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Medical Policy Manual

Topic: Percutaneous Vertebroplasty and Kyphoplasty

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Percutaneous Vertebroplasty and Kyphoplasty

Percutaneous vertebroplasty, vertebral balloon kyphoplasty, and mechanical augmentation have been proposed as options to provide mechanical support and symptomatic pain relief in patients with osteoporotic vertebral compression, insufficiency fractures, vertebral hemangioma, or osteolytic lesions of the spine, i.e., multiple myeloma or metastatic malignancies. These procedures, sometimes referred to as vertebral augmentation, have been used in all levels of the spinal column including the sacrum and coccyx. When vertebroplasty or kyphoplasty is used to treat insufficiency fractures of the sacrum or coccyx they may be referred to as sacroplasty or coccygeoplasty, respectively.

- Percutaneous vertebroplasty is an interventional radiology technique involving the fluoroscopic- or CT-guided injection of polymethylmethacrylate (PMMA) through a needle inserted into a weakened vertebral body.
- Percutaneous kyphoplasty is a variant of vertebroplasty that is intended to restore the vertebral body height and alignment along with stabilizing the fracture, using one of the following techniques:
    - Balloon kyphoplasty involves the use of a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body. PMMA is then injected into the created cavity to stabilize the vertebral body.
    - Mechanical kyphoplasty describes techniques that do not involve a balloon device.

- In radiofrequency kyphoplasty, ultrahigh viscosity cement is injected into the fractured vertebral body. Radiofrequency energy is used to achieve the desired cement consistency. The ultrahigh viscosity cement is intended to restore height and alignment to the fractured vertebra, along with stabilizing the fracture.
- The Kiva® procedure uses an implant inserted into the vertebral body for structural support and to provide a reservoir for injection of bone cement. The proposed benefit of this technique is the adjustable height of the implant, which is made from a biocompatible polymer (e.g., PEEK-OPTIMA®), and a potential reduction in cement leakage.
- Vertebral body stenting utilizes an expandable scaffold instead of a balloon to restore vertebral height. The proposed advantages of vertebral body stenting are to reduce the risk of cement leakage by formation of a cavity for cement application and to prevent the loss of correction that is seen following removal of the balloon used for balloon kyphoplasty.

Although the mechanism is unknown, percutaneous vertebroplasty and kyphoplasty are intended to provide analgesic effect either through mechanical stabilization of a fractured or otherwise weakened vertebral body or through thermal damage to intraosseous nerve fibers, since PMMA undergoes a heat-releasing (exothermic) reaction during its hardening process.

Regulatory Status

Percutaneous vertebroplasty and kyphoplasty are surgical procedures and, as such, are not subject to U.S. Food and Drug Administration (FDA) approval, although the following instruments and materials used within these procedures are subject to FDA approval:

- Various equipment for percutaneous vertebral body access and delivery of bone cement for vertebroplasty have received FDA approval. Also FDA approved is the Parallax® Contour® Vertebral Augmentation device. This device creates a void in cancellous bone that can then be filled with bone cement. The void is created by removal of bone fragments; unlike balloon kyphoplasty, this procedure does not attempt to restore vertebral body height.

- 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.

- Percutaneous kyphoplasty requires the use of an inflatable bone tamp. One such tamp, the KyphX® inflatable bone tamp, received 510(k) marketing clearance from the FDA in July 1998. Other devices with FDA 510(k) marketing clearance include AVAmax® Vertebral Balloon system (Carefusion), NeuroTherm Parallax® Balloon Inflatable Bone Tamp (NeuroTherm, Inc.), Stryker iVAS® Balloon catheter, and Synthes Synflate™ Vertebral Balloon System (Synthes).

- 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. PMMA bone cements such as KyphX® HV-RTM, Spine-Fix® Biomimetic Bone Cement, StabiliT®, and Osteopal® V were

issued 510(k) marketing clearance for the fixation of pathological 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.

- The Kiva® VCF Treatment System (Benvenue Medical) received FDA 510(k) marketing clearance. Vertebral body stenting (VBS™, Synthes) is available only in Europe at this time.

The FDA also issued a "Public Health Web Notification: Complications related to the use of bone cement in vertebroplasty and kyphoplasty procedures," which is available at www.fda.gov/cdrh/safety/bonecement.html. This notification is intended to inform the public about reports on safety and to encourage hospitals and other user facilities to report adverse events related to bone cement malfunctions either directly to manufacturers or to MedWatch, the FDA's voluntary reporting program.

MEDICAL POLICY CRITERIA

I. Percutaneous vertebroplasty or percutaneous balloon kyphoplasty may be considered **medically necessary** for the treatment of *no more than* 3 symptomatic vertebral fractures of the T5-L5 spine, on any single date of service, when **all** of the following criteria are met:

A. Appropriate imaging (plain film x-ray or MRI) has been performed preoperatively and the findings of such imaging correlate unequivocally with the patient's pain; and

B. It has been established in the clinical record that the patient's pain is predominantly, if not solely, related to the demonstrated fracture(s); and

C. Functional impairment attributed to vertebral fracture is documented in the clinical record as limiting performance of instrumental activities of daily living (ADLs). Instrumental ADLs are defined as feeding, bathing, dressing, grooming, meal preparation, household chores, and occupational tasks that are required as a daily part of job functioning.

Clinical records must specifically document the following:

1. The specific instrumental ADL(s) that is impaired; and

2. A description of how performance of the instrumental ADL is limited.

D. The patient has failed to respond to conservative treatment (e.g., analgesics, physical therapy, rest) for at least 6 weeks; and

E. A pre-procedure assessment has documented the absence of the following contraindications:

1. Untreated symptomatic foraminal or canal stenosis, facet arthropathy, or other significant coexistent spinal or bony pain generators

2. Bone fragment retropulsion

3. Symptoms that cannot be related to a fracture

4. Unstable fracture or requirement for stabilization procedure in same or adjacent spinal region

5. Active osteomyelitis whether fungal, bacterial or mycobacterial, or any other active infection, including urinary tract infection (UTI)

6. Presence of painful metastases to areas other than the spine, spinal cord compression, primary bone and osteoblastic tumors, solitary plasmacytomas

7. Uncorrected coagulation disorders

8. Known allergy to any of the materials used in these procedures

9. Chronic (>6 months) fracture at the same vertebral level

II. Percutaneous vertebroplasty or percutaneous balloon kyphoplasty is considered **investigational** for all other indications, including but not limited to the following:

A. Vertebral hemangioma

B. Acute vertebral fractures due to osteoporosis or trauma

C. Vertebrae of the cervical spine and thoracic levels T1-5

D. Stabilization of insufficiency fractures or lesions of the sacrum (sacroplasty) or coccyx (coccygeoplasty)

E. Prophylactic treatment for osteoporosis of the spine or for chronic back pain of long-standing duration, even if associated with old compression fracture(s).

III. Percutaneous mechanical vertebral augmentation using any device other than a balloon device is considered **investigational**, including but not limited to the following:

A. The Kiva® system

B. Radiofrequency-assisted vertebral augmentation with ultrahigh viscosity cement, including but not limited to Radiofrequency-Targeted Vertebral Augmentation™ (RF-TVA™) with the StabiliT® System

C. Vertebral body stenting

SCIENTIFIC EVIDENCE

For treatment of vertebral body fractures related to osteoporosis or malignancy with percutaneous vertebroplasty or kyphoplasty, the primary beneficial outcomes of interest are relief of pain and improvement in ability to function. Both of these outcomes can be influenced by nonspecific effects, placebo response, and natural history of the disease. Therefore, data from large, blinded, randomized

controlled trials (RCT) of sufficient long-term follow-up are required to control for the placebo effect, determine its magnitude, and determine whether any treatment effect from vertebroplasty or kyphoplasty provides a significant advantage over sham or nonsurgical treatment. Further, adverse effects related to complications from percutaneous vertebroplasty or kyphoplasty, such as risk of additional fractures or cement leakage, must be considered in evaluating the net health impact of these technologies.

Literature Appraisal

The focus of this literature appraisal is on technology assessments, systematic reviews, randomized trials, and clinical practice guidelines.

This policy was originally based on a 2000 BlueCross BlueShield Association Technology Evaluation Center (TEC) Assessment on vertebroplasty and/or kyphoplasty for vertebral lesions from osteoporosis and malignancy.[1] This TEC Assessment was subsequently updated in 2004[2], 2005[3], 2008[4], 2009[5], 2010[6], and 2011[7]. The 2010 update concluded that methodological limitations of available RCTs preclude any determination of the clinical effectiveness of vertebroplasty or kyphoplasty.

Percutaneous Vertebroplasty

Technology Assessments

An update to the 2010 TEC assessment concluded: "The two published randomized, double blind, sham-controlled trials provide evidence that vertebroplasty may not improve health outcomes when compared with a sham procedure" although "interpretation of these data is unclear" due to small sample sizes in these trials.[7]

Systematic Reviews and Meta-analyses

A systematic review of the safety and efficacy of vertebroplasty in malignancy was reported by Chew et al. in 2011.[8] Thirty relevant studies were identified, totaling 987 patients. Included in the review was a single randomized controlled trial and seven prospective studies. Most centers reported treating no more than four vertebrae per session. Pain reduction ranged from 20% to 79%. Five deaths were attributable to vertebroplasty, two from chest infections following general anesthesia, one from a cement pulmonary embolus, and two 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 most in studies with a mean cement volume of more than 4 ml, suggesting a possible association between the volume of cement injected and increased risk of adverse events.

Two meta-analyses were published in 2013:

- Anderson et al. included six studies (total n=827) that compared pain relief, functional improvement, and quality of life following conservative care or cement augmentation. [9] Cement augmentation included both vertebroplasty and kyphoplasty. There were significantly superior early and late outcomes in the augmentation group for pain ($p<0.001$) and function (p-value not provided). The number of secondary fractures was not statistically different between the 2 groups. The meta-analysis did not compare outcomes between vertebroplasty and kyphoplasty.
- Xing et al. compared the safety and efficacy of vertebroplasty with that of kyphoplasty in a total of 10 studies (n=783).[10] The patients who underwent kyphoplasty had significantly superior outcomes

for long-term kyphosis angle (p=0.01), anterior vertebral body height (p=0.002), and cement leakage (p =0.02). No significant difference was found in short- and long-term pain and function scores, or in the rate of adjacent level fractures. The authors noted that these results required verification in a large randomized controlled trial.

Randomized Controlled Trials (RCTs) with Sham Controls

No new sham-controlled RCTs have been published since the most recent TEC Assessment. The 2 randomized blinded sham-controlled trials that were included in the TEC assessment[7] noted above compared vertebroplasty to a sham procedure which mimicked the vertebroplasty procedure up to the point of cement injection.[11,12] The following is a summary of these two RCTs and related articles:

- Buchbinder and colleagues reported results of a four-center, randomized, double-blind, sham-controlled trial conducted in Australia, where 78 participants with 1 or 2 painful osteoporotic vertebral fractures of duration less than 1 year were assigned to undergo vertebroplasty or sham procedure (i.e., injection of local anesthetic into the facet capsule and/or periosteum).[11] Following surgery, participants were evaluated at baseline, then with a mailed questionnaire at 1 week and 1, 3, and 6 months after the procedure. Ninety-one percent of participants completed 6-month follow-up. The primary outcome was average weekly pain (over the course of the previous week) measured on a 0 to 10 Visual Analogue Scale (VAS), with 1.5 representing the minimal clinically important difference. All analyses were performed according to intention-to-treat principles. At all three time points, the authors observed reductions in pain and improvements in quality of life compared with baseline measurements in both groups; however, there was no significant difference in VAS pain score between the treatment and control groups at any time point. Based upon these results, the authors concluded vertebroplasty provided no benefit.

- Kallmes and colleagues also conducted a multicenter, randomized, double-blind, sham-controlled trial in the U.S. in which 131 participants with 1 to 3 painful osteoporotic vertebral fractures of duration less than 1 year were assigned to undergo vertebroplasty or sham procedure (injection of local anesthetic into the facet capsule and/or periosteum).[12] Ninety-seven percent completed a 1-month follow-up and 95% completed 3 months. 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. All primary analyses were performed according to intention-to-treat principles and primary outcomes presented as mean score for the Roland Morris Disability Questionnaire (RDQ) and pain intensity during the preceding 24 hours. Evaluation of primary outcomes at 1 month showed no difference between the treatment and control group. There was a trend toward a higher clinically meaningful improvement (30% reduction from baseline) [8] in pain at 1 month, in the vertebroplasty group (64% vs. 48%), although the difference between the treatment groups was not significant. At 3 months, the trial allowed for patients to cross over to the other treatment group, thus ending the comparative portion of the trial; 43% from the control group and 12% from the vertebroplasty group crossed over (p<0.001). By 1 year, 16% of vertebroplasty patients and 60% of control subjects had crossed over to the alternative procedure (p<0.001).[13] No significant difference in RMDQ or pain scores was found between the 2 groups. There was a significant difference in favor of the vertebroplasty group in the percentage of patients showing a 30% or greater improvement in pain (70% vs. 45% of patients of the control group).

The two randomized, blinded sham controlled trials concluded that vertebroplasty showed no benefit above sham for painful osteoporotic fractures. However, the following considerations must be made in the interpretation of these findings:

- Both trials may have been underpowered to observe and compare the proportion of participants experiencing a clinically meaningful difference in pain (2.5 on the VAS), which is the most informative outcome measure. A fundamental limitation of comparing change in continuous effect measures is failing to identify the proportion of patients experiencing a meaningful clinical response.[14] Since a clinically meaningful important improvement has been established, the proportion of patients responding is the most informative outcome.[15] However, to detect this kind of response would have required a study with 200 or more patients.

- Comments accompanying the published results of both studies cited the lack of sufficient inclusion criteria to evaluate the effect of vertebroplasty on chronic or acute osteoporotic vertebral fractures.[16-18] This indicates that outcomes for patients with acute fractures (< 6weeks) were conflated with outcomes of patients with chronic fractures (6 weeks to 1 year), thus potentially obscuring the treatment effect in either of the patient groups. The inclusion criteria of other studies (detailed below) differentiated between these two patient populations.[19-21]

- Staples, Buchbinder, Kallmes, and colleagues 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.[22] 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 numerical 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 (not statistically significant) trend for a higher proportion of the vertebroplasty group to achieve at least 30% improvement in pain scores, 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.

- The major methodological strength of these trials was that they employed a sham procedure to control for nonspecific (placebo) effects, which are reported to be quite large for invasive procedures, on the order of 6 to 7 mm on a 100-mm scale.[23-26] Although some initially noted the sham used in the trial may have acted as an active control, the effect of injecting open-label local anesthetic in the facet capsule and/or periosteum was subsequently studied in 16 patients and was determined to not significantly improve pain or daily function from baseline to 1 day after injection (16 of 19 patients underwent PV 3 days to 3 months after treatment, limiting interpretation of other time points).[27] Improvement in pain and activities of daily living was compared with the treatment effect observed by patients randomized to the sham-control group in the 2009 Kallmes et al RCT 1 day following treatment, and was found to be significantly less than that observed by the placebo-controlled group, leading the researchers to conclude that placebo, rather than active control sham, was more likely responsible for the treatment effect observed in the RCT. However, the small sample size and the loss of participants to PV after day 1 limit the interpretation of the short and long-term treatment effect of local anesthetic.

- In 2011, investigators who were part of the Kallmes et al. study published results of a nonrandomized trial designed to investigate whether the source of the pain experienced by some patients with osteoporotic vertebral fractures may be related to another vertebral structure, such as the facet joint.[28] The intent of this trial was to determine whether the pain of patients referred for vertebroplasty could be alleviated by local anesthetic and steroid facet joint injection (FJI) into the level of their most painful vertebrae, before considering these patients for vertebroplasty. Although nearly a quarter (21 of 91) of the patients had their pain alleviated by FJI, results of this study are best considered hypothesis-generating and do not offer conclusive findings regarding the contribution of facet joints in vertebral pain.

RCTs without Sham Controls

Several other non-blinded RCTs have also been conducted on the use of vertebroplasty for osteoporotic vertebral fracture:

- Rousing et al. reported on a non-blinded randomized trial in which participants were randomized to either vertebroplasty or conservative management.[19] 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 two groups. The authors concluded that conservative management should be used in the acute phase. The primary limitations of this study include lack of blinding of assessors, its small size and incomplete pain assessment at the baseline visit.

- In 2007, Voormolen and colleagues published results of the VERTOS 1 study, a small randomized clinical trial of 34 patients.[29] Patients refractory to medical management for at least 6 weeks and no longer than 6 months were selected for inclusion. 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. Nevertheless, lack of appropriate treatment randomization (due to patients self-selecting out of the conservative medical treatment group), small sample size and short follow-up time (2 weeks) preclude any conclusions about the effectiveness of this procedure in the short or long term.

- Klazen et al. conducted an industry-supported open-label prospective randomized trial, VERTOS II, of 202 patients, at 6 hospitals in the Netherlands and Belgium.[20] Participants with at least one painful osteoporotic vertebral fracture of duration of 6 weeks or less and a severity of at least 5 on the VAS were assigned to undergo vertebroplasty or conservative management (i.e., bed rest, analgesia, and cast and physical support). There was no blinding of participants, investigators, or outcome assessors to treatment assignment. Of 431 patients eligible for participation, pain spontaneously resolved in 229. Of the remaining 202 participants, 101 were enrolled into the treatment group and 101 into the control arm. Participants were clinically evaluated at baseline, 1 day, 1 week, 1 month, 3 months, 6 months and 12 months after treatment; 81% completed 12

months' follow-up. All analyses were performed according to intention to treat principles, although 10% of patients in the conservative treatment group crossed over to PV and it is not clear how their results were analyzed. The primary outcome was difference in pain relief at 1 month and 12 months measured on a 10 point VAS scale. Clinically significant pain relief was defined as ≥3 point change on the VAS (0-10 scale).

- Vertebroplasty resulted in significantly greater, though not clinically relevant, pain relief than did medical management at 1 month (2.6 difference in VAS) and 1 year (2.0 difference in VAS). 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. Overall, this study fails to provide evidence of significant and clinically relevant pain relief with vertebroplasty over the short and long-term.

- 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 and colleagues also provided an a priori definition of clinically significant change in pain as one that registered a 30% difference on the 10-point VAS. Additionally, the study was adequately powered to find differences between groups, and the study duration was long enough to provide comparisons between groups for up to a year. Although this study was limited by lack of blinding of study assessors and personnel, which increases risk of over-estimating any association between vertebroplasty and pain relief, clinically relevant pain relief was not identified. In a subsequent comment on this study (authored by Buchbinder, the primary author of a RCT detailed above), it was noted that among the 431 patients eligible for enrollment, pain spontaneously resolved in 229 within the first month of the study, rendering them ineligible for further treatment, and potentially over-estimating the success of vertebroplasty on acute fractures.[30]

- A subsequent report from the VERTOS II study described the 12-month natural history of pain in the patients in the conservative treatment arm.[31] 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.

- In 2011, Farrokhi and colleagues reported a randomized trial that compared vertebroplasty with optimal medical management in 82 patients.[32] 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. After 1 month, patients in the conservative treatment group were allowed the option of crossing over to vertebroplasty, and between 1 to 36 months, 10 of 42 patients in this

group did so. 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. Beyond 6 months, there were no between-group differences in pain. Group differences on the Oswestry 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. This study provides support for long-term improvements in function, but not pain, among a small group of patients. However, interpretation of these findings is limited by the small sample size and the crossing over of patients from the control to the treatment group (effectively breaking the study randomization scheme).

- A 2012 report of a prospective open-label single-center RCT conducted by Blasco Andaluz and colleagues, described the effect of vertebroplasty compared with standard medical management on pain (VAS) and quality of life (measured with the Qualeffo-41 instrument) among 125 patients over the course of 12 months.[21] Patients were selected based upon acute, painful osteoporotic fracture of duration less than 12 months with a VAS score ≥ 4. Intent-to-treat analyses was used and moderately high loss to follow-up (24% of patients at 12 months) was compensated for with a statistical procedure assuming that loss-to-follow up may have been influenced by pain. Although the vertebroplasty group initially showed significantly larger improvements in pain alleviation at 2 months, by 12 months there were no significant differences in pain between groups. Quality of life significantly improved from baseline at all measured time points for the treatment group, although it only improved at one time point for the control group (at 6 months). Patients in the treatment group were nearly 3 times more likely to develop new radiological vertebral fractures compared with those in the control group (OR=2.78; 95% CI, 1.02-7.62, p=0·046).

    - In a discussion of their results, the authors point out that lack of difference in proportion of patients with pain between the groups at 12 months could be attributed to one or both of these factors: greater usage of "rescue therapy" used among controls versus treatment group, or higher incidence of subsequent vertebral fractures within the treatment group. The authors place these findings in the context of other randomized trials by stating that both vertebroplasty and conservative treatment are associated with significant improvements in pain and mobility in patients with painful osteoporotic vertebral fractures. Although the pain level of patients in the vertebroplasty group initially responded much more quickly to treatment, this may have been due to the lack of treatment blinding given that differences were not significant at 12 months. However, improvement in a sub-category of function (fitness mobility) was significantly improved for the treatment group throughout the course of the study, indicating a potential advantage of treatment over conservative therapy. Therefore, the authors recommend that, "Further efforts should be addressed to the selection of patients most likely to benefit from [vertebroplasty] with the lowest risk of complications."

In summary, despite the completion of five RCTs, including two with sham control, the efficacy of vertebroplasty for painful osteoporotic compression fractures remains uncertain. Findings from the most recent RCTs concur with earlier nonrandomized reports that vertebroplasty may be associated with significant improvements in pain and/or function. However, the lack of significant improvements in pain or function in the sham-controlled trials and in some other RCTs is suggestive that this treatment effect may not be universal. A synthesis of these findings points to the need for more careful, standardized

patient selection for vertebroplasty, including ensuring that pain management allows for the existence of "multifactorial causes"[33]. In addition, it remains unclear whether the potential benefits of the procedure outweigh harms (such as risk of additional vertebral fractures).

Percutaneous Balloon Kyphoplasty

Technology Assessment

Regarding the use of kyphoplasty, the most recent update to the 2010 TEC Assessment cited the lack of randomized placebo-controlled trials and stated, "While there is one randomized trial of kyphoplasty, without the employment of a sham procedure it is not possible to quantify the real benefit of the procedure over a nonspecific effect to determine the effect of kyphoplasty on the net health outcome."[7]

Systematic Reviews and Meta-analyses

The 2 new meta-analyses[9,10] summarized in the vertebroplasty section above included both vertebroplasty and kyphoplasty. There have been no other systematic reviews or meta-analyses for kyphoplasty.

Randomized Controlled Trials (RCTs)

- The Fracture Reduction Evaluation (FREE) trial, funded by Medtronic Spine, LLC, was designed to examine short-term efficacy and safety of balloon kyphoplasty for the treatment of acute vertebral compression fractures. There was no blinding in this trial. Participants were recruited from 21 sites in eight countries and were randomly assigned to undergo kyphoplasty or conservative care. Primary outcomes were the changes in quality of life, function, pain and disability outcomes in 300 adults with 1 to 3 acute vertebral fractures with back pain for no longer than 3 months randomly assigned kyphoplasty or conservative therapy. For the first 6 months, the treatment group led the control group in every measured outcome, but thereafter, gaps in improvement between the two groups narrowed. Pain was the major outcome which differed throughout the study period; the treatment group saw a consistent, if not clinically relevant, difference in this outcome.

  The following outcomes were reported in three separate articles:[34-36]

  - A total of 138 participants who underwent kyphoplasty and 128 control patients completed 1 month of follow-up. Scores for the primary outcome, 1-month change in SF-36 and Physical Component Summary (PCS) score, were significantly higher for those in the kyphoplasty group (average difference was 5.2 points; $p<0.0001$). Participants in the kyphoplasty group also reported greater improvements in quality of life and Roland Morris disability score.
  - Quality of life: While statistically significant improvement in quality of life was seen at 6 months (3.39 point difference in PCS scores), there was no significant difference in these scores between the groups at 12 and 24 months. The authors noted that this may be due to natural healing of fractures.
  - Pain: Greater improvement in back pain was observed over 24 months for kyphoplasty (-1.49 points) and remained statistically significant at 24 months. At 12 months, fewer kyphoplasty patients (26.4% vs. 42.1%) had received physical therapy or walking aids, back braces, wheelchairs, miscellaneous aids, or other therapy. Fewer kyphoplasty patients used opioid medications through 6 months (29.8% vs. 42.9%) and fewer pain medications through 12 months (51.7% vs. 68.3%).

- Other differences between the groups were no longer apparent at 12 months, possibly due to natural healing of fractures. At 24 months, there was no significant difference between groups in the number of patients with new radiographic vertebral fractures (47.5% for kyphoplasty, 44.1% for control).
- While not a study outcome, the authors noted that patients who received kyphoplasty had approximately 60 fewer days of restricted activity during the year than controls.
- There were no differences between the two groups in subsequent fractures.
- Two device-related serious adverse events were reported: a spondylitis and an anterior cement migration.
- Limitations of this study included the lack of clinically meaningful outcomes (2.5 is considered a clinically meaningful change in VAS), moderate loss to follow-up (24% at 24 months follow-up), and the lack of placebo control for subjective outcomes. In addition, due to the sham effect observed in the recent trials of vertebroplasty, results from a non-sham-controlled trial, as published by Wardlaw, are questionable as the placebo effect may be substantial.[23,24] The analyses were appropriate; however, it would have been preferable to have the number of participants reporting a clinically meaningful change as the primary outcome. In cases of chronic pain, continuous measures can miss responders. The authors acknowledge that their participants at baseline had substantially reduced quality of life compared with other patients with chronic disease, which may have affected their results.

- Berenson and colleagues reported the results of an international randomized multicenter clinical trial.[37] They enrolled 134 patients with cancer who were at least 21 years of age. Participants had at least one and not more than 3 painful vertebral compression fractures (VCF). (These appear to be due to osteoporosis, rather than from a metastatic lesion.) The primary outcome was change in functional status from baseline at 1 month as measured by the Roland Morris Disability Questionnaire (RMDQ). Treatment allocation was not blinded, and the primary outcome at 1 month was analyzed using all participants with data both at baseline and at 1 month. Crossover to the balloon kyphoplasty arm was allowed after 1 month. The authors report baseline scores in the kyphoplasty and nonsurgical groups of 17.6 and 18.2, respectively and 9.10 and 18.0 at 1-month follow-up. P-value for the between group difference in scores p=0.0001. However, conclusions based upon this trial are limited due to lack of blinding and short follow up (1 month).

Due to the lack of comparative trials of sufficient size and rigor, it is difficult to reach conclusions regarding the effectiveness of kyphoplasty. Despite most case series showing consistent improvements in pain after the procedure, and the same conclusion being reached in the RCTs, it is difficult to separate placebo and natural history effects from actual treatment efficacy.

Adverse Events

The most commonly reported adverse effects of vertebroplasty or balloon kyphoplasty are new compression fractures and cement leakage. 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).[38] 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. 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).

Cement leakage remains a concern, though it has been shown to be reduced in kyphoplasty relative to vertebroplasty.

There continue to be case reports of right ventricle perforation, cardiac tamponade, and embolism of cement into pulmonary vessels.

Mechanical Vertebral Augmentation with Kiva®

The Kiva technique and radiofrequency-assisted mechanical vertebral augmentation are in the early stages of development and study. For the reasons noted above, randomized controlled trials of sufficient size and duration are needed to determine the effectiveness, safety, and durability of these techniques compared with conventional balloon kyphoplasty, vertebroplasty, and conservative therapies.

Randomized Controlled Trials (RCTs)

In 2013, Korovessis et al. reported a randomized trial comparing mechanical vertebral augmentation with the Kiva device versus balloon kyphoplasty in 180 patients with osteoporotic vertebral body fractures.[39] Mean follow-up was 14 months (range 13-15 months). The groups showed similar improvements in VAS for back pain, SF-36, and ODI. For example, there was a greater than 5.5 point improvement in VAS in 54% of patients in the Kiva group and 43% of patients in the balloon kyphoplasty group. Radiological measures of vertebral height were similar in the two groups. Kiva reduced the Gardner kyphotic angle, while residual kyphosis of more than 5 degrees was more frequently observed in the balloon kyphoplasty group. Patients and outcome assessors were reported to be unaware of the group assignment, although it is not clear if the Kiva device was apparent in the radiographs. Cement leakage into the canal occurred in two patients treated with balloon kyphoplasty, necessitating decompression, compared with none following the Kiva procedure.

Radiofrequency-assisted Mechanical Vertebral Augmentation

Current published evidence is limited to a few very small, short-term feasibility studies. These preliminary studies do not permit conclusions due to methodological limitations, including but not limited to the lack of randomized comparison to alternative treatments, small study populations, and the lack of long-term follow-up.

Vertebral Body Stenting

A randomized controlled trial by Werner et al, performed independent of industry support, found no advantage of vertebral body stenting (VBS) over balloon kyphoplasty.[40] The study included sixty-five patients with 1 or more fresh osteoporotic vertebral compression fractures (100 fractures total) and marked pain. Patients were randomized to either VBS or balloon kyphoplasty with the condition that if there were multiple levels in a single patient the same procedure was used for all levels. There was no significant difference between the procedures in radiation time, or in the mean reduction of kyphosis (4.7˚ after VBS and 4.5˚ after kyphoplasty). There was also no significant difference between the two intervention arms in cement leakage (20% balloon kyphoplasty and 30% VBS). Intraoperative pressure was higher and material-related complications were greater in the VBS group (9 of the 50 levels,

including failure of the cannulas, incomplete or no opening of the stent, and balloon rupture) compared to 1 of the 50 vertebral levels (balloon rupture) in the kyphoplasty group. The authors concluded that there was no advantage of VBS over balloon kyphoplasty.

Sacroplasty and Coccygeoplasty

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 evidence on sacroplasty is limited to several small, unreliable case reports or series.[41-57] These initial pilot studies reported rapid pain relief with few complications. 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 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.[58] Coccygeoplasty has been reported, but no adequate clinical trial data has been published.

Clinical Practice Guidelines and Position Statements

American Academy of Orthopaedic Surgeons (AAOS)

In 2010, the AAOS Board of Directors approved a new clinical practice guideline on the treatment of osteoporotic spinal compression fractures, which is available online at: http://www.aaos.org/Research/guidelines/SCFguideline.asp.[59] 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'." This recommendation was based on 5 RCTs[11,12,19,29,60], 2 of which were graded Level I (defined as reliable), and 3 of which were graded Level II (defined as moderately reliable). In coming out with a strong recommendation, the committee expressed their confidence that future evidence is unlikely to overturn the existing evidence. The Board also downgraded the recommendation supporting the use of kyphoplasty from "moderate" to "limited" based upon low quality and inconclusive evidence comparing this procedure with conservative care and vertebroplasty, respectively.

American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine (ASA/ASRA)

Practice guidelines from the ASA/ASRA support the use of "minimally invasive spinal procedures" (including vertebroplasty and vertebral augmentation), stating: "Consultants, ASA members, and ASRA members strongly agree that minimally invasive spinal procedures should be performed for pain related to vertebral compression fractures."[61] The practice guidelines go on to make the specific recommendation in favor of these procedures in "treatment of pain related to vertebral compression fractures" despite a review of the literature which found that available randomized sham-controlled trials had either not found differences associated with treatment groups, or that differences were inconsistent across available studies.

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)

- An updated 2012 joint practice guideline addresses the performance of vertebral augmentation in general and refers to all available percutaneous techniques used to achieve internal vertebral body stabilization, including vertebroplasty, balloon kyphoplasty, radiofrequency ablation and coblation, mechanical void creation, and injection of bone graft material or bone substitutes.[62] The ACR, ASN, ASSR, SIR, and SNIS consider vertebral augmentation to be an established and safe procedure, and provide guidelines for patient selection, qualifications and responsibilities of personnel, specifications of the procedure, equipment quality control, and quality improvement and documentation.

- These societies (ACR, ASN, ASSR, SIR, and SNIS) also published a joint position statement on percutaneous vertebral augmentation in 2014.[63] This document states that percutaneous vertebral augmentation using vertebroplasty or kyphoplasty and performed in a manner in accordance with public standards is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures. 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.

Society of Interventional Radiology (SIR)

In a 2014 quality improvement guideline from SIR, failure of medical therapy includes the following situations :[64]

1. Patients who are 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. Patients 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. Patient with a weakened or fractured vertebral body, and 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.

American College of Radiology (ACR)

The ACR published updated appropriateness criteria on the management of vertebral compression fractures in 2013.[65] While generally supportive of vertebroplasty and kyphoplasty in specified conditions, the guidelines state the following:

- Conservative management is the traditional first-line management for osteoporotic compression fractures.
- Controversy exists over the use of vertebral augmentation due to two previous independent level 1 trials that demonstrated no clinical validity for VP over the sham control groups. Conclusions from these studies have divided the medical community with respect to the efficacy of vertebral augmentation.
- Despite this controversy, increased use of vertebral augmentation for managing painful osteoporotic and malignant vertebral fractures has been the trend, with the literature favoring patient outcomes over conservative medical management up to 1 year.
- If VP is recommended for osteoporosis or malignant fractures, it should be used for patients who have failed or cannot tolerate conservative or traditional management.
- Kyphoplasty data are less extensive but have shown similar results to VP for uncomplicated vertebral compression fractures.

- Kyphoplasty may have an advantage over traditional VP in complex cases (e.g., burst fractures with neurological compromise) or fractures in which height restoration or deformity correction may be beneficial.
- This slight mechanical advantage over VP may also affect long-term outcomes.
- More level 1 studies are needed to determine the medical and societal cost of the palliative effect on pain related morbidity associated with osteoporotic vertebral compression fractures. Smaller sample studies and use trends indicate vertebral augmentation has benefits over conservative medical management for the first year.

Summary

Despite the large volume of published evidence on the use of percutaneous vertebroplasty or kyphoplasty for treatment of vertebral fractures, reported conclusions about the impact of either of these procedures on health outcomes are in conflict. However, given that several open randomized controlled trials have shown that these procedures may alleviate pain and/or improve function in select patients, the absence of alternative treatment options, and the morbidity associated with extended bed rest, percutaneous vertebroplasty or balloon kyphoplasty may be considered medically necessary in select patients with vertebral fractures.

The current evidence for mechanical vertebral augmentation using techniques other than balloon kyphoplasty (e.g., the Kiva VCF System, radiofrequency-assisted vertebral augmentation, vertebral body stenting) is limited to preliminary randomized trials. Vertebral body stents have not received approval/clearance by the FDA at this time. In addition, there are no clinical practice guidelines from U.S. professional societies that recommend these techniques. Therefore, mechanical vertebral augmentation techniques using devices other than balloon devices are considered investigational.

Sacroplasty and coccygeoplasty are under development. Varying techniques, patient indications, and small numbers of treated patients leaves uncertainty regarding the impact of sacroplasty on health outcomes and does not permit conclusions concerning its use for sacral insufficiency fractures or other indications. Currently, there is no literature reporting clinical outcomes associated with coccygeoplasty. Therefore, sacroplasty and coccygeoplasty are considered investigational.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	22520	Percutaneous vertebroplasty (bone biopsy included when performed), 1 vertebral body, unilateral or bilateral injection; thoracic
	22521	; lumbar
	22522	; each additional thoracic or lumbar vertebral body (List separately

CODES	NUMBER	DESCRIPTION
		in addition to code for primary procedure)
	22523	Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device, 1 vertebral body, unilateral or bilateral cannulation (e.g., kyphoplasty); thoracic
	22524	; lumbar
	22525	;each additional thoracic or lumbar vertebral body (list separately in addition to code for primary procedure)
	72291	Radiological supervision and interpretation, percutaneous vertebroplasty, vertebral augmentation, or sacral augmentation (sacroplasty), including cavity creation, per vertebral body or sacrum; under fluoroscopic guidance
	72292	; under CT guidance
	0200T	Percutaneous sacral augmentation (sacroplasty), unilateral injection(s), including the use of a balloon or mechanical device, when used, 1 or more needles
	0201T	Percutaneous sacral augmentation (sacroplasty), bilateral injection(s), including the use of a balloon or mechanical device, when used, 2 or more needles
HCPCS	S2360	Percutaneous vertebroplasty, one vertebral body, unilateral or bilateral injection; cervical
	S2361	; each additional cervical vertebral body (list separately in addition to code for primary procedure)