Buchbinder R, Osborne RH, et al. A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures. N Engl J Med 2009;361:557-68.

Design: Randomized clinical trial

Population/sample size/setting:

- 78 patients (62 women, 16 men, mean age 76) treated for painful osteoporotic vertebral fractures at an interventional radiology department at the University of Melbourne, Australia
- Eligibility criteria were back pain of no more than 12 months duration and the presence of one or two recent vertebral fractures of Grade 1 or higher, with MRI showing edema, a fracture line, or both
- Exclusion criteria were more than 2 recent vertebral fractures, spinal cancer, neurological complications, osteoporotic vertebral collapse of > 90%, fracture through or destruction of posterior vertebral wall, retropulsed bony fragment or fragments impinging on spinal cord, medical conditions making the patient ineligible for emergency decompressive surgery if needed, inability to give informed consent, and likelihood of noncompliance on follow-up

Main outcome measures:

- 468 patients were screened for eligibility; 248 did not meet inclusion criteria; 141 declined to participate
- Randomization was to either vertebroplasty (n=38) or a sham intervention
    - The vertebroplasty group received about 3 ml of PMMA cement into the vertebral body confirmed radiographically plus cephalothin intravenously immediately after the procedure
    - The sham intervention was the same as the vertebroplasty procedure except that a blunt stylet replaced the sharp stylet after a 13 gauge needle was inserted and made contact with the lamina; the vertebroplasty cement was prepared so that its smell permeated the room
- After the procedures, all patients received usual care at the direction of the treating physician, using up to date osteoporosis guidelines
- Baseline and follow-up data were collected by a blinded assessor
- Primary outcome was the score for overall pain on a scale from 0 to 10; the minimal clinically important difference was 1.5 points, and the primary score was measured at 3 months after the procedure
- Secondary outcomes included quality of life measures, a 41-item questionnaire specific for osteoporotic vertebral fractures, rest pain, night pain, a modified version of the Roland-Morris Disability Questionnaire (RDQ), and perceived recovery (responses of “moderately better” or “a great deal better” were scored as successful outcomes)
- Complete data were available for 71 of the 78 patients at 6 months; 3 had died for reasons unrelated to the procedures, and 4 were lost to follow-up
- At the 3-month primary data endpoint, there were no group differences for overall pain

    - Mean pain reductions were 2.6 points for the vertebroplasty group and 1.9 points for the sham vertebroplasty group; the mean between-group difference was 0.6 points, with a 95% confidence interval between -0.7 and 1.8 points, a statistically non-significant difference which was also less than the minimally clinically important difference of 1.5 points
- For the other outcomes, there were also no significant group differences, except for one of the quality of life measures which favored the vertebroplasty group at the 1 week assessment after the procedure
- For both groups, use of opioids decreased over time
- Duration of pain was not seen to influence the response to treatment
- 7 new clinical vertebral fractures were reported within 6 months of the procedures, 3 in the vertebroplasty group and 4 in the sham group

Authors' conclusions:

- No beneficial effect of vertebroplasty over a sham procedure was seen
- Outcome assessors were blinded to the procedure received by the patients; crossover was not permitted during the trial, and the attrition rate was low
- It is possible that there was some selection bias arising from the fact that 30% of potentially eligible patients declined to participate in the randomized trial
- The study had a relatively small sample size, but only 2 patients in each group had pain for more than 6 months, and all were required to have bone edema on MRI, which is reported to predict a beneficial effect of vertebroplasty
- The use of vertebroplasty for osteoporotic vertebral fractures is called into question

Comments:

- Among eligible patients who consented to participate, the study had good control of potential sources of bias
- When the authors report that 30% of potentially eligible patients declined to participate (141 out of 468 patients), they understate the potential selection bias, which should be based on the percentage of actually eligible patients who declined to participate (141 out of 218), which is 64% of patients who could have been randomized but who declined to participate
- Unlike the SPORT studies, which reported the characteristics of patients who declined randomization, the authors do not report on these patients, who are likely to have elected to undergo immediate vertebroplasty when available, perhaps because they perceived their pain as too great to risk a sham procedure
- Patient selection was based on symptoms plus MRI evidence of fracture; there was no criterion from physical examination to decide eligibility for the study
    - Specifically, tenderness of the vertebral body on examination, which can localize "overall" back pain to a specific vertebra, was not used for patient selection
    - If this physical finding in fact localizes back pain to an osteoporotic vertebra, the study may have enrolled patients whose overall pain arose from other structures

    - Since guidelines emphasize that imaging studies must be correlated with clinical findings, this point may be nontrivial in its implications
- The internal validity of the study is high; the external validity is not clear, but does apply to patients who are selected on the basis of symptom duration and MRI criteria for osteoporotic fracture and are willing to participate
- The usual (e.g., Cochrane Collaboration) ways of assessing bias operate on patients who consent to be randomized; selection bias that arises prior to obtaining consent may elude detection by these measurements
- A vertebroplasty and a sham vertebroplasty procedure do not represent decisions that clinicians must make in the real world; the decision that must be made is between vertebroplasty and some form of conservative care; while a sham vertebroplasty control sheds light on the specific effects of the cement injection, it does not illuminate the comparative success of vertebroplasty and ongoing conservative care
- The number of thoracic and lumbar fractures is not reported either in the article or the supplementary data appendix

Assessment: Methodologically high quality study which provides good evidence that vertebroplasty does not differ from sham vertebroplasty in patients with acute (less than 6 months duration) osteoporotic vertebral fractures demonstrated by MRI criteria of edema and or/a fracture line, but that may apply to only a minority of patients with painful vertebral fractures