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Priority Updates from the Research Literature from the Family Physicians Inquiries Network

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Vertebroplasty for osteoporotic fracture? Think twice

Two new studies suggest that this widely used procedure should be used less often—and more cautiously.

PRACTICE CHANGER

Think twice before recommending vertebroplasty (VP) for symptomatic osteoporotic compression fractures. New studies suggest that it has little benefit; thus, VP should be considered only after other, more conservative options fail.[1,2]

STRENGTH OF RECOMMENDATION

A: Consistent, high-quality randomized controlled trials (RCTs)

Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med*. 2009;361:569-579.

Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med*. 2009;361:557-568.

ILLUSTRATIVE CASE

A 72-year-old woman with a history of osteoporosis is being treated with a bisphosphonate, calcium, and vitamin D. She's in your office today because of the sudden onset of midline lower back pain after minor trauma. X-ray reveals an uncomplicated osteoporotic fracture of L2, with 50% loss of vertebral height. When she returns in a few weeks, the patient still has significant pain (7 on a scale of 0-10) that is not well controlled with hydrocodone and acetaminophen. Should you refer her for vertebroplasty?

Each year in the United States, approximately 750,000 vertebral fractures occur.[3] The traditional treatments for osteoporotic vertebral compression fractures include bed rest, pain medication, braces, and therapy for osteoporosis. Since the late 1990s, however, vertebroplasty (VP)—the percutaneous injection of acrylic bone cement (polymethylmethacrylate, or PMMA) into the affected vertebra under radiologic guidance—has become the preferred treatment, particularly for painful vertebral fractures that do not respond to conservative treatment.

Widely used, but not much evidence

Despite a lack of rigorous scientific evidence of VP's efficacy, the number of procedures nearly doubled from 2001 to 2005 among Medicare enrollees—from 45 per 100,000 to 87 per 100,000.[4] A meta-analysis of 74 (mostly observational) studies of VP for osteoporotic compression fractures found good evidence for improved pain control in the first 2 weeks. At 3 months, the analysis found only fair evidence of benefit, and at 2 years, there was no apparent benefit.[5]

Complications are primarily related to cement extravasation, but are usually not symptomatic. The overall symptomatic complication rate is less than 4%.[6] There is conflicting evidence regarding whether VP increases the risk of fracture in other vertebrae.[7]

Prior to the 2 studies reviewed in this PURL, there were only 2 RCTs comparing vertebroplasty with conservative medical management. The VERTOS trial[8] randomized 34 people with osteoporotic vertebral compression fractures (of 6 weeks' to 6 months' duration and refractory to medical therapy) to either VP or conservative treatment. The VP patients had improved pain scores and de-

creased use of analgesic agents at 24 hours, compared with the conservative treatment group. But at the end of the 2-week trial, there was no difference in pain scores between the 2 groups.

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The other RCT of VP vs conservative therapy randomized 50 patients with acute or subacute osteoporotic fractures (the average age of fracture was 6-8 days) to VP or conservative care.[9] There was significant pain improvement in VP patients at 24 hours, but no significant difference in pain scores between the 2 groups at 3 months. This study was significantly flawed, however, because the researchers failed to collect pain measurements at study entry for a substantial number of patients.

STUDY SUMMARIES

Vertebroplasty lacks benefits

Both INVEST (the Kallmes study)[1] and the Buchbinder study[2] were blinded, randomized, placebo-controlled trials of VP. INVEST, performed at 11 sites in the United States, United Kingdom, and Australia, enrolled 131 patients. The Buchbinder study enrolled 78 patients at 4 sites in Australia. Both enrolled patients with painful osteoporotic fractures of less than 1 year's duration. Exclusions for both trials included a suspicion of neoplasm in the vertebral body, substantial retropulsion of bony fragments, medical conditions that would preclude surgery, and an inability to obtain consent or conduct follow-up.

Participants in both trials had similar baseline characteristics: They were primarily Caucasian and female, with an average age in the mid-70s. The average pain intensity at enrollment was about 7 on a 0- to 10-point visual analog scale (VAS). The average time since the fracture causing the pain was 4 to 5 months in INVEST and about 2 months in the Buchbinder study. Both trials used appropriate randomization, blinding, and intention-to-treat analysis.

Blinding featured sham procedures. In both studies, the researchers used elaborate measures to ensure blinding: The control patients were prepped in the fluoroscopy suite as if they were about to undergo VP. They received local anesthesia down to the periosteum of the vertebra. The PMMA was opened and mixed in the room to allow its distinctive smell to permeate. Patients also received verbal and physical cues that simulated the procedure, and spinal images were obtained.

INVEST used pain and disability at 1 month as the primary end points. There was minimal difference in pain intensity (3.9 on VAS for the VP group, vs 4.6 for the controls). There was also little difference in back pain-related disability at 1 month, with scores on the Roland Morris Disability scale decreasing (from a baseline of 16.6 for the VP group and 17.5 for the control group) to 12 and 13, respectively (P=.49). Nor were there any statistically significant differences in pain or disability at earlier intervals (the researchers compared the scores of the VP and control groups at 3 days and 14 days.) The authors also looked at 7 other measures of pain and functioning and found no significant differences in any of them at the end of 1 month.

To encourage enrollment, patients in the INVEST trial were allowed to cross over after 1 month. At that time, 12% of those in the VP group and 43% of those in the control group took advantage of this provision and had the alternate "procedure." Both groups of cross-over patients had more pain than those who did not make the switch. Although both of these groups showed improvement at the 3-month mark, they still had higher pain levels than their counterparts who did not cross over.

The Buchbinder study used overall pain on a 10-point VAS at 3 months as its primary end point. The researchers also recorded 7 other measurements and assessed participants at 1 week, 1 month, 3 months, and 6 months. At 3 months, there was no significant difference in the change in pain scores between the treatment and placebo groups: Mean pain scores for those who underwent VP decreased from 7.4 to 5.1, while the placebo group's average pain scores went from 7.1 to 5.4. Similarly, there was no difference between the treatment and placebo groups in the change in pain scores at 1 week or 6 months—and no difference between the groups at any time for the other 7 measures of pain and function.

CONTINUED

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INSTANT POLL QUESTION

Under what circumstances do you recommend vertebroplasty for a patient with an osteoporotic compression fracture? (Check all that apply)

- *Shortly after the fracture is diagnosed.*
- *Only after conservative treatment has failed to bring pain relief.*
- *On a case-by-case basis, depending on factors such as compression severity, duration of fracture, level of pain, and comorbidities.*
- *None; I do not recommend VP for osteoporotic compression fracture.*
- *Other* _____

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WHAT'S NEW

Trials cast doubt on established procedure

VP has essentially become the standard of care for painful osteoporotic vertebral fractures, bolstered by a long list of methodologically inferior studies that have lent support to the procedure's efficacy. These 2 studies are the first to incorporate a sham procedure that supports true placebo control. The complete lack of benefit for VP compared with conservative management in these well-done trials calls into question the results of prior reports.

In 2005, the rate of vertebroplasty among Medicare beneficiaries was 87 per 100,000—nearly double the 2001 rate.

CAVEATS

Sample size, study design

Researchers in both studies had considerable difficulty enrolling patients. Both were multicenter trials and enrolled patients over a 4-year period; nonetheless, taken together, only about 200 patients consented. The researchers faced opposition from referring doctors and patients alike, who believed that the possibility of receiving a placebo treatment rather than VP constituted inferior care.

In addition to their relatively small size, these studies enrolled patients with fairly chronic fractures. It has been postulated that VP has a higher likelihood of success with acute fractures, but that was not the focus of these trials. The majority of the fractures in trial participants were not acute (<4 weeks). Neither trial was designed for analysis based on the chronicity of the fracture, and neither found a difference in outcome based on fracture duration.

Because these trials were not designed, or robust enough, for subgroup analysis, we don't know if there is a population that might benefit (ie, severity of the compression, acuteness of the fracture, or premorbid health, etc). In addition, these results do not apply to the use of VP for other reasons—malignant spinal neoplasms or vertebral hemangiomas, for example.

Finally, it is important to remember that these trials did not strictly compare VP with conservative treatment. The sham treatment may have had significant placebo power that is greater than that of typical conservative treatment.

CHALLENGES TO IMPLEMENTATION

Support for VP is well established

Anecdotal results, established treatment patterns, and numerous low-quality studies support the use of VP for vertebral compression fracture. Medicare and other insurers had reviewed the evidence prior to these 2 trials and agreed to reimburse for the procedure. It remains to be seen whether these 2 trials will be sufficient to overcome these barriers and change practice patterns.

At a minimum, however, it is prudent to reserve VP for patients who have intractable symptoms until further trials are undertaken to determine whether VP really works, and if so, for which patients. JFP

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