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Trends, Costs, and Complications of Anterior Cervical Discectomy and Fusion With and Without Bone Morphogenetic Protein in the United States Medicare Population

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Abstract

Study Design: Retrospective database review.

Objectives: After the Food and Drug Administration approved bone morphogenetic protein–2 (BMP) in 2002, BMP was used off-label in the cervical spine to increase bone growth and bony fusion. Since then, concerns have been raised regarding complication rates and safety. This study was conducted to examine the use of BMP in anterior cervical discectomy and fusion (ACDF) in the Medicare population and to determine risk of complications and associated costs within 90 days of surgery.

Methods: Patients who underwent ACDF were identified using Current Procedural Terminology (CPT) and International Classification of Diseases, Ninth Revision Procedure codes (ICD9-P). Complications were identified using ICD9 diagnostic codes. Charges were calculated as amount billed, and reimbursements were calculated as amounts paid by Medicare. Data for these analyses came from a nationwide claims database.

Results: A total of 215 047 patients were identified who had ACDF from 2005 to 2011. For the majority of the procedures (89.0%), BMP was not used. BMP use rose from 11.84% in 2005 to a peak of 16.73% in 2007 before decreasing to 12.01% in 2011. BMP was used 16% more in women than men. BMP use was the highest in the West (13.6%) followed by Midwest (11.8%), South (10.6%), and Northeast (7.5%). There was a higher overall complication rate in the BMP group (2.1%) compared with the non-BMP group (1.9%) (odds ratio [OR] = 1.11, 95% CI = 1.01-1.22). The BMP group also had a higher rate of wound complications (0.98% vs 0.76%, OR = 1.29, 95% CI = 1.12-1.48). In this study population, there was no difference in dysphagia/hoarseness, neurologic, medical, or other complications. During the 90-day perioperative period, BMP surgeries were charged at 17.6% higher than non-BMP surgeries.

Conclusions: The use of BMP in ACDF in the Medicare population has decreased since a peak in 2007. The rate of wound and overall complications for BMP use with ACDF was higher than without. Our results regarding dysphagia/hoarseness did not show a statistically meaningful difference, which is in contrast with many other studies. Charges associated with BMP use were higher during the 90-day perioperative period.

Keywords

anterior cervical discectomy and fusion, bone morphogenetic protein, trends

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Introduction

Back and neck pain are significant contributors to morbidity and health care costs in the United States.[1,2] Many patients fail the first-line treatment of non-surgical interventions and proceed to surgical treatment. Cervical arthrodesis has evolved as a treatment for neck pain caused by disc disease and herniated discs that result in bony fusion of spinal segments. Cervical arthrodesis has been associated with a complication rate of about 3.9%, increasing with patient age.[3] These complications include infections, swallowing problems and dysphagia, neurological problems, and failure of bony fusion, which can lead to pain, instability, and require revision surgery.

Bone morphogenetic protein–2 (BMP) was approved by the US Food and Drug Administration (FDA) in 2002 to promote fusion in anterior lumbar surgery.[4] The use of BMP has increased from 2002 to 2011 with off-label applications accounting for the majority of use.[5] One of these off-label uses is in the cervical spine to increase bone growth and bony fusion while decreasing risk of pseudarthrosis and nonunion.[6] Over time, concerns have been raised regarding complication rates and safety, including a public health notification from the US FDA in 2008.[7-9]

This study was conducted to examine the use of BMP in anterior cervical discectomy and fusion (ACDF) in the Medicare population and to determine risk of complications and associated costs within 90 days of surgery. We hypothesized that the use of BMP would increase complication rates and increase costs associated with care. As has previously been documented, we hypothesized that safety concerns regarding use of BMP would have a dramatic effect on its use for ACDF. We attempted to quantify the impact of these concerns on clinical utilization.

Methods

Records for patients who underwent ACDF were collected using the PearlDiver Patient Record Database (PearlDiver Technologies, Warsaw, IN). This is a publicly available national database of Medicare insurance records. Patients were identified by International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. We performed a retrospective review over 48 million patients from January 1, 2005 through December 31, 2011. Region was defined as Midwest, Northeast, South, and West (Table 1). Charges were calculated as amount billed by the institution for each patient for care surrounding the index procedure. Our institutional review board deemed this study exempt from review, as all patient information was deidentified. Incidence was calculated as procedures per 100 000 members. *P* values less than .05 were considered significant. Patient data was completely deidentified therefore did not require institutional review board approval.

Patients were eligible if they had ACDF from January 1, 2005 to October 2, 2011. Patients who underwent primary ACDF were identified by use of ICD-9 code for arthrodesis of C2 level or below: anterior (interbody) technique anterolateral technique (ICD-9 81.02). Use of BMP2 was identified by ICD-9 code 84.52.

Table 1. Regional Breakdown of States.

Region	States
Midwest	IA, KS, MN, MO, NE, IL, IN, MI, WI, OH, NO, SD
Northeast	CT, MA, ME, NH, NJ, PA, RI, NY, VT
South	AL, AR, DC, DE, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV, PR
West	AK, AZ, CA, CO, ID, MT, NM, NV, OR, UT, WA, WY, HI

Complications were identified using ICD-9 and CPT codes for each patient 90 days following their index procedure, from January 1, 2005 to December 31, 2011. The following complications were identified: dysphagia/hoarseness (478.30, 478.31, 478.32, 478.33, 478.34, 784.4, and 787.2), nervous system complications (997.0, 997.00, 997.01, 997.09), wound complications (998.1, 998.11, 998.12, 998.13, 998.3, 998.31,998.32, 998.83, 998.5, 999.3, 998.51, 998.59, 998.83, and 999.3), medical complications (997.1-997.3, 410.0-410.9, 415.1, 998.0), and other complications (998.81, 998.89, 998.9, 999.9).

Unadjusted relative risk (RR) and 95% confidence intervals (CIs) were used to determine patient characteristics and complications from BMP use. Student's *t* tests and chi-square tests were used for cost comparisons. *P* values less than .05 were considered significant.

Results

A total of 215 047 patients were identified who underwent primary ACDF. For the majority of the procedures (89.0%, n = 191 421), BMP was not used. BMP use rose from 11.84% (n = 3222) of all ACDFs within 2005 to a peak of 16.73% (n = 5198) in 2007 before decreasing to 12.01% (n = 4595) in 2011 (Figure 1). The number of ACDF with BMP also rose from 3222 to 4595 over the same time period, but incidence of ACDF with BMP paralleled percent use; it increased from 7.58 in 2005 with a peak in 2007 with 11.74 before decreasing to 9.41 in 2011. The number of total cases of ACDF without BMP increased steadily throughout, from 23 996 in 2005 to 33 677 in 2011. Incidence of ACDF without BMP also increased from 56.46 in 2005 to 68.94 in 2011.

There were differences among BMP use according to sex, age, and region (Table 2). Use of BMP was highest in the 70- to 74-year age group compared with <65-year age group (RR = 1.06, 95% CI = 1.02-1.09). BMP use was least in the >84-year age group (RR = 0.81, 95% CI = 0.73-0.90) followed by the 80- to 84-year old age group (RR = 0.90, 95% CI = 0.85-0.96). Women were more likely to receive BMP than men (RR = 1.16, 95% CI = 1.13-1.19). BMP use was highest in the West compared with Midwest (RR = 1.15, 95% CI = 1.11-1.19) and lowest in the Northeast compared with Midwest (RR = 0.63, 95% CI = 0.60-0.66).

There was an 11% higher overall complication rate in the BMP group (2.1%) compared with the non-BMP group (1.9%) (odds ratio [OR] = 1.11, 95% CI = 1.01-1.22). The BMP group also had a higher rate of wound complications (0.98% vs

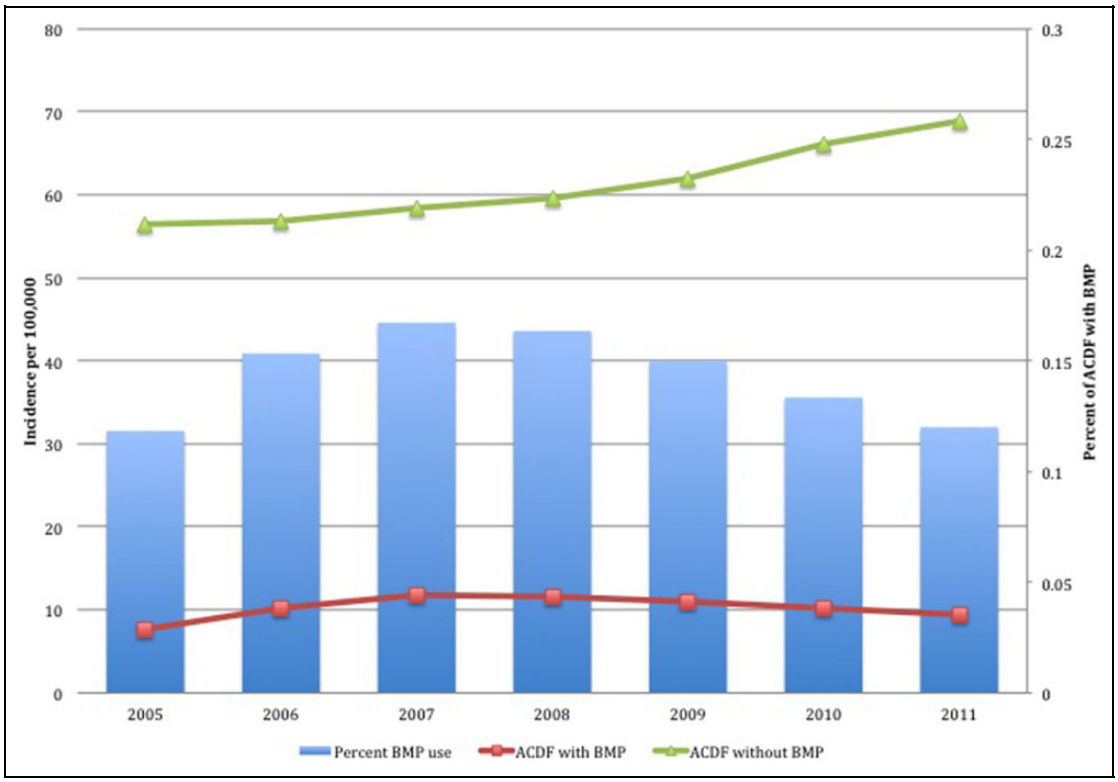

Figure 1. Incidence of anterior cervical discectomy and fusion (ACDF) with and without use of bone morphogenetic protein (BMP) from 2005 to 2011.

Table 2.

Patient Characteristics.Characteristics	No BMP (n = 191 421), n (%)	BMP (n = 23 626), n (%)	Relative Risk of BMP Use (95% CI)
Age group, years			
<65	73 639 (38.5)	9862 (41.7)	Reference
65-69	50 617 (26.4)	6604 (28.0)	0.98 (0.95-1.01)
70-74	33 160 (17.3)	4734 (20.0)	1.06 (1.02-1.09)
75-79	19 891 (10.4)	2691 (11.4)	1.01 (0.97-1.05)
80-84	9035 (4.7)	1075 (4.6)	0.90 (0.85-0.96)
>84	3301 (1.7)	349 (1.5)	0.81 (0.73-0.90)
Sex			
Male	90 038 (47.0)	10 160 (43.0)	Reference
Female	98 784 (51.6)	13 191 (55.8)	1.16 (1.13-1.19)
Region			
Midwest	40 909 (21.4)	5480 (23.2)	Reference
Northeast	20 905 (10.9)	1692 (7.2)	0.63 (0.60-0.66)
South	98 119 (51.3)	11 654 (49.3)	0.90 (0.88-0.93)
West	31 557 (16.5)	4971 (21.0)	1.15 (1.11-1.19)

Abbreviation: BMP, bone morphogenetic protein.

Table 3. Complications With and Without BMP in ACDF Within 90 Days.

Complication	No BMP (n = 191 421), n (%)	BMP (n = 23 626), n (%)	Odds Ratio (95% CI)
Any	3650 (1.9)	497 (2.1)	1.11 (1.01-1.22)
Dysphagia or hoarseness	986 (0.52)	127 (0.54)	1.04 (0.87-1.26)
Wound	1461 (0.76)	232 (0.98)	1.29 (1.12-1.48)
NS	98 (0.05)	11 (0.05)	0.91 (0.49-1.70)
Medical	794 (0.41)	85 (0.36)	0.87 (0.69-1.08)
Other	311 (0.16)	42 (0.18)	1.09 (0.79-1.51)

Abbreviations: ACDF, anterior cervical discectomy and fusion; BMP, bone morphogenetic protein; NS, neurologic symptoms.

Table 4. Charges for ACDF With and Without BMP.

	Without BMP			With BMP			
	Mean ($)	SD ($)	n	Mean ($)	SD ($)	n	*P*
Total	57 245	72 034	191 421	61 838	58 914	23 626	<.0001
Age group, years							
<65	52 645	70 197	73 639	67 461	64 871	9862	<.0001
65-69	55 830	69 134	50 617	72 564	63 726	6604	<.0001
70-74	58 095	64 640	33 160	74 797	62 846	4734	<.0001
75-79	63 990	75 935	19 891	78 232	77 031	2691	<.0001
80-84	74 319	92 678	9035	85 107	81 253	1075	.0003
>84	93 625	119 054	3301	89 370	75 319	349	.5132
Region							
Midwest	48 236	48 380	40 909	64 706	50 672	5480	<.0001
Northeast	59 822	95 313	20 905	64 808	67 473	1692	.0349
South	52 571	55 030	98 119	65 481	53 341	11 654	<.0001
West	81 827	28 414	31 557	98 100	95 598	4971	<.0001
Sex							
Female	52 811	57 489	98 784	70 709	60 552	13 191	<.0001
Male	62 302	85 370	90 038	73 913	73 803	10 160	<.0001

Abbreviations: ACDF, anterior cervical discectomy and fusion; BMP, bone morphogenetic protein.

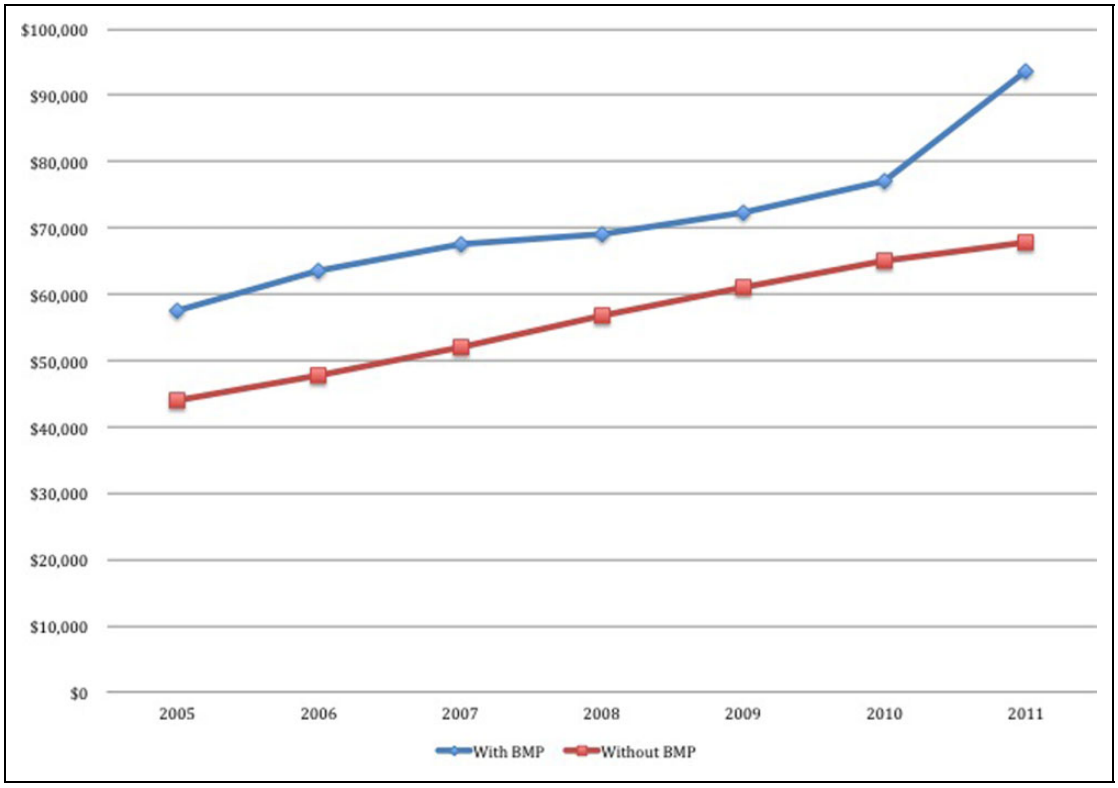

Figure 2. Charges for anterior cervical discectomy and fusion (ACDF) over time.

0.76%, OR = 1.29, 95% CI = 1.12-1.48). In this study population, there was no difference in dysphagia/hoarseness, neurologic, medical, or other complications (Table 3).

Averages charges for ACDF with BMP ($61 838) were significantly higher than those without BMP ($57 245) ($P < .0001$) (Table 4). There were significant differences in costs for the BMP and non-BMP in every demographic subgroup with the exception of patients aged older than 84 years. ACDF charges were significantly higher for males compared with females without and with BMP use ($62 302 and $73 913 compared with $52 811 and $60 552, $P < .001$). Charges for both groups increased over time (Figure 2). In 2005, ACDF without BMP averaged $43 927 and with BMP $57 927 for a difference of $13 528. By 2011, ACDF without BMP was $67 690 and with

$93 532 for a difference of $25 842. The differences remained significant throughout $P < .0001$.

Discussion

This data shows that the rate of use of BMP in ACDF in the Medicare population increased from 2005 to 2007 and then decreased thereafter. By 2011, BMP was being used in just over 12% of ACDF's in this population. This trend temporally matches the US FDA Public Health Notification indicating "life-threatening complications associated with BMP in cervical spine fusion," which was released in 2008.[9] This announcement, in addition to a growing body of literature warning against potential adverse effects of BMP, including radiculitis, soft-tissue swelling, dysphasia, heterotopic ossification, hematoma, seroma, and cancer may have led to this decrease in utilization.[3,6,7,10] This decrease in BMP use is consistent with other trends of physician use following the US FDA advisory.[11] Still, utilization of 12% four years after the announcement is potentially concerning given the known serious adverse effects. Further study as to what the utilization and complication rate today are warranted.

We found that BMP utilization in ACDF to be highest in the Western region followed by Midwest, South, and Northeast. Overall use was lowest in the Northeast. Lao et al[12] found similar results; that BMP use in single level anterior interbody fusion was highest in the West and lowest in the Northeast. Singh et al[5] reported that overall BMP use in all spine surgery was highest in the South and lowest in the Northeast. Use of BMP was highest in the 70- to 74-year-old age group and least in the >84-year-old group. The lower use in the older age group may be due to the fact that these patients likely have lower life expectancy compared with younger patients; therefore, lifetime risk of pseudarthrosis, which BMP would help prevent, is decreased. It is unclear why the 70- to 74-year-old patients would have the highest rate of BMP use. Women were more likely to receive BMP, as has been found in other studies.[7] This may be because of women, especially elderly women, having lower bone density than men,[13,14] which creates greater concern for pseudarthrosis.

The rate of overall complications for ACDF was higher with BMP than without, consistent with many other studies.[8,15] Our data indicated that wound complications occurred at a higher rate for patients treated with BMP than without (0.98% vs 0.76%). It is unclear whether this is due to BMP itself or selection bias of patients who had BMP used on them. Patients with risk factors suggestive of poor healing may be more likely to receive BMP. Our data regarding dysphagia/hoarseness did not show a statistically meaningful difference. Studies on this topic have had conflicting results. Lu et al[16] demonstrated that use of BMP2 increases severity of dysphasia while not affecting overall incidence of dysphasia. Singh et al[17] concluded a systematic review of the literature in 2014 and concluded that that rates of dysphagia were not affected by BMP. Several other studies have found a higher dysphasia rate with use of BMP.[18,19]

In 2011, Carragee et al[18] published the under reporting of adverse events related to BMP use in clinical trials, which had been underreported. Our data contributes to the growing body of literature that use of BMP contributes to perioperative morbidity and suggest that use of BMP is decreasing.

The differences in costs are not fully explained by the higher cost of BMP as the magnitude of the difference is much larger than the cost of BMP. Therefore, other factors such as increased complication rate probably contribute to the difference in cost. It is possible surgeons chose to used BMP in patients in with higher risk of complications. Our data shows that the >84-year-old age group, whom presumably would be a higher risk group for medical comorbidities did not have a significant cost differences. This is an area for further study. While charges increased for both groups over time, the difference between the 2 groups increased from $13 528 to $25 842, almost doubling, for reasons that are unclear.

There are several limitations to this study. The study is retrospective and based on medical coding, therefore subject to billing and coding errors. In addition, although it encompasses a large database, the Medicare population is not necessarily representative of the population at large. The <65-year age group covered by Medicare is a special population with end-stage renal disease or severe disability, therefore may be predisposed to risks compared with the >65-year group Medicare population who qualify for coverage based on age alone.[20] Our complication outcomes were not risk adjusted, therefore we were not able to identify whether patients who had BMP used were at inherently higher risk of complications.

Appendix

Complications by International Classification of Diseases, Ninth Revision (ICD-9) Code

Dysphagia, vocal cord paralysis	
478.30-34	Paralysis of vocal cords or larynx
784.4	Voice and resonance disorder
787.2	Dysphagia
Nerve system complications	
997.0	Nervous system complication
997.00	Nervous system complication, unspecified
997.01	Central nervous system complication
997.09	Other nervous system complication
Wound complication	
998.1	Hemorrhage or hematoma or seroma
998.11	complicating a procedure
998.12	Hemorrhage complicating a procedure
998.13	Hematoma
998.3	Seroma
998.31	Disruption
998.32	Disruption of internal surgical wound
998.5	Disruption of external operation wound
998.51	Postoperative infection
998.59	Infected postoperative seroma
998.83	Other postoperative infection
999.3	Nonhealing surgical wound
	Other infection

(continued)

(continued)

Medical complications	
997.1	Cardiac complication
997.2	Peripheral vascular complication
997.3	Respiratory complication
410.0-410.9	Myocardial infarction
415.1	Pulmonary embolism and infarction
998.0	Postoperative shock
Other complications	
998.8	Other specified complication of procedure, not elsewhere classified
998.89	Other specified complication
998.9	Unspecified complication of procedure, not elsewhere classified
999.9	Other and unspecified complication of medical care, not elsewhere classified

Declaration of Conflicting Interests

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