

<b>Title:</b>	<b>Review of interim funded service: Vertebroplasty and New review of Kyphoplasty</b>
<b>Agency:</b>	Commonwealth Department of Health and Ageing GPO Box 9848 Canberra ACT 2601 on behalf of the Medical Services Advisory Committee (MSAC) <a href="http://www.msac.gov.au">http://www.msac.gov.au</a>
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### **Aim**

In 2004–05, an assessment of **vertebroplasty** and **kyphoplasty** for the treatment of vertebral compression fracture was conducted on behalf of the Medical Services Advisory Committee (MSAC). On the basis of the evidence presented in that report, the then Minister for Health and Ageing accepted MSAC's recommendation that vertebroplasty be granted public funding on an interim basis for patients with painful vertebral fracture, caused by osteoporosis or malignant tumours, which were unresponsive to conservative management. A review of funding within 5 years was planned. At that time, MSAC concluded that there was insufficient evidence to support public funding of kyphoplasty.

This review updates and expands upon the initial assessment of these procedures. The safety, effectiveness and cost-effectiveness of the addition of vertebroplasty to conservative medical management for the treatment of painful vertebral fracture was assessed, and compared to (1) conservative medical management alone, and (2) kyphoplasty in addition to conservative medical management.

The safety, effectiveness and cost-effectiveness of the addition of kyphoplasty to conservative medical management for the treatment of painful vertebral fracture was assessed, and compared to (1) conservative medical management alone, and (2) vertebroplasty in addition to conservative medical management. For the purposes of assessing impact on functional kyphotic deformity, kyphoplasty was compared with spinal surgery.

### **Methods**

The previous MSAC assessment report included literature identified between 1987 and 2004, as both procedures were developed and published in the peer-reviewed literature from 1987. For this review update, the search period was therefore restricted from 2004 until 08/2010, except for those studies comparing the safety, effectiveness or cost-effectiveness of kyphoplasty against conservative management or vertebroplasty, for which searches were again extended back until 1987. Medline, Embase, The Cochrane Library, and several other biomedical databases, HTA and other internet sites were searched. Specific journals were handsearched and reference lists perused. Studies were included in the review using pre-determined PICO selection criteria. Study quality was appraised and data extracted in a standardised manner. The results were synthesised and reported narratively.

## **Results and Conclusions**

### **Vertebroplasty**

#### *Safety*

One hundred and nine studies relevant to the safety of vertebroplasty were identified that had been published since the previous review. In total, the studies from which safety data were extracted included approximately 10 000 patients with an estimated 16 000 vertebral fractures treated. While cement leakage was found to

occur frequently with vertebroplasty, clinically important adverse events were rarely associated with the leaks, or with the procedure. The frequency of cement leakage varied from 8 to 72 per cent. Serious adverse events were uncommon, with spinal cord injury occurring in approximately 0.6 per 1000 patients treated, symptomatic pulmonary cement embolism (PCE) occurring in 0.5 per 1000 patients, and one death reported in approximately 10 000 patients. The most common adverse events were rib fracture and radicular pain, which occurred in approximately 4 per cent of patients undergoing vertebroplasty.

### ***Effectiveness***

Since 2005, two double-blind (placebo-controlled) randomised controlled trials (RCTs), three open-label RCTs and three non-randomised comparative studies were identified as assessing the effectiveness of vertebroplasty compared with conservative management. Both of the placebo-controlled trials found vertebroplasty to be no better than placebo with respect to its effect on patient-assessed pain, quality of life, functional capacity, psychological wellbeing and analgesia usage. Although there are concerns regarding patient selection and technique used in the placebo-controlled trials, these trials provide evidence of the best methodological quality to determine the effectiveness of vertebroplasty with respect to conservative management in the majority of patients with osteoporotic vertebral fractures. With respect to hospital length-of-stay, the results varied and appear to be confounded. One open-label RCT provided evidence that vertebroplasty significantly reduces the risk of progressive fracture of the treated vertebral body. Vertebroplasty may also have a role in the management of a subgroup of patients with acute, unstable osteoporotic vertebral fractures and intractable pain, but further information is required from good-quality research before any such treatment effect modification can be confirmed. No comparative studies were identified concerning patients with vertebral fracture caused by malignant tumours.

### ***Cost-effectiveness***

A cost-effectiveness analysis is undertaken only if there is evidence that the new procedure is more effective or less harmful than the designated comparator; otherwise, MSAC requires only a financial impact analysis. The balance of benefit and harm in the evidence base did not favour vertebroplasty relative to conservative management in the treatment of osteoporotic patients with painful vertebral fracture. No comparative evidence was available for the population with painful fractures caused by vertebral tumours. As a consequence, no modelled cost-effectiveness analyses were presented. In terms of financial impact, the average cost of treating one patient with painful vertebral fracture with conservative management alone, including all non-trivial expenses over 1 year, is estimated to be \$6074. The average additional cost of treating one patient with vertebroplasty, assuming no change to analgesia usage or duration of hospitalisation, is \$1593. The total cost to the Medicare Benefits Schedule (MBS), other government agencies and patient or private insurers of providing vertebroplasty in addition to conservative management was estimated to be \$6 186 880 per annum. If all factors remain unchanged, with the exception of an ageing population and a slight increase in uptake of the procedure to match the levels of use in NSW, this total annual cost was estimated to rise to \$13 263 076 by 2020.

## **Kyphoplasty**

### ***Safety***

Sixty-one studies were identified that had been published since the previous review, which reported on the safety of kyphoplasty to treat painful vertebral fractures. No studies reported on harms associated with the use of kyphoplasty to relieve symptoms associated with kyphotic deformity.

In total, the studies for which safety data were extracted included 2675 patients with approximately 4000 vertebral fractures treated. Cement leakage is commonly associated with kyphoplasty, but adverse clinical consequences are rare. The frequency of cement leakage at any site varied from 7 to 47 per cent of procedures. No cases of spinal cord injury or PCE were observed, but one case of permanent partial paralysis of one leg was observed in one of the smaller studies. The most common adverse event was radicular pain associated with cement leakage, which was reported in up to 1.5 per cent of patients, and urinary tract infection, which occurred in 6 per cent of patients in one series. Most other adverse events were reported in only one or two studies. Also observed in a small number of cases were haematoma and rib fracture. No deaths were found to be directly associated with kyphoplasty.

### ***Effectiveness***

The best-quality evidence for the effectiveness of kyphoplasty was provided by one good-quality RCT that compared kyphoplasty with conservative management. Moderate-quality evidence was also provided by two non-randomised studies. Kyphoplasty was found to have statistical and clinically important benefits in pain reduction at 1 week in the RCT and for later time points in one of the other studies. The RCT provided evidence of statistically significant and clinically important benefits of kyphoplasty over conservative management in improving patient-assessed quality of life and functional status. Similarly, significantly fewer patients required opioid analgesia at 1, 3, and 6 months' follow-up, but not at 1 week or 1 year. One moderate-quality non-randomised study provided evidence that kyphoplasty increased hospital length-of-stay by an average of just less than 1 day, and the other provided evidence that kyphoplasty increased vertebral height, while conservative management resulted in progressive loss of vertebral height.

The contrasting results between blinded and unblinded studies assessing the similar vertebroplasty procedure provide some evidence for the existence of a placebo effect in the minimally invasive treatment of osteoporotic vertebral fracture. This finding creates uncertainty about the degree to which a placebo effect is implicated in the treatment effects reported in the kyphoplasty evidence base, considering that the primary outcomes reported in the literature are (appropriately) subjective in nature (eg pain)—and thus susceptible to placebo effect—and because patient selection in the key kyphoplasty RCT was similar to that in the vertebroplasty RCTs.

Only one poor quality non-randomised study compared kyphoplasty with spinal surgery. It found that open surgery resulted in substantially more blood loss than kyphoplasty and a benefit of kyphoplasty over surgery in improving patient-assessed pain at 1 day follow-up. There was no difference in the degree of vertebral height restoration. On the basis of this limited evidence, no conclusions can be drawn with respect to the comparative safety or effectiveness of kyphoplasty and spinal surgery.

### ***Cost-effectiveness***

The effectiveness of kyphoplasty relative to conservative management in osteoporotic patients with painful vertebral fracture could not be established without a placebo control, and there was also a likelihood of increased harm relative to conservative management. Similarly, there were insufficient data comparing kyphoplasty and surgery to determine the relative safety and effectiveness in osteoporotic patients with kyphotic deformity. No comparative evidence was available in the population with painful fractures caused by vertebral tumours. As a consequence, no modelled cost-effectiveness analyses or cost-consequence analyses were presented.

Commercial-in-confidence information supplied by the applicant confirmed that additional costs would accrue to the MBS, other government agencies and patient or private insurers if kyphoplasty was provided in addition to conservative management.

## **Vertebroplasty vs Kyphoplasty**

### ***Safety***

Fifteen studies were available that directly compared vertebroplasty to kyphoplasty. One of these studies compared the procedures in patients with multiple myeloma, while the rest treated patients with osteoporotic fractures. There was moderate-quality evidence that rates of cement leakage and clinical complications associated with cement leakage are lower in kyphoplasty than in vertebroplasty, although much of this evidence was provided through indirect comparison. Because clinically important adverse events associated with cement leakage are rare, a reduction in their frequency in kyphoplasty could be outweighed by a small increase in the risk of subsequent or adjacent vertebral fracture observed with kyphoplasty. There is, however, insufficient evidence at this time to come to any firm conclusions regarding this potential trade-off.

### ***Effectiveness***

All of the studies in the evidence base had moderate or high risks of confounding or bias, which makes it difficult to draw conclusions regarding any of the effectiveness outcomes. In the moderate-quality non-randomised study which, together with the poor-quality RCT, provided the best evidence available, there was a mid-term decline in many outcome measures in the group treated with vertebroplasty. The reason for this

deterioration is unclear, and the pattern is not represented in the rest of the literature on vertebroplasty. Therefore, there was limited poor- to moderate-quality evidence that indicated that kyphoplasty may be more effective than vertebroplasty, although none of the effects observed in the literature were demonstrated to be both clinically important and statistically significant.

#### *Cost-effectiveness*

Given the uncertainties regarding the effectiveness of vertebroplasty and kyphoplasty in osteoporotic patients with painful vertebral fracture relative to a placebo control, a cost-effectiveness analysis was not undertaken to compare the two active treatments.