

Vertebroplasty, Research Design, and Critical Analysis

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RECENT statements from the Association of American Medical Colleges and the Howard Hughes Medical Institute urge medical schools to design a major overhaul of educational curricula with the goal of achieving greater scientific competency of physicians-in-training (1). Interventional radiologists, like all physicians, must be able to critically analyze the medical literature and draw conclusions relevant to their practice. In particular, readers should be able to critically appraise published trials for their research design, results, validity, and generalizability (2–4).

Two recent trials on vertebroplasty published by the *New England Journal of Medicine* (5,6) illustrate these issues quite well. The studies by Buchbinder et al (5) and Kallmes et al (6) represent a useful addition to the growing body of literature analyzing vertebroplasty. However, as is often the case, these first published randomized trials of a relatively new treatment are the starting point for the discussion, and are by no means the final word on the proce-

dures (7,8). There were a number of potential flaws within both studies. First, both studies involved a relatively low number of patients because of difficulty in patient recruitment. In the study of Kallmes et al (6), the initial statistical power calculation resulted in a goal of enrolling 250 patients based on primary endpoint delta values between treatment groups of 2.5 on the Roland-Morris Disability Questionnaire and 1 point on the pain rating scale (6). However, after difficulty in patient accrual, the authors revised their power analysis based on higher delta values for the Roland-Morris Disability Questionnaire and pain rating scale, and set a new midtrial goal of 130 patients despite an interim analysis that could not have shown a larger-than-expected treatment effect. Therefore, raising the clinically relevant thresholds for these two outcomes biased the study to a negative result. Second, both trials involved patients with relatively low preprocedural pain scores; patients with greater preprocedural pain were likely unwilling to be randomized and risk placebo treatment. Both trials demonstrated a trend toward the favor of vertebroplasty; had the trials included greater patient numbers, especially focusing on the more symptomatic patients, the trend may have been statistically and clinically significant. Based on these studies (5,6), we do not believe that vertebroplasty should be discontinued, but rather the appropriate population and endpoints need to be examined in more studies. Given the need for further research, the Research Reporting Standards for Percutaneous Vertebral Augmentation by Radvany et al (9) are intended to

help create a standardized framework for reporting vertebroplasty.

The two recent randomized controlled trials (5,6) comparing vertebroplasty versus a sham procedure published in the *New England Journal of Medicine* demonstrate the challenges of clinical research in general and the need for physicians to enrich their participation in good-quality, methodologically sound randomized clinical trials that pertain to patients and diseases they treat routinely. There is often reluctance of procedure-based specialists to randomize their patients into such trials, which is probably multifaceted in origin. Although economic disincentives and the desire to please referring doctors may come into play, it is likely that enrollment in such treatment strategy trials of invasive versus conservative therapies is more challenged by the sincere belief among procedural practitioners in the benefits of the procedures they provide and a reluctance to potentially deprive their patients of them. These two studies illustrate the challenges in acquiring scientific knowledge if physicians are unable to recruit participants into these important trials, and we encourage broad support for these endeavors not only generally, but also specifically if the opportunity to conduct future randomized clinical trials of vertebroplasty comes along.

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