

Subsequent Vertebral Fracture Risk Is Not A Contraindication to Vertebroplasty or Kyphoplasty

To THE EDITOR:

It was with great interest that we read the article by Zou et al, "The Long-Term Incidence of Subsequent Vertebral Body Fracture After Vertebral Augmentation Therapy: A Systemic Review and Meta-Analysis," (1) published in the 2012 July/August issue of *Pain Physician*.

Currently, many surgeons have raised suspicions about the efficacy of vertebroplasty since the publication of negative outcomes in 2 placebo-armed randomized controlled trials (RCTs) (2,3). Partly due to the Kallmes et al's (3) and Buchbinder et al's (2) publications, a general decline of utilization of both vertebroplasty and kyphoplasty was observed from 2009 to 2010 (4). In this instance, concerns about the safety of vertebroplasty and kyphoplasty should be raised, especially the possibility that they increase the morbidity of new vertebral fracture (VF). Unfortunately, the effect of vertebroplasty or kyphoplasty on future fracture incidence is still contentious. The main dispute lies in whether new-onset VFs are the result of the natural progression of osteoporosis or a consequence of augmentation.

This is a well-prepared article which explored the relationship between cement augmentation and subsequent vertebral fracture by comparing the incidence of subsequent VF among patients with painful osteoporotic vertebral compression fracture (VCF) who underwent cement augmentation versus patients who did not. And the negative relationship between cement augmentation and subsequent VF may provide clinicians more confidence to recommend these minimally invasive procedures for the management of osteoporotic VCF associated pain and disability. The outcome of this article is encouraging, but we still have some concern about review method employed in this meta-analysis.

First, this meta-analysis only included 2 RCTs. One compared the fracture risk of vertebroplasty while the other evaluated the risk of kyphoplasty. However, clinical studies had demonstrated different frequencies of VF between vertebroplasty and kyphoplasty (5). In this case, would the inclusion criteria lead to the introduction of clinical heterogeneity? Could a fixed-effects

model well account for the clinical heterogeneity?

Second, it is known that subsequent fracture is a time-based event with most of the cases occurring in the first 3 months after undergoing cement augmentation (6,7). Meanwhile, the duration for most published randomized trials is relatively short, usually not more than 2 years. For example, the 2 sham-armed randomized studies have reported clinical outcomes one month and 6 months after vertebroplasty in patients with chronic or subacute VCFs (2,3). Klazen et al (8) revealed their outcome one year after vertebroplasty in patients with acute VCFs. However, the purpose of the research was restricted to evaluating the long-term incidence of subsequent vertebral body fracture following cement augment although the duration was not explicitly documented. In this instance, would the fracture incidence be underestimated with most of the eligible literature excluded?

Third, the efficacy and safety of vertebroplasty or kyphoplasty was often evaluated by comparison with an inactive control intervention (e.g., conservative treatment or optimal medical therapy) (8,9) or with an active control intervention (e.g., sham operation) (2,3). In our opinion, a pair-wise comparison across vertebroplasty versus a sham operation or vertebroplasty versus optimal medical therapy could balance the confounding effect of the natural history of osteoporosis. Thus, a broad review scope could be employed so that a larger sample size would provide us with much more statistical power to detect the treatment effect?

What's more, when studies involve time-to-event data the most appropriate statistics are hazard ratio and its variance, which take into account of the number and timing of events (10). Mainly due to the rigorous inclusion criteria, only 2 randomized studies were eligible for inclusion. And it was not possible to employ a hazard ratio for further analysis. Thus, a broad scope would provide us with more a flexible effect size so that the fracture risk could be better evaluated?

In conclusion, a more specific review question (participants, interventions, comparisons, and outcomes) might help better document the fracture topic. To be

honest, despite questions about the review protocol, the outcome of this meta-analysis is supportive of the recommendation of vertebroplasty or kyphoplasty for the treatment osteoporotic vertebral compression fracture even when the efficacy of these minimally invasive procedures still cannot be established.

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REFERENCES

1. Zou J, Mei X, Zhu X, Shi Q, Yang H. The long-term incidence of subsequent vertebral body fracture after vertebral augmentation therapy: A systemic review and meta-analysis. *Pain Physician* 2012; 15:E515-E522.
2. Buchbinder R, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedt C, Graves S, Staples MP, Murphy B. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med* 2009;361: 557-568.
3. Kallmes DF, Comstock BA, Heagerty PJ, Turner JA, Wilson DJ, Diamond TH, Edwards R, Gray LA, Stout L, Owen S, Hollingworth W, Ghdoke B, Annesley-Williams DJ, Ralston SH, Jarvik JG. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med* 2009;361: 569-579.
4. Long SS, Morrison WB, Parker L. Vertebroplasty and kyphoplasty in the United States: Provider distribution and guidance method, 2001-2010. *Am J Roentgenol* 2012; 199:1358-1364.
5. Rho YJ, Choe WJ, Chun YI. Risk factors predicting the new symptomatic vertebral compression fractures after percutaneous vertebroplasty or kyphoplasty. *Eur Spine J* 2012;21: 905-911.
6. Trout A, Kallmes D, Kaufmann T. New fractures after vertebroplasty: Adjacent fractures occur significantly sooner. *Am J Neuroradiol* 2006;27: 217-223.
7. Li YA, Lin CL, Chang MC, Liu CL, Chen TH, Lai SC. Subsequent vertebral fracture after vertebroplasty: Incidence and analysis of risk factors. *Spine (Phila Pa 1976)*. 2012; 37:179-183.
8. Klazen CA, Lohle PN, de Vries J, Jansen FH, Tielbeek AV, Blonk MC, Venmans A, van Rooij WJ, Schoemaker MC, Juttman JR, Lo TH, Verhaar HJ, van der Graaf Y, van Everdingen KJ, Muller AF, Elgersma OE, Halkema DR, Franssen H, Janssens X, Buskens E, Mali WP. Vertebroplasty versus conservative treatment in acute osteoporotic vertebral compression fractures (Vertos II): An open-label randomised trial. *Lancet* 2010; 376:1085-1092.
9. Rousing R, Hansen KL, Andersen MO, Jespersen SM, Thomsen K, Lauritsen JM. Twelve-months follow-up in forty-nine patients with acute/semiacute osteoporotic vertebral fractures treated conservatively or with percutaneous vertebroplasty: A clinical randomized study. *Spine (Phila Pa 1976)* 2010; 35:478-482.
10. Higgins J, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1. 0 [updated March 2011]. The Cochrane Collaboration 2011.