Vertebral Augmentation

- Conservative treatment of vertebral compression fractures (VCFs) (bed rest, pain medications, and back bracing) is not risk free

- Augmentation therapy, including kyphoplasty and vertebroplasty, is a treatment in which cement is placed percutaneously into a fractured vertebral body or metastatic bone lesion

- Two recent small blinded prospective randomized clinical trials (RCTs) failed to demonstrate any statistically significant benefit from augmentation in osteoporotic patients, although numerous clinical case series and several prospective RCTs have shown rapid improvements in pain score

- Bone augmentation is recommended for pain control when there is good clinical and imaging evidence of a recent vertebral compression fracture or a metastatic bone lesion

In August 2009, the New England Journal of Medicine (NEJM) published two randomized controlled trials (RCTs) on vertebroplasty for the treatment of osteoporotic compression fractures. Both studies concluded that there was no evidence that vertebroplasty was better than a sham procedure for relieving pain or disability. These results were greeted with surprise and even disbelief by many practitioners, especially because an RCT published in The Lancet earlier in the year on the effectiveness of a closely related procedure, kyphoplasty, had shown that it was effective, with a high degree of statistical significance. Moreover, physicians who have performed these procedures, the patients themselves, and their primary care providers have witnessed dramatic pain relief, often within hours of the intervention. However, at times the lay press seemed to respond to these articles by proclaiming that vertebroplasty was worthless and, because of its expense, wasteful ignoring the value of shorter hospitalizations and realistic costs of alternative therapies.

RCTs are regarded as the optimal studies to determine the effectiveness of a treatment and, in this era of rising health care costs, it is important to make use of the best available evidence for selecting treatment for patients. However, every clinical study has limitations and, therefore, it is worth taking a close look at study design, especially patient selection criteria, procedures used, and the analytical methods used to draw conclusions. In Table 1, we show some differences in study design and patient enrollment in the three RCTs mentioned above, two on vertebroplasty (Buchbinder and Kallmes) and one on kyphoplasty (Wardlaw).

Patient Selection

Both Buchbinder and Kallmes had difficulty recruiting patients, as can be seen by the low percentage of eligible patients they were able to recruit, possibly because the control arm involved a sham procedure rather than medical management. The high refusal rate may have introduced some selection bias. Furthermore, neither of these studies reached their original recruitment goals.
Table 1. Differences in Study Design, Enrollment, and Outcome in RCTs for Vertebral Augmentation

<table>
<thead>
<tr>
<th></th>
<th>Buchbinder</th>
<th>Kallmes</th>
<th>Wardlaw</th>
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<tbody>
<tr>
<td>Number of patients enrolled</td>
<td>78 (73)</td>
<td>131 (128)</td>
<td>300 (266)</td>
</tr>
<tr>
<td>(Number assessed at 1 month)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Eligible patients enrolled</td>
<td>36%</td>
<td>30%</td>
<td>59%</td>
</tr>
<tr>
<td>Age of fracture</td>
<td>&lt;12 months</td>
<td>&lt;12 months</td>
<td>&lt;3 months</td>
</tr>
<tr>
<td>Advanced imaging requirement</td>
<td>Yes/no*</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>for acute fracture assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain score (0-10)</td>
<td>No threshold stated</td>
<td>≥3</td>
<td>≥4</td>
</tr>
<tr>
<td>Treatment</td>
<td>Vertebroplasty</td>
<td>Vertebroplasty</td>
<td>Kyphoplasty</td>
</tr>
<tr>
<td>Control</td>
<td>Periosteal injection of local anesthetic</td>
<td>Periosteal injection of local anesthetic</td>
<td>Medical</td>
</tr>
<tr>
<td>Outcome</td>
<td>Difference in overall pain score at 1 month, 0.5 (95% CI, -0.8 to 1.7)</td>
<td>Difference in back pain score at one month, 0.7 (P = 0.19)</td>
<td>Difference in back pain score at one month, 2.2 (P &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td>Difference in RDQ† score at 1 months, 1.7 (95% CI, -1.8 to 5.2)</td>
<td>Difference in RDQ score at 1 month, 0.7 (P = 0.49)</td>
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</tr>
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</table>

*Although advanced imaging (MRI or CT and bone scan) was required, a fracture line was accepted as evidence of a fracture; that evidence is not sufficient to show that a fracture is acute.

†RDQ, Roland-Morris Disability Questionnaire

One striking difference between the Wardlaw study and Kallmes and Buchbinder studies is that the Wardlaw RCT included patients with fractures up to three months old while the latter two studies included patients with fractures up to one year old. While we believe that there is potential value in treating subacute fractures, such a decision is typically undertaken with specific historical, physical examination and imaging data supporting such intervention in that particular patient. Moreover, only under very rare circumstances would we not examine the patient or utilize advanced imaging to help optimize therapy. This standard was not universally applied or necessarily required in these RCTs.

The causes of back pain are multiple. Fracture lines in radiographs are not necessarily helpful in assessing acuity of compression fractures. MRI or bone scans are much more sensitive than are radiographs for the diagnosis of acute fractures. In the Kallmes study, there was no requirement for advanced imaging unless the fracture was of an uncertain age. In the Buchbinder study, advanced imaging was a requirement but either edema or a fracture line was considered sufficient evidence for enrollment, despite the fact that a fracture line is not necessarily evidence of an acute fracture. The Wardlaw study used rigorous imaging criteria and accepted patients who showed signs of edema on MRI and a 15% loss of height or more for a single level fracture. There were additional MRI-based requirements for enrolling patients with more than one fracture.

Comparison of Procedures

Although the Wardlaw study was on the effectiveness of kyphoplasty, not vertebroplasty, both techniques involve the injection of the same kind of cement into vertebrae. In kyphoplasty, a balloon is employed to create a cavity within the bone prior to injection of cement. Proponents of kyphoplasty have argued advantages of kyphoplasty over vertebroplasty, but pain relief has not typically been one of them. Therefore, we believe that is it reasonable to compare the outcomes of RCTs of kyphoplasty and vertebroplasty for pain control.
In the Wardlaw study, the control population was treated medically and, therefore, could not be blinded as to whether or not they were treated. It is worth noting that this control group more reasonably approximates the treatments patient would normally receive in lieu of augmentation. In the Kallmes and Buchbinder studies, the control population received an injection of local anesthetic simulating a facet joint block, albeit with far higher medication dosing than routinely used for this purpose. Although the effects of this would be short-lived, it is nonetheless a form of treatment that, depending on the etiology of the pain, may have had an effect.

The patients in both the Kallmes and Buchbinder studies were blinded and theoretically did not know which treatment they received. Questions have arisen regarding blinding in the Kallmes trial because patients undergoing vertebroplasty had their insurance billed. The investigators made every effort to simulate the vertebroplasty procedure, which included periosteal injection of local anesthetic. Even so, in the Kallmes study, the majority of patients correctly guessed which group they were in. Furthermore, patients were permitted to cross over to the alternate treatment after one month, and there was a higher crossover rate in the control group than in the vertebroplasty group (48% vs. 12%, P<0.001).

**Outcome Assessment**

All three of these studies measured changes in pain and disability scores at set times during the studies. However, the Buchbinder study did not specify the initial pain intensity required for inclusion in the RCT and measured overall pain rather than back pain. The Kallmes study set the pain threshold at a relatively low score, >3 (out of 10), and had the statistical power to measure a 1.5 point difference in pain score. Assessment of pain after treatment was by telephone interview (Kallmes) and questionnaire (Buchbinder), not physical examination, and it is not clear how the investigators distinguished continuing pain from vertebral fracture from other sources of pain, including new vertebral fractures, in these studies. In the Wardlaw study, standing lateral radiographs, taken at 3 and 12 months, were used to determine the presence of a new or worsening fracture.

In the Wardlaw study, the benefits of kyphoplasty were found to be highly significant and lasting on all measures of back pain, quality of life, and disability scores. Neither the Kallmes nor the Buchbinder studies showed any benefit from vertebroplasty. However, in the Kallmes study, a trend towards clinically meaningful improvement was observed (a 30% decrease in baseline scores, p = 0.06). It is unfortunate that the Kallmes trial did not achieve their originally planned recruitment goals.

**Conclusions and Recommendations**

Vertebral augmentation has played a role in the management of vulnerable geriatric patients for almost two decades in the United States. The performance of RCTs for such widely accepted procedures is a challenging endeavor and we salute the investigators involved in the trials described above for embarking on such a daunting task. However, we believe that the negative conclusions on the effectiveness of vertebroplasty from the Kallmes and Buchbinder studies do not provide definitive answers. For this reason, we continue to offer bone augmentation for properly selected patients with osteoporotic VCFs as well as metastatic bone lesions.

The figures in this article make use of a clinical vignette to illustrate the critical role that advanced imaging plays in patient selection. These images are of an elderly patient with multiple medical co-morbidities who fell and developed acute back pain. After several weeks of conservative outpatient management, the patient was unable to cope with the pain and required admission to the hospital for pain control. The MRI demonstrates its utility in evaluation of patients for vertebral augmentation.
Scheduling
A consultation or office visit for bone augmentation therapy can be scheduled by contacting Interventional Neuroradiology / Endovascular Neurosurgery (617-726-1767).

Further Information
For further questions about augmentation therapy, contact Joshua A. Hirsch, M.D., Vice Chief of Interventional Care, Director of Interventional Neuroradiology / Endovascular Neurosurgery at 617-726-1767.

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References


