Resurrection of evidence for vertebroplasty?

Although over 500 articles have been published in the last 5 years on vertebroplasty, a fundamental question remains—is vertebroplasty a safe and effective procedure to reduce pain and disability for patients with vertebral compression fractures?

Initial enthusiasm for vertebroplasty was driven by clinician experience and meta-analysis of large observational series showing patient benefit.1 This enthusiasm was dampened after publication of two randomised controlled trials (RCTs)2,3 in the New England Journal of Medicine, which showed no statistically significant benefit to performing vertebroplasty compared with a placebo procedure. Although there were legitimate criticisms of these two trials, their highly publicised nature led to a marked reduction in the use of the procedure in the USA, and removal of public funding for vertebroplasty in Australia.4,5

Subsequent open-label RCTs compared vertebroplasty with optimum medical management for osteoporotic fractures.6,4 These trials all showed consistent statistically significant benefit from vertebroplasty, and better reflected the real-world comparator that we use in clinical practice. This finding led to endorsement in 20136 of vertebroplasty for osteoporotic fractures by the National Institute for Health and Care Excellence that advises the National Health Service of England and Wales and by many international medical societies.10,11 Nonetheless, over this time of continuing scientific discourse, many patients and caregivers were unable to access vertebroplasty as a potential treatment option.

In The Lancet, William Clark and colleagues12 report the VAPOUR trial, a thoughtful and important multicentre, masked, placebo-controlled RCT to assess the efficacy of vertebroplasty in the subgroup of patients with recent (<6 weeks) vertebral compression fractures causing severe pain (Numeric Rating Scale [NRS] score of ≥7 out of 10). The trial recruited 120 patients; 61 patients were randomly assigned to vertebroplasty and 59 to a placebo procedure (subcutaneous local anaesthetic infiltration). The primary outcome was the proportion of patients achieving an NRS score of less than 4 at 14 days post-treatment. A significantly greater proportion of patients in the vertebroplasty group achieved the primary outcome compared with the control group (44% vs 21%; between-group difference 23 percentage points, 95% CI 6–39; p=0.011). This treatment advantage persisted at all timepoints to 6 months. Moreover, there were also statistically significant reductions in Roland-Morris Disability Questionnaire scores from 1 month to 6 months post-treatment.

VAPOUR was different from other studies in a number of respects. First, VAPOUR included earlier treatment of vertebral compression fractures compared with previous masked RCTs, and focused on patients with severe pain (NRS ≥7). Second, the placebo group was different, and closer to a true sham procedure. In the previous masked RCTs, the sham procedure involved periosteal local anaesthetic infiltration, an active control, which could have provided pain relief particularly for patients with more chronic fractures and secondary mechanical pain.13 The authors used subcutaneous local anaesthetic infiltration followed by medical management, thus providing a better comparator more akin to conservative therapy. Additionally, VAPOUR showed that medical management is not always benign, and can also be associated with risk—two patients in the control group developed spinal cord compression from further collapse and retropulsion of their vertebral compression fractures.

Third, the major benefit was driven by fractures in the thoracolumbar (T11 to L2) segment. In this subgroup, 61% of the vertebroplasty group achieved the primary outcome compared with 13% of the control group (between-group difference 48 percentage points, 95% CI 27–68). The authors hypothesise that this segment is subject to increased dynamic weight-bearing load and thus there is potentially greater benefit from restoration of structural integrity after vertebroplasty.

Fourth, there was at least a 30% greater vertebral height preservation from 6-month radiographs in the vertebroplasty group without increase in additional vertebral fractures.

Finally, 57% of patients enrolled were hospital inpatients, and the median duration of hospital stay was reduced by 5·5 days in the vertebroplasty group. Although there was no cost-effectiveness analysis in VAPOUR, such marked reduction in hospital stay will presumably translate to overall health-care cost saving, even when accounting for procedural costs.
There are several limitations to the trial. Although the authors of VAPOUR advocate their adequate-fill technique to prevent future vertebral collapse, it remains unclear whether their results were driven by the greater cement volumes injected when compared with previous RCTs. In some investigations, volume of cement injected was not considered to affect analgesic response, and these questions might need to be addressed in future research efforts. Moreover, 85% of procedures were done at a single centre by experienced surgeons, which could limit generalisability.

Overall, the implications from VAPOUR as a stand-alone trial are clear: patients with severe pain from a recent osteoporotic fracture appear to benefit from vertebroplasty. Benefits might be more pronounced for fractures closer to the thoracolumbar junction, and importantly, for patients admitted to hospital, there could be significant reduction in length of hospital stay. VAPOUR also highlights that conservative medical therapy is not always risk free. Clinicians involved with this cohort of patients should offer patients and their caregivers the option to consider vertebroplasty.

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