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

These procedures involves the injection of a polymethylmethacrylate (PMMA), a cement, into a fractured or weakened vertebral body to provide stabilization as an alternative to spinal fusion.

Background

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 shaped memory coil and a Kiva 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 systems 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 reduce 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 in 2014.

- 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 http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm062126.htm. 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**

1. Percutaneous vertebroplasty, percutaneous balloon kyphoplasty, or Kiva® may be considered **medically necessary** for 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, MRI, CT, or bone scan) 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 at the planned treatment level
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 plasmacytomasa
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, percutaneous balloon kyphoplasty, or Kiva 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. Radiofrequency-assisted vertebral augmentation with ultrahigh viscosity cement, including but not limited to Radiofrequency-Targeted Vertebral Augmentation™ (RF-TVA™) with the StabiliT® System
B. Vertebral body stenting
SCIENTIFIC EVIDENCE

For treatment of vertebral body fractures related to osteoporosis or malignancy with percutaneous vertebroplasty (VP), kyphoplasty (KP), or Kiva, 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 (RCTs) 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 systematic reviews, randomized trials, and clinical practice guidelines.

Percutaneous Vertebroplasty

Systematic Reviews

In 2015, Buchbinder et al. published results from a systematic review to better understand the benefits and harms of vertebroplasty for the treatment of osteoporotic vertebral fractures.[1] Eleven randomized controlled trials and one quasi-RCT were included in the review and were deemed moderate quality evidence. Two trials compared vertebroplasty with usual care (209 participants), and four compared vertebroplasty with kyphoplasty (545 participants). Based on their review, the authors found that the evidence does not support a role for vertebroplasty for treating osteoporotic vertebral fractures in routine practice. Furthermore, there was no difference in the duration of pain when compare with a sham procedure. Sensitivity analysis confirmed that open trials comparing vertebroplasty with usual care are likely to have overestimated any benefit of vertebroplasty. Finally, adverse events have been observed following vertebroplasty; however, based on the current research it is challenging to determine if vertebroplasty results in a clinically important increase risk of new symptomatic vertebral fractures and/or other serious events.

In 2015, Xiao et al. published results from a systematic review and meta-analysis that compared complications between percutaneous vertebroplasty (PVP) and balloon kyphoplasty (BK) for the treatment of osteoporotic vertebral compression fractures.[2] Nineteen studies encompassing 1,787 patients (887 PVP, and 900 BKP) were included in the analysis. The authors reported that the two procedures suffer from equal risk of subsequent spinal fractures; however, PVP had a higher cement leakage rate when compare to BK.

In 2015, Wang et al. published results from a systematic review and meta-analysis that examined the safety and efficacy of percutaneous balloon kyphoplasty (PKP) compared to percutaneous vertebroplasty (PVP) in the treatment of single level osteoporotic vertebral compression fractures (OVCF).[3] Eight studies that encompassed 845 patients were included in the review. Overall, the results indicated that PKP and PVP for the treatment of OVCF are both safe and effective treatments; however, PKP is superior to PVP for the injected cement volume, the short-term pain relief, the improvement of short-and-long term kyphotic angle, and lower cement leakage rate.
In 2015, Shi-Ming et al. published results from a systematic review and meta-analysis to better determine the efficacy and safety between percutaneous vertebroplasty (PVP) and balloon kyphoplasty (BKP) for osteoporotic vertebral compression fractures (OVCF).\[4\] Eleven studies that encompassed 789 patients were included in the review. The average length of follow up was 17 months and a total of 4.6% of the patients were lost to follow-up. Results indicated that BKP is more effective for short term pain relief, and more effective to restore the anterior vertebral body height, functional capacity, and kyphotic angle of OVCFs. Therefore, the authors concluded that BKP was superior over PVP for the treatment of osteoporotic vertebral compression fractures.

A 2015 meta-analysis of prospective studies comparing VP and KP included six RCTs and 14 comparative studies (N=1,429).\[5\] There was no difference between the two techniques in short-term (≤1 week post-procedure) and long-term (>6 months post-procedure) pain reduction, improved function, or adjacent level fractures. Cobb angle at long-term follow-up was significantly better in the KP group. The KP group had significantly fewer incidents of cement extravasation, though the clinical significance of this difference is uncertain.

In 2014 Stevenson et al. published a technology assessment on the outcomes following percutaneous VP and KP for osteoporotic vertebral compression fractures (VCFs).\[6\] A robust literature search through November 2011 was conducted using a broad search of a number of databases, contact with clinical experts, and manual searches of the bibliographies of retrieved studies. The assessment of effectiveness included only RCTs while the assessment of safety included data from RCTs, large case series, and individual case reports. A network meta-analysis of the data on pain scores was also undertaken. Six scenarios were analyzed and extensive sensitivity analyses were conducted. Twenty-eight articles on nine RCTs were included in the effectiveness review, two of which\[7,8\] were double-blind, placebo controlled trials.

The quality of the review is subject to the limitations of the included studies. The methodological limitation of most concern to the authors was the lack of blinding in all studies except the INVEST study\[7,9\] and Buchbinder et al.\[8\] This lack of blinding could result in a significant overestimation of treatment effect. The authors also noted controversy over the use of pain as a primary outcome and suggested that pain-related disability and quality of life could provide more objective and clinically meaningful measure. However, heterogeneity in the outcomes measured across studies precluded statistical aggregation of data. In addition, this review was limited to people with painful osteoporotic VCFs, making generalizability to other fracture causes (e.g., multiple myeloma; traumatic injury) questionable.

The authors concluded that VP and KP resulted in significantly better pain and disability reduction and improved quality of life for refractory osteoporotic VCFs compared to optimal pain management. However, the evidence was insufficient to determine whether VP or KP resulted in better outcomes compared to operative placebo. In addition, changes in mortality rates related to these procedures compared to optimal pain management or surgical placebo could not be established due to the lack of data on causes of death and the lack of long-term data.

In 2014, Khan et al. published a systematic review of the efficacy of VP and KP in patients with vertebral fractures associated with multiple myeloma (MM).\[10\] Twenty-three studies (N=923) met inclusion criteria. The primary outcomes studied were pain, disability, and analgesic drug use following vertebral augmentation. Based on changes in a 10-point pain scale, KP and VP were reported as equally effective in reducing pain. Post-procedure decrease in pain was found early and was sustained over time.
One significant limitation of this analysis was the lack of a conservative therapy control group which does not permit conclusions about whether these effects were due to KP and VP or the natural history of MM related fracture. Other limitations were related to the methodological limitations of the included studies including small sample sizes, heterogeneity across studies in adjunctive therapy, disease stage, reporting of outcome measures, and the inclusion of retrospective and uncontrolled case series.

In 2013, Anderson et al. published results from a systematic review and meta-analysis that included six studies (total n=827) that compared pain relief, functional improvement, and quality of life following conservative care or cement augmentation for osteoporotic spinal fractures.[11] 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 two groups. The meta-analysis did not compare outcomes between vertebroplasty and kyphoplasty. The authors noted a number of limitations in the interpretation of this meta-analysis including heterogeneity between studies in inclusion/exclusion criteria (e.g., time from fracture to treatment), treatment methods (e.g., unilateral vs. bilateral injections), and study endpoints.

Also in 2013, Xing et al. published results from a systematic review and meta-analysis that analyzed different studies since their focus was on comparison of the safety and efficacy of vertebroplasty with that of kyphoplasty for the treatment of osteoporotic spinal fractures. A total of 10 studies (n=783) were included.[12] 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. The authors considered the primary limitation of this meta-analysis to be the limited number of included studies which decreased the statistical power.

A 2012 systematic review by Robinson and Olerud analyzed RCTs on VP and KP compared to standard medical therapy in patients over 60 years of age with osteoporotic vertebral compression fractures.[13] A total of eight studies[8,9,14-19] were included, two of which were properly blinded and placebo-controlled by sham operation (i.e., the INVEST trial[7,9] and Buchbinder et al.[8]). Cross-over was allowed after two weeks in one study[14] which was terminated prematurely due to massive cross-over, and after a month in another study[9]. All six RCTs that compared VP or KP to medical treatment found significantly superior improvements in pain and function over medical treatment, at least in the first month after the procedure. The authors also discussed comparison between VP and KP, noting two conflicting 2007 meta-analyses in which Taylor et al.[20] reported significantly greater improvement in pain for KP while Eck et al.[21] reported opposite findings. A more recent RCT in which 100 patients were randomized to either VP or KP found no significant clinical difference between the procedures.[22] While VP consistently resulted in more cement leakage than KP, the vast majority of cement leakage was asymptomatic and required no treatment.

A number of limitations of the included studies were listed. The lack of adequate blinding was a cause for possible significant bias in six of the eight studies. In addition, 43% of the sham-control patients in the Kallmes et al. study crossed over after three months. Also, many RCTs were financed by the device manufacturers, causing potential for bias. The authors concluded that VP, KP, and standard medical treatment had similar outcomes and recommended continued sham-controlled trials.

In 2011 Staples, Buchbinder, Kallmes, and colleagues published a patient-level meta-analysis of the two sham-controlled trials to determine whether vertebroplasty is more effective than sham in specific
subsets of patients.[23] 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, 27% with pain of recent onset and 47% with severe pain at baseline. The primary outcome measures, pain scores and function on the RMDQ at one 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 not statistically significant. This difference was a higher proportion of the vertebroplasty group achieving 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 did 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.

A systematic review of the safety and efficacy of vertebroplasty in malignancy was reported by Chew et al. in 2011.[24] Thirty relevant studies were identified, totaling 987 patients. Included in the review were 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.

Randomized Controlled Trials (RCTs) with Sham Controls

Since the above systematic reviews were published, Kroon et al. reported the 12- and 24-month outcomes of a double-blind RCT comparing VP (n=38) with sham procedure (n=40) for acute osteoporotic vertebral fractures.[25] The initial report of 6-month outcomes (Buchbinder et al. 2009[8]) found no benefit of VP over sham procedure. Complete data were available for 67 (86%) and 57 (73%) of participants at 12 and 24 months, respectively. VP patients had significantly higher overall pain reduction at both time points compared to sham. There were no significant between-group differences in disability, quality of life, perceived recovery, or adverse event including subsequent vertebral fractures. The authors concluded that these outcomes provide evidence that use of VP as routine care for vertebral fractures is unsupported. Methodological limitations in the RCT included small sample size that may have had inadequate power to show significant differences in subsequent vertebral fractures.

RCTs without Sham Controls

In 2015, Lui et al. published results from a five year follow-up study of 100 patients who had vertebral compression fractures and were randomly assigned to either receive the kyphoplasty or vertebroplasty.[22,26] The authors found that vertebral body height, kyphotic wedge angle, and VAS scores were not altered. Eight patients in the kyphoplasty group had an adjacent fracture after the procedure, whereas seven patients in the vertebroplasty group had an adjacent fracture after the procedure. These adjacent fractures occurred within one year of surgery in both treatment groups except in one kyphoplasty-treated patient in whom the adjacent fracture was noted 16 months after treatment. Three patients in the vertebroplasty group had a nonadjacent fracture, and four patients in the kyphoplasty group had a nonadjacent fracture. The link between angular correction and the occurrence of adjacent fracture was statistically significant in the vertebroplasty group.
In 2015 Wang et al. randomized 107 patients with painful osteoporotic vertebral compression fractures to undergo KP (n=54) or VP (n=53) using high viscosity cement.\cite{27} Patients were blinded to the group assignment. Both groups reported significant pain relief and improved quality of life (p<0.05) beginning at postoperative day 1 compared to baseline. Pain and function scores continued to improve through 1-year follow-up. There were no significant between-group differences in outcomes. In the PV group there was one new adjacent vertebral fracture and no symptomatic cement leakage, neurological deficit, or embolism. In the KP group, there were four new nonadjacent vertebral fractures as well as one patient who experienced severe discogenic pain due to disc leak and required discectomy with fusion. The rate of subsequent fractures was not statistically significant between the two groups, and all new fractures were treated surgically. The authors concluded that these two procedures were safe and effective. This study had a number of methodological limitations. The randomization and concealment methods were not reported. Sample size was relatively small. The authors also noted that they did not distinguish between dynamic and fixed fractures which could impact outcomes since dynamic fractures can achieve greater height restoration.

In 2014, Chen et al. reported a nonblinded RCT comparing VP with conservative management.\cite{28} Included patients (n=89) had MRI-confirmed chronic compression fractures with persistent severe pain for 3 months or longer. At 12 months follow-up, pain scores decreased from 6.5 to 2.5 in the VP group and from 6.4 to 4.1 in the control group (p<0.001). Complete pain relief was reported by 84.8% of VP patients and 34.9% of controls. The final Oswestry Disability Index (ODI) score in the VP group and the conservative management group was 15 and 32.1, respectively (p<0.001) and the final Roland Morris Disability Score was 8.1 and 10.7, respectively (p<0.001).

\textit{Conclusion}

It remains unclear whether vertebroplasty provides additional beneficial effects compared to sham procedure for painful osteoporotic compression fractures. 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”\cite{29}. In addition, it remains unclear whether the potential benefits of the procedure outweigh harms (such as risk of additional vertebral fractures). Despite these concerns, use of VP has become increasingly widespread as a treatment of refractory vertebral fracture.

\textbf{Percutaneous Balloon Kyphoplasty}

\textit{Systematic Reviews}

As discussed above, Shi-Ming et al. published results from a systematic review and meta-analysis to better determine the efficacy and safety between percutaneous vertebroplasty (PVP and balloon kyphoplasty (BKP) for osteoporotic vertebral compression fractures (OVCF).\cite{4} Results indicated that BKP is more effective for short term pain relief, and more effective to restore the anterior vertebral body height, functional capacity, and kyphotic angle of OVCFs. Therefore, the authors concluded that BKP was superior over PVP for the treatment of osteoporotic vertebral compression fractures. Also discussed above, Xiao et al. published results from a systematic review and meta-analysis that compared complications between percutaneous vertebroplasty (PVP) and balloon kyphoplasty (BK) for the
treatment of osteoporotic vertebral compression fractures. Nineteen studies encompassing 1,787 patients (887 PVP, and 900 BKP) were included in the analysis. The authors reported that the two procedures suffer from equal risk of subsequent spinal fractures; however, PVP had a higher cement leakage rate when compare to BK. In 2014 Huang et al. published a systematic review with meta-analysis and noted controversy over which technique, unilateral or bilateral KP, was superior in terms of effectiveness and safety. No large studies were found that directly compared these two approaches. Five studies with 253 patients met inclusion criteria. No clinically significant difference between unilateral and bilateral KP was found for improvement in pain and function, kyphosis angle reduction, and anterior vertebral height restoration. The rate of adverse events was also similar between the two approaches. However, the quality of the evidence was graded as very low and the authors recommended high-quality RCTs be conducted to resolve this question.

There were two systematic reviews included in the vertebroplasty (VP), kyphoplasty (KP) sections above that also addressed percutaneous balloon kyphoplasty. In those instances the authors noted a number of limitations in the interpretation to these systematic reviews and meta-analyses, including but not limited to, heterogeneity between studies in inclusion/exclusion criteria (e.g., time from fracture to treatment), treatment methods (e.g., unilateral vs. bilateral injections) and study endpoints, and a limited number of included studies which decreased the statistical power, and called for more research to determine the efficacy of this treatment.

**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 one to three acute vertebral fractures with back pain for no longer than three months randomly assigned kyphoplasty or conservative therapy. For the first six 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:

- A total of 138 participants who underwent kyphoplasty and 128 control patients completed one 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%
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 Visual Analogue Scale [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.[33,34] 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.

In 2011, Berenson et al. published results from an international randomized multicenter clinical trial.[35] 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-term (one month) follow up.

Conclusion

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. However, as with VP, the use of KP has become increasingly widespread as a treatment of refractory vertebral fracture.

Adverse Events

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

In a 2014 report published by Yi et al. they 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).[36] 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 one 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).

- In a 2014 report from the SWISSspine registry (SSR), 375 single-level osteoporotic vertebral fracture patients were followed for a mean follow-up of 3.6 months following KP.[37] Post-KP adjacent segment fractures were found in 37 (10%) patients, occurring on average at 2.8 months postoperatively. Significant risk factors included preoperative segmental kyphosis >30 degrees (p=0.026), rheumatoid arthritis (p=0.038), and cardiovascular disease (p=0.047). Patients with postoperative adjacent segment fractures had significantly higher back pain at final follow-up.

- Zhang et al. conducted a systematic review and meta-analysis of four RCTs[8,17-19] (N=454) published through April 2013.[38] The aim was to analyze the causal relationship between vertebroplasty and new-onset vertebral fractures in osteoporotic vertebral fracture patients. Authors noted a number of limitations to the meta-analysis. The authors reported that the RCTs did not support a conclusion that VP significantly increased the occurrence of new postoperative or adjacent vertebral fractures. Due to inclusion of only four RCTs, some with modest sample sizes, could allow over- or under-estimation of results. In addition, there was heterogeneity between RCTs in fracture age, intervention, duration of follow-up, and study design. Attrition bias was also of concern due to moderately high drop-out rates, though one trial did balance missing outcome data across intervention groups.

- In a retrospective analysis of 171 post-KP patients at a mean follow-up of 41 months, Civelek et al. also found higher preoperative kyphotic angle to be a risk factor significantly associated with adjacent level fractures.[39] Female sex was also found to be a significant risk factor. The severity of osteoporosis was not a determining factor.

- Cement leakage remains a concern, though it has been shown to be reduced in kyphoplasty relative to vertebroplasty. Most incidents of cement leakage were reported to be asymptomatic.

- There continue to be case reports of cardiac 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**

In 2015, Tutton et al. published results from an RCT that where vertebral augmentation with the Kiva® VCF System® was compared with balloon kyphoplasty in the KAST trial, a 2015 pivotal non-inferiority RCT.[40] This industry-sponsored multicenter open-label trial was conducted in 300 patients with one or two osteoporotic vertebral compression fractures. The Kiva group included 153 patients and the KP group included 147 patients. Included were patients with VAS for back pain of at least 70 mm out of 100 after two to six weeks of conservative care or a VAS of at least 50 mm after six weeks of conservative care, and an ODI of at least 30%. The primary endpoint at 12 months was a composite of a
reduction in fracture pain by at least 15 mm on VAS, maintenance or improvement in function on ODI, and absence of device-related serious adverse events. The primary endpoint was met for 94.5% of patients treated with Kiva® and 97.6% of patients treated with kyphoplasty (Bayesian posterior probability of 99.92% for non-inferiority, using as-treated analysis). In the 285 treated patients, Kiva® resulted in a mean improvement of 70.8 points in VAS, compared with a 71.8 point improvement for kyphoplasty. There was a 38.1 point improvement in ODI for the Kiva® group, compared to a 42.2 point improvement for the kyphoplasty group. There were no device-related serious adverse events. The total volume of cement was 50% less with Kiva® and there was lower cement leakage compared with kyphoplasty (16.9% vs 25.8%, respectively).

In a 2014 RCT Korovessis et al. compared Kiva with low viscosity PMMA in 23 patients to KP with high viscosity PMMA in 24 patients. All patients had vertebral body osteolysis. None of the patients survived after 3 months. PMMA leakage occurred in 4 (9.3%) of the KP group. Anterior, posterior, and middle vertebral body height ratio did not improve significantly in either group. Pain and function scores improved significantly in both groups with no significant between-group difference. The authors noted the lack of PMMA leakage in the Kiva group. The small sample size limits the ability to reach conclusions on safety and effectiveness but supports further study.

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. 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 five 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.

Conclusion

The Kiva procedure appears to be at least equivalent to KP in pain reduction and improved functional outcomes with a lower rate of cement leakage.

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

Systematic Review

In 2015, Martin-Lopez et al. published results from a systematic review that examined the effectiveness and safety of stentoplasty in patients with osteoporotic vertebral body fractures. Five studies were included in the review, two clinical trials and three observational studies. The authors found there was
no difference between the two procedures in terms of reduction of kyphosis, time of exposure to radiation or postoperative loss of cement. Although stentoplasty in comparison to vertebroplasty showed an improvement of restoration of vertebral height ($P=0.042$), kyphosis correction and volume of bone cement, no differences were found between two procedures in terms of loss of vertebral body volume. Based on observational studies, stentoplasty improved vertebral height, pain and functional disability at six and 12 months follow-up, and corrected the angle vertebral fractures in patients with osteoporotic vertebral body. The authors concluded that there was no advantage of stentoplasty 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 case reports or series. 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. Coccygeoplasty has been reported, but no adequate clinical trial data has been published.

**Clinical Practice Guidelines**

**American Academy of Orthopaedic Surgeons**

In 2010, the American Academy of Orthopaedic Surgeons (AAOS) Board of Directors approved a clinical practice guideline on the treatment of osteoporotic spinal compression fractures. 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 five RCTs, two 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**

Practice guidelines from the American Society of Anesthesiologist (ASA) and the American Society of Regional Anesthesia and Pain Medicine (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.” 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, American Society of Neuroradiology, American Society of Spine Radiology, the Society of Interventional Radiology, and the Society of NeuroInterventional Surgery

The American College of Radiology (ACR), American Society of Neuroradiology (ASNR), American Society of Spine Radiology (ASSR), the Society of Interventional Radiology (SIR), and the Society of NeuroInterventional Surgery (SNIS) along with the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons (CAN), and the Canadian Interventional Radiology Association (CIRA) published a joint position statement on percutaneous vertebral augmentation in 2014.[68] 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.

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.[69] 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.

Society of NeuroInterventional Surgery

In 2014 the Society of NeuroInterventional Surgery (SNIS) published a report that included a systematic review with meta-analysis and the following recommendations:[70]

1. Kyphoplasty in selected patients is superior to conservative medical therapy in reducing back pain, disability and improving Karnofsky performance status and quality of life for patients with cancer.
2. and disabling back pain from a vertebral fracture (AHA Class IIA, Level of Evidence B).
3. Vertebroplasty and kyphoplasty are reasonable therapeutic options in selected patients with cancer and severe back pain from a vertebral fracture that is refractory to conservative medical therapy (AHA Class IIA, Level of Evidence B).
4. Vertebroplasty and kyphoplasty are reasonable therapeutic options in selected patients with severe back pain from an osteoporotic vertebral fracture that is refractory to conservative medical therapy (AHA Class IIA, Level of Evidence B).

Society of Interventional Radiology

In a 2014 quality improvement guideline from Society of Interventional Radiology (SIR), failure of medical therapy includes the following situations:[71]

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**

The American College of Radiology (ACR) published updated appropriateness criteria on the management of vertebral compression fractures in 2013.[72] 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 one 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 published about 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 the Kiva procedure consists of several randomized controlled trials that consistently found this technique to be at least equivalent to kyphoplasty for pain reduction and improved functional outcomes in patients with vertebral fractures. In addition, the Kiva procedure required less cement and may result in fewer incidents of cement leakage than kyphoplasty. While this evidence is not extensive, it is sufficient to determine that the Kiva procedure may be considered medically necessary in select patients with vertebral fractures that do not respond adequately to medical treatment.
The current evidence for mechanical vertebral augmentation using techniques other than balloon kyphoplasty (e.g., 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.

REFERENCES


40. Tutton, SM, Pflugmacher, R, Davidian, M, Beall, DP, Facchini, FR, Garfin, SR. KAST Study: The Kiva(R) System as a Vertebral Augmentation Treatment - A Safety and Effectiveness Trial: A Randomized, Non-inferiority Trial Comparing the Kiva(R) System to Balloon Kyphoplasty in


CROSS REFERENCES

Sacroiliac Joint Fusion, Surgery, Policy No. 193

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