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A review of vertebroplasty for osteoporotic and malignant vertebral compression fractures

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Abstract

Vertebral compression fractures are a common clinical problem and the incidence of them will increase with the ageing population. Traditionally management has been conservative; however, there has been a growing trend towards vertebroplasty as an alternative therapy in patients with persisting severe pain. NICE produced guidance in 2003 recommending the procedure after 4 weeks of conservative management. Recent high-quality studies have been contradictory and there is currently a debate surrounding the role of the procedure with no agreement in the literature. We examine the evidence in both osteoporotic and malignant vertebral compression fractures; we also describe the benefits and side effects, alternative treatment options and the cost of the procedure. Finally, we recommend when vertebroplasty is most appropriately used based on the best available evidence.

Keywords: *vertebroplasty, osteoporosis, malignant, compression fractures, elderly*

Introduction

The incidence of a new vertebral compression fracture in Europe is, at age 50–79 years, 1% per year in women and 0.6% per year in men and at age 75–79 years 2.9% per year in women and 1.4% per year in men [1]. Osteoporosis and osteolytic lesions of the spine, caused by myeloma or spinal metastases, are most commonly responsible for these fractures, although more unusual causes, such as trauma and vertebral haemangiomas, are also seen. Approximately two-thirds of patients with vertebral fractures will respond well to conservative management and improve with analgesia alone; however, the remaining third do not improve and may suffer with chronic pain [2], which may lead to immobility, kyphosis, deterioration in respiratory function and an overall reduction in quality of life [3].

Since Galibert *et al.* first described vertebroplasty in 1987; it has been developed to become an increasingly important tool in the management of vertebral compression fractures [4]. This minimally invasive technique involves the use of radiological guidance to inject acrylic bone cement, percutaneously into the affected vertebrae. An interventional radiologist usually performs this, although many spinal surgeons now offer the procedure. This review will concentrate on vertebroplasty for compression fractures rather than kyphoplasty. Kyphoplasty differs from vertebroplasty in so far as the vertebral fracture is first reduced using an inflatable balloon, before injecting cement into the vertebral body. NICE (2003) suggests that there is sufficient evidence on safety and efficacy to support the use of vertebroplasty in individuals with compression fractures secondary to severe osteoporosis, and also for those with vertebral body tumours and symptomatic vertebral haemangiomas, following a period of at least 4 weeks conservative treatment [5]. However, the treatment should be undertaken in an environment that has arrangement for audit and governance of the procedure. We aim to review the current best evidence for the use of vertebroplasty in those with severe osteoporosis and osteolytic lesions of the spine and recommend for which vertebroplasty is best utilised.

Search strategy

We systematically searched Medline database from 1966 to July 2011 with the following terms:

Vertebroplasty and osteoporosis
Vertebroplasty and spinal neoplasm or bone neoplasm
Vertebroplasty and spinal metastases or bone metastases

A total of 499 articles were retrieved and the abstracts were reviewed. If the abstract was not available the title was considered. If the article was not in English it was not reviewed. As the procedure was developed in France and is currently used more extensively in Europe, then excluding articles that were not written in English could have potentially raised difficulties. We feel that these difficulties are minimal as the majority of the larger trials, including the randomised control trials have been published in the English language. We identified 122 papers, which were then read so that pertinent articles were identified. After identifying these articles their references were reviewed for secondary references. Reviewing and filtering was performed by two reviewers and differences in opinion resolved by a third reviewer. Articles were used if the focus of the article was the use of vertebroplasty in either osteoporosis or malignant disease of the spine. We included case reports, case series, randomised control trials and review articles.

Vertebroplasty in osteoporotic vertebral fractures

Observational studies of the use of vertebroplasty for osteoporotic compression fractures have shown that it is a safe procedure that offers good reduction in pain when compared with conservative management [6–9]. However, until recently there have been few high-quality randomised controlled trials to generate sufficient evidence upon which to base practice.

Two studies published in 2009 randomised patients to either vertebroplasty or a control arm who underwent a blinded sham procedure [10, 11]. The primary outcome was reduction in pain. Both studies failed to show an increased effect of vertebroplasty over the control. The sham procedure in both studies involved the injection of local anaesthetic into the periosteum of the posterior elements of the spine where the vertebroplasty needles would be inserted, which some authors have argued is an active treatment akin to a perifacetal injection [12, 13]. Many of the criticisms of these trials; patient selection, low pain scores and small numbers with acute fractures have been rebutted by a meta-analysis of the two papers, adequately powered for subgroup analysis which found no benefit in acute fractures or in patients who reported high pain scores [14].

As one of the initial investigators for the Kallmes trial [15], points out, 85% of all patients in these trials were successfully treated despite many months of pain, supporting the theory that the sham procedure was in fact therapeutic. He subsequently published a prospective audit, where all patients suitable for vertebroplasty received initially a paraspinal injection at the level of the pain. This resulted in 34% having good pain relief. The remaining patients then underwent vertebroplasty with a greater than 90% success [13].

Significant benefit of vertebroplasty has been demonstrated in the non-blinded randomised VERTOS II trial, which compared vertebroplasty to best conservative management thus reproducing the choice that the clinician has [16]. Patients included in the study were 50 or older, had back pain for 6 weeks or less and had radiographic evidence of vertebral compression fractures at T5 or lower. Those in the intervention group demonstrated significant improvements in pain, quality of life and spinal disability at both 1 month and 1 year compared with conservative management [16]. Critics of this study suggest that the benefit is due to placebo, although since the results persist for 12 months it is unlikely to be placebo alone.

Clearly, further trials are needed and randomised sham controlled trials are in the process of being performed with modified selection criteria [15].

Vertebroplasty for malignancy

Vertebral compression fractures are a major cause of morbidity in patients with primary or metastatic skeletal malignancy. Vertebral metastases most commonly occur in lung, breast and prostate cancer. Multiple myeloma also frequently affects the bone. Approximately 10% of cancer patients will present with symptoms related to vertebral metastases, and of these 40–70% will have multiple vertebral levels involved [17]. All malignancies that metastasise to bone have the highest incidence in the elderly population [18].

When considering the use of vertebroplasty for malignancy, the majority of evidence comes from prospective and retrospective observational studies; our search revealed only one randomised control trail [19]. The majority of studies have investigated vertebroplasty for metastatic disease of the spine; however, there have also been studies that have investigated the use of vertebroplasty for multiple myeloma [20, 21].

As with osteoporotic fractures, the main indication for performing vertebroplasty was pain, with the main outcome measure being reduction in pain after the procedure. A recent systematic review of vertebroplasty in malignancy found that the vertebral levels most commonly treated were lumbar and thoracic [22]. Few studies have used vertebroplasty for cervical spine lesions [21, 23]. The majority of studies have found a reduction in pain after vertebroplasty, with the improvement in pain ranging from 20 to 79% at 1 month [20, 24, 25]. The studies that have assessed pain at 6 months post-intervention have found a sustained reduction in pain [24, 25]. Other outcome measures, including functional activities and quality of life measures, have been sporadically reported [22].

The main difficulty in deciding on the appropriateness of vertebroplasty in malignancy is the lack of robust evidence from randomised controlled trails. In the studies performed so far, there is heterogeneity in study design, underlying diagnoses and outcome measures employed. Some studies have reported serious adverse outcomes (see below); however, few have reported precise detail on outcome, in particular 30-day mortality (the accepted standard for invasive surgical procedures).

Side effects/adverse events

Although considered to be a low-risk procedure, vertebroplasty does have recognised serious adverse events; however, with meticulous technique and excellent image guidance fortunately these are very rare [9, 26]. The two most serious complications reported, both of which are rare, are cement leak resulting in significant neural compression and symptomatic pulmonary embolism [10, 11, 16, 27, 28]. In addition, a few cases of osteomyelitis, rib/transverse process fracture and anaesthetic complications have been reported [3].

Asymptomatic cement leak, where cement extends out of the vertebral body into the adjacent soft tissues or intervertebral disc, avoiding neural structures or vessels is common. A systematic review of 69 studies conducted by Hulme *et al.* revealed leakage of cement as the most common adverse event, occurring in 41% of treated vertebrae [3]. Ninety-six per cent of cases remained asymptomatic, although the long-term effects are not known. In one series of 134-treated vertebral bodies, CT identified cement leakage in 72% [16]. In none of these cases did cement leak into the spinal canal, with only one entering the venous system.

New fractures adjacent to the cemented vertebral body have been reported as an adverse event following vertebroplasty [3]. However, several recent randomised controlled trials have found no difference in vertebral fracture following vertebroplasty compared with the control group [10, 11, 16]. Given that Lindsay *et al.* found a 19% incidence of new vertebral fractures in the year following a vertebral fracture, further fractures are common whether or not a patient undergoes vertebroplasty [29].

When considering vertebroplasty in malignancy higher complication rates have been observed. It has been suggested that there is an increased risk in patients with fractures secondary to malignancy, due to loss of cortical integrity and tumour angiogenesis [30]. A systematic review found that 2% of individuals undergoing vertebroplasty for malignant disease suffered a serious complication [22]. Serious complications included neuropathy requiring emergency decompression and venous thrombo-embolism. In this population, the slightly higher risks of vertebroplasty must be weighed against the potentially debilitating pain and disability in patients with a reduced life expectancy.

Alternative treatments

Alternatives to vertebroplasty include conservative management, kyphoplasty and in the case of malignancy either surgery or radiotherapy. Decisions about radiotherapy and surgery should be undertaken in a multi-disciplinary environment, involving oncologists and spinal surgeons. Conservative management involves rest, analgesia, support bracing and physiotherapy. There are no randomised control trials evaluating oral analgesics for vertebral compression fractures, to guide which analgesic is preferred. Analgesia should be utilised according to the World Health Organisation analgesic ladder, remembering that non-steroidal anti-inflammatory drugs are contra-indicated in many elderly people. Calcitonin has been shown to hasten the relief of pain from vertebral fractures, and it can be a useful adjunct to traditional analgesics in the acute setting [31–33]. In a randomised placebo-controlled trial, performed in a group of 56 women who had sustained osteoporotic vertebral fractures, mean pain scores and analgesic consumption in the calcitonin group were significantly

lower than in the placebo group by the fourth day [31]. The main problems with calcitonin are its relative expense, difficulties with administration (either parenteral or nasal) and it's frequency of side effects (nausea, vomiting and flushing). There are no clinical trials evaluating the effect of skeletal muscle relaxants in the relief of pain following vertebral compression fractures. Although bracing is sometimes used for the management of compression fractures, there is a paucity of evidence for its use. The use of bracing is most likely based on the extrapolation of evidence from the management of traumatic spinal fractures [34]. In addition, it must be remembered that the use of braces should be balanced against the risks of reducing mobility. Prevention of future osteoporotic compression fractures should be considered, with individuals undergoing osteoporosis assessment and management started accordingly.

Introduced in 1998, kyphoplasty first reduces the vertebral fracture using an inflatable balloon before injecting cement into the vertebral body, helping to restore vertebral height and realign the spine [**35**]. The FREE study was a randomised control trial comparing kyphoplasty with conservative management in those with acute vertebral compression fractures [**36**]. Kyphoplasty appears to be as effective as vertebroplasty in relieving pain [**16**] and the adverse events, and the rate at which they occur, are similar to vertebroplasty. Its main disadvantages, however, when compared with vertebroplasty are that it must be performed using deeper sedation or general anaesthesia, requires hospital admission and is up to 20 times more expensive [**37**, **38**]. A randomised controlled trial, randomly assigning 100 patients with vertebral compression fractures at the thoraco-lumbar junction to vertebroplasty or kyphoplasty, found little difference in the clinical outcome, and concluded vertebroplasty should be used over kyphoplasty due to its lower costs [**38**].

Cost

Masala *et al*. studied the cost-effectiveness of vertebroplasty versus conservative therapy in those with osteoporotic vertebral fractures using three statistical scales; the Mann–Whitney *U* test, the Wilcoxon signed rank test and the Fischer exact method [**39**]. They found that it was cost-effective at 1 week, 3 and 12 months using all three scales, although this was not statistically significant at 3 and 12 months. The VERTOS II trial reports a procedural cost of €2,463. It also reports that the procedural cost accounts for the main increase in cost between those treated with vertebroplasty compared with those treated conservatively (i.e. conservative treatment cheaper by €2,463 at 1 year). The cost of one pain-free day was €20 and for one QALY was €22,685 [**16**]. The authors concluded that if society is willing to spend €30,000 per quality of adjusted life years gained then vertebroplasty is acceptable [16]. In the UK, NICE does not have 'hard' decision rules on cost per QALY, but generally procedures of £20–30,000 per QALY are acceptable.

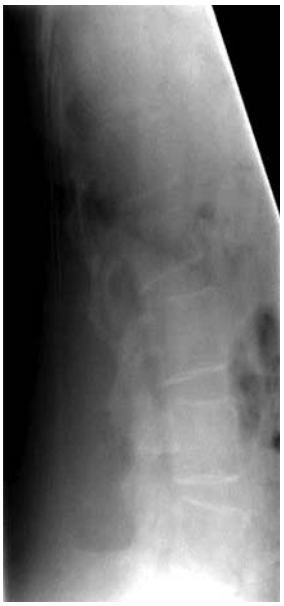

Figure 1. Conventional radiograph of a 6-week-old fracture of the L1 vertebral body in a 46-year-old female with steroid induced osteoporosis who was admitted with immobility secondary to severe back pain.

Patient selection

Defining exact patient selection criteria is difficult in the face of lack of consensus in the literature. We would suggest that all patients should first undergo a course of conservative treatment. Although vertebroplasty is used as a first line treatment in some countries, for example, Australia, the evidence for using it first line is at present lacking, and as previously discussed many patients will respond to conservative management, thus obviating the need for an interventional procedure with its associated risks and costs. If conservative treatment is unsuccessful, a significant proportion of patients may respond to minimally invasive facet joint injections at the level of their pain. Vertebroplasty, essentially a low-risk procedure, can then be considered once an MRI scan has been performed to confirm the fracture level and activity (Figures 1, 2 and 3). The VERTOS 2 and FREE trials support the use of vertebral augmentation within 6 weeks of sustaining a fracture, with patients admitted to hospital with severe pain and immobility secondary to an acute vertebral fracture especially good candidates [12]. Procedures in patients with older fractures, assuming there is high signal on the STIR sequence of the MRI, can also be contemplated, although some practitioners believe that fractures greater than 4 months of age are less likely to respond successfully. In addition, although there are case reports of people with little bone oedema gaining benefit from vertebroplasty,

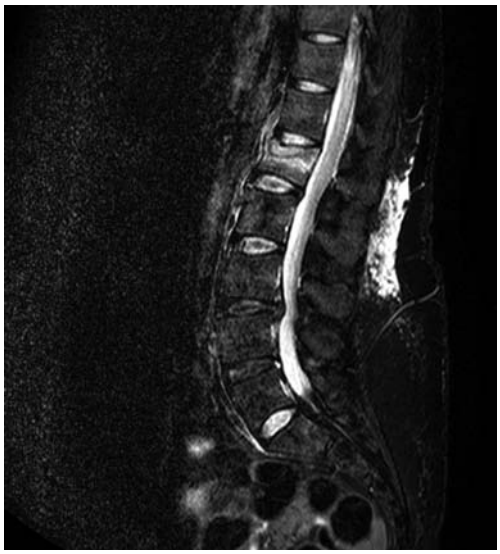

Figure 2. The STIR high signal corresponding with the acute nature of the fracture.

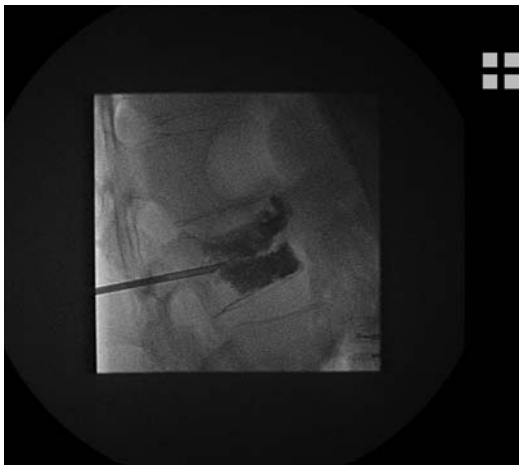

Figure 3. Post-vertebroplasty showing good cement filling and a very small anterior leak of no clinical significance. The patient's pain reduced from 10 to 2 on the visual analogue scale and she was discharged shortly after the procedure.

there is currently no randomised control evidence to support this.

Conclusion

The evidence for vertebroplasty in osteoporotic fractures is controversial with the only placebo-controlled randomised controlled trials finding no benefit for vertebroplasty versus a sham procedure [**10**, **11**]. A meta-analysis of the two trials further supported the original findings that vertebroplasty has no benefit over placebo (sham treatment arm) [**14**]. This is contrary to other non-blinded randomised controlled trials, which found significant benefit for vertebral augmentation persisting for 12 months [**16**, **36**]. As discussed earlier, one reason the blinded studies may have found no benefit for vertebroplasty is the potential active treatment of the sham control arm. When considering malignant vertebral compression fractures there is a paucity of high-quality evidence; however, what is available demonstrates that it provides effective pain relief. The complication rates for both vertebroplasty in malignant and osteoporotic fractures are low, and it has been shown to be cost-effective.

In conclusion, vertebroplasty cannot be recommended as a first line therapy for painful vertebral fractures, but may be considered in combination with less invasive facet joint injections in patients with severe pain and disability, preferably within 6 weeks.

Key points

- Vertebroplasty should be considered for patients with pain and disability due to vertebral compression fractures, where conservative management has not been successful.
- At present the evidence for the use of vertebroplasty is controversial.
- Vertebroplasty should be employed on a case-by-case basis after discussion with a practitioner experienced in the procedure.

Conflicts of interest

None declared.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in *Age and Ageing* online.

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The very long list of references supporting this review has meant that only the most important are listed here and are represented by bold type throughout the text. The full list of references is available on the Supplementary data are available in *Age and Ageing* online.

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