Vertebral Augmentation for Symptomatic Compression Fractures Is Supported by Randomized Clinical Trials

To The Editor We read with interest the Invited Commentary by Dr Bauer.1 We believe there are portions of his comments that lack scientific support.

The author states that “Although uncontrolled studies have consistently demonstrated reduced short-term pain and disability after vertebral augmentation, randomized trial results have been inconsistent.”4(p1523) In fact, if all Oxford level I and level II data are considered, there are 27 studies, including 8 randomized clinical trials. This collection of articles shows significant reductions in pain, improvement in quality of life, fewer subsequent fractures, and greater kyphosis reduction.2

The statement “compared with conservative therapy, kyphoplasty treatment improved pain and function scores at 6 and 12 months of follow-up, but by 24 months differences were attenuated and mostly nonsignificant”4(p1523) when referencing the Fracture Reduction Evaluation (FREE) trial is unsubstantiated. In fact, the reduction in back pain remained statistically significant at all time points.3

Dr Bauer4(p1523) states that “The highest-quality evidence...do not provide a compelling rationale for augmentation procedures and suggest that there are little or no differences in long-term pain and function compared with conservative management.” The sham randomized clinical trials that were referred to as “the highest-quality data” were recently downgraded to level II data based on flawed inclusion criteria in both studies and a subsequent high crossover rate in the Investigational Vertebroplasty Safety and Efficacy Trial (INVEST). This downgrade was based on an analysis by Anderson et al2 using standard methods for literature quality analysis. Lastly, Dr Bauer4(p1523) states that “as summarized in a recent independent technology assessment addressing vertebral augmentation, until better evidence becomes available, the potential benefits of vertebral augmentation remain unproven, and it should not be routinely offered to patients with osteoporotic vertebral fractures.” This strong statement is based on a reference to the BlueCross BlueShield Association Technology Evaluation Center,5 a non-peer-reviewed insurance company document previously available but is no longer online. Unless additional information is provided this document would not be considered unbiased and was formulated prior to the consideration and analysis of all of the level I and II data by Papanastassiou et al2 and the high-quality meta-analyses by Anderson et al.4

We believe that treatment decisions should be based on the entire set of literature data and do not believe that Dr Bauer’s assessments are accurate depictions of the existing evidence.

Jason R. Levy, MD
Douglas P. Beall, MD

Author Affiliations: Department of Interventional Radiology, Northside Hospital, Atlanta, Georgia (Levy); Clinical Radiology of Oklahoma, Edmond (Beall).

Corresponding Author: Jason R. Levy, MD, Director, Interventional Radiology, Northside Hospital, 1000 Johnson Ferry Rd, Atlanta, GA 30342 (jlevy@bellsouth.net).

In Reply Drs Levy and Beall, both of whom perform vertebral augmentation procedures and serve as consultants for 1 or more companies that manufacture vertebral augmentation equipment, believe that my Invited Commentary lacks scientific support. They offer an industry-funded study by Papanastassiou et al,1 pooling 27 randomized and nonrandomized studies as evidence that vertebral augmentation is associated with improved subjective outcomes such as pain and quality of life. Unfortunately, unblinded studies with subjective outcomes are particularly prone to bias, and some or all of the apparent superiority of vertebral augmentation in that meta-analysis might be attributed to the fact that all but 2 of the 27 studies were unblinded. They further claim that the 2 blinded randomized trials, which showed no pain or quality-of-life advantage with augmentation,2 had been “downgraded” to “Oxford level 2” in a meta-analysis of randomized trials by Anderson et al,3 but that publication does not provide a detailed description of the process or who made such a decision. The study by Anderson et al3 follows the approach of the industry-sponsored meta-analysis and pools the 2 blinded and 4 unblinded randomized trials with predictable results: pain and quality of life appear to be improved among those who receive vertebral augmentation compared with nonsurgical treatment. Had Anderson et al3 performed a sensitivity analysis limited to the 2 blinded studies, as others have done, they would have found that vertebral augmentation had no meaningful effect on pain or quality of life.

Regarding the Fracture Reduction Evaluation (FREE) trial, Levy and Beall should examine Table 3 in the article by Boonen et al,4 which shows that after 24 months of follow-up, 6 of the 10 reported pain and quality-of-life outcomes, including the primary outcome (the 36-Item Short-Form Health Survey Physical Component Summary), did not differ between those who received kyphoplasty and those who received conservative treatment.

Lastly, Drs Levy and Beall contend that the independent assessment of vertebral augmentation efficacy by the highly
regarded Technology Evaluation Center,5 conducted by a panel of experts using strict evidence rules and referenced in PubMed in 2011, is not compelling and may not be up to date. It is reassuring that a more recent technology assessment by another panel of experts without industry ties has independently reviewed the available evidence, including all of the studies in the meta-analysis by Papanastassiou et al1 and all but one of the trials pooled by Anderson et al,3 and reached the same conclusion: currently there is insufficient evidence that vertebral augmentation for osteoporotic vertebral fracture is effective and improves health outcomes.5 Only additional randomized and adequately blinded trials will resolve the issue.

Douglas C. Bauer, MD

Author Affiliations: Department of Medicine, University of California, San Francisco (Bauer); Department of Epidemiology and Biostatistics, University of California, San Francisco (Bauer).

Corresponding Author: Douglas C. Bauer, MD, Department of Epidemiology and Biostatistics, University of California, San Francisco, 185 Berry St, Ste 5700, San Francisco, CA 94143 (dbauer@psg.ucsf.edu).

Conflict of Interest Disclosures: None reported.


EDITOR’S NOTE
Vertebroplasty: Changing Levels of Evidence and Conflict of Interest

At JAMA Internal Medicine we take scientific rigor, high quality of evidence, and objective data very seriously. Drs Levy and Beall suggest that Dr Bauer overlooked or ignored studies that show reduction in pain with vertebroplasty. As Dr Bauer explains in his letter in reply, however, his statements are based on randomized, blinded clinical trials, which are considered the highest-quality evidence. Drs Levy and Beall fail to appreciate the greater reliability of randomization and blinding, which are particularly important for trials that have a powerful placebo effect.2 They assert that 2 randomized trials of vertebroplasty cited by Dr Bauer (both of which included blinding and sham controls) were “recently downgraded” in an article by Anderson and colleagues.2 Dr Bauer explains why the analysis by Anderson and colleagues is flawed. Moreover, Drs Levy and Beall, who acknowledge their own financial ties to the manufacturers of vertebroplasty devices, fail to mention that Dr Anderson receives hundreds of thousands of dollars from Medtronic, a major manufacturer of such products.

In fact, it is reported that Dr Anderson’s financial ties to Medtronic are so extensive that the University of Wisconsin-Madison has set up special oversight procedures for him, including annual meetings with his department chairman to review his relationship with Medtronic and its potential influence on his university activities. Unfortunately, such conflicts (and failures to disclose them) are rampant in the orthopedic surgery community—recent investigations have shown that nearly half of orthopedic surgeons who received more than $1 million per year in consulting fees failed to disclose any conflicts in their subsequent publications.3 We remind all our authors and readers of the importance of supporting their views with the highest-quality scientific evidence, free from bias, so that we can rely on the best published data in caring for our patients.

Rita F. Redberg, MD, MSc


CORRECTION
Typographic Data Reporting Error: In the Original Investigation titled “Atrial Fibrillation and the Risk of Myocardial Infarction” published in the January issue of JAMA Internal Medicine (2014;174[1]:SWK. doi:10.1001/jamainternmed.2013.11912), the number of all participants with no atrial fibrillation (AF) reported in Table 2 was incorrect. The correct number is 22,297.