



Trends-in-Medicine

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by D. Woods

Quick Pulse

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MEDICARE COVERAGE ADVISORY COMMITTEE WANTS MORE STUDIES ON VERTEBROPLASTY AND KYPHOPLASTY Baltimore, MD May 24, 2005

The Medicare Coverage Advisory Committee (MCAC) called for long-term clinical studies on both vertebroplasty and kyphoplasty, two procedures used to treat spinal fractures and deformities, particularly in osteoporosis patients. The panel concluded that both procedures are effective – at least in the short term. Although the panel said it does not have any say in national Medicare coverage for the procedures, it is influential in reimbursement decisions made by the Centers for Medicare and Medicaid Services (CMS).

Percutaneous vertebroplasty is a procedure in which bone cement is inserted into the compressed and fractured vertebrae to provide mechanical stabilization. Kyphon's kyphoplasty is a variation on vertebroplasty, using a patented inflatable balloon to expand the compressed vertebral body before injecting the cement. A doctor explained that when patients don't get either procedure, "Some feel good and don't come back...some are hospitalized...and some die. Demographically, they look the same (as those who undergo the procedure)."

The all-day MCAC meeting was called by CMS to discuss and vote on the effectiveness of vertebroplasty and kyphoplasty for patients with vertebral compression fractures (VCFs) vs. conservative care. A panel member explained, "The purpose of this panel is to listen to the evidence and make recommendations to CMS. The panel is here to ask: What's the quality of evidence and what does that evidence show?"

Speakers generally agreed that there is evidence that both procedures succeed in easing pain in the short term. However, they pointed out that the difference between the procedures and medical management narrows in the long term. Kyphon supporters also claimed that kyphoplasty adds some height to patients. There were questions about the long-term safety of both procedures as well as concerns about whether they actually cause adjacent vertebral fractures. A panel member said, "There is not much doubt that there is some height restored."

During the morning session, most speakers insisted there are no significant differences between vertebroplasty and kyphoplasty. Dr. Greg Przybylski of the North American Spine Society (NASS) said, "The two methods are similar, with a smaller (cement) leak with kyphoplasty, although that may not be clinically relevant...NASS believes that both procedures are equally effective for problems that persist despite non-operative treatment. We recommend that facility and non-facility payments for procedures be based on the least expensive supply costs."

Dr. John Mathis, chair of radiology at Lewis-Gale Medical Center, said, “Vertebroplasty and balloon kyphoplasty, at the end of the day, are the only way we’ve found so far to make the pain go away...Everyone agrees that they relieve pain acutely...Whether to use kyphoplasty or vertebroplasty? Patient selection is the key to the whole process.”

Blue Cross and Blue Shield Association Technology Evaluation Center Assessment: Randomized clinical trials are needed.

Dr. David Mark presented Blue Cross/Blue Shield’s technology assessment, which was based on a review of articles about the two procedures. He said, “We studied procedure and relevant clinical outcomes of pain, functional status, or quality of life...and we looked at some comparative trials and randomized trials in abstract form...So what are the effects of vertebroplasty for osteoporosis-assisted fractures? What we found mostly is case series studies; that is the predominant form of study out there...There is a lack of randomized clinical trials in this field. So the Blue Cross/Blue Shield panel made the decision that it (vertebroplasty) did not meet our particular criteria as an effective procedure, based on the type of evidence that exists for the procedure so far.”

University of Alabama at Birmingham (UAB) Study: The procedures help in the short term, but randomized trials and long-term data are needed.

Kenneth Saag MD and John Bian PhD of UAB presented the results of a new study UAB is doing in collaboration with the FDA and Blue Cross/Blue Shield of Alabama. Dr. Bian said, “We see a major gap in the evidence...(Vertebroplasty) offers short-to-moderate-term pain relief and restoration of vertebral height, but there is little evidence on long-term effectiveness and safety from randomized clinical trials. The studies are mostly observational studies and case series without comparison groups.”

The UAB study used two major data sources, including the administrative database of the ~3 million Blue Cross/Blue Shield of Alabama enrollees, most of whom were under the age of 65, to examine whether vertebroplasty is associated with a higher risk of recurrent VCFs. He concluded:

- A large body of evidence supports short-term pain relief.
- There may be a greater risk of fractures, particularly at adjacent levels, but controlled studies are needed to determine this.
- Randomized clinical trials with well-designed outcomes and sufficient duration of follow-up are required to address effectiveness and safety questions.
- With the paucity of high-grade scientific evidence, there is little consensus on the indications and contraindications for vertebroplasty.

A non-voting panel member expressed concern about problems with working with a database of patients under age 65, and speakers agreed that is a problem. The panel member said, “The purpose of presenting this wasn’t really to provide answers but to highlight some of the questions. We focused on one particular area, and we are more concerned about the long term. The short term shows height restoration and pain relief, but the key area, the area we feel is understudied and where concern exists, is how do the results of this procedure compare with the results of medical management 2, 5, 10 years later?”

Cleveland Clinic experience: The procedures are effective but patient selection is important.

The Cleveland Clinic Spine Institute treated more than 500 patients between 1999 and 2005 with either vertebroplasty or kyphoplasty, and Dr. Isador Lieberman – a Kyphon consultant – said those patients improved in terms of pain as well as increased body height. He added that none had neurologic complications, and (as far as complications) there were fewer than 10% cement extravasations from fractured fistulas. Dr. Lieberman concluded, “Vertebral augmentation does make a difference if you look at the literature. In good hands, in qualified hands, you can get very good results with these techniques.” However, Dr. Lieberman emphasized that patient selection is “absolutely critical.”

Johns Hopkins literature review: Randomized clinical study with long-term follow-up is needed.

A Johns Hopkins medical engineering expert who reviewed more than 400 articles on the two procedures found most of them lacking. He commented, “Of all the studies, there are perhaps five that I recommend reading...It’s a bit frustrating because vertebroplasty has been around for more than 20 years, and it’s time to have a prospective, randomized, controlled study with long-term follow-up. I’m a big fan of clinical outcome studies, and I’d like to see one...I wish I had more to tell you. The bottom line is that we don’t even know which patients are indicated for vertebroplasty, what constitutes an acute or chronic compression or which patients respond better to vertebroplasty or kyphoplasty and which don’t.”

As for deformity corrections, he said, “If you can show a decrease in premature sciatic, increased lung capacity, depressing, altered kinematics, such as dowager’s hump – those are all good reasons to consider the procedure – but that has to be shown, and so far that data are not available...What are the risks and benefits of all this? The bottom line is the information is just not there.”

Complications: Generally within an acceptable range, but concerns remain.

➤ **Subsequent adjacent and remote fractures.** Dr. Lieberman called this a big issue, “If you put a block of cement in the spine, can it generate other fractures? We looked at 115 patients and saw that 26 had 33 fractures, but we realized that this was a mixed bag. If we took out the primary osteoporotic patients, we found only an 11.25% rate of subsequent fractures, and if you took out the secondary osteoporosis patients, we saw they had a 45% rate. I still don’t know why, in patients with secondary osteoporosis, the rate is so high, but I suspect it’s because they are younger patients, more active, and go out and try to do things like shovel snow and get hurt.” A non-voting panel member said that the most important thing to him was getting the pain level down immediately, and that the risk of adjacent fracture could be dealt with down the line. He said that it is unlikely just putting cement into the spine will cause fractures, but it is likely that the cement actually causes pain relief.

➤ **Other complications.** Potential short-term complications and adverse outcomes with vertebroplasty are bone cement leaks, rib fractures, and cement and other embolic complications. Longer term, Dr. Bian raised a concern about the possibility of an increased risk of adjacent VCFs and PMMA toxicity.

Sources generally viewed the two vertebroplasty and kyphoplasty as equally safe, but a Kyphon official, Dr. Dan Jolivet, argued that kyphoplasty is safer than vertebroplasty. He said that, as part of his company’s 510K submission to the FDA comparing balloon kyphoplasty and vertebroplasty safety, “We found 77 balloon kyphoplasty and 39 vertebroplasty studies. Overall procedure-related complication rates include both cement-related and non-cement-related adverse events. For balloon kyphoplasty it was 0.9% versus 5.44% for vertebroplasty, and the difference was statistically significant.”

Comments by other speakers: Overwhelmingly positive about the benefits of both vertebroplasty and kyphoplasty.

- *Dr. Lee Jensen, American Society of Interventional and Therapeutic Neuroradiology (ASITN):* “This is a safe, efficacious, and durable procedure in appropriate patients who are symptomatic and who have failed medical therapy.”
- *Dr. Joshua Hirsch, ASITN:* “This has a remarkable impact on patients’ lives.”
- *Dr. Kevin McGraw, Ohio interventional radiologist:* “Conservative therapy is not without risk and includes bed rest, immobilization, and narcotic analgesics. Bone density declines about 2% per week in patients already suffering from osteoporosis, and muscle strength is halved in 4-6 weeks of bed rest.”

- *Dr. Richard D. Fessler, American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS):* “The AANS and CNS consider these to be safe, effective, and durable treatments for relief of pain due to certain fractures. These procedures offer immediate pain relief for those patients. Vertebroplasty and kyphoplasty should be available to Medicare patients, when deemed appropriate by the treating physician if the patient has not improved within several weeks (on medical therapy). We don’t believe patients should be required to endure pain...In the elderly population, immobilization, prolonged bed rest, and pain medications have serious consequences, and we believe (the procedures) should be reimbursed appropriately by Medicare.”
- *Dr. Deborah Gold, Duke University medical sociologist:* “There is a misconception that VCFs automatically get better with non-operative treatment. After a VCF, patients show no significant improvement at six months in pain, function, and disability. Two years after a fracture, patients show no improvement in physical function, and they remain physically impaired. Also, non-operative care doesn’t always prevent spinal deformity...VCF patients also have worse outcomes than patients with hip fractures.”
- *Dr. Steven Garfin, a spine surgeon at the University of California, San Diego, and a Kyphon consultant:* “We see continuing significant improvement in physical and emotional health following kyphoplasty for painful vertebral body compression fractures.”
- *Dr. Michael Marks, Connecticut orthopedic surgeon:* “In my practice, kyphoplasty works extremely well. It works in both acute and chronic fractures to decrease pain and achieve some correction in body collapse. The beneficial results definitely improve functional status on a long-term basis.”

The one exception was Dr. Fergus McKiernan of the Marshfield Clinic who demanded better science: “I question the reporting method for height restoration...Is it height restoration inflation?...And there are questions about the quality of the scientific evidence. Is the issue of dynamic mobility rigorously addressed? Accountability? Integrity? Is it science or is it marketing?”

In the afternoon, there was an extended and sometimes heated discussion of why there are no randomized clinical trials. Defenders of the procedures said it was impossible to conduct such trials, insisting that they would have a hard time getting people to voluntarily enroll if they knew there was a chance they would not be getting an operation. Panel members argued that it is indeed possible to do comprehensive studies, citing Germany and Australia as examples. The Australian government funded a study, and so did Merck, Kyphon, and

the German government together. A procedure defender disagreed, saying, “When I tell patients about the paperwork, they walk down the street...I’ve tried to come up with a trial five times...I’m willing to randomize my patients. I’m willing to take off my emotional hat to answer this scientific question.”

Panel member questions: **More, better, and longer-lasting studies are needed.**

Panel members expressed unhappiness with current study designs as well as what they perceived as lack of adequate follow-up. Comments by panel members included:

- “What kind of assurances can you give us, given the lack of adequate control, that trials will not turn out to be like the gastric bubble, the endoscopic repair to the knee – examples where medical interventions have been adopted, proven of limited benefit, and ultimately hurt patients in the end? I need to hear a little bit more about details – practicality – and you’re not giving me the evidence...I want you to raise the bar.”
- “A randomized trial would not have to be very large. I’m actually thinking that if you’re plugging away at 10 patients a year, I think you’d be able to reach some of those primary endpoints – sooner than some of you who think the studies cannot be done.”
- “Have you looked at ways other than randomized clinical trials to get at Class 1 evidence? Randomized clinical trials aren’t always the way.”

Panel members wanted to know why there are so little control group data. A doctor told the panel that his patients usually wait six weeks before getting their operations. A panel member said, “Hearing that makes me even more frustrated. Here you have a patient for which you can be collecting data for six weeks and why isn’t that data being collected? We need to be made more comfortable.”

Panel members also pressured speakers about trial design flaws and incomplete follow-up at two years. One asked, “How can you be sure that, at your last follow-up period, there isn’t an increased incidence of adjacent fractures? I don’t see how you can convince me that there isn’t.” Questions were also raised about why some patients weren’t followed up. A panel member said, “I’d like to know if anyone can characterize the kinds of patients who aren’t followed up and not measured...In our case it was 39%. Will someone help me understand the people who drop out? Dr Lieberman answered, “We try to follow them up to one year, but they disappear...We try as best we can and those are the numbers I have; I can’t comment on what happened.”

The panel discussion

Among the interesting comments made during the panel’s discussion were:

- *Public health representative:* “It seems to work, but that’s not enough...As we move toward limited resources, we really need to get this right. When does it work, for whom, and what are the indications? There are a lot of vertebrae there. Do we do it once, twice, three times? We can’t pay for it all. And does it improve quality of life? Can we pay for it? We need to be collecting data. Saying that it seems to work isn’t enough.”
- *On patient selection:* “We don’t have the data to say who are the best patients...They may be the same patients who get better without vertebroplasty.”
- “The data probably aren’t as good as what the people are standing up here and saying they are.”
- “We’ve treated 500 patients over five years. Of those patients, about 40% already had (a prior) procedure done, although at a different location (on the spine).”
- “My biggest concern is what the morbidity is in the six to 12 week treatment period vs. no treatment? I’m a little confused because we’re debating feasibility of randomized clinical trials in this population, and perhaps we’re a little off track here...I’d like to see data on side effects, such as pulmonary embolism, pneumonia rates, narcotic use, and pressure ulcerations of the skin in different populations. There are a whole host of things – not just how much height restoration or angle of the body. I think we’re missing some of the important parameters...I don’t think we’ve collected any data as far as those things go.”

Panel votes on vertebroplasty

The panel voted on six questions for each procedure, concluding that more studies and more data are needed. The votes below are the averages for **voting** members.

1. **How well does the evidence address the effectiveness of vertebroplasty or kyphoplasty for patients with a compression fracture as compared to conservative care?** (1-5 scale: with 1 poorly, 3 reasonably well, and 5 very well)

Vertebroplasty: Voting member average: 2.0

Kyphoplasty: Voting member average: 2.0

Confidence in the Validity of the Scientific Data

2. How confident are you in the validity of the scientific data on the following outcomes with respect to vertebroplasty or kyphoplasty for patients with:

(1-5 scale: 1 no confidence, 3 moderate confidence, 5 high confidence)

Patients with:	Vertebroplasty		Kyphoplasty	
	Acute and sub-acute compression fracture	Chronic compression fracture	Acute and sub-acute compression fracture	Chronic compression fracture
Short-term – morbidity	2.17	2.17	2.17	2.17
Long term – morbidity	2.0	2.0	2.0	2.0
Mortality	1.5	1.5	1.5	1.5
Morbidity- functional status	2.17	2.0	2.17	2.0
Pain relief	2.17	2.0	2.17	2.0
Overall average	2.00	1.93	2.00	1.93

3. How likely is it that vertebroplasty or kyphoplasty, in the following circumstances, will positively affect the following outcomes when compared to conservative care? (1-5 scale: 1 not likely, 3 reasonably likely, 5 very likely)

(1-5 scale: 1 not likely, 3 reasonably likely, 5 very likely)

Likeliness of Positive Impact on Outcomes

Patients with:	Vertebroplasty		Kyphoplasty	
	Acute and sub-acute compression fracture	Chronic compression fracture	Acute and sub-acute compression fracture	Chronic compression fracture
Short term – morbidity	3.83	3.67	3.83	3.67
Long term – morbidity	3.33	3.17	3.33	3.17
Mortality	2.67	2.33	2.67	2.33
Morbidity- functional status	3.67	3.50	3.67	3.50
Pain relief	4.17	3.67	4.17	3.67
Overall average	3.53	3.27	3.53	3.27

4. How likely is it that vertebroplasty or kyphoplasty, in the following circumstances, will positively affect the following outcomes when compared to conservative care? (1-5 scale: 1 not likely, 3 reasonably likely, 5 very likely)

Likeliness of Positive Impact on Outcomes by Fracture Type

Type of fracture	Vertebroplasty net health benefit	Kyphoplasty net health benefit
Acute and sub-acute compression fracture	3.17	3.0
Chronic compression fracture	2.83	3.0

5. How confident are you that vertebroplasty or kyphoplasty will produce a clinically important net health benefit for patients with a compression fracture as compared to conservative care for patients with: (1-5 scale: 1 no confidence, 3 moderate confidence, 5 high confidence)

Confidence in Net Clinical Benefit

Patients with:	Vertebroplasty		Kyphoplasty	
	Acute and sub-acute compression fracture	Chronic compression fracture	Acute and sub-acute compression fracture	Chronic compression fracture
Short-term – morbidity	3.83	3.67	3.83	3.67
Long term – morbidity	3.33	3.17	3.33	3.17
Mortality	2.67	2.33	2.67	2.33
Morbidity- functional status	3.67	3.50	3.67	3.50
Pain relief	4.17	3.67	4.17	3.67
Overall average	3.53	3.27	3.53	3.27

6. Based on the literature presented, how likely is it that the results of vertebroplasty and kyphoplasty in the treatment of relief of pain and improvement in ability to function for the patients with a compression fracture can be generalized to: (1-5 scale: 1 not likely, 3 reasonably likely, 5 very likely)

Likeliness of Pain Relief and Improvement in Function Can Be Generalized

Population	Vertebroplasty: Generalizability of pain relief and ability to function	Kyphoplasty: Generalizability of pain relief and ability to function
The Medicare population	2.83	2.83
Providers (facilities/physicians) in community practice	2.67	2.67

Panel member comments after the vote included:

- “I voted based on the current evidence.”
- “Much as I would have liked to give lower scores, I have confidence it works.”
- “These are promising and effective procedures that need to be better documented.”
- “I was influenced by the very poor follow-up in the data that we saw relative to assessing effectiveness. With respect to mortality, I gave low scores because I didn’t see any data.”
- “I wasn’t particularly impressed by the data. On the other hand, we need to listen to the patients, and having heard about them and from them really helped...This procedure does work and will work, and that needs to be taken into consideration.”
- “We have some physicians who really care and believe in this. On the other hand...we have two to three medium studies, and it’s somewhat shameful. So, I’d hope that CMS, working with the community and NIH, would (know more) before the baby boomers get on board. In other words, do the right thing.”
- “The scientific data is sorely lacking, but we need to listen to the clinical experts. Patient care needs to be at the forefront of what we do.”
- “We need improvements in the scientific data, and I guess I’d look to see if there’s any assistance CMS can provide to do that. It has the wherewithal to get it done.”
- “This is a mandate in the sense of what we need, and I hope the funding is somewhere to execute the mandate.”
- “I’m impressed by the dedication and the passion. You heard loud and clear that we are moved by, and confident that, if you do the right study, the outcomes you think will happen are likely to happen.”
- “My votes were based on the science.”
- “There are lots of pieces to the puzzle. I suspect that the procedures will help patients, but the final hurdle – that of invention versus non-operative therapy – remains.”

Asked the significance of the votes, one of the leading clinicians in favor of the procedures said, “We have to do a better job documenting our outcomes. There’s still a lot of work to do. But the glass is three-quarters full, and I’m hopeful.” A panel member who criticized the lack of data throughout the session said, “The message is that controlled investigations are extremely important to really determine if an intervention is helpful.”

The CMS view of the panel meeting

The panel’s discussion and recommendations are not likely to change Medicare coverage of vertebroplasty or kyphoplasty since no national coverage decision on those procedures is pending. Currently, vertebroplasty and kyphoplasty are covered by Medicare on a region-by-region basis. The head of CMS’s coverage and analysis group said, “We have no open national coverage determination to make any decision that we could not be providing coverage for this.”

This CMS official also made several other interesting comments, including:

- “Where do we go from here? Perhaps we can use (this) for the *new* technologies, those that are coming into the field of orthopedics today, so that five, seven, or 10 years from now this panel won’t be saying that we don’t have the right data. We need to know what are the appropriate trials that we need to do so that we know risks and benefits.”
- “We have some information, and we have some recommendations on the quality of evidence.”
- “We’ll take this back and say, ‘Is there a next step for us?’ We are interested in the further collection of data.”
- “I need to say that we don’t fund the administrative cost of doing trials. If you want administrative money to do a trial, we’re not the people to come to. If there’s a way we can work to stimulate trials through other matters, for example, through the reimbursement cost process, we can do that. We also have relationships with our sister agencies...where we can perhaps stimulate some interest on their part.”
- “I do expect that over the next several weeks to a month we’ll produce a guidance document in draft form which may describe how we feel about the evidence.”

