Kallmes DF, Comstock BA, et al. A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures. N Engl J Med 2009; 361:569-79.

Design: Randomized clinical trial

Population/sample size/setting:

- 131 patients (99 women, 32 men, mean age 74) treated for osteoporotic vertebral fractures at specialty sites in the US, UK, and Australia
- Eligibility criteria were age 50 or over, 1-3 osteoporotic vertebral compression fractures between T4 and L5, inadequate pain relief with standard medical therapy, a current pain rating of at least 3 on a scale from 1 to 10, and symptom duration less than one year
- Exclusion criteria were suspicion of neoplasm in the target vertebral body, retropulsion of bone fragments, concomitant hip fracture, active infection, uncorrectable bleeding diathesis, surgery within past 60 days, and dementia or inability to communicate in English

Main outcome measures:

- 1813 patients were assessed for eligibility; 1682 were excluded, 431 were eligible to participate; 300 declined, and 131 underwent randomization
- Patients were randomized to vertebroplasty (n=68) or to a sham vertebroplasty procedure (n=63)
- All procedures were performed with fluoroscopic guidance under conscious sedation; all patients were injected with 1% lidocaine in the subcutaneous tissues overlying the pedicle of the target vertebra and 0.25% bupivacaine in the periosteum of the vertebra
    - Randomization was done after the initial infiltration with local anesthetics; the vertebroplasty group had radiopaque PMMA infusion into the vertebral body until the cement reached the posterior aspect of the vertebral body or until it entered an extraosseous space such as the disc or paravertebral vein
    - During the sham intervention, pressure was applied to the patient's back, a container of PMMA was opened to simulate the odor of the actual vertebroplasty infusion, but the needle did not enter the vertebral body and no PMMA was infused
- Both groups of patients were monitored in the supine position after the procedure before discharge
- At the time of consent, patients were told that they would be allowed to cross over to the other intervention after one month, when the primary outcome was measured
- Primary outcomes were the group differences in the Roland-Morris Disability Questionnaire (RDQ) score at 1 month and in the average back pain intensity in the preceding 24 hours
    - A secondary analysis was also done to count the number of patients who had both a 30% or more decrease in the RDQ and pain intensity,

which were considered the minimally clinically important changes in these measures

- Several other secondary outcomes were obtained, including quality of life, activities of daily living, use of opioid medication, and ability to guess which procedure they had undergone
- 3 patients (1 vertebroplasty, 2 control) missed the 1-month interview because they crossed over to the other intervention before 1 month had elapsed
- Both groups had substantial improvement in pain and disability as soon as 3 days after the procedures, but the improvements were about equal
- The RDQ scores at 1 month did not differ between groups (mean score for vertebroplasty was 12.0 and for control group was 13.0); the adjusted group difference was 0.6, which was less than the 3 point minimally clinically important difference and whose 95% confidence interval included zero
- Similarly, the 1 month pain scores were similar in the two groups (mean of 3.9 for vertebroplasty and 4.7 for control, with a small group difference of 0.7 (less than the minimally clinically important difference of 2 points) and whose 95% confidence interval included zero
- The proportions of patients who reported at least 30% improvements in RDQ and pain also did not differ (40% for the vertebroplasty group and 40% for the control group)
- At 3 months, there were differences in the patients who asked to cross over to the other intervention group; 8 patients (12%) in the vertebroplasty group and 27 patients (43%) of the control group elected to cross over before 3 months
    - Patients who crossed over had greater pain scores than those who did not cross over, and the crossovers experienced less improvement in RDQ and pain after 3 months than patients who did not cross over
- 1 patient in the vertebroplasty group had injury to the thecal sac during the procedure requiring hospitalization; 1 patient in the control group had tachycardia and rigors of unknown cause and also had to be hospitalized overnight

Authors' conclusions:

- Patients with osteoporotic vertebral fractures experience similar improvement from true and sham vertebroplasty in RDQ and pain scores at 1 month from the performance of the procedure
- Factors other than the infusion of PMMA may account for the improvements observed after the procedures; these can include local anesthesia, the placebo effect of positive expectations, the natural history of vertebral fractures, and regression to the mean
- The reason for the greater crossover in the sham vertebroplasty group is not clear; this may arise from differences in pain relief which eluded detection from the commonly used and standardized measurements used to compare treatment groups
- Persistence of pain after or fracture healing may indicate causes of pain other than the vertebral fracture

- Long term effects of vertebroplasty could not be compared because patients were allowed to cross over after 1 month, and separate study is needed to assess long term improvement

Comments:

- Presumably the vertebroplasty patients who chose to cross over received the placebo procedure, but this is not further described
- Some selection bias could arise from the fact that so many eligible patients (300 of the 431 or 69.6%) who met the inclusion criteria) declined to be randomized; if these patients had more intense pain and wanted more urgent treatment, their presence in the population of acute vertebral fracture patients could affect the generalizability of the study results to all fracture patients
    - The slow accrual rate which forced changes in the original study protocol may be accounted for partly by high refusal to participate
- The inclusion criteria were symptom duration and imaging evidence of a fracture; there were no correlations of imaging with physical findings such as local tenderness on physical examination
    - This may be important, since guidelines stress the importance of interpreting imaging in the light of the clinical examination
- It is possible that the crossover differences show that the commonly used standardized outcome scores of pain and RDQ are not capturing all relevant information about patient response to vertebroplasty and other procedures
- The distribution of fractures between the thoracic and lumbar spine is not described
- The sham intervention should not be interpreted as equivalent to continuation of standard conservative medial treatment for purposes of decision making for patients with osteoporotic vertebral fractures
- To conclude that vertebroplasty is ineffective is not warranted from the data

Assessment: A methodologically high quality study which supports good evidence that pain and function scores in patients with osteoporotic vertebral fractures improve about equally both with vertebroplasty and with a well-simulated sham vertebroplasty which includes infiltration of the periosteum with local anesthesia, but may apply to only a minority of patients with these fractures