Utilizing Big Data to Determine the Safety Profile of Recombinant Human Bone Morphogenetic Protein-2 in Spinal Fusion Surgery: An Analysis of 5 Databases from 2003 to 2017

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INTRODUCTION: The use of recombinant human bone morphogenetic protein (rhBMP) in spinal fusion remains controversial. While rhBMP safety concerns revealed misrepresentations in industry-sponsored research, prior observational studies reached conflicting conclusions regarding rhBMP safety and effectiveness.

METHODS: This study compared first-time spinal fusion patients who received rhBMP to a comparative group who did not receive rhBMP from 2003 to 2017 and investigated re-fusion rates and postoperative complications, including infection, seroma/hematoma, radiculitis, heterotopic ossification, and cancer. A secondary analysis was performed investigating 18 subtypes of benign and malignant neoplasms. Five longitudinal observational databases were utilized, including four insurance claims databases and one electronic medical record. Confounding was controlled for using propensity score matching and analyzed resultant covariate balance as an indicator of successful confounding control. Negative and positive controls were utilized to control for unmeasured confounding and calibrate the observed confidence intervals.

RESULTS:
Across all five databases, 60,427 patients were identified with rhBMP and 349,771 patients without, totaling 161,213 and 923,822 years of patient observation, respectively. rhBMP was associated with statistically significantly fewer postoperative infections, with a hazard ratio of 0.88 (95% CI: 0.78-0.99). No significant difference was seen with the other outcomes, including benign and malignant neoplasms. Substantial control of measured confounding was demonstrated by propensity score adjustment, and negative and positive controls revealed noticeable residual bias that was controlled for through confidence interval calibration.

DISCUSSION AND CONCLUSION: In the largest longitudinal observational study to date, rhBMP was determined to be safe and effective as compared to non-BMP usage in spinal fusion, with lower rate of postoperative infections. Importantly, no increased rates of cancer were detected. Coding error and the retrospective design may be an important source of bias. Despite these limitations, the large population size and statistical design give considerable significance to the results and conclusions of this study.