Vertebroplasty and kyphoplasty: new evidence adds heat to the debate

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Purpose of review
Cement bone augmentation has become very popular worldwide in treating painful noncomplicated spine fractures. Controversy about the effectiveness was raised by two randomized trials in 2009. Recent new evidence contradicts those findings giving credit to vertebroplasty/kyphoplasty.

Recent findings
Well designed prospective clinical trials in cancer and noncancer vertebral fractures as well as an excellent meta-analysis showed that painful vertebral compression fractures have better and faster pain relief, better functional outcomes, and with low complication rate when treated with percutaneous cement than conservatively.

Summary
The saga is unfinished. The treatment of vertebral compression fractures with cement augmentation is still in its infancy. The potential for development with new materials and the injection of biologic and active bone cements or anticancer products, in metastatic disease, will revolutionize the treatment of this condition.

Keywords
cancer, kyphoplasty, pain osteoporosis, vertebral compression fractures, vertebroplasty

INTRODUCTION

The treatment of painful vertebral compression fractures can be divided into two periods: before and after the development of vertebral bone augmentation (VBA). Before, the only effective way to control the excruciating pain from a spine fracture was an epidural infusion of local anesthetics nearby the affected vertebra for a few days. For anesthesiologists not involved in interventional pain management, it is worth noting that vertebroplasty was described in 1987 by Deramond *et al.* [1] in France in helping neurosurgeons stabilize and reinforce the structure of a cervical vertebra weakened by a hemangioma. VBA consists of percutaneously injecting cement into a fractured vertebra to stabilize it, control pain, and increase its strength. VBA may be done via vertebroplasty or kyphoplasty. Kyphoplasty was developed subsequently in North America by Kyphon (later acquired by Medtronic) and entails placing transpedicular percutaneous cannulas in the vertebral body (like a standard vertebroplasty) that serve as channels to introduce inflatable balloons in the vertebral body with the purpose of creating a cavity and re-expanding the fractured vertebra (like an angioplasty) and then filling the cavity with cement at low pressure.

CURRENT INDICATIONS AND CONTRAINDICATIONS FOR VERTEBRAL BONE AUGMENTATION

Vertebral bone augmentation is performed mostly by spine surgeons and interventional radiologists, but also by highly trained interventional pain physicians [2]. Worldwide vertebroplasty and kyphoplasty are mainly used in osteoporotic as well as metastatic cancer/myeloma fractures of the spine. Fewer cases are done in patients with painful or destructive vertebral hemangiomas, traumatic fractures, and radiotherapy-induced osteonecrosis (Kumell's disease). Spine surgeons are also injecting vertebroplasty cement to reinforce the vertebra before placing transpedicular screws for spine fusions in weakened spines. The clinical indication

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KEY POINTS

- Vertebral compression fractures are common and frequently very painful.
- Vertebroplasty and kyphoplasty reinforce the bone structure and control the incidental pain much faster and longer than medical management.
- Both osteoporotic and cancer-related fractured patients benefit from the therapy.
- Promising data will be available soon from ongoing well designed studies on new cements and clinical trials.
- More research is necessary to confirm possible improvements in life expectancy in cancer patients with vertebral compression fractures treated with VBA.

to perform a VBA is based on incidental pain on movement of the spine (coming out of bed, in and out of the car, etc.), an MRI with bone marrow edema visible in T2-weighed cuts, and the absence of neurologic signs. VBA is not indicated in vertebral compression fractures (VCFx) associated with neurologic damage, vertebra plana, in patients with uncorrected coagulopathies, or infections in the surgical area.

PROPHYLACTIC VERTEBRAL BONE AUGMENTATION IN CANCER AND OSTEOPOROSIS

New VCFx may develop in adjacent or distant vertebrae after VBA. Kamano *et al.* [3] reported on the use of prophylactic VBA to prevent new VCFx. They found 18 and 24% new fractures at 3 and 12-month follow-up, respectively. The more vertebrae are affected, the higher is the incidence of new fractures after VBA, pointing to a lack of preventive effect. These numbers, however, are not different of the usual subsequent fracture rate without vertebroplasty [3]. Becker *et al.* randomized 60 patients to treat only the fractured unit or to add an adjacent prophylactic kyphoplasty to the fractured one. The 1-year re-fracture rate was 22 and 25%, respectively (NS). They suggested that there is no indication for pre-emptive kyphoplasty to the adjacent segment [4]. Its expanded use in the vertebra just above the upper level of a spine fixation is not analyzed in this study.

TYPE OF ANESTHESIA

In performing VBA the type of anesthesia seems to follow the pattern of the practitioner. Interventional radiologists use predominantly local anesthesia and mild sedation [5]. Spine surgeons typically are more comfortable with general anesthesia and interventional pain anesthesiologists use more epidurals, spinals, and local anesthetic infiltration with sedation [6].

TECHNICAL ASPECTS AND CLINICAL PEARLS

Movement of the spine triggers excruciating pain so the patient should be carefully positioned, prone, on the table. Standard monitoring and intravenous access are applied. Frequently some analgesia or propofol sedation is required, unless a spinal or epidural has been given beforehand. It is the authors' practice to review again the MRI or computed tomography (CT) scan, and measure the angles and distances for the needle trajectory immediately before the procedure (Fig. 1). Regardless of the choice of anesthesia, once the skin entry sites are identified, we use local anesthesia with bupivacaine 0.25% with epinephrine 5 ug/ml to infiltrate the skin to the periosteum of the pedicle. This is to provide intraoperative and postoperative analgesia as well as vasoconstriction. The techniques for vertebroplasty and KP kyphoplasty have been well described elsewhere and differ only in that kyphoplasty requires larger cannulae and drilling to indwell the inflatable balloon into the vertebral bone. After expanding the balloons in the vertebral bone the cement is injected into the cavity. Studies have shown that unipedicular or bipedicular approaches are acceptable as long as the distribution of the cement is bilateral in the vertebral bone [7,8]. There is no consensus on the injection of contrast before the cement and it is not the practice of some authors [9]. Injection of the cement must be done carefully with live fluoroscopy in the lateral view or simultaneous antero-posterior and lateral to

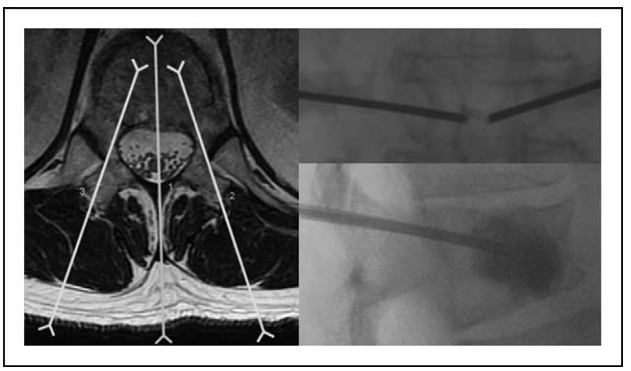

FIGURE 1. Preprocedure measurements and angle calculations (left). Final needle position in antero-posterior and lateral fluoroscopic views (right).

monitor the spread of the contrast/cement mixture. If it is seen going to the posterior third of the vertebra or into a vein, the injection must be stopped for 1–2 min before resuming the procedure. There are some cements that have the proper viscosity right after mixing along with good visibility properties. VBA is an ambulatory procedure, but factors like prior admission for pain relief, severe comorbidities, reimbursement, and complications may ultimately drive the decision whether the patient is sent home the same day. In our practice 100% of ambulatory patients go home after 2 h in the post anesthesia care unit. An abdominal binder and minor analgesics are recommended for the first few days with follow-up at 4 weeks. Patients are suggested to resume progressively normal activities as permitted by their condition since different levels of activity were not significantly associated with time to new postvertebroplasty fracture [10].

IS IT WORTH THE RISK OF DOING SPINE CEMENT AUGMENTATION?

Is it possible that the infiltration of only the posterior elements could control pain from VCFx? Two recent studies by Mitra *et al.* [11] and Bogduk *et al.* [12] commented on the possibility that part of the pain in VCFx could be due to facet subluxation and changes in loads over the facet joints/capsule as a consequence of the vertebral collapse. Two types are identified according to the nature of fracture. Figure 2a shows subluxation of the superior facet joint in wedge-type fractures and Fig. 2b shows subluxation of the inferior facet joint in flat-type VCFx. The model is very provocative and may explain good outcomes with facet/medial branch blocks in VCFx. However, there are negative results from RCT studies, discussed below, in which no differences were found between the control and vertebroplasty groups. Against this hypothesis is a study on local anesthetic infiltration versus vertebroplasty [13]. This interesting study by Brinjikji *et al.* [13] compared Rolland-Morris Questionnaire (RMQ) results at days 1 and 3 after injection of local anesthetic versus vertebroplasty patients from their INvestigational Vertebroplasty Efficacy and Safety Trial study. The patients who only had local anesthesia improved dynamic pain at 24 and 72 h, whereas 'control'-vertebroplasty patients had better scores in all measurement time periods. Clearly more research is needed in this area.

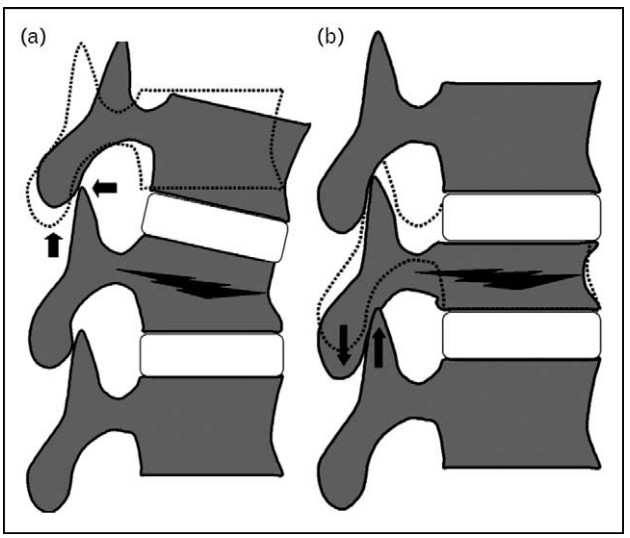

FIGURE 2. Left-hand side shows a wedge-type VCFx with above-level facet subluxation. Right-hand side shows flat-type VCFx with inferior-level facet stress. VCFx, vertebral compression fractures. Reproduced with permission from [12].

OUTCOMES IN CANCER

Pain relief of painful malignant VCFx is paramount in improving quality of life in terminal patients. In Japan, in a small series of mostly metastatic VCFx, with very strict criteria for efficacy, 70% of patients receiving a vertebroplasty showed very good results at 1 week [14].

In 2011 the Cancer Patient Fracture Evaluation (CAFE), a multicenter prospective randomized trial (PRT) study, evaluated the RMQ at 1 month; up to three VCFx were allocated to kyphoplasty or medical management [15▪▪]. The patients in the kyphoplasty group had much better pain relief and improved their functional status as evidenced by the decrease in the RMQ from 17.6 to 9.1 compared with the control group (18.2 to 18.0). Chew *et al.* [16] prospectively collected data on all patients undergoing percutaneous vertebroplasty over a 9-year period. In the second half they used visual analogue pain scores [Visual Analogue Scale (VAS)] and RMQ as well as complications and long-term outcome. Forty-one patients with myeloma and 87 with spinal metastases were followed and documented a reduction in VAS score from 7.75 ± 1.88 before vertebroplasty to 4.77 ± 2.69 after vertebroplasty ($P = 0.001$). RMQ scores improved from 18.55 ± 4.79 to 13.5 ± 6.96 ($P = 0.001$). Complications were recorded in 2%: cement extension to vena cava ($n = 1$), local hematoma ($n = 1$), and loss of sensation over T1 dermatome ($n = 1$). The Kaplan–Meier estimate of 5-year survival after vertebroplasty was 40% for patients with myeloma and 25% for those with metastases. They suggested that vertebroplasty is an important part of the multimodality treatment for cancer with VCFx [16]. A recurrent clinical question is whether radiation therapy

should be used before or after VBA in this population. Hirsch *et al.* [17] reported a series of 200 patients with cancer who received VBA and radiation therapy. In 39% there was complete resolution of the back pain with 88% responding with significant relief. They concluded that the timing of the radiation is irrelevant in relation to the side-effects or efficacy of VBA. However, the study was not randomized and marginally addressed the topic [17].

Conclusion

Vertebral bone augmentation may be a reasonable treatment option for selected patients with severe back pain secondary to destruction of the vertebral body due to osteolytic vertebral metastasis or multiple myeloma, or for painful and/or aggressive hemangioma or eosinophilic granuloma of the spine when conservative medical management has failed to alleviate symptoms. Timing of radiation therapy in relation to the vertebroplasty does not seem to be relevant.

VERTEBROPLASTY VERSUS KYPHOPLASTY

There is a long-standing controversy on the safety and efficacy of vertebroplasty versus kyphoplasty. A recent meta-analysis compared the efficacy and safety of vertebroplasty with kyphoplasty in osteoporotic fractures. The study included only trials reporting pain relief (VAS), disability (Oswestry disability score), and complications (i.e. cement leakage, new fractures) as the primary outcome. Data from eight studies with 848 patients were extracted showing that in the first week vertebroplasty was superior to kyphoplasty, at 3 months kyphoplasty was better than vertebroplasty, and at 1-year there was no difference in functional improvement and pain relief. The risk of cement leakage and subsequent fracture was similar between both techniques [18▪]. An earlier meta-analysis concluded that both kyphoplasty and vertebroplasty provide good pain relief but with some superiority of vertebroplasty. However, the vertebroplasty patients had more leaks and refracture rates [19]. Goz *et al.* compared the trends in the utilization of vertebroplasty and kyphoplasty in the USA. They found that in 2008, the growth of kyphoplasty was faster than vertebroplasty, interventional radiologists performed more vertebroplasty, whereas orthopedic surgeons performed more kyphoplasty, and that more medical complications were related to kyphoplasty [2]. It is interesting that the Kyphoplasty And Vertebroplasty In the Augmentation and Restoration of Vertebral Body Compression Fractures trial (NCT00323609), a large head-to-head comparison between vertebroplasty and kyphoplasty in osteoporotic VCFx sponsored by Medtronic (the manufacturer of the kit for kyphoplasty), was terminated prematurely.

KYPHOPLASTY

The Fracture REduction Evaluation (FREE) trial [20] assessed the efficacy and safety of kyphoplasty mostly in patients with osteoporotic fractures. In a well designed study that enrolled 300 patients it was found that the Short Form 36 (SF-36) score improved from 26.0 at baseline to 33.4 at 1 month in the kyphoplasty group, and from 25.5 to 27.4 in the nonsurgical group (difference between groups 5.2 points, $2.9 - 7.4$; $P < 0.0001$). In another PRT sponsored by Medtronic, Boonen *et al.* [21] compared kyphoplasty to conservative management over a 24-month period. Kyphoplasty was associated with greater improvements in SF-36 Physical Component scores when averaged across the 24-month follow-up period compared with conservative therapy ($P < 0.0004$); the treatment difference remained significant at 6 months ($P < 0.003$) but not at 12 or 24 months. Greater improvement in back pain was observed over 24 months for kyphoplasty ($P < 0.0001$) and the difference between groups remained significant at 24 months ($P < 0.009$). There were two device-related serious adverse events in the second year that occurred at the index vertebrae (a spondylitis and an anterior cement migration). There was no significant difference between groups in the number of patients with new radiographic vertebral fractures (47.5% for kyphoplasty, 44.1% for control). As stated, both qouted studies were supported by Medtronic.

A meta-analysis by Taylor *et al.* [22] showed that pain was clearly reduced with kyphoplasty at 3, 6, 12, and 36 months of follow-up ($P < 0.001$). Pain reductions were greater ($P < 0.0001$) than those observed at the same time points with conservative treatment. Functional capacity and office visits were also reduced in the kyphoplasty groups [22].

VERTEBROPLASTIES

The vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (VERTOS) study is a RCT evaluating osteoporotic VCFx treated with vertebroplasty against conservative treatment with possible cross-over at 2 weeks follow-up. Although small, this is a well designed trial showing that pain relief and improvement of mobility, function, and stature after vertebroplasty

is immediate and significantly better in the short term compared with optimal pain medication [23]. VERTOS II is a PRT of vertebroplasty versus conservative treatment in 202 patients. Vertebroplasty resulted in greater pain relief than conservative treatment; the difference in mean VAS score between baseline and 1 month was 5.2 after vertebroplasty and 2.7 after conservative treatment. Between baseline and 1 year, it was 5.7 after vertebroplasty and 3.7 after conservative treatment. The difference between groups in reduction of the mean VAS score from baseline was 2.6 ($P < 0.000$) at 1 month and 2.0 ($P < 0.0001$) at 1 year [24]. Interestingly, this nicely done study did not receive the media and insurance carrier attention given to the articles published in the *New England Journal of Medicine* [25,26]. Several letters that questioned the methodology and results were published in the *NEJM* and an editorial was published in the *European Spine Journal* titled 'Vertebroplasty: about sense and nonsense of uncontrolled 'controlled randomized prospective trials' [27]. The authors of the *NEJM* studies suggested that the placebo effect could be partially responsible for the positive effect of VBA [28].

In another PRT, Rousing *et al.* [29] reported immediate pain improvement after vertebroplasty in osteoporotic VCFx. The better pain relief persisted at 1-month follow-up, but was not present at 3 and 12 months [29]. The VERTOS IV, an extremely well designed ongoing study (and without industry sponsor), compares vertebroplasty versus active sham procedure in a prospective randomized double-blind fashion and should be able to shed light into this controversy [30▪▪].

Did the referral of patients for VBA change significantly after the *NEJM* studies in 2009? This is a very interesting question because it takes into consideration the opinion of the clinicians following the literature on VBA. The same authors of one of the *NEJM* studies showed that the referral decreased by only 40% (18.9 to 11.3 patients per month), but the percentage of patients receiving the actual treatment out of the smaller pool of referrals increased but not significantly from 67.3 to 76% [31].

It seems also relevant to consider the potential of survival from VBA. Gerling *et al.* [32▪] compared the survival in patients with osteoporotic VCFx who received cement augmentation versus conservative controls. They controlled for comorbidities, age, and number of fractures. The group of patients having VBA had a significant improvement in survival compared with the control group ($P < 0.001$) regardless of age comorbidities and the number of fractures. They concluded that cement augmentation improved survival for up to 2 years when compared with bed rest, opioid analgesia, and bracing regardless of age, sex, number of fractures, and comorbidities [32▪].

COMPLICATIONS

The most frequent complications after VBA are the following:

Leak risk

Considering only prospective data, asymptomatic cement leaks occur in 52 versus 13% for vertebroplasty and kyphoplasty, respectively. Symptomatic leaks are 0.8 versus 0% and the rate of leaks in pathologic fractures seems to be higher than in osteoporosis [33].

Neurologic

This is a very uncommon but feared complication [34].

Potential increase in vertebral compression fractures

In a prospective study with 166 patients undergoing single level vertebroplasty for osteoporosis, Li *et al.* [35▪] found that a factor for new adjacent vertebral fracture was the volume of cement injected. Adjacent new fracture rate was 38% occurring mostly in the first 3 months postprocedure. For nonadjacent VCFx, a low bone density T-score seems to be the main risk factor [35▪]. In a retrospective analysis of 155 vertebroplasty patients, there was a 27% subsequent refracture rate with 48% occurring in the first 3 months after procedure for both adjacent and nonadjacent fractures. Again, a low T-score was the only risk factor [36].

Pulmonary cement embolism

VERTOS II confirmed a striking 26% incidence of pulmonary cement embolism with vertebroplasty. However, there were very small cement pieces only demonstrated with CT scan, probably similar in size to the ones seen in large joint replacements, and did not generate lung reaction. The authors recommended against routine chest X-rays or CT after vertebroplasty [37].

COST–BENEFIT

A cost-effectiveness study in the UK found that kyphoplasty was associated with quality-adjusted life-year (QALY) gains of 0.17 and cost/QALY gains at £8800. The results were supportive of the

assumptions on decreased length of hospital stay and persistence of kyphoplasty-related quality-of-life (QoL) benefits. They concluded that in their setting, treating in-patients with VCFx with kyphoplasty was cost-effective [38]. In a retrospective study of 140 patients comparing vertebroplasty with conservative therapy [39], the cost-effectiveness of vertebroplasty was measured as the average cost per patient per reduction of 1 point in the VAS, ambulation, or activity of daily living scale. After 1 week, vertebroplasty was significantly more cost-effective for all the measured outcomes compared to medical management ($P < 0.05$). From a database with nearly 12 000 patients out of New England, it was found that the cost of kyphoplasty versus vertebroplasty was between 50 and 120% higher, whether the patient was admitted or treated as an outpatient. The higher cost was mainly driven by the expenses related to supplies [40]. In a PRT sponsored by the US Food and Drug Administration (FDA), Cortoss, a new bioactive type of cement, has been recently compared with polymethylmethacrylate in vertebroplasty, and demonstrated promising results [41].

CONCLUSION

A review of the most relevant studies and meta-analysis (Kallmes, Buchbinder, VERTOS, VERTOS II, CAFÉ, FREE, Han's meta-analysis), there appears to be a case for VBA in selected patients with VCFx. These include VCFx in cancer patients, multiple myeloma, and osteoporotic fractures with bone marrow edema. The procedure is increasingly done by properly trained anesthesiology interventional pain specialists with a low rate of complications and excellent clinical outcomes.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

1. Deramond H, Depriester C, Galibert P, Le Gars D. Percutaneous vertebroplasty with polymethylmethacrylate. Technique, indications, and results. Radiol Clin N Am 1998; 36:533–546.
2. Goz V, Koehler SM, Egorova NN, *et al.* Kyphoplasty and vertebroplasty: trends in use in ambulatory and inpatient settings. Spine J 2011; 11:737–744.
3. Kamano H, Hiwatashi A, Kobayashi N, *et al.* New vertebral compression fractures after prophylactic vertebroplasty in osteoporotic patients. Am J Roentgenol 2011; 197:451–456.
4. Becker S, Garoscio M, Meissner J, *et al.* Is there an indication for prophylactic balloon kyphoplasty? A pilot study. Clin Orthopaed Related Res 2007; 458:83–89.
5. Cagli S, Isik HS, Zileli M. Vertebroplasty and kyphoplasty under local anesthesia: review of 91 patients. Turkish Neurosurg 2010; 20:464–469.
6. Peters S, Brecht K, Bracco D, Asenjo JF. Vertebroplasty/kyphoplasty: good alternatives in managing incidental pain in patients with vertebral compression fractures. Reg Anesth Pain Med 2009; PS2:11.
7. Chen L, Yang H, Tang T. Unilateral versus bilateral balloon kyphoplasty for multilevel osteoporotic vertebral compression fractures: a prospective study. Spine 2011; 36:534–540.
8. Kim AK, Jensen ME, Dion JE, *et al.* Unilateral transpedicular percutaneous vertebroplasty: initial experience. Radiology 2002; 222:737–741.
9. Gaughen JR Jr, Jensen ME, Schweickert PA, *et al.* Relevance of antecedent venography in percutaneous vertebroplasty for the treatment of osteoporotic compression fractures. Am J Neuroradiol 2002; 23:594–600.
10. Rad AE, Gray LA, Sinaki M, Kallmes DF. Role of physical activity in new onset fractures after percutaneous vertebroplasty. Acta Radiol 2011; 52:1020–1023.
11. Mitra R, Do H, Alamin T, Cheng I. Facet pain in thoracic compression fractures. Pain Med 2010; 11:1674–1677.
12. Bogduk N, MacVicar J, Borowczyk J. The pain of vertebral compression fractures can arise in the posterior elements. Pain Med 2010; 11:1666–1673.
13. Brinjikji W, Comstock BA, Gray L, Kallmes DF. Local Anesthesia with Bupivacaine and Lidocaine for Vertebral Fracture trial (LABEL): a report of outcomes and comparison with the Investigational Vertebroplasty Efficacy and Safety Trial (INVEST). Am J Neuroradiol 2010; 31:1631–1634.
14. Kobayashi T, Arai Y, Takeuchi Y, *et al.* Phase I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant vertebral compression fractures (PMVCF): JIVROSG-0202. Ann Oncol 2009; 20:1943–1947.
15. ■■ Berenson J, Pflugmacher R, Jarzem P, *et al.* Balloon kyphoplasty versus nonsurgical fracture management for treatment of painful vertebral body compression fractures in patients with cancer: a multicentre, randomised controlled trial. Lancet Oncol 2011; 12:225–235.

This well designed multicenter randomized trial highlights the efficacy of kyphoplasty in the short-term pain relief related to VCFx in cancer population.

16. Chew C, Ritchie M, O'Dwyer PJ, Edwards R. A prospective study of percutaneous vertebroplasty in patients with myeloma and spinal metastases. Clin Radiol 2011; 66:1193–1196.
17. Hirsch AE, Jha RM, Yoo AJ, *et al.* The use of vertebral augmentation and external beam radiation therapy in the multimodal management of malignant vertebral compression fractures. Pain Phys 2011; 14:447–458.
18. ■ Han S, Wan S, Ning L, *et al.* Percutaneous vertebroplasty versus balloon kyphoplasty for treatment of osteoporotic vertebral compression fracture: a meta-analysis of randomised and nonrandomised controlled trials. Int Orthopaed 2011; 35:1349–1358.

Interesting meta-analysis comparing vertebroplasty versus kyphoplasty efficacy and safety. It shows that in terms of pain relief and complications both procedures have only some slight differences.

19. Eck JC, Nachtigall D, Humphreys SC, Hodges SD. Comparison of vertebroplasty and balloon kyphoplasty for treatment of vertebral compression fractures: a meta-analysis of the literature. The Spine J 2008; 8:488–497.
20. Wardlaw D, Cummings SR, Van Meirhaeghe J, *et al.* Efficacy and safety of balloon kyphoplasty compared with nonsurgical care for vertebral compression fracture (FREE): a randomised controlled trial. Lancet 2009; 373:1016–1024.
21. Boonen S, Van Meirhaeghe J, Bastian L, *et al.* Balloon kyphoplasty for the treatment of acute vertebral compression fractures: 2-year results from a randomized trial. J Bone Mineral Res 2011; 26:1627–1637.
22. Taylor RS, Fritzell P, Taylor RJ. Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis. Eur Spine J 2007; 16:1085–1100.
23. Voormolen MH, Mali WP, Lohle PN, *et al.* Percutaneous vertebroplasty compared with optimal pain medication treatment: short-term clinical outcome of patients with subacute or chronic painful osteoporotic vertebral compression fractures. The VERTOS study. Am J Neuroradiol 2007; 28: 555–560.
24. 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; 376:1085–1092.
25. Buchbinder R, Osborne RH, Ebeling PR, *et al.* A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. New Engl J Med 2009; 361:557–568.
26. Kallmes DF, Comstock BA, Heagerty PJ, *et al.* A randomized trial of vertebroplasty for osteoporotic spinal fractures. New Engl J Med 2009; 361:569–579.
27. Aebi M. Vertebroplasty: about sense and nonsense of uncontrolled 'controlled randomized prospective trials'. Eur Spine J 2009; 18:1247–1248.
28. Miller FG, Kallmes DF, Buchbinder R. Vertebroplasty and the placebo response. Radiology 2011; 259:621–625.
29. Rousing R, Hansen KL, Andersen MO, *et al.* Twelve-months follow-up in forty-nine patients with acute/semiacute osteoporotic vertebral fractures treated conservatively or with percutaneous vertebroplasty: a clinical randomized study. Spine 2010; 35:478–482.

30. Firanescu C, Lohle PN, de Vries J, *et al.* A randomised sham controlled trial of ■■ vertebroplasty for painful acute osteoporotic vertebral fractures (VERTOS IV). Trials 2011; 12:93.
This well designed trial probably will bring high-quality evidence to the use of vertebroplasty in acute VCFx.
31. Luetmer MT, Kallmes DF. Have referral patterns for vertebroplasty changed since publication of the placebo-controlled trials? Am J Neuroradiol 2011; 32:647–648.
32. Gerling MC, Eubanks JD, Patel R, *et al.* Cement augmentation of refractory ■ osteoporotic vertebral compression fractures: survivorship analysis. Spine 2011; 36:E1266–E1269.
This study demonstrates that cement augmentation procedures for VCFx brings a survival advantage at 1 year compared with match controls, and that benefit is regardless age, sex, or comorbidities.
33. Lee MJ, Dumonski M, Cahill P, *et al.* Percutaneous treatment of vertebral compression fractures: a meta-analysis of complications. Spine 2009; 34:1228–1232.
34. 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 Interventional Radiol 2004; 15:1185–1192.
35. Li YA, Lin CL, Chang MC, *et al.* Subsequent vertebral fracture after verteb- ■ roplasty: incidence and analysis of risk factors. Spine 2012; 37:179–183.
This study showed that the degree of height restoration and the volume of bone cement injected are risk factors for subsequent vertebral fractures.
36. Lu K, Liang CL, Hsieh CH, *et al.* Risk factors of subsequent vertebral compression fractures after vertebroplasty. Pain Med 2012; 13:376–382.
37. Venmans A, Klazen CA, Lohle PN, *et al.* Percutaneous vertebroplasty and pulmonary cement embolism: results from VERTOS II. Am J Neuroradiol 2010; 31:1451–1453.
38. Strom O, Leonard C, Marsh D, Cooper C. Cost-effectiveness of balloon kyphoplasty in patients with symptomatic vertebral compression fractures in a UK setting. Osteoporosis Int 2010; 21:1599–1608.
39. Masala S, Ciarrapico AM, Konda D, *et al.* Cost-effectiveness of percutaneous vertebroplasty in osteoporotic vertebral fractures. Eur Spine J 2008; 17: 1242–1250.
40. Mehio AK, Lerner JH, Engelhart LM, *et al.* Comparative hospital economics and patient presentation: vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. Am J Neuroradiol 2011; 32:1290–1294.
41. Bae H, Hatten HP, Linovitz P, *et al.* A prospective randomized FDA-IDE trial comparing Cortoss with PMMA for vertebroplasty. Spine 2012; 37:544–550.