Vertebroplasty 'Benefits' May Be Placebo Effect

BY SHERRY BOSCHERT

EXPERT ANALYSIS FROM A MEETING ON OSTEOPOROSIS

SAN FRANCISCO – Vertebroplasty worked no better than sham surgery to reduce pain and disability from vertebral fracture, according to data from recent randomized, controlled trials that put nonsurgical therapies firmly in the first line of treatment.

Osteoporotic vertebral fractures should be treated aggressively with antiresorptive or anabolic therapy for at least 6-12 weeks before considering surgery, Dr. Douglas C. Bauer said at a meeting on osteoporosis sponsored by the University of California, San Francisco. Optimize medical therapy, physical therapy, and other options that might be appropriate such as adding calcitonin or referring the patient for a facet joint injection, he said.

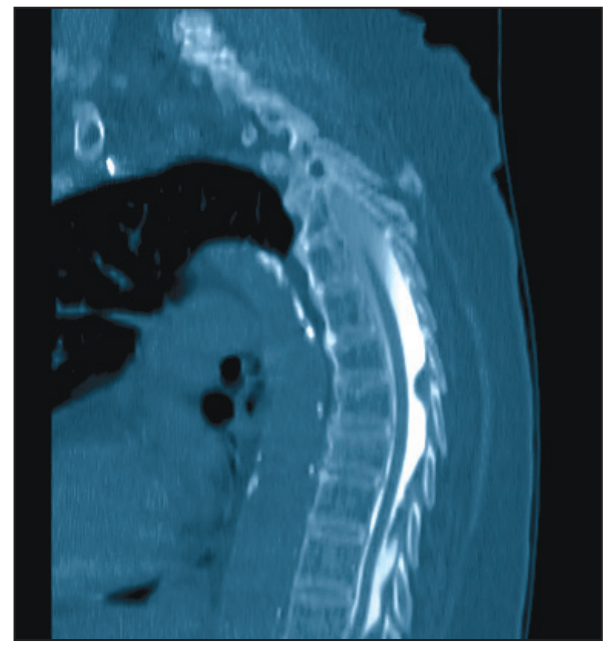
Even after all that, clinicians should consider kyphoplasty before resorting to vertebroplasty, said Dr. Bauer, who is professor of medicine and of epidemiology and biostatistics at the university.

Findings from one unblinded, randomized trial suggests that kyphoplasty may reduce pain and disability, compared with conservative care initially, though the difference in results is less apparent 1 year after surgery.

Despite data from numerous uncontrolled studies suggesting that vertebroplasty also lessens pain and improves function, findings from two well-designed controlled trials "raised a brouhaha" and surprised investigators by showing vertebroplasty to have no benefit, "suggesting that a very commonly done procedure is not helpful," he said. It's unclear whether the uncontrolled trial results were due to an extended placebo effect or some other factor.

In kyphoplasty, surgeons insert a balloon device to reduce the cervical fracture, remove the balloon, and replace it with cement. Vertebroplasty injects cement only, without the balloon, and does not attempt to increase vertebral height. Both are minimally invasive surgeries that usually are performed under general anesthesia but can be done using local anesthesia, often with conscious sedation.

The unblinded trial of kyphoplasty randomized 149 patients to kyphoplasty and 151 to usual nonsurgical care. "The patients were typical of who we see with vertebral fracture," Dr. Bauer said. One month after surgery, scores on the Short Form-36 (SF-36) Physical Component Summary had risen from 26 at baseline in both groups to 27 in the kyphoplasty group and 33 in the control group, a significant difference between groups (Lancet 2009;373:1016-24).



COURTESY DR. VICTOR JARAMILLO/DR. ARAVIND POTHINENI

CT myelogram shows an epidural hematoma and cord compression associated with a vertebral fracture.

Follow-up continued out to 3, 6, and 12 months after surgery, and results were significantly better in the kyphoplasty group at all time points for the SF-36 Physical Component, patient-reported Visual Analog Scale (VAS) scores for back pain, and the number of days of limited activity in the previous 2 weeks.

Although statistically significant, some of the differences between groups were more clinically significant than others. The self-reported VAS pain scores, for example, differed between groups by only 1 point on a 10-point scale at 12 months. The kyphoplasty group, however, enjoyed an average of 60 fewer days of limited activity during those 12 months, compared with the control group, he said.

At 24 months, only the difference in pain scores remained statistically significant between groups (J. Bone Miner. Res. 2011;26:1627-37).

More trials of kyphoplasty are needed before the surgery becomes widespread, Dr. Bauer said.

A separate uncontrolled trial that randomized 202 patients to vertebroplasty or usual care similarly found statistically greater improvements in the vertebroplasty group in VAS pain scores at 1 month (a decrease of 5 points) and 1 year (a 6-point drop), compared with usual care (a 3- and 4-point drop, respectively). Patients in the surgery arm also reported less narcotic use (Lancet 2010;376:1085-92).

The two well-designed controlled trials of vertebroplasty contradict other findings, however. Patients were taken to the operating room before randomization. The control group received sham surgery that included needle insertions in their backs and the breaking of a vial of chemicals to disperse a chemical smell. Outcomes assessors were blinded to randomization.

In one study of 71 patients, scores for back pain decreased significantly in both the real and sham surgery groups, but outcomes did not differ significantly between groups at any time point out to 6 months (N. Engl. J. Med. 2009;361:557-68).

In the other study of 131 patients, both groups showed immediate improvements in disability and pain scores but no outcomes differed significantly between groups at 1 month (N. Engl. J. Med. 2009;361:569-79).

While it's conceivable that the benefits reported for vertebroplasty and kyphoplasty in uncontrolled studies are due to an extended placebo effect, the likelihood that the placebo effect would last for as much as 24 months of follow-up is unclear, Dr. Bauer said.

Some have suggested that the sham-surgery studies included a harder-to-treat population by accepting patients with vertebral fractures up to 1 year in duration, but a subsequent analysis of data limited to fractures of less than 6 weeks duration found no change in the overall results.

Case series have shown that anesthetic or steroid injections alone can reduce vertebral fracture pain, which may explain the improvement in pain scores in both the real and sham-surgery groups in the vertebroplasty trials, he suggested.

There also may be a difference between the two surgeries that produce different results from kyphoplasty or vertebroplasty. Randomized controlled trials comparing the two are underway.

Dr. Bauer has received research funding from Amgen and Novartis. ■

Mortality Risk Doubles During Year After Hip Fracture

BY MARY ANN MOON

FROM ARCHIVES OF INTERNAL MEDICINE

Mortality risk doubles during the year after hip fracture among women aged 65 years and older, then returns to baseline in many women; but this pattern doesn't apply in all cases, according to a large, prospective cohort study.

Mortality risk in patients who have sustained a hip fracture differs by age, underlying health, and the interval since the injury occurred in this population, said Dr. Erin S. LeBlanc of the center for health research at Kaiser Permanente Northwest Region, Portland, Ore., and her associates.

Previous studies of this issue have had methodological limitations and have yielded inconsistent results. Most have shown increased short-term mortality, but have had mixed findings on long-term mortality. "Our data suggest that previous mixed results … may have been the result of differences in the underlying age and health status of the population being studied," the researchers said (Arch. Intern. Med. 2011 Sept. 26 [doi: 10.1001/archinternmed.2011.447]).

They used data from the SOF (Study of Osteoporotic Fractures) to address these methodological limitations. The subjects were identified before hip fractures occurred, and extensive data on comorbidities allowed adjustment for potential confounders.

The SOF subjects were 5,580 community-dwelling women aged 65 and older who resided in Maryland, Minnesota, Oregon, and Pennsylvania at baseline in 1986-1988. This population included 1,116 women who sustained incident hip fractures during a mean follow-up of 14 years, and 4,464 age-matched control subjects without hip fracture.

Mortality risk was highest in the first year after hip fracture. The rate was 16.9% among cases, versus only 8.4% in controls. This doubling of risk persisted after adjustment to account for factors such as total hip bone mineral density.

Moreover, deaths in the control group were evenly spread throughout the year, whereas those in the case group were concentrated within the first 6 months of the year, with more than half the deaths occurring in the first 3 months. When the subjects were categorized by age (younger than 70 years, 70-79 years, or 80 years and older), the youngest group showed a fivefold rise in mortality risk during the first year after hip fracture (16.3%), compared with women younger than 70 who did not sustain a hip fracture (3.7%). In contrast, the oldest women showed no increased mortality risk in the year following hip fracture, and the middle group showed an intermediate risk.

In addition, mortality risk remained elevated for years 1-10 in the youngest group, but it was somewhat lower than the mortality risk in the first year. Mortality risk declined to baseline for the next 10 years in the two older groups.

"We hypothesize that age influences the risk of death after hip fracture by affecting the baseline death rate in the population. Those who are younger ... have a low risk of dying from other causes. Therefore, experiencing a hip fracture may increase their mortality risk compared with nonfracture controls.

"In contrast, octogenarians generally have a relatively high risk of dying from other causes; therefore, experiencing a hip fracture does not result in an increased risk of death during the next year compared with other women their age," the researchers said.

This study was supported by the U.S. Public Health Service, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute on Aging, and the National Center for Research Resources. No financial conflicts of interest were reported. ■

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