

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA279; Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral fractures

This guidance was issued in April 2013.

The review date for this guidance is November 2015.

1. Recommendation

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Original remit(s)

To appraise the clinical and cost effectiveness of percutaneous vertebroplasty and percutaneous balloon kyphoplasty (with or without vertebral body stenting) for the treatment of osteoporotic vertebral fractures.

3. Current guidance

1.1 Percutaneous vertebroplasty, and percutaneous balloon kyphoplasty without stenting, are recommended as options for treating osteoporotic vertebral compression fractures only in people:

- who have severe ongoing pain after a recent, unhealed vertebral fracture despite optimal pain management and
- in whom the pain has been confirmed to be at the level of the fracture by physical examination and imaging.

4. Rationale¹

The systematic review suggests that the new evidence identified is broadly consistent with the Committee's considerations in Technology Appraisal 279 (TA279). In particular, no evidence was identified to suggest that vertebroplasty and balloon kyphoplasty are substantially less effective than previously thought, and limited evidence was found to address key uncertainties about the survival benefits associated with these treatments.

¹ A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

Several developments of the original techniques and new devices have emerged after publication of TA279. It would be possible to incorporate these developments in a review of TA279, but it is not anticipated that a technology appraisal of these technologies would be of value to the NHS.

It is therefore proposed that TA279 is transferred to the static guidance list.

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development that overlaps with this review proposal.

6. New evidence

The search strategy from the original Assessment Report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from January 2012 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

The updated systematic literature searches identified a large number of publications relevant to the appraisal of percutaneous vertebroplasty and balloon kyphoplasty. These included systematic review and meta-analyses, randomised controlled trials and observational studies, examining the effectiveness and safety of vertebroplasty and kyphoplasty compared with each other and with conservative management strategies (that is, non-surgical management or optimised pain relief).

The results of the identified studies appear broadly consistent with the Committee's conclusions on clinical benefit during TA279. In particular, there remains limited evidence from blinded randomised trials to support statistically significant clinical benefits with vertebroplasty and balloon kyphoplasty compared with conservative management (Buchbinder et al. 2015). However, significant benefits have been seen in other studies, including non-blinded trials and observational studies; for example, (Chen et al. 2014b; Hao et al. 2013; Li et al. 2015). Although studies continue to highlight the potential for adverse events and complications (such as cement leakage and new fractures; (Bouza et al. 2015; Buchbinder et al. 2015; Yi et al. 2014), no substantial new safety concerns have been identified.

Additional studies comparing symptoms and fracture outcomes with vertebroplasty and balloon kyphoplasty have been identified, with inconsistent results. Although some benefits associated with balloon kyphoplasty have been seen (for example, bone deformity improvements and cement leakage; Chang et al. 2015; Dong et al. 2013; Wang et al. 2015; Xiao et al. 2015), other studies have highlighted similarities between the techniques in pain relief, quality of life and new fractures (Chen et al. 2015; Dohm et al. 2014; Evans et al. 2015; Xie et al. 2015). In TA279, there was limited evidence for differences between the techniques. The findings from the updated systematic review are therefore consistent with the evidence considered in TA279.

Notably, the updated systematic review has identified very little new evidence on the effect of vertebroplasty and balloon kyphoplasty on survival; this was highlighted as a key uncertainty in TA279. Lange et al. presented survival data from an observational registry in Germany, and found a statistically significant survival gain associated with both vertebroplasty and balloon kyphoplasty compared with conservative management, and a non-significant survival gain with balloon kyphoplasty compared with vertebroplasty (Lange et al. 2014). Goz et al. found that balloon kyphoplasty was associated with lower mortality than vertebroplasty in a US claims database (Goz et al. 2015). These findings are consistent with the Committee's conclusions in TA279.

Since publication of TA279, a number of related interventions have been developed that were not specifically considered during the previous appraisal. These include:

- Developments of the vertebroplasty and kyphoplasty techniques, such as unilateral approaches (Chen et al. 2014a; Rebolledo et al. 2013), cement delivery systems (Vogl et al. 2013), fluoroscopy guidance (Xu et al. 2014), preventative vertebroplasty (Yen et al. 2012) and curette use (Bastian et al. 2013).
- New cements and alternatives, such as Cortoss and Cerament (Bae et al. 2012; Gilula and Persenaire 2013; Marcia et al. 2012; Masala et al. 2012).
- Alternative kyphoplasty-related techniques, such as shield kyphoplasty, radiofrequency kyphoplasty and vertebral perforation (Endres and Badura 2012; Moser et al. 2013; Rollinghoff et al. 2013; Yokoyama et al. 2012).
- Studies of balloon kyphoplasty with vertebral body stenting (although this was included in the scope for TA279, there was insufficient evidence for this technique at the time of the appraisal so it was excluded; (Thaler et al. 2013; Werner et al. 2013).
- Newer devices that develop from balloon kyphoplasty, such as the Kiva polymer implant (Benvenue Medical), the Osseofix titanium mesh implant (Alphatec Spine), and the SpineJack titanium jack implant (Vexim) (Ender et al. 2014; Tutton et al. 2014; Vanni et al. 2012). SpineJack and Osseofix are currently being scoped for consideration by the NICE Interventional Procedures programme.

The published studies present promising results for these technical developments – many show similar effectiveness and safety to vertebroplasty and balloon kyphoplasty, and some benefits have been observed (for example, in surgery time, complications, bone deformity correction and cement leakage). However, no consistent, substantial improvements in clinical outcomes compared with traditional vertebroplasty and kyphoplasty have been reported. Moreover, it is unknown whether these emerging technologies and techniques are likely to be used in UK clinical practice, or whether they differ substantially in cost to the established vertebroplasty and balloon kyphoplasty technologies. These new technologies could be incorporated into a review of TA279 (subject to referral by the Department of Health), but it is unlikely that enough evidence exists to clearly differentiate between

the technologies, and it is therefore uncertain whether an appraisal of these technologies would be of value to the NHS.

It is unknown whether there have been any other significant changes in the market for vertebroplasty or balloon kyphoplasty devices since publication of TA279, such as the launch of new products in the UK or substantial price changes. Unless the prices of the devices have increased significantly since the time of TA279, a review of the guidance would not be necessary because the prices were not identified as key drivers of the cost effectiveness results in TA279. Three companies have confirmed that the price of their product has not increased since TA279.

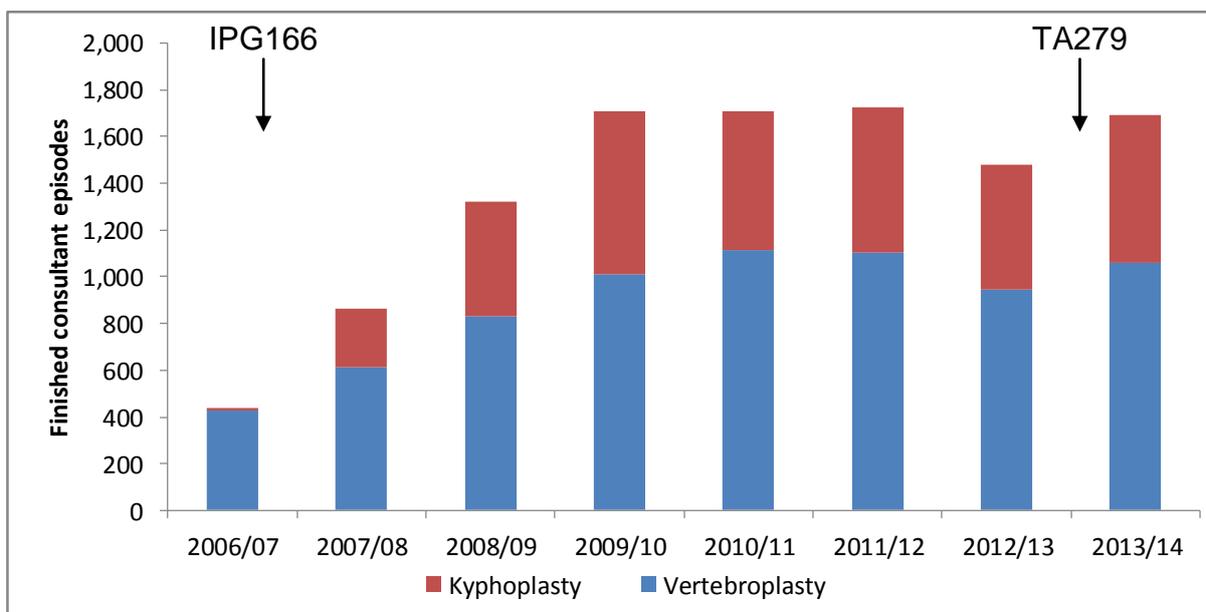
8. Implementation

No submission was received from Implementation.

Analysis of Hospital Episode Statistics suggests that approximately 1700 vertebroplasty and balloon kyphoplasty operations are performed each year in England. The number of operations has stayed relatively constant since 2009/10 (figure 1), although it is too early to identify the effect of TA279 on uptake of these procedures.

NICE has previously estimated that there are 2.5 million people with osteoporosis in England and Wales, and approximately 11,900 osteoporotic vertebral compression fractures per year (although this figure may not include all fractures, as many may be undiagnosed; source: NICE TA279 guidance and costing statement). This suggests that only a small proportion of diagnosed vertebral compression fractures are treated with vertebroplasty or balloon kyphoplasty.

Figure 1 Vertebroplasty and balloon kyphoplasty operations in England, 2006–2014.



Finished Consultant Episodes for primary/main intervention of V44.4, vertebroplasty of fracture of spine, and V44.5, balloon kyphoplasty of fracture of spine. These figures relate to admitted patients; a small number of operations (for example, 13 in 2013/14) are performed in an out-patient setting. Statistics for these procedures prior to 2006/07 are not reported. Source: Health and Social Care

Information Centre, Hospital Episode Statistics; <http://www.hscic.gov.uk/hes> (accessed October 2015).

9. Equality issues

No equality issues relevant to the Committee's recommendations were raised during TA279.

GE paper sign off: Elisabeth George, Associate Director – 29 October 2015

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – ‘Yes/No’
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the [specify STA or MTA] process.	A review of the appraisal will be planned into the NICE’s work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE’s work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	<p>The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review.</p> <p>This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.</p>	No

Options	Consequence	Selected – ‘Yes/No’
The guidance should be updated in an on-going clinical guideline.	<p>Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn.</p> <p>Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).</p>	No
The guidance should be transferred to the ‘static guidance list’.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

- i. The technology falls within the scope of a clinical guideline (or public health guidance)
- ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement
- iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment
- iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;
 - Spending on a treatment for the indication which was the subject of the appraisal continues to rise
 - There is evidence of unjustified variation across the country in access to a treatment
 - There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff
- v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

NICE interventional procedure guidance [IPG12] Percutaneous vertebroplasty.
Published date: September 2003

NICE interventional procedure guidance [IPG166] Balloon kyphoplasty for vertebral compression fractures. Published date: April 2006

NICE technology appraisal guidance [TA161] Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (amended). Published date: October 2008 (partial review in progress)

NICE guideline [CG146] Osteoporosis: assessing the risk of fragility fracture.
Published date: August 2012

In progress

NICE technology appraisal guidance. Bisphosphonates for preventing osteoporotic fragility fractures (including a partial update of NICE technology appraisal guidance 160 and 161). Anticipated publication date: November 2015

Details of new products

Drug (company)	Details (phase of development, expected launch date)	In topic selection
SpineJack (Vexim)	<p>“Vexim will supplement its regulatory submission for the use of SpineJack® in the U.S. with a prospective European multicentric randomized study that compares the safety and efficacy at one year follow-up of the New Generation SpineJack® device with Medtronic’s balloon in 160 patients suffering from vertebral compression fractures due to osteoporosis. Expected to submit a 510(k) application in 2017.”</p>	Nothing relevant
Kiva VCF Treatment System (Benvenue Medical)		Nothing relevant
Osseofix (Alphatec Spine)		Nothing relevant

Registered and unpublished trials

Trial name and registration number	Details
Complete	
Comparison of Balloon Kyphoplasty and Vertebroplasty in Subacute Osteoporotic Vertebral Fractures (OSTEO+6) (NCT00749086)	Enrolment: 97 Study Completion Date: June 2012
Unipedicular vs. Bipedicular Kyphoplasty for the Treatment of Osteoporotic Vertebral Fractures (NCT01383616)	Enrolment: 45 Study Completion Date: December 2012
Ongoing	
Safety and Efficacy Study of Percutaneous Vertebroplasty for Painful Acute Osteoporotic Spine Fractures (NCT01677806)	Estimated Enrolment: 140 Estimated Study Completion Date: December 2014 This study is currently recruiting participants (by invitation only)
Study About the Effect of Preventive Adjacent Level Cement Augmentation After Osteoporotic Vertebral Compression Fractures (NCT02489825)	Estimated Enrolment: 100 Estimated Study Completion Date: June 2017 This study is currently recruiting participants
Study on the Treatment of Osteoporotic Vertebral Fractures Using Vertebral Body Stenting (NCT01847898)	Enrolment: 100 Estimated Study Completion Date: September 2015 This study is ongoing, but not recruiting participants

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