

BMP and Cancer Risk: Results of a Large, Propensity Matched Study

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Introduction

A number of studies have demonstrated the efficacy of BMP in increasing fusion rates. However, there has been controversy concerning the potential association between use of BMP during spinal fusion surgery and increased risk of cancer. We sought to determine whether use of BMP carried an increased risk of cancer in a national cohort of patients undergoing lumbar fusions.

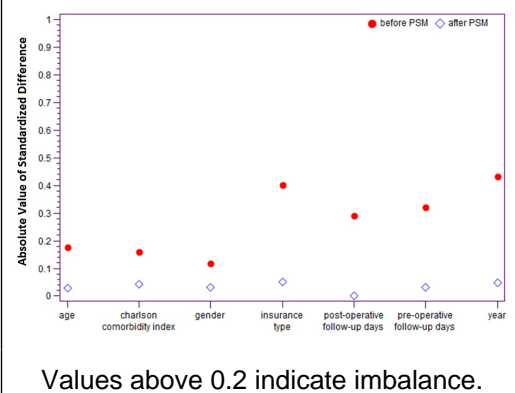
Methods

Reuter's MarketScan database was used to identify patients who had lumbar fusion between 2003 and 2009. Of the 94,166 fusions performed, we excluded those with previous diagnosis of cancer and those with less than 2 years of pre- and post-operative follow-up. The association between BMP and cancer risk was independently probed in the total cohort and a propensity matched cohort in which the non-BMP group was designed to closely resemble the BMP patients on a number of parameters related to demographics, insurance type, and comorbidities, among others. The primary outcome was all-type cancer risk at two or more years following operation.

Characteristics of All Patients and Propensity Matched Cohort

	All patients				Matched cohort			
	All (n=35854)	No BMP use (n=33505)	Yes BMP use (n=2349)	p-value	Matched patients (n=4698)	No BMP use (n=2349)	Yes BMP use (n=2349)	p-value
Age (mean (SD))	56 (12)	56 (12)	54 (12)	<0.001*	54 (12)	54 (12)	54 (12)	0.4246
Pre-operative follow-up days (mean (SD))	1365 (449)	1312 (454)	1194 (361)	<0.001*	1193 (346)	1193 (346)	1194 (361)	0.1808
Post-operative follow-up days (mean (SD))	1504 (552)	1492 (551)	1667 (538)	<0.001*	1659 (552)	1650 (565)	1667 (538)	0.5687
Gender: female [n (%)]	20554 (57.33)	19081 (56.99)	1473 (62.71)	<0.001*	2981 (63.45)	1508 (64.20)	1473 (62.71)	0.2890
Insurance type [n (%)]								
Commercial	25382 (70.79)	23747 (70.88)	1635 (70.79)	<0.001*	3323 (70.73)	1688 (71.86)	1635 (70.79)	0.2039
Medicaid	1891 (5.24)	1592 (4.79)	1991 (8.49)		70 (1.492)	342 (14.56)	1991 (8.49)	
Medicare	8521 (23.77)	8166 (24.37)	8521 (36.77)		674 (14.35)	319 (13.58)	8521 (36.77)	
Charlson index [n (%)]								
0	30652 (85.49)	28770 (85.87)	1882 (80.12)	<0.001*	3801 (80.91)	1919 (81.69)	1882 (80.12)	0.5102
1	4304 (12.00)	3925 (11.74)	369 (15.71)		713 (15.18)	344 (14.64)	369 (15.71)	
2	702 (1.96)	629 (1.88)	73 (3.13)		140 (2.98)	67 (2.85)	73 (3.13)	
3	196 (0.55)	171 (0.51)	25 (1.06)		44 (0.94)	19 (0.81)	25 (1.06)	
Year of initial operation [n (%)]								
2003	3352 (9.35)	3288 (9.81)	64 (2.72)		122 (2.60)	58 (2.47)	64 (2.72)	
2004	3508 (9.78)	3432 (10.24)	76 (3.24)		148 (3.15)	72 (3.07)	76 (3.24)	
2005	6064 (16.94)	6309 (18.92)	525 (22.59)	<0.001*	1079 (22.97)	454 (19.56)	525 (22.59)	0.6156
2006	10705 (29.86)	9940 (29.67)	765 (32.57)		1555 (33.10)	790 (33.63)	765 (32.57)	
2007	11425 (31.87)	10506 (31.36)	919 (39.12)		1794 (38.19)	875 (37.25)	919 (39.12)	

Improved Covariate Balance in Propensity Matched Cohort



All-type Cancer Diagnoses After BMP

Post-fusion outcome	All patients				Matched cohort			
	All (n=35854)	No BMP use (n=33505)	Yes BMP use (n=2349)	p-value	All patients (n=4698)	No BMP use (n=2349)	Yes BMP use (n=2349)	p-value
All-type cancer [n (%)]	3034 (8.46)	2814 (8.40)	220 (9.37)	0.1036	406 (8.64)	186 (7.92)	220 (9.37)	0.0775
Lip, oral, cavity, and pharynx [n (%)]	23 (0.09)	22 (0.07)	6 (0.26)	0.0007*	8 (0.17)	2 (0.09)	6 (0.26)	0.2866
Digestive organs and peritoneum [n (%)]	233 (0.65)	224 (0.67)	9 (0.38)	0.0061	18 (0.38)	9 (0.38)	9 (0.38)	1.0000
Respiratory and intra-thoracic organs [n (%)]	205 (0.57)	193 (0.58)	12 (0.51)	0.6855	23 (0.49)	11 (0.47)	12 (0.51)	0.8344
Bone, connective tissue, skin, breast and genitourinary organs [n (%)]	676 (1.89)	644 (1.92)	32 (1.36)	0.0538	68 (1.45)	36 (1.53)	32 (1.36)	0.6251
Other and unspecified sites [n (%)]	359 (1.00)	335 (1.00)	24 (1.02)	0.9181	44 (0.94)	20 (0.85)	24 (1.02)	0.5446
Lymphatic, hematopoietic tissue and neuroendocrine tumors [n (%)]	135 (0.38)	124 (0.37)	11 (0.47)	0.4526	15 (0.32)	4 (0.17)	11 (0.47)	0.0703
Benign neoplasms [n (%), aOR (95% CI)]	1743 (4.86)	1596 (4.76)	147 (6.26)	0.0011*	261 (5.56)	114 (4.85)	147 (6.26)	0.0356*
Carcinoma in situ, neoplasms of uncertain behavior, neoplasms of unspecified nature [n (%)]	640 (1.79)	594 (1.77)	46 (1.96)	0.5118	80 (1.92)	44 (1.87)	46 (1.96)	0.8314

Risk Factors for Cancer Diagnosis in Total Cohort

	All-type cancer aOR (95% CI)	Benign tumors aOR (95% CI)
BMP (1 vs. 0)	1.112 (0.961, 1.287)	1.254 (1.051, 1.496)
Age (1 year increase)	1.016 (1.011, 1.021)	0.996 (0.991, 1.002)
Charlson (1 unit increase)	1.123 (1.051, 1.201)	1.050 (0.957, 1.151)
Insurance type (Medicaid vs. commercial)	1.499 (1.286, 1.748)	1.549 (1.288, 1.861)
Insurance type (Medicare vs. commercial)	1.127 (0.995, 1.277)	1.045 (0.886, 1.233)

Odds ratios have been adjusted for age, sex, comorbidities, and insurance type

Benign Tumor Diagnoses After BMP in Total Cohort

Benign Tumor Type	All patients			Matched cohort		
	All (n=35854)	No BMP use (n=33505)	Yes BMP use (n=2349)	All patients (n=4698)	No BMP use (n=2349)	Yes BMP use (n=2349)
All-type benign neoplasms [n (%)]	1743 (4.86)	1596 (4.76)	147 (6.26)	261 (5.56)	114 (4.85)	147 (6.26)
Lip, oral, pharynx [n (%)]	15 (0.04)	14 (0.04)	1 (0.04)	1 (0.04)	1 (0.04)	1 (0.04)
Other part of digestive tract [n (%)]	464 (1.29)	436 (1.30)	28 (1.19)	28 (1.19)	28 (1.19)	28 (1.19)
Respiratory and intra-thoracic [n (%)]	50 (0.14)	46 (0.14)	4 (0.17)	4 (0.17)	4 (0.17)	4 (0.17)
Bone and articular cartilage [n (%)]	89 (0.25)	79 (0.24)	10 (0.43)	10 (0.43)	10 (0.43)	10 (0.43)
Lipoma [n (%)]	51 (0.14)	48 (0.14)	3 (0.13)	3 (0.13)	3 (0.13)	3 (0.13)
Connective and soft tissue [n (%)]	38 (0.11)	35 (0.10)	3 (0.13)	3 (0.13)	3 (0.13)	3 (0.13)
Skin [n (%)]	29 (0.08)	26 (0.08)	3 (0.13)	3 (0.13)	3 (0.13)	3 (0.13)
Breast [n (%)]	10 (0.03)	10 (0.03)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Leiomyoma [n (%)]	636 (1.77)	575 (1.72)	61 (2.60)	61 (2.60)	61 (2.60)	61 (2.60)
Other benign uterine neoplasm [n (%)]	34 (0.09)	29 (0.09)	5 (0.21)	5 (0.21)	5 (0.21)	5 (0.21)
Other benign female genital organ [n (%)]	27 (0.08)	27 (0.08)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Male genital organs [n (%)]	7 (0.02)	7 (0.02)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Ovary [n (%)]	141 (0.39)	130 (0.39)	11 (0.47)	11 (0.47)	11 (0.47)	11 (0.47)
Kidney and urinary tract	23 (0.06)	23 (0.07)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Eye	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Brain and other nervous system	124 (0.35)	105 (0.31)	19 (0.81)	19 (0.81)	19 (0.81)	19 (0.81)
Endocrine glands and related structures	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Hemangioma and lymphangioma, any site	36 (0.10)	29 (0.09)	7 (0.30)	7 (0.30)	7 (0.30)	7 (0.30)
Benign tumors of other unspecified sites	55 (0.15)	46 (0.14)	9 (0.38)	9 (0.38)	9 (0.38)	9 (0.38)

Results

The propensity matched cohort comprised a set of 2349 patients who underwent fusion with BMP and a matched group of 2349 without BMP. The covariate balance was markedly improved in the propensity matched cohort. In this cohort, the all-type cancer risk was not significantly different between the patients who did not get BMP and those who did (7.92% vs. 9.37%, p= 0.0775). In both the propensity matched and total cohorts, BMP use was associated with an increase in benign tumor diagnoses (propensity matched cohort: aOR=1.31, 95% CI: 1.02, 1.66, p = 0.035). When those benign tumor diagnoses were stratified in the total cohort, BMP was associated with increases in the frequency of the diagnosis of leiomyomas, benign hemangiomas/lymphangiomas, benign brain/nervous system tumors, and benign tumors of unspecified sites.

Conclusions

In a large, independent, propensity matched cohort, the use of BMP in lumbar fusions was associated with an increased risk of benign tumor diagnoses. The risk of malignant tumors was not significantly different between BMP-treated and non-treated patients.