Advances in Clinical Radiology 1 (2019) 233–241
ADVANCES IN CLINICAL RADIOLOGY

Vertebral Augmentation

Nicole S. Carter, MBBS[a,b,c], Julian Maingard, MBBS, FRANZCR[b,d,e], Ronil V. Chandra, MBBS, FRANZCR[a,b,*], Hamed Asadi, MD, PhD, FRANZCR[b,d,e,1], Joshua A. Hirsch, MD[f]

[a]Monash University Faculty of Medicine, Nursing and Health Sciences, Melbourne, Victoria, Australia; [b]NeuroInterventional Radiology, Monash Imaging, Level 2 Monash Medical Centre, 246 Clayton Road, Clayton 3168, Australia; [c]Alfred Hospital, Commercial Rd, Melbourne, VIC 3004, Australia; [d]Interventional Neuroradiology, Radiology Department, Austin Hospital, Melbourne, Victoria, Australia; [e]School of Medicine – Faculty of Health, Deakin University, Waurn Ponds, Australia; [f]Neuroendovascular Program, Massachusetts General Hospital, Harvard Medical School, MGH 55 Fruit Street, GRB 241, Boston, MA 02114, USA

KEYWORDS

• Vertebral augmentation • Vertebroplasty • Kyphoplasty • Vertebral compression fracture • Osteoporosis • Metastasis

KEY POINTS

- Vertebral augmentation is a minimally invasive, image-guided procedure that involves the insertion of bone cement into the fractured vertebral body. It is a treatment option for vertebral compression fractures that cause severe pain despite medical management.
- Data from blinded randomized trials on vertebroplasty diverge regarding its efficacy in osteoporotic vertebral compression fractures (VCFs). Several sham-controlled trials have found no benefit over placebo, yet were flawed by methodological limitations. A recent trial has demonstrated vertebroplasty to confer benefit over sham.
- Data from large randomized trials support the use of kyphoplasty for osteoporotic and neoplastic VCFs.
- The risk of complications from vertebral augmentation is low. Unrecognized leakage of bone cement outside the vertebral body is the major source of complications, yet most leaks are asymptomatic.

INTRODUCTION

Vertebral compression fractures (VCFs) are a common complication of osteoporosis and vertebral neoplasms, and constitute a major source of morbidity and mortality from these conditions [1]. For most patients with VCFs, conservative therapies form the mainstay of treatment, including analgesic medications, adjunct devices such as orthotic braces, a period of bed rest, or physical therapy. In those with milder pain and minimal restriction of function, this management approach may be sufficient. However, a subset of patients will have severe pain and functional limitations despite these measures, or may experience unacceptable adverse effects from narcotic analgesia and immobilization. In this population, vertebral augmentation is an effective, minimally invasive treatment option.

Vertebral augmentation procedures involve the percutaneous, image-guided infiltration of bone cement into a fractured vertebral body. The primary goal is relief from back pain, and secondary goals include biomechanical stabilization of the

Disclosure Statement: J.A. Hirsch reports providing consulting services for Medtronic. The remaining authors have no relevant financial interests that relate to the research or techniques described in this article.

[1] Present address: 145 Studley Road, Heidelberg, Victoria 3084, Australia.

*Corresponding author. NeuroInterventional Radiology, Monash Imaging, Monash Health, Melbourne, Victoria, Australia. *E-mail address:* ronil.chandra@monash.edu

https://doi.org/10.1016/j.yacr.2019.05.002
2589-8744/19/

vertebral body and improved mobility and functional status. In vertebroplasty, cement is injected directly into the VCF, while kyphoplasty involves the creation of a cavity within the vertebral body for cement infiltration, commonly with the insertion of a balloon tamp.

Experience has shown favorable patient outcomes in pain relief and improved functional status. However, there remains divided opinion as to the utility of vertebral augmentation procedures, with mixed results from large randomized trials. This article will discuss current issues in vertebral augmentation for VCFs and present the latest data on efficacy and safety.

CONSIDERATIONS IN PROCEDURAL TECHNIQUE

Indications

Vertebral augmentation is best performed in the following situations

Acute (≤6 weeks) symptomatic osteoporotic VCF, refractory to medical management

Symptomatic VCF caused by spinal neoplasia refractory to medical management

Subacute or chronic (>12 weeks) fractures refractory to medical management may be considered with advanced imaging selection and careful correlation with clinical findings

Failure of medical management can be defined as

- Pain persisting to a level that compromises quality of life, despite medical therapies
- Unacceptable adverse effects occurring because of the analgesic doses required to relieve pain

A reasonable trial of medical management is 2 to 4 weeks, but earlier treatment may be considered for those requiring high-dose narcotic analgesia or hospitalization because of pain.

Contraindications

Absolute contraindications include: sepsis or spinal infection, known allergy to bone cement, uncorrectable coagulopathy, myelopathy caused by facture retropulsion or epidural tumor extension, and inability to tolerate procedural sedation or anesthesia because of cardiopulmonary risk.

Relative contraindications are procedures with these conditions should be treated only by experienced operators. They include: procedure above the level of T5, loss of at least 75% of vertebral height, substantial destruction of vertebral body walls, disruption to the posterior cortex of the vertebral body, and epidural extension into the central spinal canal or neural foramina.

Preprocedural Imaging

Imaging of the spine should be performed in all potential augmentation procedures to confirm the fracture level, assess acuity, and evaluate for possible contraindications or technical difficulties.

The initial imaging modality is often conventional radiographs or computed tomography (CT). However, these modalities are limited in their capacity to assess fracture acuity. MRI is the investigation of choice. Acute fractures are optimally shown on a combination of fluid-sensitive short-tau inversion recovery (STIR) or T2-weighted fat-saturated fast spin echo sequences, with bone marrow edema represented by a T2 hyperintense signal, and a T1 hypointense fracture line occasionally visible. Through MRI, the operator can assess the vertebral body posterior cortex, spinal canal, neural foraminal, and presence of avascular necrosis. The operator can also evaluate for fracture retropulsion and epidural tumor extension. CT may be used as an adjunct, predominantly to assess integrity of the posterior cortex.

Technetium-99m (99mTc) nuclear scintigraphic bone scan is a useful alternative for patients with contraindications to MRI. Higher intake of the injected radiotracer represents acute unhealed fractures. A combination of bone scan and single-photon emission CT (SPECT-CT) allows 3-dimensional imaging and anatomic evaluation.

Image Guidance

Fluoroscopic guidance is optimal for vertebral augmentation procedures, allowing real-time monitoring of needle placement (Figs. 1 and 2) and cement infiltration. Biplane fluoroscopy is preferred because of multiple imaging plane assessment without the need to move or realign equipment. Fixed fluoroscopic equipment confers higher image quality and lower risks of radiation exposure when compared with mobile C-arms. As with preprocedure imaging, CT may be utilized as an adjunct, and may here allow the detection of small cement leaks because of high contrast resolution [2,3].

Special Considerations

Vertebra plana

Safe placement of the augmentation needle becomes challenging in cases of vertebra plana, in which vertebral body height is nearly completely lost. A bow-tie

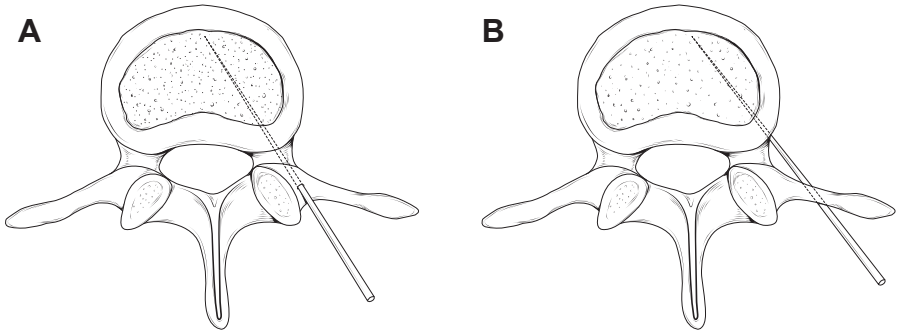

FIG. 1 (**A**) Transpedicular and (**B**) parapedicular approaches to the vertebral body. (**A**) The transpedicular approach takes the needle from the posterior surface of the pedicle, through the pedicle's length, and into the vertebral body. (**B**) The parapedicular advances the needle along the lateral surface of the pedicle and penetrates the vertebral body at its junction with the pedicle. This approach may achieve a more medial position of the needle when treating smaller pedicles.

configuration of the vertebral body is commonly seen, in which the center is maximally compressed, which typically requires operators to place bilateral needles with a more lateral final position of the needle [4]. Only a small amount of cement is generally necessary for pain relief [5].

Multilevel treatments

Patients may have multiple painful VCFs that could be treated in a single procedural setting, yet currently no clear guidelines or evidence exist regarding the maximal or optimal number of levels to treat. Multilevel treatment has potential risks including increased postprocedural pain, extended operative time, or cement toxicity. Two deaths have been reported in the literature in patients undergoing multilevel treatment of more than 8 concurrent levels [6]. Treating a maximum of 3 levels in a single session is thus recommended [7,8].

EVIDENCE FOR EFFICACY

Evidence for the efficacy of vertebral augmentation has evolved over time. Early positive results in observational studies and meta-analyses led to increased uptake [9]. However, since that time, contrasting results have been demonstrated by large trials.

Vertebroplasty

Early evidence

The 2007 VERTOS trial was the first to compare vertebroplasty with medical management in the treatment of osteoporotic VCFs [10]. In the 34 patients randomized to receive vertebroplasty (n = 18) or medical management (n = 16), significant pain relief was reported by 1 day after the procedure. Vertebroplasty resulted in significant reduction in visual analogue scale (VAS) pain scores (from 7.1 to 4.7), as well as reductions in

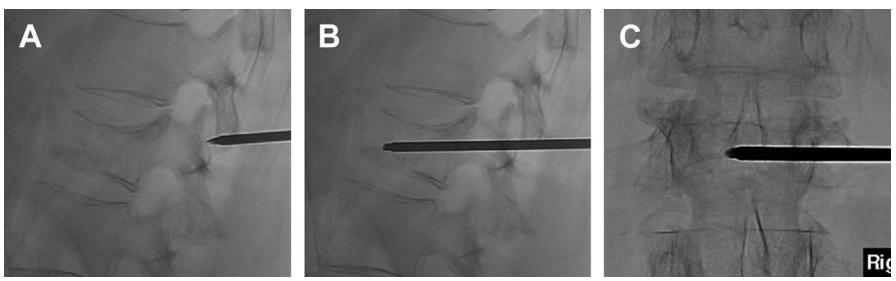

FIG. 2 Needle trajectory for a unilateral transpedicular approach in the lumbar spine. (**A**) Lateral fluoroscopic image of the vertebral body prior to vertebroplasty. The needle trajectory is extrapolated during initial transpedicular access to achieve final needle position in the midline on (**B**) lateral and (**C**) anteroposterior fluoroscopic images.

postprocedural analgesic requirements and improvements in disability and quality of life questionnaire scores. However, this trial was limited by its small size and lack of blinding.

In 2009, 2 high-profile multicenter randomized controlled trials (RCTs) were published in the *New England Journal of Medicine* (NEJM), comparing vertebroplasty with a sham procedure. The results of both trials diverged from earlier data, calling into question the effectiveness of vertebroplasty. The INVEST trial randomized 131 patients to receive vertebroplasty (n = 68) or a sham procedure that consisted of injecting local anesthetic onto the periosteum of the pedicle combined with placing pressure on the patient's back [11]. At 1 month after the procedure, there was no difference between groups in back pain scores or disability measures (quantified by Roland Morris Disability Questionnaire [RMDQ]). The second 2009 trial, by Buchbinder and colleagues [12], included 78 patients allocated to undergo vertebroplasty (n = 38) or a sham procedure involving the insertion of a blunt stylet needle onto the lamina. As with INVEST, no significant difference was observed between groups in terms of pain scores, disability, or quality of life at any follow-up time point.

These studies are subject to methodological limitations. Both trials included fractures of up to 12 months in age. Neither study required patients to undergo physical examination prior to the procedure. INVEST did not require advanced imaging with MRI or bone scan prior to the procedure; this may have caused radiologically occult adjacent fractures, which may have contributed to back pain, to be missed. The sham procedure utilized in INVEST-involved infiltrating local anesthetic into the periosteum of the fractured vertebral body, which may have acted as an active control by resolving pain originating from adjacent structures. Neither study performed long-term follow-up. In response to criticism of the liberal inclusion criteria and the lack of long-term outcome evaluation, Kallmes and colleagues [13] published a 2013 study that followed the INVEST cohort over 12 months. At 12-month follow-up, there was a modest pain reduction in the vertebroplasty arm, although no differences in disability measures were found.

In 2012, a meta-analysis was published that included prospective randomized and nonrandomized trials comparing vertebroplasty with conservative or sham therapy for osteoporotic VCFs [14]. In the 9 trials analyzed, including INVEST, Buchbinder, and VERTOS II, no difference in pain relief was found between vertebroplasty and sham procedure groups. However, vertebroplasty was superior to conservative medical management at all time points studied, in both pain relief and quality-of-life measures.

There remained no large RCT comparing vertebroplasty and medical management until the publication of VERTOS II in 2010 [15]. The authors included only acute fractures of less than 6 weeks duration, with pain severity of at least 5 of 10, focal tenderness on examination, and acute unhealed fracture demonstrated as bone marrow edema on MRI. In total, 202 patients were randomized equally to receive vertebroplasty or medical therapies. After 1 month, significant reductions in back pain were observed in the vertebroplasty group compared with conservative management, and this effect was durable at 1-year follow-up. Quality of life (measured by several questionnaires) was also improved in the vertebroplasty group. However, this trial was limited by a lack of blinding.

Further similar trials followed. In 2011, Farrokhi and colleagues [16] compared vertebroplasty with medical management for osteoporotic VCFs, randomizing 82 patients to receive vertebroplasty or conservative therapies. At 1 week, vertebroplasty resulted in greater reductions in back pain and quality-of-life measures; these effects were durable to 6 months and 36 months, respectively. Vertebroplasty also resulted in increased vertebral body height and reduction in kyphosis. Blasco and colleagues [17] performed a similar RCT in 2012, randomizing 125 patients to receive vertebroplasty (n = 64) or medical management (n = 61). Significant reductions in VAS and analgesic requirements were observed in the vertebroplasty group.

Recent evidence

In 2016, the VAPOR trial (Vertebroplasty for Acute Painful Osteoporotic Fractures) was released, aiming to compare vertebroplasty with a sham procedure, thus ensuring blinding, while also addressing some of the limitations of the 2009 trials [18,19]. The 120 enrolled patients were randomized to receive vertebroplasty (n = 61) or a sham procedure that involved the injection of local anesthetic into subcutaneous tissue (n = 59). All fractures were less than 6 weeks old; all were imaged with MRI or SPECT, and a pain threshold of greater than 7/10 was required for inclusion. After 2 weeks, significant pain reduction was observed in the vertebroplasty group, and this effect was durable to 1 and 6 months follow-up. Vertebroplasty resulted in improved quality-of-life measures, improved functional capacity, reduced analgesic requirement, and increased vertebral body height.

A 2016 prospective study by Yang and colleagues [20] followed, with 135 patients enrolled to receive

vertebroplasty or conservative management. Vertebroplasty resulted in faster and greater pain relief and improved quality of life at all time points: 1 week, 1 month, 3 months, 6 months and 1 year. Follow-up surveys indicated that patients who received vertebroplasty had greater overall satisfaction with their treatment compared with those receiving medical management.

VERTOS IV, published in 2018 in the *British Medical Journal* (BMJ), is the most recent large RCT of vertebroplasty for osteoporotic VCFs [21]. In contrast to more recent trials, but in line with the findings of the 2009 studies, VERTOS IV found that vertebroplasty conferred no benefit over a sham procedure. The 176 patients were aged 50 years or older, with VCFs of up to 9 weeks in age, and were randomly allocated to receive vertebroplasty or a sham procedure. All patients received infiltration of local anesthetic into each pedicle. The sham procedure then involved periosteal placement of needles followed by simulated cement injection, while those in the vertebroplasty group underwent cementation. At all time points over the 12-month period, both groups demonstrated clinically and statistically significant reduction in pain and improved quality of life. However, there was no significant difference between groups in these measures.

The findings of VERTOS IV suggest a potential for periosteal anesthetic infiltration in VCF patients, which may be evaluated in further open-label trials. However, results should be carefully scrutinized and viewed in conjunction with those of other recent trials. VAPOR included hospitalized patients and outpatients with severe pain (>7/10), in whom vertebroplasty was offered without delay; VERTOS IV included only outpatients. In VAPOR, vertebroplasty was performed earlier than in VERTOS IV (mean pain duration of 2.8 weeks compared with 6.1 weeks), while VERTOS IV had a delay of 13 days between recruitment and the procedure. Indeed, the findings of VAPOR showed the maximal benefits of vertebroplasty to occur in fractures less than 3 weeks in duration; 88% of VAPOR patients had fractures aged 4 weeks or less, compared with only 25% in VERTOS IV. This later treatment is of particular importance, given the potential for vertebroplasty to prevent spinal deformation and collapse, if performed early enough before these effects progress. Notably, both VAPOR and VERTOS IV compared radiographs of both cohorts over time, demonstrating improved anatomic outcomes after vertebroplasty compared with placebo.

Kyphoplasty

The first large multicenter RCT to evaluate kyphoplasty for VCFs was the 2009 FREE trial (Fracture Reduction Evaluation) [22]. In total, 300 patients were enrolled, with inclusion criteria of severe back pain of less than 3 months duration, focal tenderness on examination, and MRI demonstrating bone marrow edema, loss of vertebral body height or pseudoarthrosis. Both osteoporotic and neoplastic fractures were included. At 1 month, patients receiving kyphoplasty (n = 149) demonstrated significantly improved back pain and quality of life (measured by RMDQ and Short Form 36 Health Survey [SF-36] physical component summary scale) when compared with those receiving medical management (n = 151). Reduced pain scores and reduced analgesic requirements were also observed in the kyphoplasty group, and these effects were durable to 6 months. At 2-year follow-up, there remained a significant reduction in pain scores in the kyphoplasty group, although there were no longer significant differences in quality-of-life scores.

The CAFE (Cancer Patient Fracture Evaluation) trial was a multicenter RCT comparing kyphoplasty with conservative management for malignant VCFs [23]. One hundred thirty-four patients were included, with neoplastic fractures causing severe pain of no more than 4 of 10, RMDQ disability score of no more than 10, and vertebral fracture demonstrated on plain radiographs or MRI. Kyphoplasty resulted in significantly reduced RMDQ scores, pain, and analgesic use, as well as improved quality-of-life measures. However, despite all participants being cancer patients, the precise histology of VCFs was not known or histologically investigated. It was not known if the fracture was caused by metastasis, osteoporosis, or radionecrosis; it is also possible that the etiology was a combination of the factors mentioned. CAFE was also limited by a lack of blinding.

EVOLVE is the most recent and largest study of kyphoplasty efficacy to date [24]. In total, 350 patients received kyphoplasty for painful VCFs, and were prospectively followed to evaluate short- and long-term outcomes. By 1 week, kyphoplasty had resulted in significantly reduced back pain, functional status, and quality-of-life scores, as well as reduced opioid analgesic requirement. These effects were durable at all time points measured (1 week and 1, 3, 6, and 12 months), with 12-month follow-up revealing an average 72% reduction in back pain scores across participants.

A curette may be utilized as an adjunct in kyphoplasty, either before or after inflation of the balloon,

to scrape away sclerotic bone that might prevent the restoration of vertebral body height. The 2013 SCORE trial aimed to evaluate this method in 112 patients receiving kyphoplasty for osteoporotic VCFs [25]. Patients were randomly allocated to receive kyphoplasty procedures in which curetting was performed either before balloon inflation (n = 57), or after inflation, followed by a second balloon tamp (n = 55). Both treatment approaches resulted in significantly improved pain relief and vertebral body height, with no significant difference observed between groups.

Comparing Vertebroplasty with Kyphoplasty

The 2014 KAVIAR trial directly compared vertebroplasty and kyphoplasty for osteoporotic VCFs [26]. The 381 enrolled patients with acute painful VCFs caused by osteoporosis were randomized to receive vertebroplasty (n = 190) or kyphoplasty (n = 191), and were not blinded to the treatment received. All fractures were confirmed by imaging with MRI, bone scan, or CT. Although the trial was terminated early, similar improvements in back pain and functional outcomes were observed across both groups. Operative time was shorter in vertebroplasty, while kyphoplasty led to lower rates of cement extravasation, as demonstrated on CT.

In a smaller trial, Liu and colleagues [27] compared vertebroplasty and kyphoplasty for osteoporotic VCFs. The 100 patients were randomized equally into vertebroplasty and kyphoplasty arms, with both groups demonstrating reductions in back pain and improved vertebral body height and kyphotic wedge angle. There was no significant difference in clinical outcomes between groups, yet because of the higher procedural costs of kyphoplasty, the authors recommended vertebroplasty for osteoporotic VCFs.

Similar results were demonstrated by Rollinghof and colleagues [28], who performed a prospective study of 90 patients receiving either vertebroplasty or kyphoplasty. Both procedures resulted in significantly improved back pain and quality of life, with no difference seen between groups. However, kyphoplasty was superior in restoring height of the vertebral body.

EVIDENCE FOR SAFETY

Overall Complications

The overall risk of complications from vertebral augmentation is low. Across major RCTs evaluating augmentation for osteoporotic VCFs, the rate of serious complications is approximately 1% [6,29,30]. In VERTOS II, the only complications in the vertebroplasty group were 1 urinary tract infection (UTI) and 1 case of asymptomatic cement leakage into a pulmonary artery branch. The Buchbinder trial reported 1 self-resolving thecal sac injury, while in INVEST, there was 1 case of osteomyelitis in a patient who did not receive prophylactic antibiotics. In VAPOR, 1 patient suffered respiratory arrest following sedation prior to vertebroplasty, yet was able to undergo the procedure uneventfully 48 hours later. One patient in the vertebroplasty group sustained a humeral fracture during transfer onto the procedure table.

Cement Leakage

Extravasation of bone cement outside the vertebral body constitutes the major source of vertebral augmentation complications (Fig. 3). When postprocedural CT is performed, asymptomatic leakage is commonly seen. Symptomatic leakage is rare. VERTOS II found that 72% of VCFs treated by vertebroplasty demonstrated some degree of leakage on CT, yet no leakage occurred into the spinal canal, and all patients remained symptomatic. Lower rates of leakage have been reported by other RCTs: 36% in a study by Buchbinder and colleagues, and 34% in VAPOR.

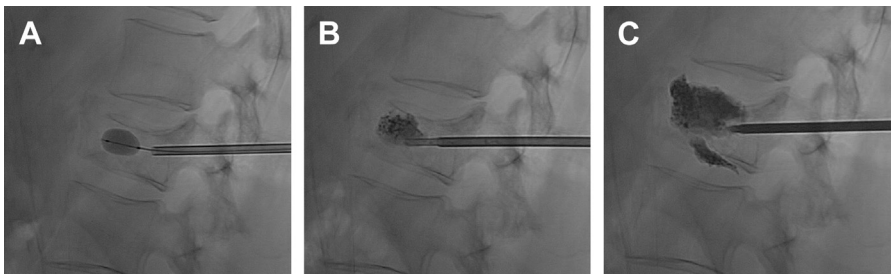

FIG. 3 During percutaneous kyphoplasty, (**A**) a balloon is inflated to create a cavity into which PMMA cement can be instilled. (**B**) The cavity is filled with PMMA, which then extends into the remaining vertebral body. (**C**) A small asymptomatic cement leak was observed from the inferior endplate.

Embolization of cement toward the pulmonary arteries is not uncommon, with rates of 5% to 23%, yet most embolization events are asymptomatic and produce no adverse outcomes.

Kyphoplasty was developed as an alternative to vertebroplasty with a theoretically lower risk of cement leakage due to cement being injected into the low-resistance cavity created by the balloon tamp [31]. Indeed, rates of leakage are consistently lower in trials of kyphoplasty compared with vertebroplasty, occurring in 27% of treated VCFs in the FREE trial and only 2 of 70 patients in the CAFE trial.

The risk of cement leakage is potentially higher in VCFs because of malignant neoplasms, due to regions of tumor-destroyed bone at the vertebral cortex. In a retrospective study of CT-guided vertebroplasty for malignant VCFs, local cement leakage occurred in 59% of vertebrae. Pulmonary cement emboli were evident on 2% of plain chest radiographs and 11% of chest CT scans [32].

Subsequent Vertebral Fractures

Despite claims that vertebral augmentation increases the risk of new or adjacent-level VCF, it is unlikely that this is the case [33]. In 2017, Zhang and colleagues [34] performed a meta-analysis of 12 comparative studies encompassing 1328 patients, comparing the rate of new VCFs following augmentation and conservative treatment. No difference was seen between groups in the number of total new vertebral fractures or adjacent fractures. Anderson and colleagues found comparable results in their meta-analysis, which revealed no significant differences between vertebral augmentation and conservative groups in rates of subsequent VCF. Papanastassiou and colleagues [35] evaluated level 1 and 2 data on vertebral augmentation; they demonstrated that the rate of subsequent fracture for patients treated with vertebral augmentation was 12%, compared with 23% for those treated with conservative management.

In 2017, a biomechanical study of cadaveric spines aimed to evaluate the effect of VCFs and vertebroplasty on vertebral deformation and loading [36]. Vertebral fractures resulted in deformations to both the fractured vertebral level and the adjacent level, and caused transferred loading onto the neural arch. Vertebroplasty of the VCF resulted in significant reduction of these effects, reducing anterior vertebral body deformation by 62% at fractured levels, and 52% at adjacent levels.

Eichler and colleagues [37] aimed to assess the potential benefits of prophylactic vertebroplasty to reduce postaugmentation adjacent level VCF. Thirty-seven patients treated with kyphoplasty for osteoporotic VCFs were included and received either kyphoplasty alone (n = 19) or kyphoplasty with additional vertebroplasty at the adjacent level (n = 18). Adjacent-level prophylactic vertebroplasty did not reduce the rate of subsequent VCFs after kyphoplasty. The authors concluded that adjacent-level VCFs following vertebral augmentation are most likely attributed to underlying disease mechanisms rather than the procedure.

Mortality Benefit?

The excess mortality risk from osteoporotic VCF is considerable [38]. There is some evidence that vertebral augmentation may confer mortality benefit, although none of the currently published large RCTs were powered to assess mortality reduction.

In 2017 to 2018, a review of US Medicare data was performed, encompassing 261,756 kyphoplasty patients and 117,232 vertebroplasty patients [39]. The years following the 2009 NEJM RCTs saw a sharp decline in vertebral augmentation procedures. During this time period, an elevated mortality risk was seen in VCF patients when compared with the years preceding 2009 when vertebral augmentation was more commonly performed.

The first population-based comparison of mortality risk between augmentation, and conservative management was performed in 2011 and included 858,978 patients treated with kyphoplasty, vertebroplasty, or medical management [40]. There was a significantly higher survival rate in those patients receiving augmentation (60.8% compared with 50%). At 4-year follow-up, median life expectancy was 2.2 to 7.3 years greater across the interventional groups compared with conservative management. The same authors published a similar retrospective comparison in 2015, with 1,038,956 VCF patients (141,343 kyphoplasty; 75,365 vertebroplasty) [41]. The conservatively-managed cohort had a 55% higher mortality risk than the kyphoplasty arm, and a 25% higher risk than the vertebroplasty arm. Notably, in the conservative arm there were higher rates of pneumonia, urinary tract infection (UTI), deep vein thrombosis, and cardiac complications than the augmentation cohort.

Contrasting results were reported by McCullough and colleagues, who utilized Medicare claims data to select 9017 patient pairs treated with vertebral augmentation or conservative management, matched by demographics and comorbidities [42]. Although initial mortality rates were lower in the vertebral augmentation cohort, there were no significant differences between groups in mortality at 1 year. However, authors attempted to control selection bias by matching

comorbidities between groups, yet only considered a narrow set of comorbidities, thus not accounting for other conditions that may have potentially led to VCFs.

SUMMARY

The current status of vertebral augmentation as a treatment for painful VCFs remains in some ways controversial. Evidence for its efficacy has evolved over time, particularly because of the difficulties designing an adequately blinded trial that is able to compare augmentation with its real-world alternative. The negative results from 2 2009 sham-controlled RCTs of vertebroplasty cast doubt onto its efficacy. Subsequent trials aimed to mitigate the methodological limitations of these studies, utilizing robust inclusion criteria and finding vertebroplasty to be effective. However, a recent sham-controlled RCT follows the path of the 2009 trials, showing no difference in pain outcomes between vertebroplasty and placebo. Two large RCTs comparing kyphoplasty with conservative management demonstrated its benefit, although a trial comparing kyphoplasty with a sham has not yet been performed. The risk of serious complications from vertebral augmentation is extremely low, and there is meaningful evidence to suggest that vertebral augmentation confers a mortality benefit in VCF patients compared with medical management.

REFERENCES

[1] Ensrud KE, Schousboe JT. Clinical practice. Vertebral fractures. N Engl J Med 2011;364(17):1634–42.

[2] Caudana R, Renzi Brivio L, Ventura L, et al. CT-guided percutaneous vertebroplasty: personal experience in the treatment of osteoporotic fractures and dorsolumbar metastases. Radiol Med 2008;113:114–33.

[3] Vogl TJ, Proschek D, Schwarz W, et al. CT-guided percutaneous vertebroplasty in the therapy of vertebral compression fractures. Eur Radiol 2006;16:797–803.

[4] O'Brien JP, Sims JT, Evans AJ. Vertebroplasty in patients with severe vertebral compression fractures: a technical report. AJNR Am J Neuroradiol 2000;21:1555–8.

[5] Guglielmi G, Andreula C, Muto M, et al. Percutaneous vertebroplasty: indications, contraindications, technique, and complications. Acta Radiol 2005;46:256–68.

[6] Nussbaum DA, Gailloud P, Murphy K. A review of complications associated with vertebroplasty and kyphoplasty as reported to the Food and Drug Administration medical device related web site. J Vasc Interv Radiol 2004;15:1185–92.

[7] Zoarski GH, Snow P, Olan WJ, et al. Percutaneous vertebroplasty for osteoporotic compression fractures: quantitative prospective evaluation of long-term outcomes. J Vasc Interv Radiol 2002;13:139–48.

[8] Mathis JM, Barr JD, Belkoff SM, et al. Percutaneous vertebroplasty: a developing standard of care for vertebral compression fractures. AJNR Am J Neuroradiol 2001;22:373–81.

[9] Jensen ME, McGraw JK, Cardella JF, et al. Position statement on percutaneous vertebral augmentation. J Vasc Interv Radiol 2007;18:325–30.

[10] Voormolen MH, Mali WP, Lohle PNM, et al. Percutaneous vertebroplasty compared with optimal pain medication treatment. AJNR Am J Neuroradiol 2007;28:555–60.

[11] Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. N Engl J Med 2009;361:557–68.

[12] Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. N Engl J Med 2009;361:557–68.

[13] Comstock BA, Sitlani CM, Jarvik JG, et al. Investigational vertebroplasty safety and efficacy trial (INVEST): patient-ported outcomes through 1 year. Radiology 2013;269(1):224–31.

[14] Shi MM, Cai XZ, Lin T, et al. Is there really no benefit of vertebroplasty for osteoporotic vertebral fractures? A meta-analysis. Clin Orthop Relat Red 2012;470(10):2785–99.

[15] Klazen CA, Lohle PN, De Vries J, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet 2010;376:1085–92.

[16] Farrokhi MR, Alibai E, Maghami Z. Randomized controlled trial of percutaneous vertebroplasty versus optimal medical management for the relief of pain and disability in acute osteoporotic vertebral compression fractures. J Neurosurg Spine 2011;14(5):561–9.

[17] Blasco J, Martinez-Ferrer A, Macho J, et al. Effect of vertebroplasty on pain relief, quality of life and the incidence of new vertebral fractures: a 12-month randomized follow-up, controlled trial. J Bone Miner Res 2012;27(5):1159–66.

[18] Clark W, Bird P, Gonski P, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet 2016;388(10052):1408–16.

[19] Hirsch JA, Chandra RV. Resurrection of evidence for vertebroplasty? Lancet 2016;388(10052):1356–7.

[20] Yang EZ, Xu JG, Huang GZ, et al. Percutaneous vertebroplasty versus conservative treatment in aged patients with acute osteoporotic vertebral compression fractures: a prospective randomized controlled clinical study. Spine (Phila Pa 1976) 2016;41(8):653–60.

[21] Firanescu CE, de Vries J, Lodder P, et al. Vertebroplasty versus sham procedure for painful acute osteoporotic vertebral compression fractures (VERTOS IV): randomised sham controlled clinical trial. BMJ 2018;361:k1551 [Erratum in: BMJ 2018;362:k2937].

[22] Wardlaw D, Cummings SR, Van Meirhaeghe J, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Lancet 2009; 373:1016–24.
[23] Berenson J, Pflugmacher R, Jarzem P, et al. Balloon kyphoplasty versus non-surgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. Lancet Oncol 2011;12:225–35.
[24] Beall DP, Chambers MR, Thomas S, et al. Prospective and multicenter evaluation of outcomes for quality of life and activities of daily living for balloon kyphoplasty in the treatment of vertebral compression fractures: the EVOLVE trial. Neurosurgery 2014. https://doi.org/10.1093/neuros/nyy017.
[25] Bastian L, Schils F, Tillman JB, et al. A randomized trial comparing 2 techniques of balloon kyphoplasty and curette use for obtaining vertebral body height restoration and angular deformity correction in vertebral compression fractures due to osteoporosis. AJNR Am J Neuroradiol 2013;34(3):666–75.
[26] Dohm M, Black CM, Dacre A, et al. A randomized trial comparing balloon kyphoplasty and vertebroplasty for vertebral compression fractures due to osteoporosis. AJNR Am J Neuroradiol 2014;35(12):2227–36.
[27] Liu JT, Liao WJ, Tan WC, et al. Balloon kyphoplasty versus vertebroplasty for treatment of osteoporotic vertebral compression fracture: a prospective, comparative and randomized clinical study. Osteoporos Int 2010; 21(2):359–64.
[28] Röllinghoff M, Siewe J, Zarghooni K, et al. Effectiveness, security and height restoration on fresh compression fractures: a comparative prospective study of vertebroplasty and kyphoplasty. Minim Invasive Neurosurg 2009;52(5–6):233–7.
[29] McGraw JK, Cardella J, Barr JD, et al. Society of Interventional Radiology Standards of Practice Committee quality improvement guidelines for percutaneous vertebroplasty. J Vasc Interv Radiol 2003;14(1):311–5.
[30] Chandra RV, Yoo AJ, Hirsch JA. Vertebral augmentation: update on safety, efficacy, cost-effectiveness and increased survival. Pain Physician 2013;16(4):309–20.
[31] Lieberman IH, Dudeney S, Reinhardt MK, et al. Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures. Spine 2001;26(14):1631–7.
[32] Trumm CG, Pahl A, Helmberger TK, et al. CT fluoroscopy-guided percutaneous vertebroplasty in spinal malignancy: technical results, PMMA leakages, and complications in 202 patients. Skeletal Radiol 2012;41: 1391–400.
[33] Uppin AA, Hirsch JA, Centenera LV, et al. Occurrence of new vertebral body fracture after percutaneous vertebroplasty in patients with osteoporosis. Radiology 2003; 226(1):119–24.
[34] Zhang H, Xu C, Zhang T, et al. Does percutaneous vertebroplasty or balloon kyphoplasty for osteoporotic vertebral compression fractures increase the incidence of new vertebral fractures? A meta-analysis. Pain Physician 2017; 20(1):13–28.
[35] Papanastassiou ID, Phillips FM, Van Meirhaeghe J, et al. Comparing effects of kyphoplasty, vertebroplasty, and nonsurgical management in a systematic review of randomized and non-randomized controlled studies. Eur Spine J 2012;21(9):1826–43.
[36] Luo J, Annesley-Williams DJ, Adams MA, et al. How are adjacent spinal levels affected by vertebral fracture and by vertebroplasty? A biomechanical study on cadaveric spines. Spine 2017;17(6):863–74.
[37] Eichler MC, Spross C, Ewers A, et al. Prophylactic adjacent-segment vertebroplasty following kyphoplasty for a single osteoporotic vertebral fracture and the risk of adjacent fractures: a retrospective study and clinical experience. J Neurosurg Spine 2016;25(4):528–34.
[38] Sattui SE, Saag KG. Fracture mortality: associations with epidemiology and osteoporosis treatment. Nat Rev Endocrinol 2014;10:592–602.
[39] Ong KL, Beall DP, Frohbergh M, et al. Were VCF patients at higher risk of mortality following the 2009 publication of the vertebroplasty 'sham' trials? Osteoporos Int 2018;29(2):375–83.
[40] Edidin AA, Ong KL, Lau E, et al. Mortality risk for operated and non-operated vertebral fracture patients in the Medicare population. J Bone Miner Res 2011;26(7): 1617–26.
[41] Edidin AA, Ong KL, Lau E, et al. Morbidity and mortality after vertebral fractures: comparison of vertebral augmentation and nonoperative management in the Medicare population. Spine 2015;40(15):128–41.
[42] McCullough BJ, Comstock BA, Deyo RA, et al. Major medical outcomes with spinal augmentation vs conservative therapy. JAMA Intern Med 2013;173(16): 1514–21.