

HEALTH SERVICES RESEARCH

Does Bone Morphogenetic Protein Increase the Incidence of Perioperative Complications in Spinal Fusion?

A Comparison of 55,862 Cases of Spinal Fusion With and Without Bone Morphogenetic Protein

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Study Design. Retrospective review of a multi-institutional, multisurgeon database.**Objective.** Assess for associations between bone morphogenetic protein (BMP) use and rate of complications in spinal fusion.**Summary of Background Data.** BMP is commonly used in spinal surgery to augment fusion; however, there is limited evidence demonstrating its associated complications.**Methods.** We performed a retrospective analysis of all fusion cases submitted by members of the Scoliosis Research Society from 2004 to 2007. We stratified on the basis of the use of BMP and evaluated for complications and associated characteristics.**Results.** A total of 55,862 cases of spinal fusion were identified with BMP used in 21% (11,933) of the cases. Excluding anterior cervical fusions, there were no significant differences between fusions with and without BMP with regard to overall complications (8.4% vs. 8.5%; $P = 0.5$), wound infections (2.4% vs. 2.4%; $P = 0.8$), or epidural hematomas/seromas (0.2% vs. 0.2%; $P = 0.3$). Anterior cervical fusions with BMP were associated with moreoverall complications (5.8% vs. 2.4%; $P < 0.001$) and more wound infections (2.1% vs. 0.4%; $P < 0.001$) than fusions without BMP.On multivariate analysis for thoracolumbar and posterior cervical fusions, BMP use was not a significant predictor of complications ($P = 0.334$; odds ratio = 1.039; 95% confidence interval = 0.961–1.124; covariates were BMP use, patient age, revision vs. primary surgery). Multivariate analysis for anterior cervical spinal fusion demonstrated that BMP use remained a significant predictor of complications ($P < 0.001$, odds ratio = 1.6; 95% confidence interval = 1.516–1.721), after adjusting for the effects of patient age and whether the surgery was a revision procedure.**Conclusion.** BMP use with anterior cervical fusion was associated with an increased incidence of complications. Use of BMP was not associated with more complications in thoracolumbar and posterior cervical fusions.**Key words:** complication, BMP, scoliosis, spinal fusion, spondylolisthesis. **Spine 2011;36:1685–1691**

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BMP is FDA approved for anterior lumbar interbody fusion using an LT cage, but is being used off-label for the vast majority of cases in this series. The on-label uses for BMP are clearly indicated in the Introduction of the manuscript.

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Spine

Bone morphogenetic proteins (BMPs) are a family of growth factors that induce bone formation.¹ There are two commercially available BMP products for use in spinal fusion, BMP-2 (InFuse; Medtronic, Memphis, TN) and BMP-7 (OP-1 Putty; Stryker, Kalamazoo, MI).^{2,3} Clinical use of recombinant BMP-2 was approved by the US Food and Drug Administration in 2002 for anterior lumbar interbody fusion with an LT-CAGE (Medtronic, Memphis, TN).² BMP-7 has been approved under a humanitarian device exemption for use in revision intertransverse process lumbar fusion.³ The potential benefits of BMP may be the increased frequency of fusion, decreased morbidity related to harvesting of autograft, and potential cost savings.^{4,5}

Complications related to the use of BMP have been reported in relatively small series.^{6–13} There are reports that BMP use in transforaminal lumbar interbody fusion (TLIF) may be associated with postoperative radiculitis without neural compression.¹⁴ BMP use has also been associated with ectopic bone formation; however, the relation to neural compression and postoperative symptoms remains unclear.^{15–17} There has been

one large report utilizing the Nationwide Inpatient Sample database that showed increased incidence of complications with BMP use in anterior cervical spine fusions, but a more acceptable safety profile when used in other areas of spinal fusion.¹⁸ Supporting this evidence, there have been several reports of complications when BMP was used in anterior cervical fusions.^{4,11,15-17,19-21}

The Scoliosis Research Society (SRS) has been collecting morbidity and mortality (M&M) data from its members for more than 40 years. The membership of the SRS is predominantly fellowship-trained spinal surgeons and pediatric orthopedists, and the cases submitted represent a broad range of case complexities, with a substantial number of deformity cases. In the present study we sought to assess the rates of complications for spinal fusion procedures submitted to the SRS M&M database, stratified by whether BMP was used. On the basis of previous literature, we hypothesized that use of BMP for posterior cervical or thoracolumbar (anterior and/or posterior) spinal fusions would not be associated with higher rates of complications, including overall rates of complications, rates of wound infections, and rates of epidural hematomas/seromas. We also hypothesized that higher rates of complications would be associated with use of BMP for anterior cervical fusions.

MATERIALS AND METHODS

The SRS M&M database is the compilation of submissions of SRS members, predominantly within North America. For the years that the data were collected and reviewed for this report, candidate members were required to report their operative spine cases, including M&M data. Full active members were encouraged to report their cases as well.

We evaluated all surgical cases from 2004 through 2007 from the SRS M&M database. All data had previously been deidentified with regard to patient, surgeon, and institution. The database on which this project was based was submitted to an institutional review board and was deemed to be exempt from institutional review board approval on the basis of the use of deidentified data (institutional review board no. 29045).

Specific complications were collected in the database with a focus on the intraoperative and immediate postoperative periods. Examples of these included death, new neurological deficit, wound infection (superficial or deep), pulmonary embolus, deep venous thrombosis, other pulmonary complications, implant related, peripheral nerve deficit, visual deficit, and epidural hematoma. A category for "other" complications, with free text entry for description of the complication, was also included. Wound seroma was not a complication that was explicitly collected and was included in the epidural hematoma category, although a small subset of cases had documentation of wound seroma in the free text "other" category. For the purposes of this analysis, we have grouped together the epidural hematoma and seroma (from the "other" category) complications and denoted them as "epidural hematoma/seroma" complications.

All cases of spinal fusion were identified. We then evaluated for use of BMP, complications, and associated characteristics. The overall rate of complications, rate of wound infections, and rate of epidural hematoma/seroma were tabulated as the primary outcomes. Related characteristics, including patient age and revision procedure were also recorded. Data were also collected regarding delayed neurological deficit, which was defined as a neurological deficit occurring more than 24 hours after surgery.

Given previously reported associations between BMP use in anterior cervical spinal fusion and complications, this group was analyzed separately from the remainder of the spinal fusions. The primary group (including posterior cervical and thoracolumbar) was further stratified by diagnosis and method of fusion. Scoliosis cases were separated into pediatric and adult (≥ 21 years) groups to assess for potential differences in the rates of complications in these two populations.

Statistical analyses of these data were performed using SPSS for Windows v15.0 (SPSS Inc., Chicago, IL). The chi-square or Fisher exact tests were used for categorical data depending on the number of patients in each group. The two-sample unpaired *t* test with unequal variance was used for analysis of the two means. All tests were two-tailed. Multivariate analysis was performed using binomial logistic regression analysis.

The primary statistical analyses in the present study were those based on the starting hypotheses, specifically that use of BMP for posterior cervical or thoracolumbar (anterior and/or posterior) spinal fusions would not be associated with higher rates of complications, including overall rates of complications, rates of wound infections, and rates of epidural hematoma/seroma. We also hypothesized that higher rates of complications would be associated with use of BMP for anterior cervical fusions. For these primary analyses, statistical significance was based on a *P* value less than 0.05.

Post hoc analyses were also performed, with further stratification based on specific diagnoses, surgical approaches and treatments, and whether the surgery was a revision procedure. Significance for *post hoc* analyses was considered to be a *P* value less than 0.008, based upon a Bonferroni correction.

RESULTS

Patient Characteristics

A total of 55,862 cases of spinal fusion were identified, with BMP used in 21% (11,933) (Table 1) of the cases. The average age was significantly higher in the BMP fusion group than in the non-BMP group (52.1 years *vs.* 36.4 years; $P < 0.001$). On the basis of diagnosis, the proportion of fusions with BMP ranged from 9% for pediatric scoliosis to 37% for lumbar degenerative disease (Table 1). There were significantly more cases of degenerative spinal disease (46% *vs.* 30%; $P < 0.001$) and spondylolisthesis (27% *vs.* 17%; $P < 0.001$) in the fusion with BMP group, whereas there were more pediatric (36% *vs.* 13%; $P < 0.001$) and adult (10% *vs.* 8%; $P < 0.001$) scoliosis cases in the fusion without BMP group. Overall, BMP was

TABLE 1. Characteristics of Fusions With and Without BMP

Characteristic	Fusion Without BMP	Fusion With BMP
Cases (No. [%])	43929 (79)	11,933 (21)
Age (yr) [†]		
Mean ± SD	36.4 ± 22.3	52.1 ± 18.6
Median	27	54
Diagnosis (No. [%])		
Degenerative spinal disorder	13,228 (71)	5446 (29)
Anterior cervical	4532 (87)	652 (13)
Posterior cervical	776 (78)	217 (22)
Thoracic	237 (75)	79 (25)
Lumbar	7683 (63)	4519 (37)
Kyphosis	2625 (78)	731 (22)
Scoliosis		
Pediatric	15,937 (91)	1576 (9)
Adult	4586 (84)	899 (16)
Spondylolisthesis	7536 (70)	3255 (30)
Not specified	17 (77)	5 (23)
Method of fusion (No. [%])		
Anterior cervical	4532 (87)	652 (13)
Anterior/posterior thoracolumbar	3325 (62)	2049 (38)
Anterior thoracolumbar	2743 (72)	1054 (28)
Interlaminar/facet	11335 (91)	1085 (9)
Posterolateral	12241 (83)	2532 (17)
PLIF	3329 (82)	744 (18)
TLIF	2697 (49)	2773 (51)
Not specified	3727 (78)	1044 (22)
Revision procedures (No. [%])	4451 (65)	2400 (35)
[†] <i>P</i> < 0.001 (independent sample <i>t</i> test with unequal variances).		
<i>BMP</i> indicates bone morphogenetic protein; <i>PLIF</i> , posterior lumbar interbody fusion; <i>TLIF</i> , transforaminal lumbar interbody fusion.		

used more frequently in adult scoliosis cases than in pediatric scoliosis cases (16% vs. 9%; *P* < 0.001).

When stratified by the method of fusion, the proportion of fusions with BMP ranged from 9% for interlaminar/facet fusions to 51% for TLIFs (Table 1). There were significantly more anterior/posterior thoracolumbar (17% vs. 8%; *P* < 0.001), anterior thoracolumbar (9% vs. 6%; *P* < 0.001), and TLIF (23% vs. 6%; *P* < 0.001) fusions in the fusion with BMP group, whereas there were more interlaminar/facet fusions (26% vs. 9%) and posterior lumbar interbody fusions (8% vs. 6%; *P* < 0.001) in the fusion without BMP group.

Finally, there were more revision procedures in the fusion with BMP group (20% vs. 10%; *P* < 0.001).

Overall Complications

Excluding anterior cervical fusions, there were no significant differences in rates of overall complications (8.5% vs. 8.4%; *P* = 0.5), wound infections (2.4% vs. 2.4%; *P* = 0.8), or epidural hematomas/seromas (0.2% vs. 0.2%; *P* = 0.3) between the fusion with and without BMP groups, respectively (Table 2). When further stratified by deep (1.6% vs. 1.3%; *P* = 0.08) or superficial (0.8% vs. 1%; *P* = 0.2) wound infections, there remained no significant differences in the rates of complications between the fusion with and without BMP, respectively. Among revision procedures, there were no significant differences in the rates of complications between the fusion with and without BMP groups, including superficial (1.1% [n = 26] vs. 0.9% [n = 42]; *P* = 0.5) and deep (1.8% [n = 42] vs. 1.9% [n = 84]; *P* = 0.16) wound infections, epidural hematoma/seroma (0.3% [n = 6] vs. 0.4% [n = 18]; *P* = 0.3), and overall complications (9.8% [n = 236] vs. 10.9% [n = 483]; *P* = 0.2), respectively. There was no significant difference in the mortality rate between fusions with or without BMP (0.19% vs. 0.12%; *P* = 0.4).

We identified 5184 cases of anterior cervical fusion, with BMP used in 13% of the cases. Fusion with BMP was associated with more overall complications (5.8% vs. 2.4%; *P* < 0.001) and wound infections (2.1% vs. 0.4%; *P* < 0.001); however, there was no difference in the incidence of epidural hematoma/seroma (0.5% vs. 0.3%; *P* = 0.3) (Table 2). For anterior cervical fusions, both superficial (0.9% [n = 6] vs. 0.2% [n = 9]; *P* = 0.007) and deep (1.2% [n = 8] vs. 0.2% [n = 8]; *P* < 0.001) wound infections occurred more frequently in fusions with BMP. There were trends toward more episodes of dysphagia (0.6% [n = 10] vs. 0.2% [n = 4]) and higher mortality (0.6% [n = 4] vs. 0.08% [n = 4]) in fusions with BMP but neither of these associations reached statistical significance (*P* = 0.088 and *P* = 0.011, respectively).

In the fusion with BMP group, one patient each died of an ischemic stroke, pulmonary embolism, respiratory distress, and arrhythmia. In the fusion without BMP group two patients died of pulmonary embolism, one of arrhythmia, and one of respiratory-related complication (not embolic). There were 373 (7.2%) revision anterior cervical fusions performed and BMP was used in 29% (n = 107) of the cases.

Incidence of Complications Stratified by Preoperative Diagnosis

Rates of overall complications, superficial and deep wound infections, and epidural hematomas/seromas were assessed on the basis of preoperative diagnosis (Table 3). For diagnoses of degenerative spinal disease (except for cases treated with anterior cervical fusion), kyphosis, pediatric scoliosis, and spondylolisthesis, there were no significant differences in the rates of these complications. For adult scoliosis cases, use of BMP was not associated with higher rates of infection or epidural hematoma/seroma but was associated with a higher overall rate of complications (13.8% vs. 9.3%; *P* < 0.001).

TABLE 2. Overall Complications Associated With Fusion With and Without BMP, Grouped as Anterior Cervical Fusion or Posterior Cervical and Thoracolumbar Fusion

	Complications	Fusion Without BMP (No. [%])	Fusion With BMP (No. [%])	P*
Posterior cervical and thoracolumbar	Overall	3306 (8.4)	962 (8.5)	0.5
	Wound infection	963 (2.4)	266 (2.4)	0.8
	Epidural hematoma/seroma	65 (0.2)	24 (0.2)	0.3
Anterior cervical	Overall	110 (2.4)	38 (5.8)	<0.001
	Wound infection	17 (0.4)	14 (2.1)	<0.001
	Epidural hematoma/seroma	14 (0.3)	3 (0.5)	0.3

*P < 0.05 considered significant.

BMP indicates bone morphogenetic protein.

Influence of Fusion Method/Approach on Complications

Rates of overall complications, superficial and deep wound infections, and epidural hematomas/seromas were assessed on the basis of method of fusion (Table 4). For anterior-only thoracolumbar fusion, posterolateral fusion, posterior lumbar interbody fusion, and TLIF, there were no significant differ-

ences in the rates of complications, based on whether BMP was used. Combined anterior and posterior thoracolumbar fusions had a higher rate of deep wound infection if BMP was used (1.1%), than in cases in which BMP was not used (0.2%; P < 0.001). Interlaminar/facet fusions were associated with a higher rate of epidural hematoma/seroma if BMP was used (0.5%) versus if no BMP was used (0.1%; P = 0.006).

TABLE 3. Complications Associated With Spinal Fusion With and Without BMP Stratified by Diagnosis, Excluding Anterior Cervical Fusions*

Diagnosis	BMP	Superficial Infection (No. [%])	P	Deep Infection (No. [%])	P	Epidural Hematoma / Seroma (No. [%])	P	Overall (No. [%])	P
Degenerative spinal disease	No	72 (1.1)		116 (1.3)		18 (0.2)		677 (7.8)	
	Yes	56 (1.2)	0.054	56 (1.2)	0.4	8 (0.17)	0.6	378 (7.9)	0.17
Posterior cervical	No	6 (0.8)		10 (1.3)		0 (0)		60 (7.7)	
	Yes	2 (0.9)	0.7	2 (0.9)	1	0 (0)	1	8 (3.7)	0.047
Thoracic	No	2 (0.8)		0 (0)		1 (0.4)		19 (8.0)	
	Yes	0 (0)	1	1 (1.3)	0.3	1 (1.3)	0.4	7 (8.9)	0.6
Lumbar	No	64 (0.8)		105 (1.4)		17 (0.2)		592 (7.7)	
	Yes	54 (1.2)	0.06	53 (1.2)	0.3	7 (0.2)	0.6	362 (7.9)	0.6
Kyphosis	No	37 (1.4)		65 (2.5)		12 (0.46)		348 (13.4)	
	Yes	5 (0.7)	0.1	16 (2.2)	0.6	0 (0)	0.067	97 (13.4)	0.9
Adult scoliosis	No	42 (0.9)		90 (2.0)		13 (0.3)		425 (9.3)	
	Yes	12 (1.3)	0.5	16 (1.8)	0.9	1 (0.1)	0.3	124 (13.8)	<0.001
Pediatric scoliosis	No	138 (0.7)		235 (1.3)		20 (0.1)		1310 (7.0)	
	Yes	18 (1.1)	0.1	26 (1.6)	0.2	3 (0.2)	0.5	139 (8.8)	0.01
Spondylolisthesis	No	70 (0.9)		103 (1.4)		14 (0.18)		559 (7.5)	
	Yes	30 (0.9)	0.9	34 (1.0)	0.2	9 (0.27)	0.4	244 (7.6)	0.9

*P < 0.008 considered significant, based on a Bonferroni correction.

BMP indicates bone morphogenetic protein.

TABLE 4. Complications Associated With Spinal Fusion With and Without BMP Stratified by Method of Fusion, Excluding Anterior Cervical Fusions*

Category of Fusion	BMP	Superficial Infection (No. [%])	<i>P</i>	Deep Infection (No. [%])	<i>P</i>	Epidural Hematoma/Seroma (No. [%])	<i>P</i>	Overall Complications (No. [%])	<i>P</i>
Anterior/posterior (thoracolumbar)	No	43 (1.3)		8 (0.2)		5 (0.2)		391 (12)	
	Yes	21 (1)	0.4	23 (1.1)	<0.001	2 (0.09)	0.4	194 (9.5)	0.02
Anterior only (thoracolumbar)	No	25 (0.9)		25 (0.9)		3 (0.1)		227 (8.3)	
	Yes	12 (1.1)	0.5	12 (1.1)	0.5	2 (0.2)	0.6	87 (8.3)	0.9
Interlaminar/facet	No	100 (0.9)		188 (1.6)		14 (0.1)		935 (8.2)	
	Yes	13 (1.2)	0.3	16 (1.5)	0.7	5 (0.5)	0.006	101 (9.3)	0.3
Posterolateral	No	124 (1.0)		218 (1.8)		27 (0.2)		1228 (10)	
	Yes	32 (1.3)	0.3	41 (1.6)	0.6	5 (0.2)	0.8	246 (9.7)	0.7
PLIF	No	26 (0.8)		47 (1.4)		7 (0.2)		246 (7.4)	
	Yes	5 (0.7)	0.8	16 (2.2)	0.1	2 (0.3)	0.8	70 (9.4)	0.09
TLIF	No	24 (0.04)		57 (2.1)		9 (0.3)		252 (9.3)	
	Yes	32 (1.2)	0.3	42 (1.5)	0.1	8 (0.3)	0.7	259 (9.3)	0.9

**P* < 0.008 considered significant, based on a Bonferroni correction.

BMP indicates bone morphogenetic protein; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion.

Delayed Neurological Deficit

A total of 190 delayed neurological deficits (>24 hours postoperative) were reported among all fusions in the present series, with 43 occurring in fusions with BMP (22%). Overall, these deficits improved, with a partial or complete recovery occurring in most cases. There were 146 cases of nerve root deficit (82 complete recovery, 60 partial recovery, and 4 no recovery), 22 cases of cauda equina syndrome (17 complete recovery, 10 partial recovery, and 2 no recovery), 16 incomplete cord deficits (12 complete recovery and 4 partial recovery), and 5 complete cord deficits (3 complete recovery, 1 partial recovery, and 1 no recovery). Delayed neurological deficits were not associated with the use of BMP (*P* = 0.7).

Multivariate Analysis

Multivariate analysis was performed to assess for factors independently associated with increased rates of overall complications in patients undergoing posterior cervical or thoracolumbar spinal fusion. Factors in the analysis included age, BMP use, and revision surgery status. The best-fit final model included older age (*P* = 0.006, odds ratio [OR] = 1.002, 95% confidence interval [CI] = 1.001–1.003) and revision surgery (*P* < 0.001, OR = 1.227, 95% CI = 1.156–1.291), both of which were associated with more overall complications. Whether BMP was used was not part of the best-fit model. (*P* = 0.334, OR = 1.039, 95% CI = 0.961–1.124)

Multivariate analysis was performed to assess for factors independently associated with increased rates of overall complications in patients undergoing anterior cervical spinal fusion.

Factors included in the analysis included age, BMP use, and revision surgery status. The best-fit final model included only BMP use (*P* < 0.001, OR = 1.6, 95% CI = 1.516–1.721). Revision surgery (*P* = 0.126, OR = 0.669, 95% CI = 0.399–1.120) and older age (*P* = 0.1, OR = 0.988, 95% CI = 0.973–1.003) were not part of the best-fit model.

Multivariate analyses were performed to adjust for potential confounding effects on the rates of complications associated with BMP use. Specifically, for adult scoliosis patients, after adjusting for the effects of patient age (continuous variable) and revision procedure status, there was no longer a statistically significant association between BMP use and increased rate of overall complications (*P* = 0.06, OR = 0.988, 95% CI = 0.837–1.139), although older age (*P* < 0.001, OR = 1.016, 95% CI = 1.011–1.022) and revision surgery (*P* < 0.001, OR = 1.344, 95% CI = 1.193–1.467) were both independent predictors of overall complications.

Multivariate analyses were performed to adjust for potential confounding effects of other variables on the association between deep wound infections in anterior-posterior fusions and BMP use. Covariates included age (continuous variable), revision status, and BMP use. After adjusting for the effects of patient age and revision status, use of BMP remained associated with a higher rate of deep wound infections (*P* = 0.013, OR = 1.839, 95% CI = 1.138–2.973). Older age was also significantly associated with a higher rate of deep wound infections (*P* = 0.024, OR = 1.037, 95% CI = 1.005–1.071), whereas revision surgery was not significantly associated with higher rates of deep wound infection (*P* = 0.413, OR = 0.712, 95% CI = 0.432–1.174).

Multivariate analyses were also performed to adjust for potential confounding effects of other variables on the association between epidural hematoma/seroma in interlaminar/facet fusions. Covariates included age (continuous variable), revision status, and BMP use. None of the covariates were significantly associated with increased incidence of epidural hematoma/seroma (older age: $P = 0.776$, OR = 0.995, 95% CI = 0.961–1.030; revision surgery: $P = 0.167$, OR = 0.356, 95% CI = 0.122–1.038; BMP: $P = 0.051$, OR = 0.345, 95% CI = 0.118–1.006). Thus, after adjusting for the effects of patient age and revision status, there was no significant association between the use of BMP and epidural hematoma/seroma in interlaminar/facet fusions.

DISCUSSION

BMP has quickly become a commonly used adjunct to promote fusion. This is the largest report focusing on complications associated with use of BMP in spinal fusions. Collectively, these data demonstrate a lack of increased overall complications in thoracolumbar and posterior cervical fusions associated with the use of BMP. However, regarding anterior cervical fusions, we confirm that fusions with BMP are associated with higher rates of overall complications and deep and superficial wound infections.¹⁸ As with any procedure, it is important to consider the risk-benefit ratio for each patient individually. In certain cases requiring anterior cervical fusion, it is possible that the benefit of enhanced fusion rates with BMP use may offset its potential risk of increased complications. However this must be evaluated on a case-by-case basis.

It is important to recognize that in the present series, the fusion with and without BMP groups have significant differences. The fusion with BMP group had an older average age and greater proportion of revision procedures that were more often performed for pathologies such as degenerative spinal disease (42% vs. 22%) and spondylolisthesis (29% vs. 19%). This information underscores that differences in the incidence of complications between these two groups may be due to confounding variables including the complexity of the procedures performed or the pathology treated. Notably, despite having older patients and more revision procedures (two factors commonly associated with greater risk of complications), the fusions with BMP (excluding the anterior cervical fusions) had a statistically similar rate of complications compared with fusions without BMP.

Use of BMP in interlaminar/facet fusion was associated with more epidural hematomas; however, multivariate analysis controlling for revision surgery and patient age demonstrated no significant association between any of these factors including BMP use. Similarly, fusion with BMP in adult scoliosis patients was associated with more overall complications; however, multivariate analysis demonstrated no significant association between complications and BMP, after adjusting for the effects of revision surgery and patient age. Finally, anterior/posterior thoracolumbar fusions with BMP were associated with more deep-wound infections than fusions without BMP. Multivariate analysis confirmed that

BMP as well as patient age were independent predictors for deep wound infections among patients undergoing these procedures.

In a recent publication by Cahill *et al*,¹⁸ the authors used the Nationwide Inpatient Sample database to identify complications related to spinal fusion with and without BMP. They reported that 25% of spinal fusions used BMP, which is comparable to the present study (21%). The mean age for fusion with BMP was similar between the two studies, 53 versus 52 years. The fusion without BMP group was considerably younger, 36 years, in our report, in contrast to the study by Cahill *et al*, in which the average age was 53 years. In the previous report, BMP was used more frequently in revision fusions (36.6% vs. 24.3%; $P < 0.001$), which is congruent with our findings (21% vs. 11%).

In the study by Cahill *et al*, they noted that there was no difference in overall complication rates between fusions with and without BMP. They noted that the incidence of wound complications was lowest in anterior cervical fusions without BMP (0.65%) and highest in thoracic fusions without BMP (5.81%). In the present study, fusions without BMP had deep and superficial wound infection rates of 1.6% and 0.9%, respectively. For fusions with BMP, these rates were 1.3% and 1%, respectively.

In the report by Cahill *et al*, thoracic fusions without BMP were associated with the highest incidence of overall complications (17.4%), whereas anterior cervical fusions without BMP were associated with the lowest incidence of complications (4.68%). In this report we note an overall complication rate of 8.4% and 8.5% in fusion without and with BMP, respectively. The highest incidence of complications occurred in kyphosis correction procedures with or without BMP (13.4%), whereas the lowest incidence of complications was associated with fusions for correction of spondylolisthesis (7.5%).

Given the differences in methods of data collection and patient population between these two studies, there are limitations of these comparisons; however, despite these limitations, the study by Cahill *et al* and the present study remain the largest and most rigorous reports related to complications associated with BMP use in spinal fusion.

The present study has several strengths. This is the largest study to date to specifically evaluate complications related to use of BMP in spinal fusion. Furthermore, since all of these cases were submitted during a recent 4-year period, they likely reflect a relatively current standard of care.

Nevertheless, there remain several limitations of this study, as well. There is no documentation of the amount of BMP used in each case. This is a retrospective study and subject to the inherent weaknesses of this methodology. Some key information not in the database includes documentation of medical comorbidities, level of case complexity, and long-term follow-up. One outcome not evaluated is the incidence of pseudarthrosis and related sequelae. In addition, there is currently no method to determine the completeness of data submission or the accuracy of the reporting. It is dependent upon the efforts of the participants. As such, there may be limitations to the completeness of the data, as there is with any large data set.

CONCLUSION

Overall, BMP was used in 21% of all spinal fusions. It was used more commonly in revision spinal fusions and older patients. It was used more commonly in anterior/posterior, anterior thoracolumbar, and TLIF fusion procedures. For thoracolumbar and posterior cervical fusions, its use was not associated with more complications than for fusions that did not use BMP. However, BMP use was associated with more complications in specific instances, including anterior cervical fusions and anterior/posterior fusions. Additional studies incorporating prospective data collection would be useful to further define the relationship between BMP use and complications.

➤ Key Points

- BMP was used in 21% of the 55,862 spinal fusions in this series and more frequently in older patients ($P < 0.001$) and in revision procedures ($P < 0.001$).
- Within the collective group of thoracolumbar and posterior cervical fusions, there were no significant associations between use of BMP and overall complication rate ($P = 0.5$), wound infection rate ($P = 0.8$), or rate of epidural hematoma/seroma ($P = 0.3$).
- Compared with anterior cervical fusions without BMP, anterior cervical fusions that included BMP had a significantly higher rate of overall complications (5.8% vs. 2.4%; $P < 0.001$) and wound infections (2.1% vs. 0.4%; $P < 0.001$). This association remained significant after adjusting for the effects of patient age and whether the surgery was a revision procedure ($P < 0.001$).

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