcome assessors were blind to the treatment assignment. Blinding was maintained through 24-month follow-up of this trial. (18)
Recruitment took place within the practices of both general practitioners and specialists from hospital inpatient and emergency departments. In general, participants were required to have back pain of no more than 12 months and the presence of at least 1 but no more than 2 recent vertebral fractures. Participants were evaluated at baseline, then with a mailed questionnaire at 1 week and 1, 3, and 6 months after the procedure. The primary outcome was overall pain (over the course of the previous week) measured on a 0 to 10 VAS, with 1.5 representing the minimal clinically important difference. A sample size of 24 per group was calculated to provide 80% power with 2-sided α of 0.05 to show a 2.5-point post-procedure difference assuming a 3-point standard deviation (SD). All analyses were performed according to intention-to-treat principles. Results are presented as difference from baseline. For the primary outcome of overall pain, the authors reported no significant difference in VAS pain score at 3, 12 or 24 months. With reductions in pain and improvements in quality of life observed in both groups, the authors concluded vertebroplasty provided no benefit.

There was considerable variability in pain scores, which may in part be due to a lack of minimum pain score at entry. The primary outcome measure was the mean difference in VAS from baseline. For some continuous outcomes, pain being one, there is a magnitude of improvement that is clinically meaningful on an individual level; someone achieving that minimal change can be considered a responder. Under these circumstances, a fundamental limitation of continuous effect measures is failing to identify the proportion of patients experiencing a meaningful clinical response. (19) Because a clinically meaningful important improvement has been established, the proportion of patients responding is the most informative outcome that can supplement and extend the comparison of mean differences. (20) Moreover, when considered in this manner, response or meaningful improvement (2.5 on the VAS) in overall pain at 1, 3, 6, 12 and 24 months tended to be more frequent with vertebroplasty—respective relative risks (RRs) of 1.2 (95% confidence interval [CI], 0.7 to 2.0), 1.5 (95% CI, 0.9 to 2.6), 1.3 (95% CI, 0.8 to 2.1), 1.19 (95% CI, 0.7 to 2.1), and 1.31 (95% CI, 0.8 to 2.1). However, detecting an increase in response from 40% (sham) to 60% with 80% power would have required a sample exceeding 200 participants. Also, at entry, many participants had experienced pain longer than 3 months; (21) suggesting that the VAS may not be as responsive as other measures for these patients. (21) This adds to the uncertainty as to whether a mean change in VAS will capture clinically meaningful improvement.

Kallmes et al also conducted a multicenter, randomized, double-blind, sham-controlled trial (INVEST) in which 131 participants with 1 to 3 painful osteoporotic vertebral fractures were assigned to undergo vertebroplasty or sham procedure (injection of local anesthetic into the facet capsule and/or periosteum). (17) Participants had back pain for no more than 12 months and had a current pain rating of at least 3 on VAS at baseline. Participants were evaluated at baseline, then again at various time points to 1-year post-procedure. Ninety-seven percent completed a 1-month follow-up, and 95% completed 3 months. The primary outcomes were scores on the Roland-Morris Disability Questionnaire (RMDQ) and average back pain intensity during the preceding 24 hours at 1 month, with a reduction of 30% on the RMDQ and VAS pain was considered a clinically meaningful difference. (22) The study initially had 80% power to detect differences in both primary and secondary outcomes with 250 patients, with a 2-sided α of 0.05 on the basis of a 2.5-unit advantage for vertebroplasty over placebo on the RMDQ and 1.0 point difference on VAS. After recruitment difficulty and interim analysis on first 90 participants, target sample size was
decreased to 130 participants with 80% power for primary aims maintained. All primary analyses were performed according to intention-to-treat (ITT) principles and results presented as mean score for the RMDQ and pain intensity.

For the primary endpoints at 1 month, there were no significant between group differences. There was a trend toward a higher clinically meaningful improvement in pain at 1 month (30% reduction from baseline) in the vertebroplasty group (64% vs 48%, respectively; p=0.06). At 3 months, 43% from the control group vs 12% in the vertebroplasty group crossed over (p<0.001). The crossovers did not affect study outcomes, as they occurred after the primary outcome assessment. However, significantly more participants in the control group chose to cross over than in the vertebroplasty group. By 1 year 16% of patients who underwent vertebroplasty and 60% of control subjects had crossed over to the alternative procedure (p<0.001). (23) As treated analysis found no significant difference in RMDQ or pain scores between the 2 groups. ITT analysis found a modest 1 point difference in pain rating, but no significant difference in RMDQ. There was a significant difference in the percentage of patients showing a 30% or greater improvement in pain (70% of patients randomized to vertebroplasty vs. 45% of patients randomized to the control group).

Staples et al conducted a patient-level meta-analysis of the 2 sham-controlled trials to determine whether vertebroplasty is more effective than sham in specific subsets of patients. (24) This subset analysis focused on duration of pain (<6 weeks vs. >6 weeks) and severity of pain (score <8 or ≥8 on an 11-point numeric rating scale). Included in the analysis were 209 participants (78 from the Australian trial and 131 from the U.S. trial); 27% had pain of recent onset and 47% had severe pain at baseline. The primary outcome measures, pain scores and function on the RMDQ at 1 month, were not significantly different between groups. Responders' analyses were also conducted based on a 3-unit improvement in pain scores, a 3-unit improvement on the RMDQ, and a 30% improvement in each of the pain and disability outcomes. The only difference observed between groups was a trend for a higher proportion of the vertebroplasty group to achieve at least 30% improvement in pain scores (RR= 1.32; 95% CI, 0.98 to 1.76, p=0.07), a result that may have been confounded by the greater use of opioid medications in that group. Overall, this analysis does not support the hypothesis that selected subgroups of patients, including those with pain of 6 weeks’ duration or less or those with severe pain, would benefit from vertebroplasty.

**RCTs of Vertebroplasty versus Medical Management without Sham Controls**

VERTOS II, reported by Klazen et al in 2010, was an open-label prospective randomized trial of 202 patients at 6 hospitals in the Netherlands and Belgium. (25) Participants with at least 1 painful osteoporotic vertebral fracture of duration of 6 weeks or less in duration were assigned to undergo vertebroplasty or conservative management (ie, bed rest, analgesia, cast, physical support). Ninety-three participants received vertebroplasty, while 95 received conservative management; 81% of participants completed 1-year follow-up. The trial was designed to assess the efficacy of vertebroplasty compared to conservative management for the treatment of osteoporotic vertebral compression fractures. There was no blinding of participants, investigators, or outcome assessors to treatment assignment, due to the lack of a sham procedure.

Participants were recruited after referral from their primary care provider for spine radiography because of back pain. In general, participants were required to be at least 50 years of age or older,
have compression fracture with height loss of the vertebral body of at least 15% on x-ray of the spine, the level of fracture was T5 or lower back with pain of a duration of 6 weeks or less with a severity of at least 5 on the VAS. Participants were clinically evaluated at baseline, 1 day, 1 week, 1 month, 3 months, 6 months and 12 months after treatment. Primary outcome was pain relief at 1 month and 12 months measured on a 10-point VAS scale. A sample size of 100 per group was calculated to provide 80% power with an α of 0.05 to show a 25% difference in pain relief. All analyses were performed according to intention-to-treat principles. Clinically significant pain relief was defined as 30% change on the VAS (0-10 scale).

One hundred and one subjects were enrolled into the treatment group and 101 into the control arm; 81% completed 12 months’ follow-up. Except for the primary outcome, difference in mean pain score from baseline at 3 months and 12 months, vertebroplasty resulted in greater pain relief than did medical management at 1 month and 1 year; there were significant between group differences at 1 month (2.6; 1.74 to 3.37, p<0.001) and at 1 year (2.0; 1.13 to 2.80, p<0.001). Survival analysis showed significant pain relief was quicker (29.7 vs 115.6 days) and was achieved in more patients after vertebroplasty than after conservative management. There was cement leakage in 72% of patients after vertebroplasty, with all patients remaining asymptomatic, and at a mean of 11.4 months’ follow-up, there was no significant difference in number of new fractures between groups, with 18 new fractures in 15 patients who had vertebroplasty compared to 30 new fractures in 21 participants undergoing medical management.

A methodologic strength of this study is the study’s focus on acute fracture, a subset of those with osteoporotic vertebral compression fractures, while other studies (Buchbinder et al 2009; Kallmes et al 2009) enrolled participants with pain out to 1 year. The inclusion of both chronic and acute fractures may mask the efficacy of the procedure in one subset. Klazen et al also provided an a priori definition of clinically significant change in pain as one that registered a 30% difference on the 10-point VAS. These data were incorporated as events in a survival analysis as part of the analysis of the primary outcome.

A subsequent report from the VERTOS II study described the 12-month natural history of pain in patients in the conservative treatment arm. (26) Patients in the control arm were followed until pain relief was achieved, defined as a VAS score of 3 or less. Results were analyzed by Kaplan-Meier survival analysis. By 12-month follow-up, 57 of 95 patients (60%) were considered to have sufficient pain relief, with most experiencing sufficient pain relief in the first 3 months. Comparison by logistic regression analysis with the 38 patients (40%) who still had pain (VAS >4) at 12 months did not reveal any significant differences between the groups for the clinical and imaging factors that were evaluated.

Chen et al reported a nonblinded RCT of vertebroplasty compared with conservative management in 2014. (27) The study included 89 patients with chronic compression fractures confirmed by MRI and persistent severe pain for 3 months or longer. Evaluation was performed at 1 week and at 1, 3, 6, and 12 months. Over the course of the year, pain scores decreased from 6.5 to 2.5 in the vertebroplasty group and from 6.4 to 4.1 in the control group (p < 0.001). Complete pain relief was reported by 84.8% of patients in the vertebroplasty group compared with 34.9% of controls. The final ODI score was 15.0 in the vertebroplasty group and 32.1 in the conservative management group (p < 0.001).
and the final Roland Morris Disability Score was 8.1 for vertebroplasty and 10.7 for controls (p < 0.001).

In 2011, Farrokhi et al reported a randomized trial that compared vertebroplasty with optimal medical management in 82 patients. (28) Patients had painful osteoporotic vertebral compression fractures that were refractory to analgesic therapy for at least 4 weeks and less than 1 year. The patients and the physicians involved in the treatment of the patients were not aware of the treatment that the other group was receiving. Control of pain and improvement in quality of life were measured by independent raters before treatment and at 1 week and 2, 6, 12, 24, and 36 months after the beginning of treatment. Radiological evaluation to measure vertebral body height and correction of deformity was performed before and after treatment and after 36 months of follow-up. At 1 week, the mean VAS score decreased from 8.4 to 3.3 in the vertebroplasty group and from 7.2 to 6.4 in the conservative management group, with between group differences that remained significant through 6 months of follow-up. Group differences on the Oswestry Disability Index lower back pain score were significantly lower in the vertebroplasty group throughout the 36 months of the study. New symptomatic adjacent fractures developed in 1 patient (2.6%) in the vertebroplasty group and 6 patients (15.4%) in the conservative management group. In 1 patient, epidural cement leakage caused severe lower extremity pain and weakness that was treated with bilateral laminectomy and evacuation of bone cement.

Rousing et al (29) reported on a nonblinded RCT in which participants were randomized to either vertebroplasty or conservative management. These participants had no conservative therapy prior to enrolling in the trial. The study enrolled 40 participants with acute fractures and 10 with subacute (2–8 weeks). While immediate pain relief was observed in the vertebroplasty group, reductions in pain from baseline to 3-month follow-up were similar in the 2 groups. The authors concluded that conservative management should be used in the acute phase. The primary limitations of this study include its small size and incomplete pain assessment at the baseline visit.

The VERTOS study was a small randomized clinical trial of 34 patients. (30) Patients had been refractory to medical management for at least 6 weeks and no longer than 6 months. The authors noted that many patients had been referred for vertebroplasty following failed conservative treatment and did not want to be randomized to the optimized medication control group or chose to crossover to vertebroplasty after only 2 weeks of conservative treatment. Thus, the follow-up in the study was very short. Vertebroplasty was found to decrease analgesic use (1.9 to 1.2 vs 1.7 to 2.6 in the optimized medication group) and resulted in a 19% improvement in the RMDQ (vs -2% in controls) 2 weeks following the procedure. Excluding 2 patients (11%) who had adjacent vertebral compression fractures by the 2-week follow-up, mean VAS scores for pain decreased from 7.1 to 4.4 (vs. 7.6 to 6.4 for controls). Patients who crossed over from conservative management to vertebroplasty had improvements after the procedure.

Section Summary: Despite the completion of 5 RCTs, including 2 with sham control, the efficacy of vertebroplasty for painful osteoporotic compression fractures remains uncertain. The 2 randomized, sham-controlled trials concluded that vertebroplasty showed no significant benefit above sham for painful osteoporotic fractures. However some uncertainty remains around the interpretation of their conclusions. While the use of a sham procedure is a major methodologic strength to control for nonspecific (placebo) effects, the sham used in the trial is not without controversy, as it might be
considered an active control, given that the effect of injecting local anesthetic in the facet capsule and/or periosteum is unknown. Without a clear understanding of the short- and long-term effects of the injection on pain, questions will remain. Also, both trials were underpowered to observe and compare the proportion of participants experiencing a clinically meaningful difference in pain, which is the most clinically relevant outcome measure. Furthermore, the responder outcome measures in both trials showed trends toward an improvement in the rate of meaningful clinical response, although the differences between groups were not statistically significant.

In contrast, other RCTs without sham control report that vertebroplasty is associated with significant improvements in pain. Three of the 4 trials were small, and the studies included populations with different time periods of symptoms and different prior treatments. It is possible that the effect reported in these non-sham controlled trials is due to a placebo effect, given that these studies were not blinded and the outcome of pain is a subjective, patient-reported outcome that is prone to the placebo effect. It is also possible that the differences in these trials represents a true treatment effect and that the sham control had a therapeutic effect in reducing short-term pain, thus obscuring any impact of vertebroplasty.

**Other Studies**

Although not randomized, there was one other comparative study specifically aimed at patients with acute fracture. Diamond et al enrolled 79 consecutive patients with acute vertebral fractures. (31) All patients were offered vertebroplasty, and those who declined followed as a comparison group. The two groups had balanced baseline characteristics. At 24 hours, the group undergoing vertebroplasty (n=55) had much improved pain compared to the control group (n=24). However, at 6 weeks and between 6 and 12 months, there were no differences between groups in pain scores. The control group had an identical mean pain score to the vertebroplasty group at the end of follow-up. Similar findings were shown for the Barthel index of physical functioning. At long-term follow-up, there was still slightly higher functioning in the group undergoing vertebroplasty but no difference in the percent improvement from baseline between groups. The authors interpreted these findings as demonstrating that vertebroplasty produced faster resolution of symptoms than conservative management, as was shown in the Klazen trial.

In 2011, Edidin et al reported mortality risk in Medicare patients who had vertebral compression fractures and had been treated with vertebroplasty, kyphoplasty or nonoperatively. (32) This study was industry-funded. Using the U.S. Medicare data set, they identified 858,978 patients who had vertebral compression fractures between 2005 and 2008. The data set included 119,253 kyphoplasty patients and 63,693 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to 4 years). Cox regression was used to evaluate the joint effect of multiple covariates, which included sex, age, race/ethnicity, patient health status, type of diagnosed fracture, site of service, physician specialty, socioeconomic status, year of diagnosis, and census region. After adjusting for covariates, patients in the operated cohort (vertebroplasty or kyphoplasty) were found to have a higher adjusted survival rate (60.8%) than patients in the nonoperated cohort (50.0%) and were 37% less likely to die. The adjusted survival rates for vertebroplasty or kyphoplasty were 57.3% and 62.8%, respectively, a 23% lower relative risk for kyphoplasty. As noted by the authors, a causal relationship cannot be determined from this study.
Adverse Events

Yi et al assessed the occurrence of new vertebral compression fractures after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) versus conservative treatment in a randomized controlled trial with 290 patients (363 affected vertebrae). (33) Surgically treated patients were discharged the next day. Patients treated conservatively (offered pain medication, bed rest, a body brace, and physiotherapy) had a mean length of stay of 13.7 days. Return to usual activity occurred at 1 week for 87.6% of operatively-treated patients and at 2 months for 59.2% of conservatively-treated patients. All patients were evaluated with radiographs and MRI at 6 months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80), 10.7% of patients had experienced 42 new symptomatic vertebral compression fractures. There was no significant difference in the incidence of new vertebral fractures between the operative (18 total, 9 adjacent and 9 nonadjacent) and conservative (24 total, 5 adjacent, 16 nonadjacent, and 3 same level) groups, but the mean time to a new fracture was significantly shorter in the operative compared to nonoperative group (9.7 vs 22.4 months).

A systematic review of the safety and efficacy of vertebroplasty in malignancy was reported by Chew et al in 2011. (34) Thirty relevant studies were identified, totaling 987 patients. Included in the review were a single randomized controlled trial and 7 prospective studies. Most centers reported treating no more than 4 vertebrae per session. Pain reduction ranged between 20% to 79%. Five deaths were attributable to vertebroplasty, 2 from chest infections following general anesthesia, 1 from a cement pulmonary embolus, and 2 from sepsis after emergency spinal decompression. Another 19 patients suffered a serious complication related to the procedure, with 13 requiring emergency spinal decompression. Reports of complications occurred in studies with a mean cement volume of more than 4 mL, suggesting a possible association between the volume of cement injected and adverse events.

In 2012, Wang et al reported a systematic review of pulmonary cement embolism (PCE) associated with percutaneous vertebroplasty. (35) PCE was noted in 50 cases in observational studies, with a reported incidence ranging from 2.1% in retrospective observational studies to 26% in prospective observational studies that had standard post procedural chest. There were an additional 34 patients identified from case reports with PCE, 30 of whom were symptomatic. Five deaths due to PCE after vertebroplasty have been reported.

Percutaneous Sacroplasty

Sacroplasty is an evolving technique with numerous methods (short axis, long axis, balloon-assisted short axis, and iliosacral screws). No randomized trials of sacroplasty have been reported. The largest prospective report is an observational cohort study of 52 consecutive patients undergoing sacroplasty for sacral insufficiency fractures using the short axis technique. (36) Patients had a mean age of 75.9 years and a mean duration of symptoms of 34.5 days (range: 4-89 days) and mean VAS score of 8.1 at baseline. Improvement on the VAS scale was measured at 30 minutes and 2, 4, 12, 24, and 52 weeks postprocedure. At each interval, statistically significant improvement over baseline was observed and maintained through 52 weeks.
The largest series is a retrospective multicenter analysis of 204 patients with painful sacral insufficiency fractures and 39 patients with symptomatic sacral lesions treated with either the short-axis or long-axis technique. (37) One hundred and sixty-nine patients had bilateral sacral insufficiency fractures and 65 patients had additional fractures of the axial skeleton. VAS improved from 9.2 before treatment to 1.9 after treatment in patients with sacral insufficiency fractures, and from 9.0 to 2.6 in patients with sacral lesions. There was 1 case of radicular pain due to extravasation of cement requiring surgical decompression.

There are several retrospective reviews with about 50 patients each. One of these described a series of 57 patients treated with sacroplasty for sacral insufficiency fractures. (38) The short- or long-axis approach was dictated by the length and type of the fracture and patient anatomy. Follow-up data at 2.5 weeks was available for 45 patients (79%), and the outcome measures were inconsistent. For example, activity pain scores were collected from 13 patients, and rest pain scores were collected from 29 patients. Of the 45 patients with outcome data, 37 (82%) were reported to have experienced either a numerical or descriptive decrease from initial pain of at least 30%.

Additional literature reports are mostly consistent reporting immediate improvement following the procedure. Due to the small size of the evidence base, harms associated with sacroplasty have not been adequately studied. There are complications of cement leakage with sacroplasty that are not observed with vertebroplasty. Leakage of polymethylmethacrylate (PMMA) into the presacral space, spinal canal, sacral foramen, or sacroiliac joint may result in pelvic injection of PMMA, sacral nerve root or sacral spinal canal compromise, or sacroiliac joint dysfunction. (39) Performing sacroplasty only on zone 1 fractures only can minimize these risks. (40)

**Ongoing and Unpublished Clinical Trials**

Ongoing trials that might influence this policy are listed in Table 1.

<table>
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<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>April 2018</td>
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<td>NCT01200277</td>
<td>A randomized sham controlled trial of vertebroplasty for painful acute osteoporotic vertebral fractures</td>
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<td>January 2014</td>
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NCT: national clinical trial

**Practice Guidelines and Position Statements**

In 2012, a joint practice guideline on the performance of vertebral augmentation was published by the American College of Radiology (ACR), the American Society of Neuroradiology (ASN), the American Society of Spine Radiology (ASSR), the Society of Interventional Radiology (SIR), and the Society of Neurointerventional Surgery (SNIS). Methods to achieve internal vertebral body stabilization include vertebroplasty, balloon kyphoplasty, radiofrequency ablation and coblation, mechanical void creation, and injection of bone graft material or bone substitutes. The ACR, ASN, ASSR, SIR, and SNIS
consider vertebral augmentation to be an established and safe procedure and provide guidelines for appropriate patient selection, qualifications and responsibilities of personnel, specifications of the procedure, equipment quality control, and quality improvement and documentation. This guideline addresses vertebral augmentation in general and refers to all percutaneous techniques used. (41)

These societies (ACR, ASN, ASSR, SIR, and SNIS) published a joint position statement on percutaneous vertebral augmentation in 2014. It is the position of the societies that percutaneous vertebral augmentation with the use of vertebroplasty or kyphoplasty is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures, when performed in a manner in accordance with public standards. The document also states that these procedures are offered only when nonoperative medical therapy has not provided adequate pain relief or pain is significantly altering the patient’s quality of life. (42)

In a 2014 quality improvement guideline from SIR, failure of medical therapy is defined as follows (43):

1. For a patient rendered nonambulatory as a result of pain from a weakened or fractured vertebral body, pain persisting at a level that prevents ambulation despite 24 hours of analgesic therapy;
2. For a patient with sufficient pain from a weakened or fractured vertebral body that physical therapy is intolerable, pain persisting at that level despite 24 hours of analgesic therapy; or
3. For any patient with a weakened or fractured vertebral body, unacceptable side effects such as excessive sedation, confusion, or constipation as a result of the analgesic therapy necessary to reduce pain to a tolerable level.

In 2013, the American College of Radiology (ACR) updated their appropriateness criteria on the management of compression fractures. The criteria for management of these fractures state that most vertebral compression fractures are resolved within 4 to 6 weeks with the more conservative first-line treatment including the use of NSAIDS and possibly narcotic medications, and that vertebroplasty should be reserved for patients that either have failed or cannot tolerate traditional conservative treatment. (44)

In 2010, the American Academy of Orthopaedic Surgeons (AAOS) Board of Directors approved a new clinical practice guideline on the treatment of osteoporotic spinal compression fractures, which is available online. The Board approved a strong recommendation against the use of vertebroplasty for patients who “present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically “intact.” In coming out with a strong recommendation, the committee expressed their confidence that future evidence is unlikely to overturn the existing evidence. As a note, these recommendations were based on a literature review through September 2009; therefore, the Klazen et al trial was not included in the systematic review. (45)

The United Kingdom’s National Institute for Health and Care Excellence (NICE) concluded in 2003 that the current evidence on the safety and efficacy of vertebroplasty for vertebral compression fractures appears adequate to support the use of this procedure to provide pain relief for people with severe painful osteoporosis with loss of height and/or compression fractures of the vertebral
body. (46) The guidance recommends that the procedure be limited to patients whose pain is refractory to more conservative treatment. Their 2013 technology appraisal guidance TA279 states that percutaneous vertebroplasty and percutaneous balloon kyphoplasty are recommended as treatment options for treating osteoporotic vertebral compression fractures in persons having severe, on-going pain after a recent unhealed vertebral fracture despite optimal pain management and whose pain has been confirmed through physical exam and imaging to be at the level of the fracture. (47)

In 2008, NICE issued CG75 on the diagnosis and management of adults with metastatic spinal cord compression. The guideline states that vertebroplasty or kyphoplasty should be considered for the patients that have vertebral metastases and no evidence of spinal cord compression or spinal instability if they have mechanical pain resistant to conventional pain management and vertebral body collapse. (48)

U.S. Preventive Services Task Force Recommendations

Not applicable

Summary

Vertebroplasty has been investigated as an intervention to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture or in those with osteolytic lesions of the spine, ie, multiple myeloma or metastatic malignancies. After consideration of the available evidence and clinical input, it was concluded that the consistent results of numerous case series, including large prospective reports, together with the results of clinical vetting, were sufficient to determine that vertebroplasty was a reasonable treatment option in patients with vertebral fractures who fail to respond to conservative treatment (at least 6 weeks with analgesics, physical therapy, and rest). Given the absence of alternative treatment options and the morbidity associated with extended bed rest, vertebroplasty may be considered medically necessary in patients with vertebral fractures who fail to improve after conservative therapy.

Subsequent literature updates performed after 2008, including 2 sham-controlled trials, have raised questions about the efficacy of vertebroplasty for osteoporotic fractures. These trials can be interpreted as showing that vertebroplasty is ineffective. However, alternate interpretations are possible. There are methodologic issues with these studies, including but not limited to the choice of sham procedure and the potential effect of the sham procedure having a therapeutic effect by reducing pain. Also, the appropriateness of chosen outcome measures to detect clinically meaningful differences in pain may not have been optimal, as the studies were underpowered to detect differences in clinical response rates. Because of these uncertainties in the interpretation of the literature, the policy is unchanged.

Sacroplasty is under development. Small numbers of treated patients leaves uncertainty regarding the impact of sacroplasty on health outcomes and does not permit conclusion on its use for sacral insufficiency fractions or other indications. Therefore, percutaneous sacroplasty is considered investigational for all indications, including use in sacral insufficiency fractures due to osteoporosis and spinal lesions due to metastatic malignancies or multiple myeloma.
Medical National Coverage

There is no national coverage determination.

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**Policy History**

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<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tr>
<td>December 2011</td>
<td>New Policy</td>
<td>Policy updated with literature review, References added, reorganized and some removed.  Policy statements unchanged.</td>
</tr>
<tr>
<td>June 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 22, 31, 40-42, 45, and 46 added; policy statements unchanged.</td>
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<tr>
<td>June 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review; references 18 and 27 added; policy statements unchanged.</td>
</tr>
<tr>
<td>June 2015</td>
<td>Update Policy</td>
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**Keywords**

Percutaneous Vertebroplasty
Sacroplasty
Vertebroplasty, Percutaneous

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 193, 2015 and is effective July 15, 2015.

Signature on file
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