Reply:

J.A. Hirsch, R.V. Chandra, D. Beall, M. Frohbergh and K. Ong

AJNR Am J Neuroradiol 2020, 41 (8) E69-E70
doi: https://doi.org/10.3174/ajnr.A6721
http://www.ajnr.org/content/41/8/E69

REPLY:

We thank O'Reilly et al for their interest in our article.[1] To answer the specific questions posed in their letter, we used published data from the Medicare dataset on mortality risks for patients with vertebral compression fracture (VCF) stratified by kyphoplasty (BKP), vertebroplasty (VP), and nonsurgical management (NSM).[2] As described in that study, all outcomes, including death, were measured from the time of diagnosis of the incident vertebral fracture. Hence, the "clock started" at the same time for all patients. O'Reilly et al also suggested that we should have generated survival curves and hazard ratios ourselves rather than relying on data from another article. That would certainly have been the case had we relied on an article authored by other investigators. However, because our group analyzed the data and authored the original article, we, in fact, were able to calculate the summary survival curves and hazard ratios ourselves. Moreover, in that article, we adjusted the data for a multitude of variables, including fracture location. The authors of the letter highlighted a potential bias favoring survival for patients in the augmentation procedure group. Belying that is the fact that previous sensitivity analyses of the Medicare VCF population have demonstrated improved survival risks for the augmentation over the NSM group that were still observed even when comparing all patients who survived at 1 year.[3,4]

O'Reilly et al further suggested that the Current Procedural Terminology (CPT) codes for VP 22520–22522 were missing from the analysis and that CPT code 22289 should not have been used for vertebral augmentation. As described by Ong et al,[2] the VP codes were used to identify these patients. CPT 22289 was also used to identify BKP procedures before 2006.[3,4] This was the code that insurance carriers had required for BKP reimbursement during the period in question. This would have also only applied to 1 year (2005) of 10 years of data (2005–2014) from which the survival curves and hazard ratios were determined.[2] O'Reilly et al also queried about what spine fusion codes were used. So as not to become tedious, we refer the authors of the letter back to the original study details.[2]

Without question, we acknowledge the limitations of this analysis of nonrandomized observational data and the biases present that our group previously attempted to adjust for by using propensity adjustment strategies. Indeed, we point out these limitations directly in the discussion of the underlying article, stating, "Using large claims-based datasets inherently equates to a heterogeneous population being analyzed retrospectively." However, it is surprising to us that the authors of the letter do not recognize that the mortality benefit is biologically plausible. First, NSM carries its own risks, and kyphotic posture is associated with an elevated risk of mortality.[5] The immobility caused by vertebral fractures is also very well-known to lead to increased mortality that rivals or exceeds that of hip fractures.[6] Moreover, opioid treatments for NSM of compression fracture pain were widespread from 2005 to 2014, and these medications are themselves associated with disability and increased risk of death.[7]

To explore this area further, our group also performed a systematic review and meta-analysis on the mortality outcomes of patients with osteoporotic vertebral fractures treated with vertebral augmentation compared with those treated with NSM that has been recently published.[8] The pooled hazard ratio (HR) across 7 studies was 0.78 (95% CI, 0.66–0.92; $P = .003$) in favor of augmentation. Although heterogeneity was high with an I^2 of 68%, the result remained robust with sensitivity analysis. Moreover, the lower hazard for mortality has also been independently reported in large Taiwanese ($n = 7097$; HR, 0.72; 95% CI, 0.56–0.92; $P = .008$) and German studies ($n = 3607$; HR, 0.57; 95% CI, 0.48–0.70; $P < .001$).[9,10]

Although we believe the mortality benefit of augmentation is supported by the available evidence, biologically plausible, additional high-quality evidence is required. We look forward to better designed and adequately powered randomized controlled trials of vertebral augmentation and additional meta-analyses of individual patient data from randomized trials to further examine clinically relevant outcomes, including mortality.

REFERENCES

1. Hirsch JA, Chandra RV, Carter NS, et al. **Number needed to treat with vertebral augmentation to save a life.** *AJNR Am J Neuroradiol* 2020;41:178–82 CrossRef Medline
2. Ong KL, Beall DP, Frohbergh M, et al. **Were VCF patients at higher risk of mortality following the 2009 publication of the vertebroplasty "sham" trials?** *Osteoporos Int* 2018;29:375–83 CrossRef Medline
3. Edidin AA, Ong KL, Lau E, et al. **Mortality risk for operated and nonoperated vertebral fracture patients in the Medicare population.** *J Bone Miner Res* 2011;26:1617–26 CrossRef Medline
4. Edidin AA, Ong KL, Lau E, et al. **Morbidity and mortality after vertebral fractures: comparison of vertebral augmentation and nonoperative management in the Medicare population.** *Spine (Phila Pa 1976)* 2015;40:1228–41 CrossRef Medline
5. Kado DM, Huang MH, Karlamangla AS, et al. **Hyperkyphotic posture predicts mortality in older community-dwelling men and women: a prospective study.** *J Am Geriatr Soc* 2004;52:1662–67 CrossRef Medline
6. Cauley JA, Thompson DE, Ensrud KC, et al. **Risk of mortality following clinical fractures.** *Osteoporos Int* 2000;11:556–61 CrossRef Medline
7. Manchikanti L, Kaye AD, Soin A, et al. **Comprehensive Evidence-Based Guidelines for Facet Joint Interventions in the Management of Chronic Spinal Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines Facet Joint Interventions 2020 Guidelines.** *Pain Physician* 2020;23:S1–27 Medline
8. Hinde K, Maingard J, Hirsch J, et al. **Mortality outcomes of vertebral augmentation (vertebroplasty and/or balloon kyphoplasty) for osteoporotic vertebral compression fractures: a systematic review and meta-analysis.** *Radiology* 2020;295:96–103 CrossRef Medline
9. Lin JH, Chien LN, Tsai WL, et al. **Early vertebroplasty associated with a lower risk of mortality and respiratory failure in aged patients with painful vertebral compression fractures: a population-based cohort study in Taiwan.** *Spine J* 2017;17:1310–18 CrossRef Medline
10. Lange A, Kasperk C, Alvares L, et al. **Survival and cost comparison of kyphoplasty and percutaneous vertebroplasty using German claims data.** *Spine (Phila Pa 1976)* 2014;39:318–26 CrossRef Medline

http://dx.doi.org/10.3174/ajnr.A6721

J.A. Hirsch
Neurointerventional Radiology
Massachusetts General Hospital, Harvard Medical School
Boston, Massachusetts
R.V. Chandra
Faculty of Medicine
Nursing and Health Sciences, Neuroinverventional Radiology
Monash Imaging, Monash Health
Melbourne, Australia

D. Beall
Clinical Radiology of Oklahoma
Edmond, Oklahoma
M. Frohbergh
K. Ong
Exponent Inc
Philadelphia, Pennsylvania