

Klazen CAH, Lohle PNM, et al. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): an open-label randomised trial. Lancet 2010; 376: 1085–92 .

Klazen CAH, Verhaar HJJ, et al . VERTOS II: Percutaneous vertebroplasty versus conservative therapy in patients with painful osteoporotic vertebral compression fractures; rationale, objectives and design of a multicenter randomized controlled trial. Trials 2007, 8:33 [study protocol]

Design: Randomized clinical trial

Population/sample size/setting:

- 202 patients (62 men, 140 women, mean age 75) treated for osteoporotic vertebral fractures at 5 large teaching hospitals in the Netherlands and 1 in Belgium
- Eligibility criteria were a vertebral compression fracture on x-ray with at least 15% loss of height, fracture at T5 or lower, back pain for at least 6 weeks with a VAS intensity of 5 or more, bond edema of vertebral fracture on MRI, focal tenderness at the fracture level assessed by internist on physical exam, and decreased bone density (T score ≤ -1)
- Exclusion criteria were severe cardiopulmonary comorbidity, untreatable coagulopathy, systemic or local spine infection, suspected underlying malignancy, radicular syndrome, spinal cord compression syndrome, and any contraindication to MRI

Main outcome measures:

- 934 patients were screened for eligibility; 434 met eligibility criteria (229 had spontaneous pain relief to VAS of 5 or less and were excluded for this reason); 232 declined participation, and 202 were finally randomized
- Randomization was to percutaneous vertebroplasty (n=101) or conservative therapy (n=101)
 - o Percutaneous vertebroplasty was done under fluoroscopic guidance with two bone-biopsy needles placed transpedicularly and with a CT scan with 2 mm slices after the procedure to detect leakage of cement
 - All patients additionally received osteoporosis medication such as bisphosphonates plus supplemental calcium and Vitamin D
 - o Conservative treatment was based on optimum pain management (OPM), done by an internist who optimized the use of analgesics in ascending order: acetaminophen; tramadol; tramadol plus acetaminophen; morphine
 - NSAIDS were prescribed only if patients were intolerant of opiate derivatives
 - Physiotherapy was prescribed in most cases

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- Primary outcome was pain relief at 1 month and 1 year measured on VAS from 0 to 10, with clinically significant pain relief defined as a decrease of 3 points or more on the VAS
 - Pain-free days were defined as days in which the VAS was 3 or lower
- Secondary outcome was cost-effectiveness at 1 month and 1 year, derived from hospital billing systems
 - Quality-adjusted life-years (QALYs) were estimated with the EuroQol-5 questionnaire
- Tertiary outcomes were an osteoporosis-specific quality of life issue and the Roland-Morris Disability (RMD) questionnaire D
- Among the 101 patients randomized to vertebroplasty, 93 received vertebroplasty; 96 completed the 1 month follow-up, and 86 completed the 1 year follow-up
- Among 101 patients randomized to conservative treatment, 95 received treatment, 92 completed the 1 month follow-up, and 77 completed the 1 year follow-up
- CT scanning of the 134 treated vertebral bodies showed cement leakage in 97 (72%); most were into discal or segmental veins, and none were symptomatic
- Both groups decreased their VAS scores during follow-up, but the VAS improvement was greater for the vertebroplasty than for the conservative treatment group at all timepoints
 - Pain relief was apparent for vertebroplasty 1 day after the procedure compared to conservative treatment (mean VAS 3.7 vs. 6.7)
 - At the 1 month follow-up, the mean VAS improvement in the vertebroplasty group was 5.2 points compared to 2.6 points of improvement for the conservative treatment group
 - At the 1 year follow-up, the mean VAS improvement was 5.7 for the vertebroplasty group, compared to 3.7 for the conservative treatment group
 - Significant pain improvement (3 points or more) occurred earlier (29.7 days) for vertebroplasty than for conservative treatment (115.6 days)
- Mean total medical costs per patient were lower for conservative care than for vertebroplasty (difference of €2474 at 1 month and €2450 at 1 year)
- The cost differences were approximately equal to the cost of the vertebroplasty procedure (€2463)
- The incremental cost for vertebroplasty compared to conservative care was €2.685 per QALY gained, and each additional pain-free day cost €20
 - Direct medical costs (drugs, doctor visits, PT visits, cost of vertebroplasty itself) at 1 year were €182 for vertebroplasty and €6327 for conservative treatment; the data were skewed, but the p value for the difference was >0.05 (p=0.087)
- A few (10%) of patients randomized to conservative treatment crossed over to vertebroplasty during the trial period

Authors' conclusions:

- In patients with painful osteoporotic vertebral fractures, those who receive vertebroplasty an average of 5.6 weeks after symptom onset have faster and greater pain relief than those with conservative treatment
- Other randomized trials comparing vertebroplasty with sham vertebroplasty have not found differences in pain relief
 - o This study had only acute fractures; the sham controlled studies included patients with fracture duration up to 1 year, and those studies did not consistently have bone edema on MRI as an inclusion criterion
- The main limitation is that the study could not be blinded
- In a selected subgroup of patients with acute osteoporotic vertebral fractures, vertebroplasty is a safe and effective procedure
- The cost associated with vertebroplasty are acceptable, assuming that society is willing to pay up to €30,000 for QALY gained

Comments:

- Assumptions about cost-effectiveness per QALY gained may not be generalizable to the US health care system
- The authors included focal vertebral body tenderness as an inclusion criterion, increasing the likelihood that the pain being treated by vertebroplasty arose from the vertebral body in question; this was not an inclusion criterion in the sham-controlled vertebroplasty studies
- The percentage of actually eligible patients who declined randomization (232/434=53.5%) was high, but was lower than in the sham-controlled trials (64% and 69.6%); some selection bias is possible but is less than for the other trials
- The comparison between vertebroplasty and conservative treatment more closely resembles decisions that must be made in clinical practice than for the comparison between true and sham vertebroplasty
- The description of the conservative treatment program is sketchy; it included individualized medication management and some degree of physical therapy, but it is not clear whether it included active PT or cognitive-behavioral interventions which may optimize nonoperative treatment
- Disability scores were relegated to a tertiary outcome and were not fully described; they probably deserve greater priority in comparing treatment regimens

Assessment: High quality study supporting good evidence that vertebroplasty improves pain scores more rapidly than individualized pharmacological therapy for patients with acute osteoporotic vertebral fractures, with effects detectable in the first day and persisting up to one year