Balancing Science and Informed Choice in Decisions about Vertebroplasty

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Worldwide there are approximately 1.4 million persons with vertebral compression fractures. In the United States, there are approximately 750,000; only one third receive treatment. Prevalence estimates are imprecise because of heterogeneity in how vertebral fracture is defined. Annualized direct care expenditures for osteoporotic fractures in the United States were estimated to range from $12 billion to $18 billion in 2002.

Several treatments (e.g., bed rest, bracing, and pain medications) have been designed to foster pain relief and allow for increased activities. Percutaneous vertebroplasty — the injection of polymethylmethacrylate directly into the vertebral compression fracture — has emerged as a treatment option. It is proposed that cement injected directly into the fracture provides immediate stability and relief of pain. Despite several studies suggesting a positive treatment effect for vertebroplasty, as compared with control treatments, there have been no blinded or placebo-controlled, randomized trials.

During the past 6 years, the number of vertebroplasty procedures performed in the United States has doubled, from 4.3 to 8.9 per 1000 persons, with variation across geographic areas by nearly a factor of 30 (Fig. 1, and the figure in the Supplementary Appendix, available with the full text of this article at NEJM.org). The first two blinded, randomized, placebo-controlled trials of vertebroplasty are reported in this issue of the Journal, and the results may change vertebroplasty from a procedure that is virtually always considered to be successful to one that is considered no better than placebo.

In investigating the treatment of subjective reports of pain and decreased function, the only way to distinguish the effect of expectations by the patients from the intervention itself is to conceal the treatment from the patients. Two unblinded trials have compared vertebroplasty with medical management: one showed better pain relief with vertebroplasty at 1 day and 2 weeks, and the other showed no significant difference at 3 months.

In the Investigational Vertebroplasty Safety and Efficacy Trial (INVEST) (ClinicalTrials.gov number, NCT00068822), Kallmes et al. report that pain and disability outcomes at 1 month in a group of patients who underwent vertebroplasty were similar to those in a control group that underwent a sham procedure, with a trend toward a higher rate of clinically meaningful improvement in the vertebroplasty group. Both study groups showed improvement within 3 days after the procedure. The cutoff for the primary outcome was 1 month, but data were collected for 3 months. Because of crossover to the other group, the intention-to-treat analysis at 3 months probably underestimated the true treatment effect, whereas an as-treated analysis probably would have overestimated the effect.

Interestingly, patients in the two groups (who were still unaware of which procedure they had received) crossed over to the other group after 1 month. The patients who crossed over had worse outcomes than those who did not request the other intervention. Since more patients than predicted were able to guess which treatment they had received, there might have been a benefit in understanding the treatment effect in those who guessed their treatment accurately. Did those who received vertebroplasty and guessed correctly do better or worse than those who did not guess correctly?
In the other trial, Buchbinder et al. (Australian New Zealand Clinical Trials Registry number, ACTRN012605000079640) measured pain, quality of life, and functional status at 1 week and at 1, 3, and 6 months after sham and active vertebroplasty and found there were no significant between-group differences at any time point. As in INVEST, patients in the two study groups had improvement in pain.

In both trials, the placebo procedure involved the injection of a short-acting analgesic into the bony periosteum containing nociceptive fibers, which make the area very sensitive to manipulation. Given the limited effect of vertebroplasty and no significant difference between treatments, was the placebo an active treatment?

Compassionate care and tincture of time, in and of themselves, can have an effect. After all, it is natural for fractures to heal. However, there is physical evidence of altered fracture healing in osteoporotic bone, which might have important implications in the treatment of osteoporotic fractures. During 6 months of follow-up, Buchbinder et al. reported seven incident fractures.

Adverse events were infrequent in these trials; however, vertebroplasty is not without risks. Reported complications, such as soft-tissue damage and nerve-root pain and compression, are related specifically to the leakage of bone cement. Rarely reported complications include pulmonary embolism, respiratory and cardiac failure, and death.

Given the increasing use, limited benefit, and potential risk, how often should vertebroplasty be performed? When best evidence suggests a toss-up between treatment options and no benefit, informed patient choice is essential. When faced with several choices for which the evidence is less than clear, patients and doctors must thoroughly review the options together. Informed choice helps
to educate patients about treatment options and allows them to recognize that a decision can be based on their values and preferences.12

This process also applies to cases in which the evidence for various options is available and in which each decision maker might value the risk–benefit profile for each option differently. Physicians typically underestimate patients’ desires for information.13 Active involvement by patients in their treatment choice leads to decisions that reflect the patients’ values, and patients tend to choose the most effective treatment, consistent with the best evidence. Patients who use decision aids are less likely to choose an invasive surgical procedure over a more conservative approach.14,15

President Barack Obama has called for more comparative-effectiveness research as part of the American Recovery and Reinvestment Act. Although clinical trials are an integral part of such research, from a safety and effectiveness standpoint, data from clinical trials combined with those from registries or other large longitudinal databases are necessary to provide the best evidence. Americans prize advances in technology. However, if in major medical challenges, such as osteoporotic vertebral compression fractures, the alternative is to pay the cost of perpetual uncertainty, we need to support the research necessary to provide sufficient efficacy and safety information for patients to make a truly informed choice. Although the trials by Kallmes et al. and Buchbinder et al. provide the best available scientific evidence for an informed choice, it remains to be seen whether there will be a paradigm shift in the treatment of vertebral compression fractures with vertebroplasty or similar procedures.

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