Vertebral Body Augmentation: Time for Reassessment?

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Introduction

In August 2009, the *New England Journal of Medicine* simultaneously published reports of two randomized clinical trials. Both trials compared the outcomes of patients undergoing vertebroplasty for painful osteoporotic compression fractures with a sham procedure in which a needle is placed, but no polymethylmethacrylate (PMMA). Both trials concluded that vertebroplasty did not improve outcomes when compared to the placebo procedure.[1,2]

Previous Level II-IV studies reported rapid, marked pain relief in 80%–100% of patients treated. Prior to these trials, most providers regarded vertebroplasty and kyphoplasty (together, vertebral body augmentation or VBA) as highly effective and minimally risky. The reports, therefore, came as a shock and surprise.

Now, spine care providers are faced with a large chasm between these previous data and their own anecdotal experiences, and the latest, highest quality data. To assist its membership in interpreting these studies, NASS convened a panel including Christopher Bono, MD, Michael Heggeness, MD, PhD, Charles Mick, MD, Daniel Resnick, MD and William Watters III, MD. The panel reported its analysis in a *Spine Journal* commentary in March 2010.[3] In that issue, editor in chief, Eugene Carragee, MD[4] and the lead authors of the *NEJM* studies, David Kallmes, MD, and Rachelle Buchbinder, MD, commented on that analysis.[5]

We join Bono et al, James Weinstein, DO,[6] Carragee and other commentators in commending both groups of authors for this onerous, but critical undertaking. Now that 10 months have passed from publication, our purpose is to examine the impact of these studies and their criticism on physician attitudes toward VBA.

As with any comparison of two treatments, no matter how systematic or controlled, inevitably biases and technical factors can favor one treatment over another. As Bono et al remind us, "There is no such thing as an infallible PRCT." Drawing on the acumen of a *SpineLine* Editors' panel (see sidebar, next page), we will first seek to understand the trials, including their similarities and differences.

Then, we will examine the critiques. Finally, we want to explore the "seeming disconnect between the conclusions of these two PRCTs and previous experience and data." Are these studies really flawed or are we over-analyzing them because we are not happy with the result? How are we going use this data? Does it apply to kyphoplasty and other procedures?

Studies Redux

Kallmes et al[1] study:

- international multicenter
- randomized blinded study
- 131 patients
- one to three painful osteoporotic vertebral compression fractures (VCF) of up to 12 months' duration
- patients assigned to undergo either:
  1. vertebroplasty with cement injection
  2. simulated procedure: infiltration of pedicle periosteum with local anesthetic
- conclusion: with both vertebroplasty and the sham procedure, improvements in visula analog score (VAS) pain and Roland-Morris Disability Questionnaire back pain-related

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disability at one month were similar and not clinically significant

Buchbinder et al[2] study:
- Australian multicenter
- randomized, double-blind, placebo-controlled trial
- 78 patients
- one to two painful osteoporotic vertebral fractures of up to 12 months' duration
- patients assigned to undergo either:
  1. vertebroplasty
  2. sham procedure: cement was mixed but not put into the patient
- dry needle (no anesthetic) in sham group
- conclusion: no beneficial effect of vertebroplasty over control at one week or at one, three or six months after treatment

Critiques

Most critiques have explored the types of fractures included in the studies. Were the fractures too old? The wrong types? Both trials included patients with pain duration up to 12 months. Critics conclude that there were too few acute fractures and that "internal fixation of healed fractures" is not likely to help.

Some commentators questioned the clinical assessment to which the patients were subjected before inclusion in the trial. Some claim that MRI evidence of edema and bone scan findings of technetium uptake persist beyond true fracture healing. Therefore, using imaging assessment alone overestimates the impact of fractures on these elderly patients' back pain.

In the Kallmes trial, only outpatients were enrolled. Thus, inpatients hospitalized with acute fracture pain were excluded. Their protocol mandated at least four weeks of "medical therapy" before enrollment. MRIs were not ordered in all of the Kallmes patients. In his commentary, Kallmes stated that MRI or bone scans were used only in cases in which fracture age was uncertain. Many of our panelists found this "problematic" and cited the frequency with which ostensibly new fractures are found to be "cold" on MRI or bone scan. Others, Bono et al, for example, cite limitations to the physical exam finding it "useful to percuss or palpate the spinous processes systematically to find a level of maximal tenderness. This can then be marked with a radiographic marker to help localize the region of pain to a specific fractured vertebra. It is not uncommon for a patient to have pain that is distant from the fracture site, which would greatly diminish confidence that the perceived pain was originating from the fracture site." Our panel found that physical examination findings are often "inconsistent" in these patients. For example, patients with muscular pain often report tenderness at the insertion site of the muscle on the spinous process.

In the Buchbinder et al trial, the number of patients with pain for less than six weeks was too small for subgroup analysis. Several commentators debated Buchbinder's definition of acute fracture.

Others complained that enrollment rates were too low. Difficulties with patient recruitment could lead to poor patient selection or enrollment bias. As the funding interval concludes, the study sponsors are under marked pressure to meet enrollment targets. For example, most VBA proponents note that patients with the worst pain often report the greatest improvement after vertebroplasty. These patients are also the least likely to participate in a sham controlled study. Four weeks of medical/interventional management may not seem like a long time, but when the patient is in pain, asking them

Vertebroplasty Reappraisal: Our Panel

Our panel included *SpineLine* editorial board members with no direct experience with the procedures, some with experience with only kyphoplasty or vertebroplasty and two with extensive experience with both. None had active conflicts with manufacturers of kyphoplasty or vertebroplasty devices. Some, the moderator included, had (at least two years before this activity) been consultants for Kyphon and other manufacturers. The panel, listed below, provided a cross section of NASS membership and included orthopedic spine surgeons (ORS), physical medicine and rehab (PM&R) and pain management (PM):

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Attending Spine Surgeon, William Beaumont Hospital, Royal Oak, MI. No conflicts in the last four years. I have been a Kyphon consultant in the past.

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Complete contributor disclosures available on page 20.

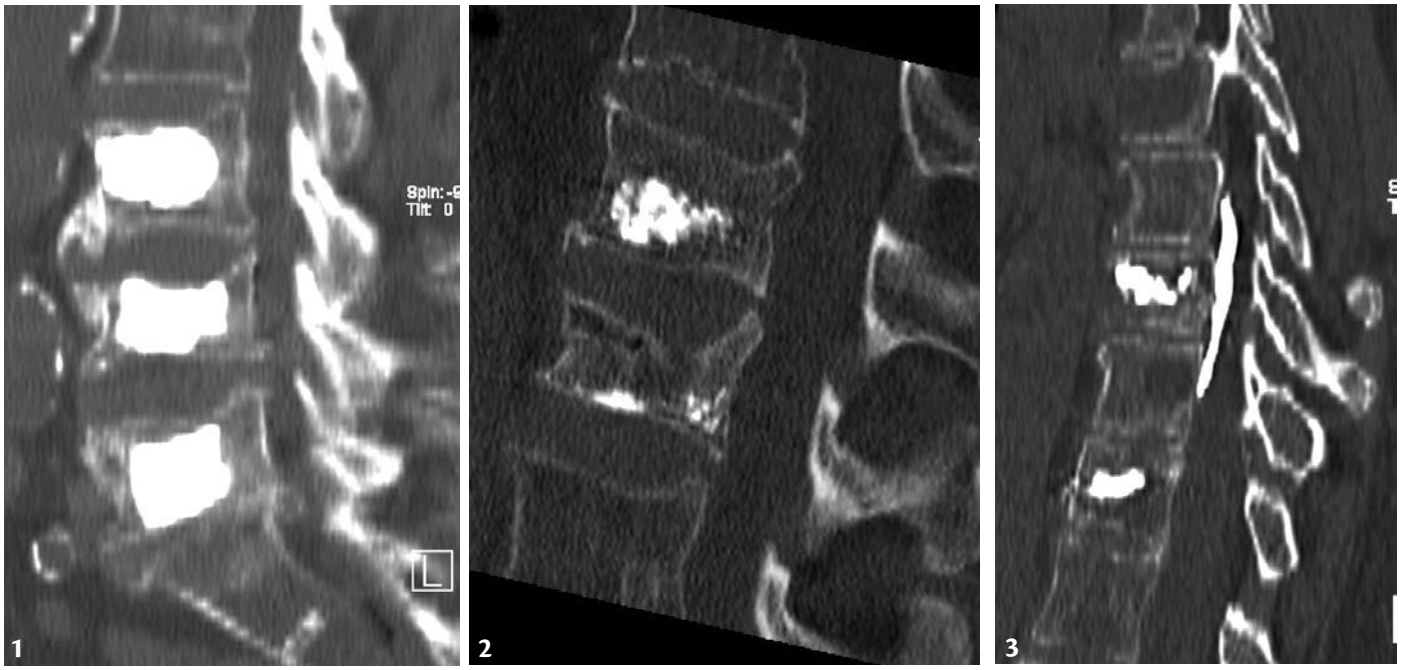

Figure 1 shows a VCF postop sagittal CT of a patient who had been admitted for intractable back pain. Despite bracing, physical therapy and IV pain medications, he was unable to ambulate. He was ambulatory the same day after a 40-minute, three-level VBA performed under local anesthesia. At two-week follow-up, he had weaned himself from all pain medications. Of course, this procedure does not meet CMS guidelines for VBA in that he had not had 4-6 weeks of nonoperative management. **Figure 2** represents a similar patient with axial pain despite 3-4 weeks of nonoperative management. Unfortunately, in this case, two-level VBA did not relieve pain. Postoperative scanning revealed underfilling of the caudal level, ie, no PMMA around the superior end plate fracture. **Figure 3** represents a patient who underwent two-level VBA with marked PMMA extravasation into the canal. The patient had no postoperative neurologic sequelae in this case, but devastating neurologic complications have been reported.

to tolerate "more of the same" for another four weeks or risk a sham procedure may be too much.

In fact, neither study reached its target enrollment. Both the Kallmes and Buchbinder studies reduced their initial target sample size due to recruitment and enrollment difficulties. In the Kallmes et al study, 1,812 patients were initially screened, yet only 131 were enrolled, with patient refusal the most common reason for nonenrollment. The rate of eligible patients declining participation was 64% and 70% in Buchbinder's and Kallmes' trials, respectively.

The Buchbinder trial, with a target enrollment of 200, required 4.5 years to accrue 78 patients at four high-volume centers. One hundred forty-one who satisfied all inclusion criteria declined randomization. These enrollment numbers markedly limited the statistical power of subgroup analysis.

Others cite the 12% treatment and 43% control group crossover rates in the Kallmes trial. Patients crossing over appeared to have worse results compared to those who did not. This, critics say, implies short-term benefits from vertebroplasty that the study was not powered to detect.

In *NEJM* editorials, critics write that describing the Buchbinder study as a multicenter trial may not be strictly accurate in that 68% of the procedures were performed in one hospital by a single radiologist. Once the Australian government decided to cover vertebroplasty, two of four sites withdrew after enrolling five patients each. Our panel found this to be a concerning point. As with any surgical procedure, vertebroplasty outcomes will be influenced by technique: "If a total hip surgeon reported bad outcomes in a prospective trial and concluded that the THA does not work, there would be similar reaction by the rest of the surgical community."

In fact, pro-VBA commentators question the techniques employed in these trials. They argue that unilateral vertebroplasty and lower cement volumes increase the potential for asymmetric cement distribution. Poor PMMA distribution could undermine vertebral body stability and allow return of micromotion and pain. The same writers state that pain relief reported in these trials was significantly lower than "multiple previous reports." Buchbinder et al reported a 2.3 point reduction of pain, "far less than other studies."

Others questioned whether injection of anesthetic represented a true control? Sometimes local anesthetic delivery benefits patients for periods exceeding the drug's half–life. Especially against a favorable short-term natural history, this longer response may blur the response between groups. According to Weinstein,[6] in both studies, "active controls may be responsible for underestimation of the true treatment effect." Our panel's response to this point varied. Some did not find

Table 1. Physician Attitudes toward Vertebral Body Augmentation (VBA)

Questions	Panel Response Summaries
Describe your experience with vertebroplasty.	Most of the panel reported generally or very positive experiences. One reported even "patients with senile dementia who clearly don't remember me, or that they had any kind of surgery, yet they and their caregivers report definite improvement."
Bono et al report that many expressed "shock and disbelief" when the vertebroplasty RCTs were first reported. What was your first reaction? Has it changed now, nine months later?	Almost all agreed they were initially quite surprised, but have become less so over time. In one case, this change came from a reassessment of the technique. For most, their surprise waned as they came to understand the study designs. "I am less surprised, but feel that some of the limitations of the studies contributed to these results and make it difficult to apply the study results to the real world patient population." Two panelists remained "mortified" these studies were published at all, especially in the *New England Journal of Medicine*.
Were the initial vertebroplasty results "too good to be true"?	Most of the respondents felt the "truth" would lie somewhere in the middle. Four of six concluded more patients fail to improve after VBA than is commonly reported, but that a significant percentage report excellent relief. The others stated these two, relatively small RCTs, are the outliers and further studies will continue to report favorable outcomes.
Carragee feels VBA complications have been under-reported. Is this true? How many of us have seen major problems from PMMA in the lungs?	Most stated that the complication rate was low, but minor perivertebral leaks may be common. Three of six concluded that complications are under-reported. Several cited differences in risk with practitioner experience and imaging equipment quality. None of the panelists (several from high volume centers) had seen a clinically significant PMMA pulmonary embolism. A typical response: "Safety is not the issue. Efficacy is."
Can these procedures get patients out of the hospital earlier?	Almost all of our panelists agreed with this statement. Several wanted to caution that, misinterpreted, this statement could lead to over-utilization.
Today, are vertebral body augmentation procedures (eg, vertebroplasty and kyphoplasty) overperformed, underperformed, or just right?	Three of six respondents felt VBA procedures are currently over-performed. Two said "just right" and one said "underperformed." Many reported significant geographical variability in overall VBA utilization, the individual rates of kyphoplasty and vertebroplasty, and the specialists offering the procedure. This variability made their answers unique to their region. Others noted that, because many with VCF never present for formal medical evaluation, the denominator is not known and our "rates" of VBA are merely guesses.
Are patients or referring doctors responding to your recommendation for or against VBA differently now?	Responses varied among the panelists. Many cited significant regional variations in tendency to refer and timing of those referrals. About half felt their referrals had declined, but none precipitously. The others have not seen a change.
Will you continue performing these procedures (or referring your patients to have them)?	While exact selection criteria varied, all of the panelists agreed VBA remains a reasonable option. Many recommended patients and their families be specifically told (as most already do) their fractures are likely to heal over time even without the procedure. A typical answer: "Yes. My indications have always been very strict and continue to be."
For the purposes of this research, should we consider kyphoplasty functionally equivalent to vertebroplasty?	Our panel varied considerably on this question. About half felt the procedures were largely identical. Most agreed pain relief was similar. Many noted that independent of the procedure employed, an adequate amount of PMMA well distributed in the body is required for lasting clinical success. Those who see these procedures as very different cited differences in leak rates and final spinal alignment as potential advantages for kyphoplasty. A typical response: "I believe that kyphoplasty is more like vertebroplasty than unlike. However, I personally don't believe that height restoration significantly affects the patient's sagittal balance, and furthermore, the balloon procedure does not change the risk of the adjacent level fracture."
Do you think payers will use this data to stop reimbursing these procedures? Have you seen changes in your area?	The panelists agreed that coverage for vertebroplasty procedures would decline. About half had seen decreased coverage or reimbursement already. A typical response: "I have to dictate more letters of medical necessity to justify what I did."
Does Scott's parabola apply? If so, where are we on the curve?	The panel was split on this question, but found this to be a useful paradigm for studying new medical technologies. Most concluded that these studies would lead to soul searching and more restrictive use of these technologies. Even those who concluded the studies were flawed reported we were in the "doubt creeps in, " "damaging survey reported" or "condemned by several authorities" phases. (**Figure 4**)

this argument convincing saying, "If lidocaine works so well, let's get rid of PMMA." Others reported the occasional long-term benefits patient report after epidural steroid injections for stenosis. It should be noted that no lidocaine was injected in the Australian trial.

Some questioned whether the outcomes measures employed were adequate to discern clinically relevant differences between groups. Pain scales, especially in elderly patients with other pain complaints, are not very sensitive. Bono et al report that "diffuse pain measures" were employed. Our panel did not find that criticism held much water given that randomization should eliminate such "background noise."

A number of other technical complaints about study mechanics were lodged, including those by William Clark, MD, Stuart Lyon, MD, James Burnes, MD,[6] who were initially involved with the Kallmes and Buchbinder studies. The follow-up interval was short and recorded by mailed questionnaire. A mailed questionnaire is unable to eliminate certain complications such as incomplete fill, cement extrusion causing radiculopathy, or even new fractures at adjacent levels. None of these would be detected by mail and could explain ongoing pain.

Responses

In a number of venues, including *The Spine Journal,* Kallmes and Buchbinder have individually and together defended their studies. First, they state that they are not "lone voices against VBA." They cite a number of other studies unable to document benefit from these procedures, eg, papers by Rousing et al,[8] Alvarez et al[9] and Diamond et al,[10] among others.

Rousing randomized 50 patients with vertebral fractures up to eight weeks old to vertebroplasty (n=26) or nonsurgical management (n=24). At a single, three-month follow-up point, the groups did not differ in quality of life (SF-36 and EQ-5D) or pain (VAS). In a concurrently controlled study, Alvarez and coworkers treated 128 consecutive patients with vertebroplasty (n=101) or nonsurgical care (n=27). Prior to enrollment, both groups received medical management for at least six weeks. They reported that vertebroplasty improved pain, function and quality of life at one and three months, but not at six or 12 months. Interestingly, at six and 12 months, function and quality of life were superior in the control arm. Diamond treated 79 consecutive patients hospitalized for acute VCF pain. Fifty-five underwent vertebroplasty, 24 had nonsurgical management as a concurrent control. Pain and function in vertebroplasty patients improved compared to control at 24 hours, but not at six weeks, or three, six or 12 months.

Most of our panel continued to conclude that these RCTs remained at odds with the larger body of VBA literature. With regard to the specific studies mentioned, the panel felt good early, but little long-term, advantage of PMMA stabilization over nonoperative management was demonstrated.

In explaining the difference in conclusion between these RCTs and previous, retrospective vertebroplasty studies, analysts suggest that non-randomized trials are biased toward overestimating treatment benefits. Typically, RCTs are felt to trump anecdote and observational studies.

Uncontrolled, nonrandomized studies can be "wrong" because of:

1. the favorable natural history of vertebral fractures.
2. regression to the mean. Very severe pain "on average" improves on repeat measurement.
3. the placebo effect which is likely accentuated by an invasive treatment.
4. the bias of unblinded assessment. Patient expectation is likely to be influenced by passionate advocates for the treatment. Assessment by the person who provided the treatment is likely to be biased in favor of the treatment.
5. loss to follow-up is generally not random and is biased toward a more favorable outcome.

In discussing the fracture acuity included in the trial,

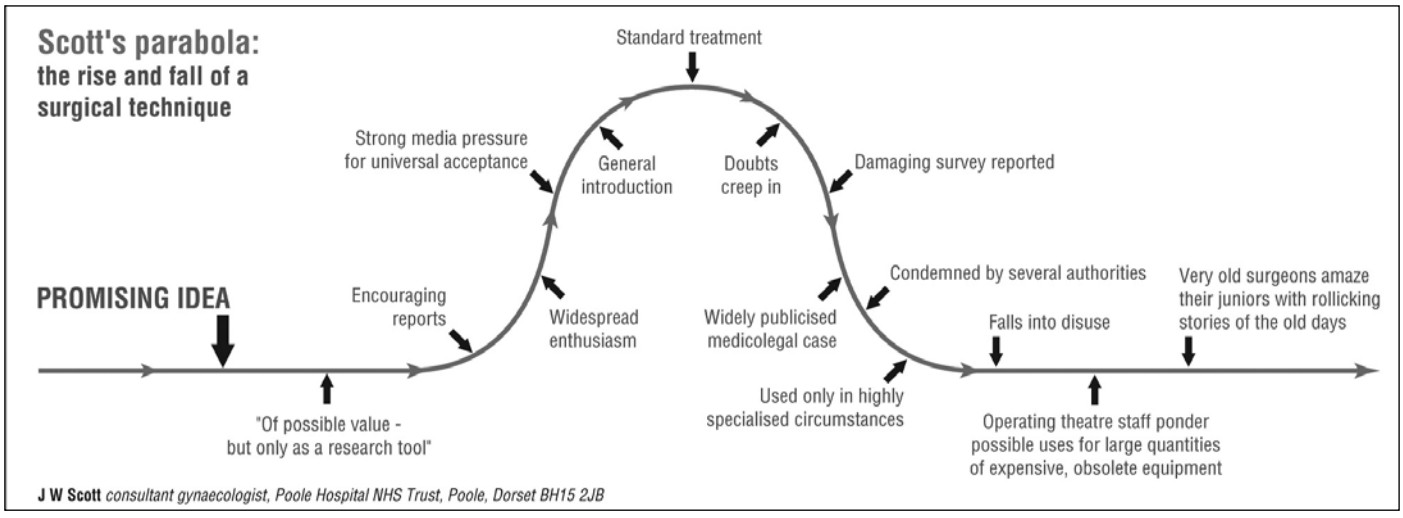

Figure 4. Scott's parabola illustrates the rise and fall of a surgical technique. Reproduced from: Scott JW. Scott's parabola. *BMJ.* 2001;323(7327):1477, © 2001 with permssion from BMJ Publishing Group, Ltd.

How Have VBA Coverage Decisions Been Affected?

PERC Conveys NASS Position on Procedure

As you read the discussion on these pages, you might ask: so what? How does this affect my patients or me? Well, it might not. On the other hand, if you perform vertebral augmentation procedures or refer patients for these procedures, payers are using the *NEJM* articles to justify non-coverage decisions.

The trend is already well underway; so far Noridian, Wellpoint and Aetna have issued non-coverage decisions and more are likely. NASS, through its Professional Economic and Regulatory Committee (PERC), has been in touch with these and other payers to explain our position and educate them about reasonable indications for PMMA augmentation of the vertebral body. So far, responses have been via mail and e-mail. Conference calls and in-person meetings are planned in the future. (Read more about PERC on page 36.)

While the terrain is rapidly evolving, multiple insurance companies are now proposing to eliminate vertebroplasty coverage and cover kyphoplasty variably. This is a dramatic shift from the current situation which is that both procedures are covered with few limitations. NASS has highlighted the weakness in the NEJM studies and the strengths of prior literature about vertebroplasty and kyphoplasty in order to make a strong argument that the procedures should be covered after 6 to 12 weeks of reasonable nonoperative treatment of an osteoporotic compression fracture. This interval has been identified based on the favorable natural history of most patients with symptomatic compression fractures to have substantial pain relief within this time period, avoiding overuse of the intervention.

At present, the NASS position is that excluding vertebral augmentation as a treatment option in lieu of nonoperative treatment only based on the randomized controlled trials that did not compare the procedure to nonoperative management would be a disservice to our patients.

Chris Bono, MD and Eeric Truumees, MD

Buchbinder states that the patients included in her trial had acute VCF. All participants had symptoms less than eight weeks. The paper lists the median duration of pain for the vertebroplasty group as nine weeks. This may be a difference of time of enrollment versus time of treatment. She maintains that their enrollment criteria were "stringent." She adds, if some subgroups were made that much better, other subgroups would have to have been made that much worse to balance the zero gain recorded.

Kallmes argues that, based on the favorable natural history, we should give patients a trial of medical/interventional management. He feels that the persistently painful, edematous fractures included in their trial probably have a less benign natural history than typical acute fractures and, thus, represent the best case for VBA.

Responding to complaints about lack of statistical power, Buchbinder reports her study was more than adequately powered to achieve its primary efficacy aim: detecting a 2.5-unit pain score advantage of vertebroplasty over placebo. Carragee adds "Most commonly, the trials were faulted for being too small. But, were they really too small to detect such an enormous purported effect? Frankly, if the vertebroplasty actually did have a '90% complete and immediate pain relief' effect and lasted perhaps a year or two, one hardly needs a baker's dozen in each study arm regardless of any amount of local anesthetic."

Neither Buchbinder nor Kallmes are willing to accept that their outcomes were worse than other VBA trials. They note that the treatment effect in the vertebroplasty arms of their trials was nearly identical to that in the treatment arm from the Fracture Reduction Evaluation (FREE) trial. "It is likely that the apparently muted improvement in these trials, in the order of 2.5 to 4 points on a 10-point scale for pain, simply reflects the fact that both studies asked specific pain questions at baseline and follow-up..." suggest Buchbinder and Kallmes. "Unfortunately, most of the augmentation literature uses nonspecific pain questions, which likely augment the baseline severity and diminish the follow-up severity, with resultant exaggeration of treatment effect." [5]

Further, in responding to enrollment and selection bias queries, Buchbinder avers that their enrollment rates compared favorably to other studies with a sham procedure arm. Specifically, in her trial, the "assertion that participants with severe pain would more often opt out of the trial and proceed with vertebroplasty is without foundation... availability of vertebroplasty outside of the trial was limited... before government-subsidized funding." Our panel found that this contention is partly refuted by the centers dropping out of the trial when government coverage became available in Australia.

Kallmes responds to this claim by citing data. Baseline pain and disability were equivalent to:

- all other available, controlled augmentation trials
- an eligible but nonenrolled cohort at our lead site
- eligible patients who declined enrollment in the INVEST trial had similar levels of pain and disability to those who participated

Further, if only the most severely affected patients were enrolled, an exaggeration of regression toward the mean would blunt any treatment effect. In Rousing et al's study,[8] those with the worst pain got the most improvement from both medical/interventional treatment and VBA. Kallmes and others cite the "volunteer bias," ie, volunteers are likely to have better outcomes than those who refuse study participation.

Kallmes reports that nearly all crossovers occurred after 30 days. Thus, crossovers could not affect primary conclusion;

there were no important differences in outcomes between the vertebroplasty and control groups at one month.

Implications

These studies have been widely quoted and discussed in other medical journals and in the lay media. Responses have ranged from righteous indignation that the authors were not able to support the obvious benefits of vertebroplasty to a cynical "I told you so."

In his editorial, Carragee offers that "comically good results were confidently proclaimed amid a stroboscopic flashing of radiographs depicting expertly placed cement; brief, blurred slides causally confirmed complications so rare that venipuncture seemed more hazardous…Spin-off products, such as kyphoplasty, reportedly improved on the practically perfect." He adds: "most impressive in this whole affair has been the relentless shrinking of the apparent vertebroplasty effect size and duration. With each increase in the quality of evidence, the apparent quantity of effect has diminished and diminished until we are searching for any traces of it at all… We have gone from 1998, when 90% of a large cohort had immediate and complete relief of symptoms, perhaps lasting a year or longer completely attributed to the procedure to arguing whether even the modest improvement now reported is a totally nonspecific effect, at even 6 weeks after treatment… Someone appears to have applied the scientific method. And not a moment too soon."[4]

A common sentiment among non–spine care specialists: the "history of vertebroplasty should remind us (again) to be cautious in embracing treatments for which the evidence of efficacy is restricted to anecdote or observation. Empirical confirmation (or refutation) of that which is observed should always be sought. The results of these randomized trials should lead to the prompt discontinuation of an ineffective therapy."

Buchbinder et al concluded: "We concur with Grey and Bolland that it would be neither appropriate nor moral to offer this treatment in routine care." She argues that Bono et al and other critiques are merely excuses to dismiss their results. "Rather than searching for spurious reasons to dismiss our results, it may be prudent to consider how vertebroplasty became the standard of care in the absence of appropriate evaluation in the first place. The onus is now on proponents of the procedure to disprove our findings in similar high-quality placebo-controlled trials."[5]

But, where are we, really? Most of our panel concluded that these results must be considered seriously, but that we cannot categorically declare vertebroplasty ineffective. Most of us feel that, after a suitable trial of medical/interventional management and with a proper and thorough discussion of the procedure's risks and benefits, it remains reasonable to offer vertebroplasty.

Just as it would be irresponsible to ignore these studies, it may be inadvisable to place too much emphasis on data from 209 patients from a handful of centers (and practitioners). Although anecdotal, the combined experience of so many practitioners has to mean something, doesn't it? While Level I data are better than Level V, can't methodological considerations temper the value of any level data? As Bono et al put it, "there is no such thing as an infallible PRCT." How many Cochrane reviews show that anything works with any certainty?

Where Do We Go from Here?

These RCTs, while important, are not likely to be the "last word" on VBA. Among the signal questions as we go forward: Are there subgroups of patients that might do well with VCF? Will kyphoplasty outcomes improve on those reported here for vertebroplasty?

For example, many assessments have questioned whether fractures with clefts behave differently. So far, neither consensus nor compelling data support a more positive outcome in this subgroup. The anti-VBA group notes that examining patients with cleft alone would markedly prolong future studies by limiting eligible patients. Most of our panel agreed that completing those studies would be technically daunting. The presence of clefts is often noted at the time of procedure positioning only.[11]

Another question is one of timing. Most of our panel agreed that vertebroplasty was most effective in hyper-acute fractures in patients admitted to the hospital in intractable pain. Of course, this group is also the most likely to get rapidly better with medical/interventional management. Further, this group is also technically difficult to randomize and follow.

Given that these two RCTs found no benefit from vertebroplasty over a sham procedure, our panel concluded that proving incremental benefit from VBA modifications would be challenging. For example, a randomized trial comparing kyphoplasty with vertebroplasty is currently underway. Similarly, makers of various, more expensive, resorbable cements will be hard pressed to demonstrate additional value. If these studies are published, it is likely that they will have been funded by industry. How will they be received?

Final Thoughts

We don't always do what the science tells us. We hold on to our beliefs long after the data suggest otherwise. The problem lies in the fact that this preponderance of the data is easier to tell with hindsight.

As it stands now, we are offered false dichotomies: vertebroplasty is either a miracle cure or worthless. Patients are either offered medical management in the form of medications, bracing and activity limitations or they undergo vertebroplasty.

In fact, no one advocates VBA in all pathologic or osteoporotic fractures. As with all invasive treatments for painful spinal disorders, patient selection is paramount for success. As Weinstein notes in his *NEJM* editorial,[6] there is a paucity of Level I evidence in approximately 50% of health care diagnostic and treatment decisions. In the absence of overwhelming evidence, the relative risks and benefits of the procedure must

be discussed with each patient.

In reality, we have a question of when to add VBA to nonoperative management. Even if everyone is the same at 12-24 weeks, how many people would be willing to wait, in pain, for 12 weeks? We suspect the answer depends on the severity of the patient's pain, the degree of relief they are getting with bracing, activity modification, etc, and the risks and pain associated with the procedure itself. Extrapolating from SPORT study data, sharing outcomes information will persuade patients with lower self-reported pain and disability to avoid vertebroplasty. Those with higher pain and disability who are not improving over time will choose to have it. For now, that might be an appropriate outcome.

Make no mistake, these studies are important. VBA procedures remain relatively new. However, their rapid increase in utilization and the huge population of affected individuals translates into large potential shifts in treatment algorithms and resource utilization.

When asked about his own current practices, Dr. Kallmes reported, "We still do a lot of vertebroplasty. Whenever possible we enroll patients into ongoing trials, which are few, unfortunately. Our volumes have not changed much, I think. My world is not as black and white as everyone wants it to be. Also, people seem not to notice that my paper showed immediate, significant and sustained improvement in the vertebroplasty patients."

Blanket noncoverage decisions based on these studies would be a mistake. But, it appears various Medicare vendors and others are doing just that.

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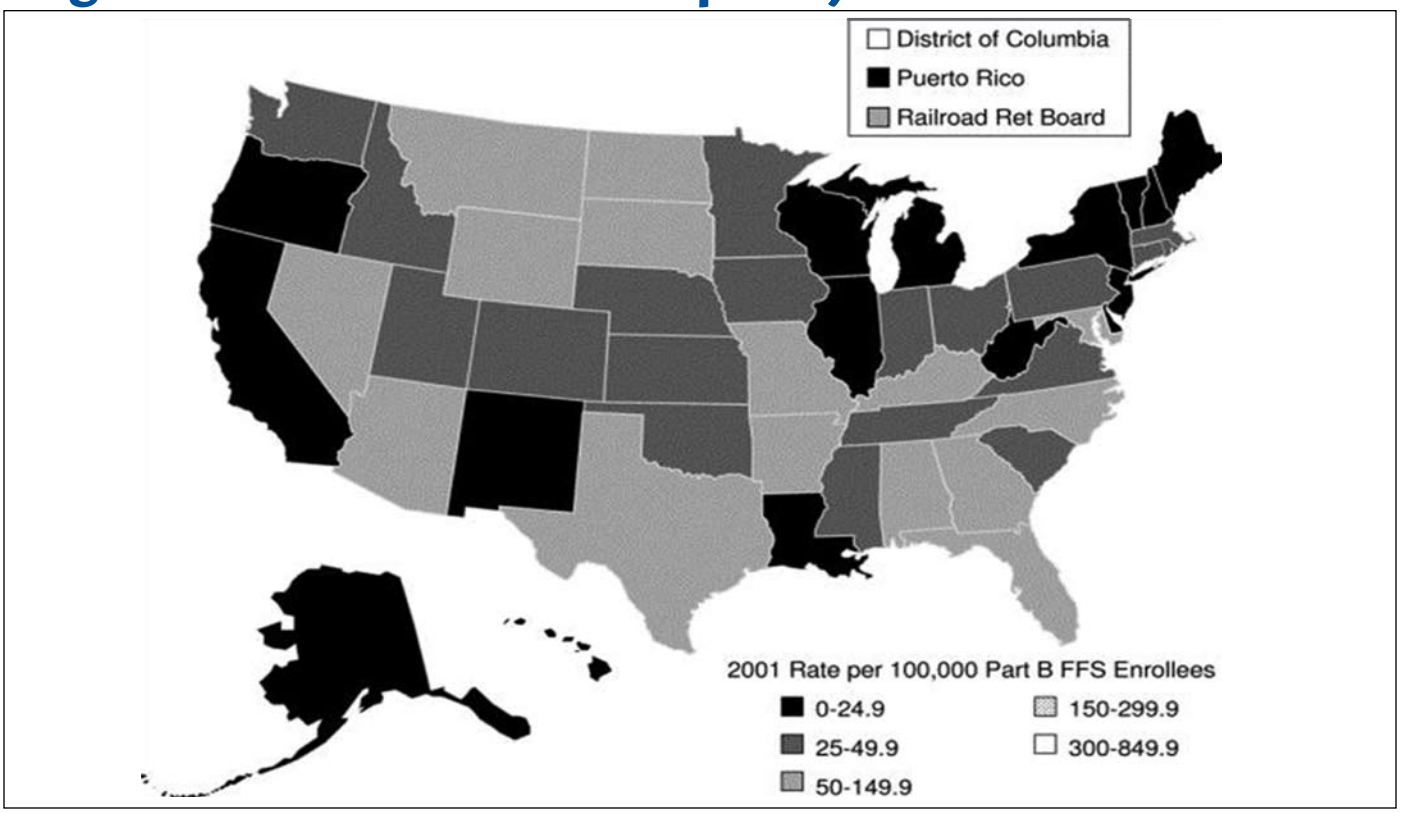
Level E.	$50,001 to $100,000		

Regional Rates of Vertebroplasty



State-wide primary vertebroplasty rates per 100,000 Part B fee-for-service enrollees for 2001. Reprinted with permission from: Gray D, Hollingworth W, Onwudiwe N, Jarvik J. Costs and state-specific rates of thoracic and lumbar vertebroplasty, 2001-2005. *Spine. 2008*;33(17):1905-1912.

For some, the vertebroplasty question is "yes" or "no." Either the procedure should be offered to patients in pain or not. Despite the *NEJM* RCTs,[1,2] for most, the debate centers on "when" and "how often" are these procedures appropriate.

Are vertebral body augmentation procedures performed too often? Answering this question is frustrated by wide variability in the rates with which the operation is offered. Studies have shown that rates vary from country to country. Vertebroplasty was developed in France and was not popularized in North American until nearly a decade later. Adoption took much longer in the Southern hemisphere. As noted by Buchbinder et al,[2] at the time their trial was initiated, vertebroplasty was not available to those not participating in the study. We know that life expectancy and osteoporosis rates also vary widely by region and nation.

As reported by Gray and others[3] in 2008, the technology assessments and literature summaries produced in different nations came to different conclusions about the effectiveness of VBA procedures. The European assessments "decried" the absence of RCT data, but were generally supportive of VBA. North American assessments have been more guarded. In most countries, these reports coincided with payor approval. With reimbursement came rapid increases in utilization.[4-9]

In the United States, Medicare began covering vertebroplasty in 2000. However, CMS never released a national coverage decision. Thus state to state and regional differences in Medicare carrier coverage continues. Additionally, Medicare vendors affected vertebroplasty performance by more or less strictly enforcing the six-week nonoperative trial. Thus, within the United States, VBA rates also vary widely within states. This hyper-local variability may arise from differences in health care–seeking behavior, reimbursement and by specialties performing the procedure. Other factors include coverage for performance in ambulatory settings and the form of anesthesia employed.[10-12]

Initially, kyphoplasty did not have its own code. In some cases, the vertebroplasty code was used. In others, unlisted codes were employed. Later, when a nationwide code for kyphoplasty was released, average reimbursements increased in some areas and decreased in others.

In 2004, Solomon and coworkers[13] were able to show marked variability in vertebroplasty rates from county to county in the Commonwealth of Pennsylvania. In several counties, no patient had vertebroplasty. In others, more than 15% of those presenting with VCF underwent the procedure. They cited patient specific factors that increased VBA utilization. Solomon et al reported those "undergoing vertebroplasty

were slightly younger (80 vs 82 years), had more physician visits, had used more medications in the prior year, and were more likely to have received a diagnosis of osteoporosis and undergone a bone mineral density test than those who had not undergone vertebroplasty."

In a study by Gray et al,[14] nationwide vertebroplasty volumes and rates doubled from 2001 to 2005. Both Solomon et al and Gray et al identified a number of physician factors that impact utilization. Most predictive, it seems, is the number of physicians in the area performing the procedure. As in Birkmeyer's data from the Dartmouth Surgical Atlas,[15] "more urgent and less discretionary procedures, such as a mastectomy have been found to vary less by geographic region."

Critics cite these and other utilization studies as evidence of a lack of procedural efficacy. That is, if major variations in procedure utilization exist without concomitant differences in outcome, that procedure must not affect outcome. If the patient populations are the same, and predicate and alternative treatments are administered in a similar, controlled way, this may be true. Osteoporotic patient populations, however, may differ widely. For example, senior populations who moved to sunbelt states from those who stayed in cold, sunless northern climates.

Gray and others[3] note that Medicare Advantage and other supplementary plans may affect decision-making by defraying some of the ancillary costs associated with the procedure. The rate of participation in these plans ranges from 0.2% in Maine to 36.9% in Rhode Island.

Regional variation in VBA procedures may also arise from the specialists who offer the procedure. Gray and coworkers[3] found significant differences in procedure rates, as well as the use of CT instead of fluoroscopy, inpatient versus outpatient procedures, and levels performed per operative session when they compared utilization data among: diagnostic/interventional radiology, orthopedic surgery, neurosurgery, and anesthesiology/pain management, and "other."

In some areas, local enthusiasm can be fostered by public relations campaigns sponsored by providers, hospitals and the companies selling the "kits." In other areas, publicized complications and warnings, such as the FDA PMMA advisory in 2004, may have a chilling effect. One of our panelists reported that, in his region, a "star" VBA proponent left the state, after which the rate of VBA fell markedly.

While the payer implications continue to evolve, it is likely that vertebroplasty rates have started to fall and are likely to continue falling. How quickly and how far remain to be seen. Have you noticed changes in vertebroplasty referrals or reimbursement? If so, we would love to hear from you at www.spineline-digital.org

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