Percutaneous Balloon Kyphoplasty, Radiofrequency Kyphoplasty, and Mechanical Vertebral Augmentation

Policy Number: 6.01.38  Last Review: 9/2019

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for percutaneous kyphoplasty when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Balloon kyphoplasty or mechanical vertebral augmentation using Kiva may be considered medically necessary for the treatment of symptomatic osteoporotic vertebral compression fractures that have failed to respond to conservative treatment (eg, analgesics, physical therapy, rest) for at least 6 weeks.

Balloon kyphoplasty or mechanical vertebral augmentation using Kiva may be considered medically necessary for the treatment of severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies.

When Policy Topic is not covered
Balloon kyphoplasty or mechanical vertebral augmentation using Kiva are considered investigational for all other indications, including use in acute vertebral fractures due to osteoporosis or trauma.

Radiofrequency kyphoplasty is considered investigational.

Mechanical vertebral augmentation using any other device is considered investigational.

Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals:</td>
<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
</tr>
<tr>
<td>• With</td>
<td>• Balloon kyphoplasty, or</td>
<td>• Conservative care</td>
<td>• Symptoms</td>
</tr>
<tr>
<td>osteoporotic</td>
<td></td>
<td></td>
<td>• Functional outcomes</td>
</tr>
<tr>
<td>vertebral</td>
<td></td>
<td></td>
<td>• Quality of life</td>
</tr>
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</table>
Percutaneous balloon kyphoplasty, radiofrequency kyphoplasty, and mechanical vertebral augmentation with Kiva are interventional techniques involving the fluoroscopically guided injection of polymethylmethacrylate into a cavity created in the vertebral body with a balloon or mechanical device. These techniques have been investigated as options to provide mechanical support and symptomatic relief in patients with osteoporotic vertebral compression fracture or those with osteolytic lesions of the spine (ie, multiple myeloma, metastatic malignancies).

For individuals who have osteoporotic vertebral compression fractures who receive balloon kyphoplasty, or mechanical vertebral augmentation (Kiva), the evidence includes randomized controlled trials (RCTs) and meta-analyses. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. A meta-analysis and moderately sized unblinded RCT have compared kyphoplasty with conservative care and found short-term benefits in pain and other outcomes. Other RCTs, summarized in a meta-analysis, have reported similar outcomes for kyphoplasty and vertebroplasty. Two randomized trials that compared mechanical vertebral augmentation (Kiva) with kyphoplasty have reported similar outcomes for both procedures. A major limitation of all these RCTs is the lack of a sham procedure. Due to the possible sham effect observed in the recent trials of vertebroplasty, the validity of the results from non-sham-controlled trials is unclear. Therefore, whether these improvements represent a true treatment effect is uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have osteolytic vertebral compression fractures who receive balloon kyphoplasty or mechanical vertebral augmentation (Kiva), the evidence includes RCTs, case series, and a systematic review of these studies. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. Two RCTs have compared balloon kyphoplasty with conservative management, and another has compared Kiva with balloon kyphoplasty. Results of these trials, along with case series, would suggest a

| compression fractures | mechanical vertebral augmentation (Kiva) | • Hospitalizations  
| | | • Treatment-related morbidity  
| Individuals:  
| • With osteolytic vertebral compression fractures | Interventions of interest are:  
| | • Balloon kyphoplasty, or mechanical vertebral augmentation (Kiva) | Comparators of interest are:  
| | | • Conservative care | Relevant outcomes include:  
| | | • Symptoms  
| | | • Functional outcomes  
| | | • Quality of life  
| | | • Hospitalizations  
| | | • Treatment-related morbidity |  
| Individuals:  
| • With osteoporotic or osteolytic vertebral compression fractures | Interventions of interest are:  
| | • Radiofrequency kyphoplasty | Comparators of interest are:  
| | | • Conservative care | Relevant outcomes include:  
| | | • Symptoms  
| | | • Functional outcomes  
| | | • Quality of life  
| | | • Hospitalizations  
| | | • Treatment-related morbidity |
reduction in pain, disability, and analgesic use in patients with cancer-related compression fractures. However, because the results of the comparative studies of vertebroplasty have suggested possible placebo or natural history effects, the evidence these studies provide is insufficient to warrant conclusions about the effect of kyphoplasty on health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

After consideration of clinical input, we concluded that, although the scientific evidence does not permit conclusions about the impact on health outcomes and that comparative studies with long-term outcomes are lacking, numerous case series, including large prospective reports, have consistently shown that vertebroplasty and percutaneous balloon kyphoplasty may alleviate pain and improve function in patients with osteoporotic vertebral fractures that have failed to respond to conservative treatment (at least 6 weeks) with analgesics, physical therapy, and rest. More recent randomized trials, which have compared percutaneous balloon kyphoplasty with medical management, have also reported benefit. Given the absence of alternative treatment options and the morbidity associated with extended bedrest, percutaneous balloon kyphoplasty and mechanical vertebral augmentation may be considered reasonable treatment options in patients with vertebral fractures who fail to improve after 6 weeks of conservative therapy and, therefore, may be considered medically necessary both for this patient population and populations with severe pain due to osteolytic lesions of the spine related to multiple myeloma or metastatic malignancies.

For individuals who have osteoporotic or osteolytic vertebral compression fractures who receive radiofrequency kyphoplasty, the evidence includes a systematic review and an RCT. Relevant outcomes include symptoms, functional outcomes, quality of life, hospitalizations, and treatment-related morbidity. The only RCT (N=80) identified showed similar results between radiofrequency kyphoplasty and balloon kyphoplasty. The systematic review suggested that radiofrequency kyphoplasty is superior to balloon kyphoplasty in pain relief, but the review itself was limited by the inclusion of a small number of studies as well as possible bias. Corroboration of these results in a larger number of patients would be needed to determine with greater certainty whether radiofrequency kyphoplasty provides outcomes similar to balloon kyphoplasty. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Background**

**Osteoporotic Vertebral Compression Fracture**

Osteoporotic compression fractures are common. It is estimated that up to 50% of women and 25% of men will have a vertebral fracture at some point in their lives. However, only about one-third of vertebral fractures reach clinical diagnosis, and most symptomatic fractures will heal within a few weeks or 1 month. A minority of patients will exhibit chronic pain following osteoporotic compression fracture that presents challenges for medical management.
Treatment
Chronic symptoms do not tend to respond to the management strategies for acute pain such as bedrest, immobilization or bracing device, and analgesic medication, sometimes including narcotic analgesics. The source of chronic pain after vertebral compression fracture may not be from the vertebra itself but may be predominantly related to strain on muscles and ligaments secondary to kyphosis. This type of pain frequently is not improved with analgesics and may be better addressed through exercise. Conventional vertebroplasty surgical intervention may be required in severe cases not responsive to conservative measures.

Osteolytic Vertebral Body Fractures
Vertebral body fractures can also be pathologic, due to osteolytic lesions, most commonly from metastatic tumors. Metastatic malignant disease involving the spine generally involves the vertebral bodies, with pain being the most frequent complaint.

Treatment
While radiotherapy and chemotherapy are frequently effective in reducing tumor burden and associated symptoms, pain relief may be delayed days to weeks, depending on tumor response. Further, these approaches rely on bone remodeling to regain vertebral body strength, which may necessitate supportive bracing to minimize the risk of vertebral body collapse during healing.

Regulatory Status
Kyphoplasty is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA). Balloon kyphoplasty requires the use of an inflatable bone tamp. In July 1998, one such tamp, the KyphX® inflatable bone tamp (Medtronic), was cleared for marketing by the FDA through the 510(k) process. Other devices with the FDA 510(k) marketing clearance include the AVAmax® Vertebral Balloon system (CareFusion), NeuroTherm Parallax® Balloon Inflatable Bone Tamp (NeuroTherm), Stryker iVAS® Balloon catheter, and Synthes Synflate™ Vertebral Balloon System (Synthes [West Chester, PA]). StabiliT® Vertebral Augmentation System (Merit Medical) for radiofrequency vertebral augmentation was cleared for marketing in 2009. FDA product code NDN.

In 2014, the Kiva® VCF Treatment System (Benvenue Medical) was cleared for marketing by the FDA through the 510(k) process. FDA product code NDN.

Polymethylmethacrylate bone cement was available as a drug product before enactment of the FDA's device regulation and was at first considered what the FDA termed a "transitional device." It was transitioned to a class III device and then to a class II device, which required future 510(k) submissions to meet "special controls" instead of "general controls" to assure safety and effectiveness. In July 2004, KyphX® HV-RTM bone cement was cleared for marketing by the FDA through the 510(k) process for the treatment of pathologic fractures of the vertebral body due to osteoporosis, cancer, or benign lesions using a balloon kyphoplasty procedure. Subsequently, other products such as Spine-Fix®
Biomimetic Bone Cement, KYPHON® HV-R® Bone Cement, and Osteopal® V (Heraeus) have received issued 510(k) marketing clearance for the fixation of pathologic fractures of the vertebral body using vertebroplasty or kyphoplasty procedures. FDA product code: NDN.

Table 1 lists examples of FDA-cleared devices for kyphoplasty and vertebral augmentation.

**Table 1. Kyphoplasty and Vertebral Augmentation Devices Cleared by the U.S. Food and Drug Administration**

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Date Cleared</th>
<th>510(k) No.</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stryker iVAS Elite Inflatable Vertebral Augmentation System</td>
<td>Stryker Corporation</td>
<td>12/21/2018</td>
<td>K181752</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>SpineJack Expansion Kit</td>
<td>Vexim SA</td>
<td>8/30/2018</td>
<td>K181262</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>SpineKure Kyphoplasty System</td>
<td>Hanchang Co. Ltd.</td>
<td>5/29/2018</td>
<td>K172871</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>KYPHON HV-R Bone Cement</td>
<td>Medtronic Sofamor Danek USA Inc.</td>
<td>5/18/2018</td>
<td>K180700</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>Modified Winch Kyphoplasty (15 and 20 mm) 11 Gauge Balloon Catheters</td>
<td>G-21 s.r.l.</td>
<td>8/23/2017</td>
<td>K172214</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>13G InterV Kyphoplasty Catheter (Micro) and 11G InterV Kyphoplasty Catheter (Mini-Flex)</td>
<td>Pan Medical Ltd.</td>
<td>11/1/2016</td>
<td>K162453</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>Kyphon HV-R Bone Cement</td>
<td>MEDTRONIC INC</td>
<td>8/24/2016</td>
<td>K160983</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>System/Procedure</td>
<td>Manufacturer</td>
<td>Date</td>
<td>K-Number</td>
<td>Description</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
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<td>--------------------------------------------------</td>
</tr>
<tr>
<td>MEDINAUT Kyphoplasty System</td>
<td>IMEDICOM Co. Ltd.</td>
<td>7/29/2016</td>
<td>K153296</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>OSTEOPAL plus</td>
<td>HERAEUS MEDICAL GMBH</td>
<td>4/22/2016</td>
<td>K153737</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>AVAflex Vertebral Balloon System</td>
<td>CAREFUSION</td>
<td>11/24/2015</td>
<td>K151125</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>Osseoflex SB Straight Balloon 10g/4ml Osseoflex SB Straight Balloon 10g/2ml</td>
<td>OSSEON LLC</td>
<td>4/9/2015</td>
<td>K150607</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>InterV Kyphoplasty Catheter (Balloon Length: 1015 and 20mm) InterV Kyphoplasty Catheter (Mini) (Balloon Length: 10 15 and 20mm)</td>
<td>PAN MEDICAL LTD</td>
<td>3/6/2015</td>
<td>K150322</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>GUARDIAN-SG Inflatable Bone Expander System</td>
<td>BM KOREA CO. LTD.</td>
<td>1/16/2015</td>
<td>K143006</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>ZVPLASTY</td>
<td>ZAVATION LLC</td>
<td>9/12/2014</td>
<td>K141419</td>
<td>To repair vertebral compression fractures</td>
</tr>
<tr>
<td>KIVA VCF TREATMENT SYSTEM</td>
<td>BENVENUE MEDICAL INC.</td>
<td>8/14/2014</td>
<td>K141141</td>
<td>To repair vertebral compression fractures</td>
</tr>
</tbody>
</table>

**Rationale**

This evidence review was created in December 2002 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through February 18, 2019.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The natural history of pain and disability associated with these conditions vary. Also, pain and functional ability are subjective outcomes, susceptible to placebo effects. Nonspecific or placebo effects can be quite large for an invasive procedure such as kyphoplasty for which there is no blinding. The placebo effect may be on the order of 6 to 7 mm on a 100-mm scale, for invasive procedures, and even larger effects (10%) have been observed in the sham-controlled vertebroplasty trials. Therefore, sham-controlled comparison studies are important to demonstrate the clinical effectiveness of kyphoplasty over and above any associated nonspecific or placebo effects.

Adverse effects related to kyphoplasty are the primary harms to be considered. Principal safety concerns relate to the incidence and consequences of leakage of the injected polymethylmethacrylate (PMMA).

**Osteoporotic Vertebral Compression Fractures**

**Clinical Context and Therapy Purpose**
The purpose of balloon kyphoplasty or mechanical vertebral augmentation (Kiva) is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with osteoporotic vertebral compression fractures (OVCF).

The question addressed in this evidence review is: does the use of balloon kyphoplasty or mechanical vertebral augmentation improve the net health outcome for individuals who have OVCF?
The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant population of interest are individuals with OVCF.

**Interventions**
The therapy being considered is balloon kyphoplasty or mechanical vertebral augmentation (Kiva). The intervention involves the fluoroscopically guided injection of PMMA into a cavity created in the vertebral body with a balloon or mechanical device to provide support and symptomatic relief in patients.

Balloon kyphoplasty is a variant of vertebroplasty and uses a specialized bone tamp with an inflatable balloon to expand a collapsed vertebral body as close as possible to its natural height before injection of PMMA. Radiofrequency kyphoplasty (RFK; also known as radiofrequency targeted vertebral augmentation) is a modification of balloon kyphoplasty. In this procedure, a small diameter articulating osteotome creates paths across the vertebra. An ultra-high viscosity cement is injected into the fractured vertebral body, and radiofrequency is used to achieve the desired consistency of the cement. The ultra-high viscosity cement is designed to restore height and alignment to the fractured vertebra, along with stabilizing the fracture.

It has been proposed that kyphoplasty may provide an analgesic effect through mechanical stabilization of a fractured or otherwise weakened vertebral body. However, other possible mechanisms of effect have been postulated, one of which is thermal damage to intraosseous nerve fibers, given that PMMA undergoes a heat-releasing (exothermic) reaction during its hardening process.

**Vertebral Augmentation**
Kiva is another mechanical vertebral augmentation technique that uses an implant for structural support of the vertebral body to provide a reservoir for bone cement. The Kiva VCF Treatment System consists of a shaped memory coil and an implant, which is filled with bone cement. The coil is inserted into the vertebral body over a removable guidewire. The coil reconfigures itself into a stack of loops within the vertebral body and can be customized by changing the number of loops of the coil. The implant, made from PEEK-OPTIMA, a biocompatible polymer, is deployed over the coil. The coil is then retracted, and PMMA is injected through the lumen of the implant. The PMMA cement flows through small slots in the center of the implant, which fixes the implant to the vertebral body and contains the PMMA in a cylindrical column. The proposed advantage of the Kiva system is a reduction in cement leakage.

**Comparators**
Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing, in a home setting as well as an outpatient clinical setting. Conventional vertebroplasty procedures may also be used to treat this condition.
Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. Kyphoplasty may also restore lost vertebral body height and reduce kyphotic deformity. Potential health outcomes related to kyphotic deformity include pulmonary or gastrointestinal compression and associated symptoms, and vertebral compression fractures may be associated with lower health-related QOL.

Timing
The existing literature evaluating balloon kyphoplasty or mechanical vertebral augmentation (Kiva) as a treatment for osteoporotic vertebral compression fractures has varying lengths of follow-up, ranging from one month to four years.

Setting
Patients with osteoporotic vertebral compression fractures are managed by orthopedic surgeons, endocrinologists, physical therapists, and primary care providers in an outpatient clinical setting. Vertebroplasty procedures would be performed in an inpatient setting.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Balloon Kyphoplasty vs Conservative Care
Wardlaw et al (2009) reported on the FREE trial, a nonblinded industry-sponsored, multisite RCT in which 300 adults with 1 to 3 painful osteoporotic vertebral compression fractures (VCFs) of less than 3 months in duration were assigned to kyphoplasty or conservative care. Scores for the primary outcome, 1-month change in the 36-Item Short-Form Health Survey Physical Component Summary score, were significantly higher for those in the kyphoplasty group. The difference between groups was 5.2 points (95% confidence interval [CI], 2.9 to 7.4 points; p<0.001). Kyphoplasty was associated with greater improvements in the 36-Item Short-Form Health Survey Physical Component Summary scores at 6-month follow-up (3.39 points), but not at 12- or 24-month follow-ups. Greater improvement in back pain was observed over 24 months for kyphoplasty (-1.49 points) and remained statistically significant at 24 months. Participants in the kyphoplasty group also reported greater improvements in QOL and Roland-Morris Disability Questionnaire (RMDQ) scores at short-term follow-up. 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 groups were no longer apparent at 12 months, possibly due to natural healing of fractures.

Edidin et al (2011) reported on mortality risk in Medicare patients who had VCFs and had been treated with vertebroplasty, kyphoplasty, or nonoperatively. This study was industry-funded. Using the U.S. Medicare dataset, the authors identified 858978 patients who had VCFs between 2005 and 2008. The dataset included 119253 kyphoplasty patients and 63693 vertebroplasty patients. Survival was calculated from the index diagnosis date until death or the end of follow-up (up to four years). Cox regression analysis was used to evaluate the joint effect of multiple covariates, which included sex, age, race/ethnicity, patient health status, type of diagnosed fracture, site of service, physician specialty, socioeconomic status, year of diagnosis, and census region. After adjusting for covariates, patients in the surgical cohorts (vertebroplasty or kyphoplasty) had a higher adjusted survival rate (60.8%) than patients in the nonsurgical cohort (50.0%) and were 37% less likely to die. The adjusted survival rates for vertebroplasty or kyphoplasty were 57.3% and 62.8%, respectively, a 23% lower relative risk for kyphoplasty. As noted by the authors, a causal relation could not be determined from this study.

Table 2. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wardlaw (2009)</td>
<td>EU</td>
<td>21</td>
<td>2003-2005</td>
<td>Patients with 1-3 vertebral fractures</td>
<td>Balloon kyphoplasty (n=149)</td>
</tr>
<tr>
<td>Boonen (2011)</td>
<td>EU</td>
<td>21</td>
<td>2003-2005</td>
<td>Patients with 1-3 vertebral fractures</td>
<td>Balloon kyphoplasty (n=149)</td>
</tr>
<tr>
<td>Van Meirhaeghe (2013)</td>
<td>EU</td>
<td>21</td>
<td>2003-2005</td>
<td>Patients with 1-3 vertebral fractures</td>
<td>Balloon kyphoplasty (n=149)</td>
</tr>
<tr>
<td>Study</td>
<td>Mean SF 36 PCS Score Improvement at 1 mo.</td>
<td>Difference in SF 36 Scores between Groups at 24 mo</td>
<td>Serious Adverse Events within 12 mo.</td>
<td>Serious Adverse Events within 24 mo.</td>
<td>Serious Adverse Events within 30 days</td>
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<tr>
<td>Wardlaw (2009)</td>
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<tr>
<td>Kyphoplasty</td>
<td>7.2</td>
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<tr>
<td>95% CI</td>
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<td>Control</td>
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<tr>
<td>95% CI</td>
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<tr>
<td>P value</td>
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<tr>
<td>Boonen (2011)</td>
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<tr>
<td>Kyphoplasty</td>
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<td>3.24 (95% CI 1.47-5.01)</td>
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<td>Control</td>
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</tr>
<tr>
<td>P value</td>
<td>0.0004</td>
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<td></td>
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<tr>
<td>Van Meirhaeghe (2011)</td>
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<td></td>
</tr>
<tr>
<td>Kyphoplasty</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>24 (16.1%)</td>
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<tr>
<td>2.71 (95% CI 1.34-4.09)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>17 (11.3%)</td>
</tr>
<tr>
<td>Study</td>
<td>Mean SF 36 PCS Score Improvement at 1 mo.</td>
<td>Difference in SF 36 Scores between Groups at 24 mo</td>
<td>Serious Adverse Events within 12 mo.</td>
<td>Serious Adverse Events within 24 mo.</td>
<td>Serious Adverse Events within 30 days</td>
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</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
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</tr>
</tbody>
</table>

CI: confidence interval; RCT: randomized controlled trial; SF-36 PCS: 36-Item Short-Form Physical Component Score.

### Table 4. Relevance Study Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population(^a)</th>
<th>Intervention(^b)</th>
<th>Comparator(^c)</th>
<th>Outcomes(^d)</th>
<th>Follow-Up(^e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wardlaw (2009)(^12)</td>
<td></td>
<td></td>
<td>3. Non-surgical treatment was not standardized</td>
<td></td>
<td>2. 12 mo. follow-up</td>
</tr>
<tr>
<td>Boonen (2011)(^13)</td>
<td></td>
<td></td>
<td>3. Non-surgical treatment was not standardized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Meirhaeghe (2013)(^14)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

\(^a\) Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

\(^b\) Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

\(^c\) Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

\(^d\) Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

\(^e\) Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.
### Table 5. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocationa</th>
<th>Blindingb</th>
<th>Selective Reportingc</th>
<th>Follow.Upd</th>
<th>Powere</th>
<th>Statisticalf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boonen (2011)13</td>
<td>3. Allocation concealment unclear</td>
<td>1,2. Not blinded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Meirhaeghe (2013)14</td>
<td>3. Allocation concealment unclear</td>
<td>1,2. Not blinded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

d Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

### Unilateral Balloon Kyphoplasty vs Bilateral Balloon Kyphoplasty

Xiang et al (2018) reviewed the literature through April 2017, evaluating the role of unilateral balloon kyphoplasty and conducted a meta-analysis to compare the efficacy and safety of unilateral and bilateral kyphoplasty in patients with OVCF16. The meta-analysis included 9 studies, 6 RCTs and 3 retrospective comparative studies, on the use of unipedicular balloon kyphoplasty in the treatment of 870 patients with OVCFs. The patients were followed for periods ranging from 2 weeks to 42.2 months with a mean age of 68.85 years. After unilateral balloon kyphoplasty, the mean postoperative visual analog score (VAS) ranged from 1.74 to 4.77, mean postoperative kyphotic angle ranged from 5.9º to 11.22º, and complications involving cement leaks ranged from 6.8 to 21.9% or adjacent level fractures was from 0 to 5.6%). Unilateral kyphoplasty had significantly shorter operative time, and less bone-cement volume; however, the postoperative VAS, Oswestry Disability Index (ODI), vertebral height restoration rate, and cement leakage and adjacent vertebral fracture rate, were similar to bilateral kyphoplasty. The meta-analysis had several inherent weaknesses. The sample size (six RCTs and three retrospective comparative studies) limited the
level of evidence for the analysis. Heterogeneity was also detected among the studies once they were pooled. In addition, incomplete data recording was discovered once clinical outcomes were extracted and pooling this data could lead to bias.

**Section Summary**

Based on the available evidence from the meta-analysis conducted by Xiang et al (2018), unilateral and bilateral balloon kyphoplasty have similar outcomes for the treatment of OCVs. Unilateral kyphoplasty had shorter operation time and radiation exposure. More RCTs are warranted to compare these surgical options.

**Balloon Kyphoplasty vs Vertebroplasty**

**Systematic Reviews**

Wang et al (2018) published a meta-analysis and systematic review aimed at exploring the overall safety and efficacy of balloon kyphoplasty vs percutaneous vertebroplasty for OVCF based on qualified studies using a search of multiple databases up to January 2018. Qualified studies included were RCTs, prospective or retrospective comparative studies, and cohort studies. Sixteen studies were included in the meta-analysis with 647 subjects in the kyphoplasty group and 758 subjects in the vertebroplasty group. The patients were from Israel, Australia, Japan, Canada, Italy, Slovenia, USA, Spain, Germany, China, and Korea. The age of the patients in both groups was over 60 years. The results indicated that kyphoplasty significantly decreased the kyphotic wedge angle (standard mean difference: 0.98; 95% CI 0.40-1.57), increased the postoperative vertebral body height (standard mean difference: −1.27; 95% CI −1.86 to −0.67), and decreased the risk of cement leakage (relative risk, 0.62; 95% CI 0.47–0.80) in comparison with vertebroplasty. However, there was no statistical difference in VAS scores (weighted mean difference, 0.04; 95% CI −0.28–0.36) and ODI scores (weighted mean difference, −1.30; 95% CI −3.34–0.74) between the two groups. The study is limited in that there are differences in the inclusion and exclusion criteria for patients between studies and a bias source could stem from the inclusion of only studies published in English and Chinese. Further, the operating techniques in the various studies differed and the low-quality of included studies and the number of included studies is limited. Lastly, pooled data were used for analysis and individual patients' data were not available which limited a more comprehensive analysis.

Chang et al (2015) reported on a meta-analysis of prospective studies that compared vertebroplasty with kyphoplasty. Included were 6 RCTs and 14 prospective comparative studies (total n=1429 patients). Outcomes were compared for the short (≤1 week after surgery) and long (>6 months) terms. The time to perform vertebroplasty was significantly shorter than kyphoplasty. There was no significant difference between groups in VAS pain scores or Oswestry Disability Index (ODI scores at either short- or long-term follow-up. There was no significant difference between treatments in adjacent-level fractures. Cobb angle at long-term follow-up was improved in the kyphoplasty group compared with vertebroplasty. Kyphoplasty had a significantly lower number of procedures with
cement extravasion, although the percentage of cases with cement leakage is high for both procedures. For example, an RCT by Dohm et al (2014; KAVIAR study) reported overall cement extravasion in 157 (73.4%) of 214 levels treated with kyphoplasty compared with 164 (81.6%) of 201 levels treated with vertebroplasty (p=0.047). Intravascular cement extravasion occurred in 59 (27.6%) of 214 levels treated with kyphoplasty compared with 76 (37.8%) of 201 levels treated with vertebroplasty. The clinical significance of a 10% difference in cement extravasion is uncertain; the occurrences of device-related cement embolism were similar, with 1 (0.5%) case in each group. Kyphosis correction was better in the kyphoplasty group by 1.42° (p=0.036). Pain and function improvements were similar for both procedures.

In a Bayesian network meta-analysis, Zhao et al (2017) examined the efficacy and safety of vertebroplasty, kyphoplasty, and conservative treatment for the treatment of OVCF. Sixteen RCTs were identified (total n=2046 participants; vertebroplasty, 816; kyphoplasty, 478; conservative treatment, 752). Eleven of the RCTs compared vertebroplasty with conservative treatment; two RCTs compared kyphoplasty with conservative treatment, and three RCTs compared kyphoplasty with vertebroplasty. Each trial assessed at least one of the following: VAS, the RMDQ, the European Quality of Life-5 Dimensions, and the observance of any new fractures. Network meta-analysis demonstrated that kyphoplasty was superior to conservative therapy as assessed by VAS (mean difference, 0.94; 95% CI, -0.40 to 2.39), European Quality of Life-5 Dimensions (mean difference -0.10; 95% CI, -0.17 to -0.01), and RMDQ (mean difference, 5.72; 95% CI, 1.05 to 10.60). Insufficient data were present to complete pairwise comparison of kyphoplasty with conservative treatment for some metrics. No significant differences were found between vertebroplasty and kyphoplasty for pain relief, daily function, and QOL. Kyphoplasty was associated with the lowest risk of new fractures, while vertebroplasty was the most effective treatment for pain relief. This review was limited by significant heterogeneity across measured outcomes and length of follow-up in studies; the presence of performing and reporting bias in studies was also a concern.

**Table 6. Systematic Reviews & Meta-Analysis Characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Dates</th>
<th>Trials</th>
<th>Participants</th>
<th>N Range.</th>
<th>Design</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang (2015)</td>
<td>2005-2014</td>
<td>20</td>
<td>Patients with osteoporotic vertebral compression fracture</td>
<td>1429 (NR)</td>
<td>RCT, Prospective</td>
<td>NR</td>
</tr>
<tr>
<td>Zhao (2017)</td>
<td>2006-2016</td>
<td>16</td>
<td>Patients with osteoporotic vertebral compression fracture</td>
<td>2046</td>
<td>RCT</td>
<td>NR</td>
</tr>
<tr>
<td>Study</td>
<td>Dates</td>
<td>Trials</td>
<td>Participants</td>
<td>N Range.</td>
<td>Design</td>
<td>Duration</td>
</tr>
<tr>
<td>----------------</td>
<td>------------</td>
<td>--------</td>
<td>-------------------------------------------------------</td>
<td>----------</td>
<td>-----------------------------</td>
<td>----------</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial; NR: no response.

### Table 7. Systematic Reviews & Meta-Analysis Results

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD in Cobb Angle Reduction</th>
<th>SMD in Long term VAS Scores</th>
<th>VAS Scores</th>
<th>Decrease in Kyphotic Wedge Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chang (2015)</td>
<td>-0.61</td>
<td>-.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>0.49-2.32</td>
<td>-0.57 to 0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.003</td>
<td>0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zhao (2017)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD</td>
<td></td>
<td>-1.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>-1.80 to -0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wang (2018)</td>
<td></td>
<td>(WMD) 0.04</td>
<td>(SMD) 0.98</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>-0.28 to 0.36</td>
<td>0.40 to 1.57</td>
<td></td>
</tr>
</tbody>
</table>

SMD: standard mean difference; WMD: weighted mean difference; CI: confidence interval; MD: mean difference; VAS: visual analog score.

### Section Summary: Balloon Kyphoplasty vs Vertebroplasty

Three systematic reviews with metanalyses compared vertebroplasty and kyphoplasty for outcomes including efficacy, pain relief, daily function, QOL, and included data for up to six months post operation. The studies each had limiting factors that lessened their evidentiary value and increased the potential for bias. Overall, the differences
between balloon kyphoplasty and vertebroplasty were either not significant or data was not sufficient.

**Mechanical Vertebral Augmentation with Kiva vs Balloon Kyphoplasty**

Vertebral augmentation with the Kiva VCF System was compared with balloon kyphoplasty in a pivotal noninferiority RCT reported by Tutton et al (2015). This industry-sponsored, multicenter open-label Kiva Safety and Effectiveness Trial was conducted in 300 patients with 1 or 2OVCFs. Included were patients with VAS scores for back pain of at least 70 mm (/100 mm) after 2 to 6 weeks of conservative care or VAS scores of at least 50 mm after 6 weeks of conservative care, and ODI scores of at least 30%. The primary composite endpoint at 12 months was a reduction in fracture pain by at least 15 mm on the VAS, maintenance or improvement in function on the ODI, and absence of device-related serious adverse events. The primary endpoint was met by 94.5% of patients treated with Kiva and 97.6% of patients treated with kyphoplasty (Bayesian posterior probability of 99.92% for noninferiority, using as-treated analysis). In the 285 treated patients, Kiva resulted in a mean improvement of 70.8 points in VAS scores, compared with a 71.8-point improvement for kyphoplasty. There was a 38.1-point improvement in ODI score for the Kiva group compared with 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 less cement extravasion (16.9%) compared with kyphoplasty (25.8%).

Korovessis et al (2013) reported on a randomized trial of 180 patients with OVCFs that compared mechanical vertebral augmentation with the Kiva device with balloon kyphoplasty in 180 patients withOVCFs. The groups showed similar improvements in VAS scores for back pain, 36-Item Short-Form Health Survey scores, and ODI scores. For example, there was a more than 5.5-point improvement in VAS scores in 54% of patients in the Kiva group and 43% of patients in the balloon kyphoplasty group. Radiologic measures of vertebral height were similar in both groups. Kiva reduced the Gardner kyphotic angle, while residual kyphosis of more than 5°was more frequently observed in the balloon kyphoplasty group. Patients and outcome assessors were reported to be unaware of group assignments, although it is not clear if the Kiva device was visible on radiographs. Cement leakage into the canal only occurred in two patients treated with balloon kyphoplasty, necessitating decompression, compared with none following the Kiva procedure.

### Table 9. Summary of Key RCT Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tutton</td>
<td>US, EU</td>
<td>21</td>
<td>2010-</td>
<td>Patients with</td>
<td>Kiva (n=153)</td>
<td>BK</td>
</tr>
</tbody>
</table>
Table 9. Summary of Key RCT Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Improvement in VAS Score at 12 mo.</th>
<th>Improvement in Oswestry Disability Index at 12 mo</th>
<th>Restoration of AVBHR</th>
<th>VAS Improvement of 5.5 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tutton (2015) 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kiva</td>
<td>70.8</td>
<td>38.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BK</td>
<td>71.8</td>
<td>42.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Korovessis (2013) 21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kiva</td>
<td></td>
<td></td>
<td>24%</td>
<td>44 (54%)</td>
</tr>
<tr>
<td>BK</td>
<td></td>
<td></td>
<td>23%</td>
<td>37 (43%)</td>
</tr>
<tr>
<td>P-value</td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
</tr>
</tbody>
</table>

RCT: randomized controlled trial; BK: balloon kyphoplasty; VAS: visual analog scale.

Table 10. Relevance Study Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population a</th>
<th>Intervention b</th>
<th>Comparator c</th>
<th>Outcomes d</th>
<th>Follow Up e</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tutton (2015) 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. 12 mo. follow-up</td>
</tr>
<tr>
<td>Korovessis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2. Average</td>
</tr>
</tbody>
</table>
### Table 11. Study Design and Conduct Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocationa</th>
<th>Blindingb</th>
<th>Selective Reportingc</th>
<th>Follow Upd</th>
<th>Powere</th>
<th>Statisticalf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tutton (2015)20</td>
<td>2. Allocation not concealed throughout study</td>
<td>1,2. Patients only blinded prior to procedure performance</td>
<td>2. Study not powered for primary or secondary endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Korovessis (2013)21</td>
<td>1,2. Not blinded</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

d Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.
Section Summary: OVCF
A moderately sized unblinded RCT reported short-term benefits of kyphoplasty for pain and other outcomes in patients with painful osteoporotic fractures compared with conservative care. Other relevant studies, including additional RCTs and meta-analysis studies, found similar outcomes for kyphoplasty and vertebroplasty.

For mechanical vertebral augmentation with Kiva, evidence includes a large industry-sponsored, multicenter investigational device exemption trial and a large independent randomized trial. These randomized comparative trials showed outcomes similar to kyphoplasty.

Osteolytic Vertebral Compression Fractures

Clinical Context and Therapy Purpose
The purpose of balloon kyphoplasty or mechanical vertebral augmentation (Kiva) is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative care, in patients with osteolytic vertebral compression fractures.

The question addressed in this evidence review is: does the use of balloon kyphoplasty or mechanical vertebral augmentation improve the net health outcome for individuals who have OVCF or osteolytic VCF?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest are individuals with osteolytic VCF.

Interventions
The therapy being considered is balloon kyphoplasty or mechanical vertebral augmentation (Kiva). The intervention involves the fluoroscopically guided injection of PMMApo into a cavity created in the vertebral body with a balloon or mechanical device to provide support and symptomatic relief in patients.

Comparators
Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing, in a home setting as well as an outpatient clinical setting by a primary care provider.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity.
Table 12. Outcomes of Interest for Individuals with osteolytic vertebral compression fractures

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of Life</td>
<td>reduced pain, disability, and analgesic use in patients</td>
</tr>
</tbody>
</table>

**Timing**
The existing literature evaluating balloon kyphoplasty or mechanical vertebral augmentation (Kiva) as a treatment for osteolytic OCF has varying lengths of follow-up. At least one year of follow-up for the primary outcome is necessary to adequately assess outcomes.

**Setting**
Patients with osteolytic VCF are actively managed by orthopedic surgeons, endocrinologists, physical therapists, and primary care providers in an outpatient clinical setting. Vertebroplasty procedures are performed in the inpatient setting.

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

In a systematic review, Health Quality Ontario (2016) assessed vertebral augmentation for cancer-related VCFs. The assessment identified 33 reports with 1690 patients who were treated with kyphoplasty for spinal metastatic cancers, multiple myeloma, or hemangiomas. For cancer-related VCFs there were 5 case series (110 patients) on multiple myeloma and 6 reports (2 RCTs, 4 case series; 308 patients) on mixed cancers with spinal metastases. Vertebral augmentation resulted in reductions in pain intensity scores, opioid or other analgesic use, and disability scores. One RCT (n=129) compared kyphoplasty with nonsurgical management for cancer-related VCFs, reporting that pain scores, pain-related disability, and health-related QOL were significantly improved in the kyphoplasty group than in the usual care group. The second RCT compared the Kiva device with kyphoplasty in 47 patients with cancer-related compression fractures, finding no significant differences between groups for improvements in VAS pain and ODI scores.

Berenson et al (2011) reported on the results of an international multicenter RCT. They enrolled 134 patients with cancer who were at least 21 years of age. Participants had at least one and not more than three painful VCFs. The primary
outcome was change in functional status from baseline at one month as measured by the RMDQ. Treatment allocation was not blinded, and the primary outcome at one month was analyzed using all participants with data both at baseline and at one month. Participants needed to have a pain score of at least four, on a 0-to-10 scale. Crossover to the balloon kyphoplasty arm was allowed after one month. Reviewers reported scores for the kyphoplasty and nonsurgical groups of 17.6 and 18.2 at baseline, respectively, and 9.10 and 18.0 at 1-month follow-ups (between-group difference in scores, p<0.001).

**Section Summary: Osteolytic VCF**

Results of RCTs and case series would suggest vertebral augmentation reduces pain, disability, and analgesic use in patients with cancer-related compression fractures. However, because the results of the comparative studies of vertebroplasty have also suggested possible placebo or natural history effects, the evidence provided is insufficient to warrant conclusions about the effect of kyphoplasty on health outcomes.

**Radiofrequency Kyphoplasty**

**Clinical Context and Therapy Purpose**

The purpose of RFK is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as conservative care, in patients with osteoporotic or osteolytic vertebral compression fractures.

The question addressed in this evidence review is: does the use of RFK improve the net health outcome for individuals who have OVCFor osteolyticVCF?

The following PICOTS were used to select literature to inform this review.

**Patients**

The relevant population of interest are individuals with osteoporotic or osteolytic VCF.

**Interventions**

The therapy being considered is RFK. The intervention uses radiofrequency energy to ablate metastatic malignant lesions in a vertebral body to provide symptomatic relief.

**Comparators**

Comparators of interest include conservative care. Treatment includes bed rest, local and systemic analgesia, and bracing, in a home setting as well as an outpatient clinical setting by a primary care provider.

**Outcomes**

The general outcomes of interest are symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity.
Table 13. Outcomes of Interest for Individuals with osteoporotic or osteolytic vertebral compression fractures

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of Life</td>
<td>reduced pain, disability, and analgesic use in patients</td>
</tr>
</tbody>
</table>

**Timing**
The existing literature evaluating RFK as a treatment for osteoporotic or osteolytic VCF has varying lengths of follow-up, ranging from 36-80 months. While studies described below all reported at least one outcome of interest, longer follow-up was necessary to fully observe outcomes.

**Setting**
Patients with osteoporotic or osteolytic VCF are actively managed by orthopedic surgeons, endocrinologists, physical therapists, and primary care providers in an outpatient clinical setting.

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Petersen et al (2016) reported on an RCT with 80 patients that compared RFK with balloon kyphoplasty. Patients had been admitted to the hospital for severe back pain and met criteria for surgery after failed conservative treatment. All had osteoporotic compression fractures. Before treatment, VAS pain scores on movement were similar in both groups (8.4 in the balloon kyphoplasty group vs 8.0 in the RFK group). Postoperatively, VAS scores improved by 4.6 after balloon kyphoplasty and 4.4 after RFK (p=NS). Pain at 12 months also did not differ significantly between both groups, with 58% of patients in the balloon kyphoplasty group and 66% of patients in the RFK group reporting no to mild pain on movement (p=NS). There was a trend for greater restoration of the kyphosis angle.

Feng et al (2017) performed a meta-analysis comparing RFK with balloon kyphoplasty in patients with VCFs. Six studies (total n=833 patients) evaluating VCFs were identified. The main outcomes were pain relief (VAS), functionality improvement (ODI), operation time, reduction of deformity (ie, the restoration of vertebral height and kyphosis angle), and incidence of cement leakage. VAS scores improved for both groups after the respective procedure; however, VAS score
dropped 3.96 points more in the RFK group (95% CI, 1.67 to 6.24; p=0.001), with improvement persisting until the 12-month mark. While functionality improvement was initially improved more after RFK than balloon kyphoplasty (p=0.04), the difference between the two groups was not significant after a year (p=0.6). No significant difference in cement leakage between groups was observed. This review was limited by the small number of studies included as well as the presence of significant bias within these studies.

**Adverse Events**

Yi et al (2014) assessed the occurrence of new VCFs after treatment with cement augmenting procedures (vertebroplasty or kyphoplasty) vs conservative treatment in an RCT with 290 patients (363 affected vertebrae). Surgically treated patients were discharged the next day. Patients treated conservatively (pain medication, bedrest, a body brace, physical therapy) had a mean length of stay of 13.7 days. Return to usual activity occurred at 1 week for 87.6% of surgically treated patients and 2 months for 59.2% of conservatively treated patients. All patients were evaluated with radiographs and magnetic resonance imaging at six months and then at yearly intervals until the last follow-up session. At a mean follow-up of 49.4 months (range, 36-80 months), 10.7% of patients had experienced 42 new symptomatic VCFs. There was no significant difference in the incidence of new vertebral fractures between the operative (n=18; 9 adjacent, 9 nonadjacent) and conservative (n=24; 5 adjacent, 16 nonadjacent, 3 same level) groups, but the mean time to a new fracture was significantly shorter in the surgical group (9.7 months) compared with the nonoperative group (22.4 months).

**Section Summary: RFK**

For RFK, the evidence includes a meta-analysis study and an RCT. While the RCT showed similar results compared with balloon kyphoplasty, an improvement in immediate pain relief after RCT was noted in the meta-analysis. Further high-quality studies are needed to determine with greater certainty whether RFK has outcomes similar to balloon kyphoplasty.

The major limitation of all these RCTs was the lack of a sham procedure. Due to the possible sham effect observed in the recent trials of vertebroplasty, the validity of results from non-sham-controlled trials is questionable. Therefore, it is not possible to conclude that these improvements are a true treatment effect. Cement leakage, although slightly reduced in kyphoplasty relative to vertebroplasty, remains a concern.

**Summary of Evidence**

For individuals who have OVCF who receive balloon kyphoplasty, or mechanical vertebral augmentation (Kiva), the evidence includes RCTs and meta-analyses. The relevant outcomes include symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. A meta-analysis and moderately sized unblinded RCT have compared kyphoplasty with conservative care and found short-term benefits in pain and other outcomes. Other RCTs, summarized in a meta-analysis, have reported similar outcomes for kyphoplasty and
vertebroplasty. Two randomized trials that compared mechanical vertebral augmentation (Kiva) with kyphoplasty have reported similar outcomes for both procedures. A major limitation of all these RCTs is the lack of a sham procedure. Due to the possible sham effect observed in the recent trials of vertebroplasty, the validity of the results from non-sham-controlled trials is unclear. Therefore, whether these improvements represent a true treatment effect is uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have osteolytic VCF who receive balloon kyphoplasty or mechanical vertebral augmentation (Kiva), the evidence includes RCTs, case series, and a systematic review of these studies. The relevant outcomes include symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. Two RCTs have compared balloon kyphoplasty with conservative management, and another has compared Kiva with balloon kyphoplasty. Results of these trials, along with case series, would suggest a reduction in pain, disability, and analgesic use in patients with cancer-related compression fractures. However, because the results of the comparative studies of vertebroplasty have suggested possible placebo or natural history effects, the evidence these studies provide is insufficient to warrant conclusions about the effect of kyphoplasty on health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have osteoporotic or osteolytic VCF who receive RFK, the evidence includes a systematic review and an RCT. The relevant outcomes include symptoms, functional outcomes, QOL, hospitalizations, and treatment-related morbidity. The only RCT (n=80) identified showed similar results between RFK and balloon kyphoplasty. The systematic review suggested that RFK is superior to balloon kyphoplasty in pain relief, but the review itself was limited by the inclusion of a small number of studies as well as possible bias. Corroboration of these results in a larger number of patients would be needed to determine with greater certainty whether RFK provides outcomes similar to balloon kyphoplasty. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**Clinical Input From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

**2014 Input**

In response to requests, input was received from 2 physician specialty societies and 3 academic medical centers while this policy was under review in 2014. Input
was sought on the treatment of acute vertebral fractures when severe pain has led to hospitalization or persists at a level that prevents ambulation, and on the treatment of traumatic fractures that have remained symptomatic after six weeks of conservative treatment. Clinical input on these issues was mixed.

**2008 Input**

In response to requests, input was received from 6 physician specialty societies (1 unsolicited) and 2 academic medical centers while this policy was under review in 2008. All reviewers disagreed with the proposed policy, referring to a body of evidence from uncontrolled studies that supported the use of kyphoplasty.

**Practice Guidelines and Position Statements**

**American College of Radiology et al**

The American College of Radiology (2014) and 7 other surgical and radiologic specialty associations published a joint position statement on percutaneous vertebral augmentation. This document stated that percutaneous vertebral augmentation, using vertebroplasty or kyphoplasty and performed in a manner consistent with public standards, is a safe, efficacious, and durable procedure in appropriate patients with symptomatic osteoporotic and neoplastic fractures. The statement also indicated that these procedures be 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**

In a quality improvement guideline on percutaneous vertebroplasty from the Society of Interventional Radiology (2014) vertebral augmentation was recommended for compression fractures refractory to medical therapy. Failure of medical therapy includes the following situations:

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. Patients 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 Academy of Orthopaedic Surgeons**

The American Academy of Orthopaedic Surgeons (2010) approved clinical guidelines on the treatment of osteoporotic spinal compression fractures, which had a weak recommendation for offering kyphoplasty to patients who "present with an osteoporotic spinal compression fracture on imaging with correlating clinical signs and symptoms and who are neurologically intact." The Academy indicated that future evidence could overturn existing evidence and that the
quality of the current literature is poor. These recommendations were based on the literature reviewed through September 2009.

**National Institute for Health and Care Excellence**
The National Institute for Health and Care Excellence (2013) issued a guidance that recommended percutaneous vertebroplasty and percutaneous balloon kyphoplasty as treatment options for treating osteoporotic vertebral compression fractures in persons having severe, ongoing pain after a recent unhealed vertebral fracture, despite optimal pain management, and whose pain has been confirmed through physical exam and imaging at the level of the fracture.\(^{29}\) This guidance did not address balloon kyphoplasty with stenting, because the manufacturer of the stenting system (Synthes) stated there is limited evidence for vertebral body stenting given that the system had only recently become available.

The Institute (2008) issued guidance on the diagnosis and management of adults with metastatic spinal cord compression. It was last reviewed in 2014, and placed on the static list (no major ongoing studies identified, with the next review in 5 years).\(^{30}\) The guidance stated that vertebroplasty or kyphoplasty should be considered for patients who have vertebral metastases, and no evidence of spinal cord compression or spinal instability if they have mechanical pain resistant to conventional pain management and vertebral body collapse. Surgery should only be performed when all appropriate specialists, agree. Despite a relatively small sample base, the Institute concluded the evidence suggests, in a select subset of patients, that early surgery may be more effective at maintaining mobility than radiotherapy.

**U.S. Preventive Services Task Force Recommendations**
Not applicable.

**Medicare National Coverage**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 14.

### Table 14. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02461810(^a)</td>
<td>A Prospective, Multicenter, Randomized, Comparative Clinical Study to Compare the</td>
<td>152</td>
<td>Feb 2018 (ongoing)</td>
</tr>
</tbody>
</table>
Safety and Effectiveness of Two Vertebral Compression Fracture (VCF) Reduction Techniques: the SpineJack® and the KyphX Xpander® Inflatable Bone Tamp

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

REFERENCES

3. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). Percutaneous vertebroplasty or kyphoplasty for vertebral fractures caused by osteoporosis or malignancy. TEC Assessments. 2008;Volume 23:Tab 5.

Billing Coding/Physician Documentation Information

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>22513</td>
<td>Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device (eg, kyphoplasty), 1 vertebral body, unilateral or bilateral cannulation, inclusive of all imaging guidance; thoracic</td>
</tr>
<tr>
<td>22514</td>
<td>Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device (eg, kyphoplasty), 1 vertebral body, unilateral or bilateral cannulation, inclusive of all imaging guidance; lumbar</td>
</tr>
</tbody>
</table>
22515 Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device (eg, kyphoplasty), 1 vertebral body, unilateral or bilateral cannulation, inclusive of all imaging guidance; each additional thoracic or lumbar vertebral body (List separately in addition to code for primary procedure)

ICD-10 Codes

C41.2 Malignant neoplasm of vertebral column
C79.51- Secondary malignant neoplasm of bone and bone marrow; code range
C75.52
C90.00- Multiple myeloma; code range
C90.02
D18.09 Hemangioma of other sites
D47.29 Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related issues
M48.50- Collapsed vertebra, not elsewhere classified; code range
M48.58
M80.08 Age related osteoporosis with current pathological fracture, vertebra(e)
M84.48 Pathological fracture, other site
M84.58 Pathological fracture in neoplastic disease, vertebrae
M84.68 Pathological fracture in other disease, other site

Codes 22523, 22524, 22525, 72291 and 72292 were deleted effective12/31/2014.

Additional Policy Key Words

N/A

Policy Implementation/Update Information

6/1/04 New indication added to the Percutaneous Vertebroplasty medical policy. Considered investigational.
2/1/05 No policy statement changes.
2/1/06 Policy changed to address only percutaneous kyphoplasty. Previously was combined with the percutaneous vertebroplasty policy. Remains investigational. Added new CPT codes for kyphoplasty.
8/1/06 No policy statement changes.
2/1/07 No policy statement changes.
8/1/07 No policy statement changes.
2/1/08 No policy statement changes.
8/1/08 No policy statement changes.
10/7/08 Policy statement revised to indicate may be medically necessary if conservative treatment has failed.
11/1/09 No policy statement changes.
11/1/10 Policy statement revised to indicate use in acute vertebral fractures as investigational.
11/1/11 No policy statement changes.
11/1/12 No policy statement changes.
11/1/13  Added to policy: Percutaneous mechanical vertebral augmentation using any other device, including but not limited to Kiva, is considered investigational.

9/1/14  Vertebral body stenting added to investigational statement.

9/1/15  Kiva considered medically necessary. Added notations that CPT 22523, 22524, 22525, 72291, 72292 were deleted 12/31/2014.

9/1/16  No policy statement changes.

9/1/17  The last investigational policy statement was revised to delete the wording, “including but not limited to vertebral body stenting”.

10/1/17  Radiofrequency kyphoplasty was added to the investigational statement and policy title

9/1/18  Updated policy statements for clarity. No change to intent.

9/1/19  No policy statement changes.

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.