Usage Trends and Safety Profile of Recombinant Human Bone Morphogenetic Protein-2 for Spinal Column Tumor Surgery: A National Matched Analysis

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INTRODUCTION:

Achievement of arthrodesis remains a significant challenge in spinal tumor surgery requiring instrumented fusion. Patients in this vulnerable cohort often experience poor bone quality, malnutrition, or concurrent use of chemotherapy or radiotherapy – all of which interfere with proper bone formation and healing. To augment fusion efforts, recombinant human bone morphogenetic protein-2 (rhBMP-2) emerged as a powerful osteogenic factor after its FDA approval in 2002. While approved solely for anterior lumbar interbody fusion, rhBMP-2's off-label use has dramatically exploded and its safety profile has remained a persistent concern necessitating several FDA and national society advisories. Although most recent evidence does not seem to suggest increased complication or carcinogenic risk due to rhBMP-2 use, these findings remain limited and poorly defined in the spinal oncology subcohort. The purpose of this study was to investigate national rates of rhBMP-2 utilization in spinal tumor cases and examine its association with postoperative complications, revisions, and carcinogenicity.

METHODS:

A retrospective query of Medicare, Medicaid, and commercial administrative claims from 2005 to 2020 was performed using a national insurance database. All patients diagnosed with primary or metastatic spinal tumors with subsequent surgical intervention involving a spinal fusion procedure were identified. Patients were organized into two cohorts according to rhBMP-2 usage and 1:1 matched based on age, gender, and Charlson Comorbidity Index. Utilization trends in rhBMP-2 usage were normalized to annual total number of fusion procedures, and then compared via a Pearson correlation between rhBMP-2 proportion and calendar year. Postoperative complications and revisions were examined at 1 month, 3 months, 6 months, and 1 year after spinal fusion. New cancer incidence following spinal tumor surgery was assessed until 5 years postoperatively. Post hoc comparisons were characterized using chi-squared analysis, and threshold for significance was established at $P < 0.05$.

RESULTS:

A total of 11,198 patients underwent fusion surgery for spinal tumors between 2005 and 2020, with 909 cases reporting the use of rhBMP-2 (8.1%). The proportion of spine tumor fusion procedures utilizing rhBMP-2 has been significantly decreasing ($R^2 = 0.859$, $P < 0.001$), with the most recent annual utilization rate at 1.1% (Figure 1). The final matched cohorts each comprised 894 patients. At least 6 months after surgery, significantly increased incidences of surgical site (7.3% vs. 1.6%, $P = 0.05$) and systemic infections (13.8% vs. 4.1%, $P = 0.01$) were observed in patients who underwent fusion with rhBMP-2 compared to nonusers (Table 1). Across all timepoints, no significant differences were observed between the groups in implant removal or revision rates (Table 2). In addition, new cancer incidence after fusion surgery was comparable between the two groups and no significant differences in individual malignant cancer types were revealed (Table 3).

DISCUSSION AND CONCLUSION:

rhBMP-2 has been widely used off-label to promote arthrodesis, however its role in spinal fusion procedures involving spinal tumors remains controversial. This analysis demonstrated significantly declining national utilization rates – likely resulting from recent FDA advisories and published clinical trials – although rhBMP-2 usage was not associated with new local or distant cancer incidence postoperatively. Compared with nonusers, spinal tumor cases utilizing rhBMP-2 sustained greater rates of surgical site and systemic infections. Furthermore, rhBMP-2 usage did not significantly reduce implant failure or revision rates – suggesting it may not be essential to fulfilling the needs of this specific patient population.

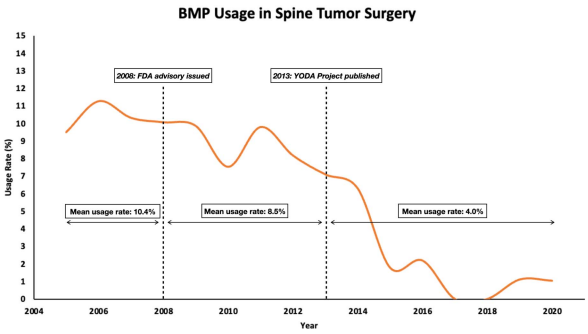

Table 1. Early and late postoperative outcomes after spinal fusion with or without BMP-2 for treatment of spinal tumor (n = 894 per age-, gender-, and CCI-matched cohort)

	1 month			3 months			6 months			1 year		
	BMP-2	No BMP-2	P-value	BMP-2	No BMP-2	P-value	BMP-2	No BMP-2	P-value	BMP-2	No BMP-2	P-value
AKI	4.1%	5.7%	0.77	4.9%	7.3%	0.59	5.7%	8.9%	0.46	5.7%	13.8 %	0.06
Cardiac Arrest	0.8%	0.8%	1	0.8%	0.8%	1	1.6%	0.8%	1	1.6%	0.8%	1
DVT	0.8%	4.9%	0.13	1.6%	5.7%	0.17	1.6%	2.4%	1	1.6%	2.4%	1
Wound Complication	5.7%	4.1%	0.77	6.5%	4.1%	0.57	6.5%	3.3%	0.37	6.5%	4.1%	0.57
Hematoma	0.8%	4.9%	0.13	0.8%	4.9%	0.13	4.1%	4.9%	1	4.9%	4.9%	1
Neural Injury	0%	0%	1	0%	0%	1	0%	0%	1	0%	0%	1
Pneumonia	8.9%	8.9%	1	10.6 %	12.2 %	0.84	15.4 %	14.6 %	1	18.7 %	17.1 %	0.87
PE	5.7%	2.4%	0.33	7.3%	2.4%	0.14	9.8%	8.1%	0.82	10.6 %	8.9%	0.83
Transfusion	2.4%	4.1%	0.72	8.1%	4.9%	0.44	9.8%	10.6 %	1	13%	12.2 %	1
UTI	10.6 %	9.8%	1	13.8 %	14.6 %	1	17.9 %	17.9 %	1	18.7 %	20.3 %	0.87
Mechanical Failure	0.8%	0%	1	1.6%	0.8%	1	1.6%	0%	0.48	3.3%	0%	0.13
Systemic Infection	8.1%	2.4%	0.17	11.4 %	4.9%	0.10	**13.8 %**	4.1%	**0.01**	**13.8 %**	4.9%	**0.03**
Spinal abscess	0%	0%	1	0.8%	0%	1	0.8%	0%	1	0.8%	0%	1
SSI	4.1%	0.8%	0.28	7.3%	2.4%	0.14	**7.3%**	1.6%	**0.05**	**7.3%**	1.6%	**0.05**