Factors predicting opioid dependence in patients undergoing surgery for degenerative spondylolisthesis: analysis from the MarketScan databases

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OBJECTIVE The opioid crisis is identified as a national emergency and epidemic in the United States. The aim of this study was to identify risk factors associated with opioid dependence in patients undergoing surgery for degenerative spondylolisthesis (DS).

METHODS The authors queried MarketScan databases to investigate the factors affecting postsurgery opioid use in patients with DS between 2000 and 2012. The outcome of interest was opioid dependence, which was defined as continued opioid use, > 10 opioid prescriptions, or diagnosis of or prescription for opioid dependence disorder in the period of 1 year before or 3–15 months after the procedure. Comparisons of outcomes were performed using nonparametric 2-group tests and generalized regression models.

RESULTS A cohort of 10,708 patients was identified from the database. The median patient age was 61 years (interquartile range 54–69 years), and 65.1% were female (n = 6975). A majority of patients had decompression with fusion (n = 10,068; 94%) and underwent multilevel procedures (n = 8123; 75.9%). Of 10,708 patients, 14.85% (n = 1591) were identified as having opioid dependence within 12 months prior to the index surgical procedure and 9.90% (n = 1060) were identified as having opioid dependence within 3–15 months after the procedure. Of all the variables, prior opioid dependence (OR 16.29, 95% CI 14.10–18.81, p < 0.001) and younger age (1-year increase in age: OR 0.972, 95% CI 0.963–0.980, p < 0.001) were independent predictors of opioid dependence following surgery for DS. The use of fusion was not associated with opioid dependence following the procedure (p = 0.8396). Following surgery for DS, patients were more likely to become opioid independent than they were to become opioid dependent (8.54% vs 3.58%, p < 0.001).

CONCLUSIONS The majority of patients underwent fusion for DS. Surgical decompression with fusion was not associated with increased risk of postsurgery opioid dependence in patients with DS. Overall, opioid dependence was reduced by 4.96% after surgery for DS. Prior opioid dependence is associated with increased risk and increasing age is associated with decreased risk of opioid dependence following surgery for DS.

<https://thejns.org/doi/abs/10.3171/2018.1.SPINE171258>

KEYWORDS lumbar decompression; fusion; opioid; degenerative spondylolisthesis

THE opioid crisis is identified as a national emergency and epidemic in the United States.¹ More than 12 million people misuse prescription opioids, and prescription opioid overdose is a leading cause of drug overdose-related deaths (60.9%) in this country.²³ Given the extent of this health care problem, it is imperative to

understand the risk factors predictive of long-term opioid dependence and to take necessary steps in curtailing this opioid epidemic.

The aim of this study was to identify risk factors associated with opioid dependence in patients undergoing surgery for degenerative spondylolisthesis (DS), which

ABBREVIATIONS CI = confidence interval; CPT-4 = *Current Procedural Terminology, Fourth Edition*; DS = degenerative spondylolisthesis; ICD-9-CM = *International Classification of Diseases, Ninth Revision, Clinical Modification*; IQR = interquartile range; OR = odds ratio; RR = relative risk.

SUBMITTED November 20, 2017. **ACCEPTED** January 11, 2018.

INCLUDE WHEN CITING Published online June 19, 2018; DOI: 10.3171/2018.1.SPINE171258.

is a frequent cause of spinal stenosis in elderly patients (male patients mean age 68 years and females mean age 71 years), affecting primarily Caucasian women (5 times higher than men) with an estimated prevalence of approximately 6%.¹³ The Spine Patient Outcomes Research Trial (SPORT) reported superior outcomes at the 2-year follow-up for surgical compared to nonsurgical management of patients with DS.²⁹ However, there is a lack of consensus regarding what type of surgical procedure provides the most effective treatment for DS, and commonly used procedures include laminectomy or decompression with or without fusion. In a recent randomized controlled trial, patients with grade 1 DS treated with laminectomy and posterolateral fusion had superior physical health–related quality of life (based on responses to the SF-36) at the 4-year follow-up compared to patients treated with laminectomy alone.¹² Interestingly, another randomized Swedish study showed no significant differences in outcomes at the 2- and 5-year follow-up after either decompression alone or decompression with fusion in patients with spinal stenosis with or without spondylolisthesis.¹¹ Despite this controversy regarding choice of treatment, a majority of patients with DS in the United States are managed with decompression combined with fusion.^{14,19} Opioids are commonly prescribed following common spine surgeries (discectomy, decompression, lumbar posterolateral arthrodesis, or lumbar interbody arthrodesis) and this use of prescription opioids may lead to prolonged use in only a minority of patients (0.1% at 6 months),²⁴ in particular those with prior opioid dependence or preexisting mental health disorders such as depression.^{4,7,20,24} A recent study using a commercial insurance database showed that re-fusion lumbar spine surgeries were associated with increased risk and anterior lumbar fusion was associated with decreased risk of opioid dependence following lumbar fusion surgeries.⁶ The use of minimally invasive procedures has been shown to reduce the duration of postoperative narcotic use to half (median 2 weeks vs 4 weeks) and result in shorter hospital stays compared to open procedures for DS.^{2,20}

Recently, there has been a surge in the use of national databases to query a variety of questions aiming to increase understanding of national trends and evaluate the efficacy of treatment modalities.^{3,7,8,18,25} In this study we used information from available databases to investigate factors that may increase the risk of opioid dependence in patients undergoing surgical treatment for DS. To the best of our knowledge, this is the first study focusing on the risk factors associated with opioid dependence in this patient population with DS, which is a common clinical problem associated with significant health care utilization.²⁶

Methods

Data Sources

We used the MarketScan Commercial claims and encounters, Medicare Supplemental, and Multi-State Medicaid databases to investigate the impact of surgery on opioid use in patients with DS ([https://truvenhealth.com/markets/life-sciences/products/data-tools/marketscan-](https://truvenhealth.com/markets/life-sciences/products/data-tools/marketscan-databases)

databases). The MarketScan databases capture patient-level data on clinical utilization, insurance enrollment, and costs linked with detailed patient, provider, and facility information. The databases include longitudinal data grouped into multiple files, including inpatient, outpatient, and prescription medication, and use an encrypted ID for each individual, which serves as a unique identifier and a linkage variable across different files.¹⁰ The information in the MarketScan databases is obtained from paid patient health insurance claims from approximately 100 data sources and is available for purchase from Truven Health Analytics–IBM Watson Health. Included are data for covered individuals and their dependents. Patient information enters the databases when patients enroll in health insurance coverage and exits when that enrollment ends; patient interactions with the health care system are captured in the MarketScan data through their claims. These data have been used extensively in comparative effectiveness research in the medical field since 1990.

Patient Selection and Inclusion/Exclusion Criteria

From the inpatient admission tables, we extracted data on patients with a primary diagnosis of acquired lumbar spondylolisthesis (ICD-9-CM [*International Classification of Diseases, Ninth Revision, Clinical Modification*] code 738.4) and concurrent procedures of either a decompression-only procedure or decompression with fusion. Another inclusion criterion was age 18 years or older at the time of index hospitalization. Exclusion criteria were pregnancy, intraspinal abscess, osteomyelitis, fracture, vertebral dislocation, accidents, or pelvic instrumentation during the index procedure. Also, data on patients lacking medical records for the period of 1 year presurgery to 2 years postsurgery were excluded (Fig. 1).

Calculation of Follow-Up Time

Preoperative follow-up time was calculated as the time difference between the start of enrollment and the index hospitalization admission. If the start enrollment time was not available because the enrollment started prior to our data window, the beginning of our data window—January 1, 2000—was used. Similarly, postoperative follow-up time was calculated as the difference between the index hospitalization discharge date and the end of enrollment. If the end of enrollment fell outside of the data period, we used December 31, 2012, which was the last date of our data window.

Explanatory Variables

We used baseline characteristics at the index hospitalization as the explanatory variables. These were age, sex, year of index hospitalization, preoperative follow-up months, postoperative follow-up months, insurance type (commercial, Medicaid, or Medicare), comorbidities, instrumentation, and number of spinal levels. Comorbidities were measured with the Elixhauser comorbidity score,⁹ computed using an adaptation to ICD-9-CM codes developed by Quan et al.²¹ The Elixhauser score is an index that quantifies the burden of comorbidities abstracted from medical or claims records using ICD codes. A total

of 30 comorbidities are checked as being present or not (present = 1, absent = 0) and cumulated to provide a comorbidity score. To check whether instrumentation was used, we screened the CPT-4 (*Current Procedural Terminology, Fourth Edition*) procedure codes 22840–22847. Cases were classified as fusion involving multiple spinal levels (≥ 2 levels) if the following codes were found: ICD-9 codes 81.62, 81.63, 81.64, and/or CPT-4 codes 22585, 22632, 22614, 63035, 63044, 63048, 63057, 63103, and 22842–22847.

Postoperative Outcome Variables

The current study aimed to identify factors predictive of postsurgery opioid dependence.

Opioid Use

Our interest was to evaluate opioid dependence postsurgery (in the period from 3 to 15 months postdischarge). However, we also looked at use prior to surgery (within 12 months before admission) in order to identify new dependence. Patients were classified as having opioid dependence if they had a diagnosis of opioid use disorder (ICD-9 305.50, 305.55, 305.52, 304.00, 304.01, 304.02, 304.70, 304.71, or 304.72),⁶ obtained a prescription for a medication used to treat opioid use disorder (buprenorphine or naltrexone), were counseled about psychological and pharmacological treatment options for opioid addiction (CPT-4 4306F),⁶ or had at least 10 prescriptions^{7,17,22,28} of opioid drugs (buprenorphine, butorphanol, codeine phosphate, dihydrocodeine, fentanyl citrate, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine sulfate, nalbuphine, opium alkaloids, oxycodone, oxymorphone, pentazocine, propoxyphene, tapentadol, tramadol, or naltrexone)¹⁶ in the look-up period (12 months prior to admission for presurgery dependence and 3–15 months^{5,28} after discharge for postsurgery dependence).

Statistical Analysis

We summarized continuous variables using means and standard deviations, medians and interquartile ranges, and full ranges (minimum to maximum). Categorical variables were summarized using counts and percentages.

To compare the patient characteristics and outcomes among different procedure groups, we used linear regression on logged values for continuous variables and logistic regression for categorical variables.¹⁵ The models included the procedure group as well as age, sex, insurance type (commercial, Medicaid, or Medicare), Elixhauser comorbidity score, presence of instrumentation, and whether multiple levels were involved as independent variables. We used the software SAS 9.4 (SAS Institute, Inc.) for data preparation and data analysis.²⁷

Results

Patient Demographics

A total of 10,708 patients with a diagnosis of degenerative spondylolisthesis (DS) who underwent a surgical procedure were identified from the MarketScan databases.

FIG. 1. Flowchart showing the inclusion and exclusion criteria used for extracting data from the MarketScan databases.

The median patient age was 61 years (interquartile range [IQR] 54–69 years). A majority of the patients were female ($n = 6975$, 65.1%). Commercial insurance was the most common insurance type (61.4%, $n = 6571$), followed by Medicare (35%, $n = 3746$). Less than half of the patients (46%, $n = 4954$) had an Elixhauser comorbidity score of 0, and a minority (8.07%, $n = 864$) had a comorbidity index of 3+. Most of the patients underwent decompression with fusion ($n = 10,068$, 94%), and approximately three-quarters had multilevel procedures ($n = 8,123$, 75.9%).

Demographic and clinical characteristics of the patients who underwent surgical treatment for DS are shown in Table 1.

Opioid Dependence

The incidence of postsurgery opioid dependence gradually increased from 11.67% (2001) to 16.12% (2011) among patients who were opioid dependent prior to the surgical procedure and from 6.67% (2001) to 10.81% (2011) among patients who were opioid independent prior to the surgery (Fig. 2). A total of 1591 patients (14.85%) were identified to have opioid dependence within 12 months prior to the index surgical procedure and 1060 (9.90%) were identified to have opioid dependence within 3–15 months after the procedure. A majority of patients (90.1%, $n = 9648$) were opioid independent following the surgical procedure. Following surgery for DS, opioid-dependent patients were 2 times more likely to become opioid independent than opioid-independent patients were likely to become opioid dependent (8.54% vs 3.58%, odds ratio [OR] 2.39, 95% confidence interval [CI] 2.12–2.69, $p < 0.0001$; Fig. 3).

Factors Predicting Opioid Dependence Following Surgery for DS

Comparison of demographic and clinical characteris-

TABLE 1. Summary of patient demographic and clinical characteristics

Variable	Combined Cohort, n = 10,708	Postsurgery Opioid Dependence		p Value
		No, n = 9648 (90.1%)	Yes, n = 1060 (9.90%)	
Age, yrs				<0.0001
Mean (SD)	60.7 (11.9)	61.1 (11.8)	57.0 (12.1)	
Median (IQR)	61.0 (54.0–69.0)	61.0 (54.0–70.0)	57.0 (49.0–65.0)	
Range, min–max	18.0–95.0	18.0–95.0	20.0–92.0	
Sex: female, n (%)	6975 (65.1%)	6244 (64.7%)	731 (69.0%)	0.0059
Insurance, n (%)				<0.0001
Commercial	6571 (61.4%)	5854 (60.7%)	717 (67.6%)	
Medicaid	391 (3.65%)	322 (3.34%)	69 (6.51%)	
Medicare	3746 (35.0%)	3472 (36.0%)	274 (25.8%)	
Elixhauser index, n (%)				0.0825
0	4954 (46.3%)	4441 (46.0%)	513 (48.4%)	
1	3386 (31.6%)	3064 (31.8%)	322 (30.4%)	
2	1504 (14.1%)	1376 (14.3%)	128 (12.1%)	
3+	864 (8.07%)	767 (7.95%)	97 (9.15%)	
Surgery: decompression, n (%)				0.6022
w/o fusion	640 (5.98%)	597 (6.19%)	43 (4.06%)	
w/ fusion	10,068 (94.0%)	9051 (93.8%)	1017 (95.9%)	
Multilevel surgery, n (%)	8123 (75.9%)	7312 (75.8%)	811 (76.5%)	

Max = maximum; min = minimum; SD = standard deviation.

Boldface type indicates statistical significance.

tics of patients with and without opioid dependence following surgery showed that younger age, female sex, and having commercial insurance were associated with opioid dependence following surgery (median age 57 vs 61 years, $p < 0.0001$; female sex 69% vs 64.7%, $p = 0.0059$; and commercial insurance 67.6% vs 60.7%, $p < 0.0001$). Comorbidity index and type of surgical procedure had no association with postsurgery opioid dependence on univariable analysis ($p > 0.05$, Table 1).

Of all the variables, prior opioid dependence (OR 16.29,

95% CI 14.10–18.81, $p < 0.001$) and younger age (1-year increase in age: OR 0.972, 95% CI 0.963–0.980, $p < 0.001$) were independent predictors of opioid dependence following surgery for DS. Type of surgical procedure (decompression alone or decompression with fusion) showed an association with postsurgery opioid dependence on univariable analysis (6.72% vs 10.10%, $p = 0.0009$; Fig. 4 and Table 2). Also, 41.9% of patients who were not opioid dependent before surgery became opioid dependent following decompression without fusion compared to 35.90% of

FIG. 2. Bar graph showing the temporal trends (2001–2011) in the incidence of postoperative opioid dependence among patients who were previously opioid dependent vs those who were not previously opioid dependent following surgery for DS.

FIG. 3. Flowchart showing changes in opioid dependence among patients who underwent surgery for DS. Figure is available in color online only.

patients who underwent decompression with fusion ($p > 0.05$, Fig. 5). However, on adjusted multivariable analysis, the use of fusion was not associated with opioid dependence following the procedure (OR 1.038, 95% CI 0.726–1.483, $p = 0.8396$). Elixhauser comorbidity score, type of insurance, and number of levels treated had no significant association with opioid dependence following surgery for DS (Table 3).

Discussion

Using the MarketScan databases, we found that 90.1% of all patients were opioid independent following DS surgery compared to 85.15% prior to surgery. Patients were twice as likely to become opioid independent after surgery as they were to become opioid dependent (OR 2.39, 95% CI 2.12–2.69, $p < 0.001$). Prior opioid dependence and young age were independent predictors of opioid dependence following surgery for DS. Type of surgical procedure had no impact on postsurgery opioid dependence.

In our study, 14.85% of patients were reported to be opioid dependent 1 year before surgery, and 9.90% were opi-

oid dependent 3–15 months after surgery. A recent study based on commercial insurance claims reported continued narcotic utilization in 62% of patients more than 1 year following lumbar fusion surgery.¹⁸ However, the number of patients with opioid dependence prior to the surgery was not reported in that study. In contrast, we found that a majority of patients (90.1%) were opioid independent after surgery for DS. Also, patients were twice as likely to become opioid independent following surgery for DS. In a recent study, Schoenfeld et al.²⁴ used the TRICARE insurance claim database to investigate factors predictive of opioid dependence in patients ($n = 9991$) undergoing spinal surgery for a variety of lumbar pathologies, including spondylolisthesis ($n = 252$) in opioid-naïve patients. In this study the authors reported that 1% of patients continued opioid use at 3 months and 0.1% continued use at 6 months postsurgery. They also reported that patients who underwent low-intensity surgical procedures, such as discectomy and decompression, were more likely to be opioid independent than those who underwent fusion procedures (HR 1.43 and 1.34, respectively). In our study we found that 3.58% of patients became opioid dependent after the

FIG. 4. Bar graph showing the rate of opioid dependence before and after surgery in the combined cohort, in patients who underwent decompression without fusion, and in patients who underwent decompression with fusion for DS.

TABLE 2. Opioid dependence before and after surgery stratified by type of surgical procedure

Opioid Dependence Group	Combined Cohort, n = 10,708 (100%)	Decompression		p Value
		w/o Fusion, n = 640 (5.98%)	w/ Fusion, n = 10,068 (94.02%)	
Previously nondependent pts who remained nondependent, n (%)	8734 (81.6%)	560 (87.5%)	8174 (81.2%)	0.0009
Previously nondependent pts who became dependent, n (%)	383 (3.58%)	18 (2.81%)	365 (3.63%)	
Previously dependent pts who became nondependent, n (%)	914 (8.54%)	37 (5.78%)	877 (8.71%)	
Previously dependent pts who remained dependent, n (%)	677 (6.32%)	25 (3.91%)	652 (6.48%)	

Pts = patients.

Boldface type indicates statistical significance.

surgical procedure for DS; 95.3% (n = 365) of these patients had decompression with fusion, and 4.7% (n = 18) had only decompression. Therefore overall, only 0.16% of patients became opioid dependent following decompression only for DS, which is in concordance with the findings of the above-mentioned study.²⁴ Schoenfeld et al. also identified depression as a factor associated with decreased likelihood of opioid independence following spinal surgery, which was also reported by Connolly et al.⁷ In contrast, we did not find any association between various comorbidities and opioid dependence in our study. This difference may be attributable to the highly selective patient population in our study—patients with a diagnosis of DS who underwent surgery treatment for that condition—compared to patients undergoing lumbar fusion procedures for a variety of spinal pathologies in the studies by Schoenfeld et al.²⁴ and Connolly et al.⁷

Another study based on a commercial insurance database reported that the duration of opioid use before surgery was significantly associated with an increased risk of long-term opioid dependence after lumbar fusion surgery.⁷ Patients using opioids for 1–22 days or more than 250 days prior to the surgery were 2.27 and 219 times, respectively, more likely to be opioid dependent after lumbar fusion surgery.⁷ This study also reported that anterior fusion was

associated with decreased risk and 360° fusion was associated with increased risk (compared to posterior fusion) of long-term opioid dependence following the procedure. Similarly, Armaghani et al.⁴ reported that young age, anxiety disorder, and increased preoperative opioid use were associated with increased opioid use during the immediate postoperative period, and major surgical procedure, revision procedure, anxiety, and increased preoperative opioid use were associated with increased opioid dependence at 12 months postsurgery. In concordance, we found that patients who were opioid dependent prior to the surgery were likely to remain dependent following the surgery (relative risk [RR] 16.29, $p < 0.0001$). However, type of surgical procedure had no impact on opioid dependence in our study. Also, we found that patients with increasing age were less likely to be opioid dependent following surgery for DS. This difference may be due to the different patient population in our study.

Strengths and Limitations of the MarketScan Databases

The advantages of using a nationwide collection of databases such as MarketScan include a larger sample size, which provides comprehensive overview of data relevant to the research question throughout the United States. Although retrospective in nature, these databases are based

FIG. 5. Bar graph showing the percentage of patients who were opioid dependent after surgery (previously opioid dependent vs not previously opioid dependent) in the combined cohort, in patients who underwent decompression without fusion, and in patients who underwent decompression with fusion for DS.

TABLE 3. The adjusted effect of patient characteristics on postoperative opioid dependence

Variable	Postsurgery Opioid Dependence	
	RR (95% CI)	p Value
Presurgery opioid dependent vs not	16.29 (14.10–18.81)	<0.0001
Age, 1-yr increment	0.972 (0.963–0.980)	<0.0001
Sex: female vs male	1.166 (0.998–1.362)	0.0536
Insurance		
Medicaid vs commercial	1.337 (0.960–1.863)	0.2275
Medicare vs commercial	1.170 (0.929–1.474)	0.9344
Elixhauser score		
1 vs 0	0.956 (0.808–1.131)	0.8980
2 vs 0	0.864 (0.686–1.088)	0.2038
3+ vs 0	1.045 (0.800–1.365)	0.4134
Decompression, w/ vs w/o fusion	1.038 (0.726–1.483)	0.8396
Multilevel vs single-level surgery	1.107 (0.931–1.316)	0.2506

Boldface type indicates statistical significance.

on insurance claims, which mitigate the issue of selection bias while providing a large sample size. MarketScan provides longitudinal information, which includes inpatient and outpatient services, medication refills, and costs.

Apart from our study's inherent limitations of being retrospective, the reliance on data from the MarketScan databases also entails limitations. The insurance claims from which the MarketScan data were acquired were used to bill for in-hospital procedures and outpatient medicine prescriptions, which may not reflect the actual clinical decision-making process used in specific cases or potential confounding variables that affect outcomes. Thus the data may not provide an accurate representation of a problem. The clinical profile of the patients, including additional procedures or clinical diagnosis during the follow-up after the surgery, cannot be determined using this database. Also, claims databases cannot be used to determine the factors that may be associated with opioid dependence such as alcohol/tobacco dependence/abuse and socioeconomic status. However, our study is representative of real-world clinical practice. Potential coding errors and inability to obtain information about the severity and duration of the clinical problem as well as the severity of postoperative complications and quality of life at follow-up are other limitations of such a database. One of the definitions of opioid dependence was based on medication refills prescribed by the physicians for the patients enrolled in the insurance plans. The patients may not have consumed these opioid medications on the refill date, and our analysis may thus overestimate the dependence if there was a delay in actually starting the medications or if they did not consume at all; accordingly, the dependence may have been underestimated in cases in which patients consumed the medications on the same date or beyond the dose prescribed by the physician. Data regarding preoperative and postoperative consumption of morphine equivalents were not included in this database. Also, illegal procurement of opioids is not captured by this database, which may also lead to underestimation of dependence. Nevertheless, our

study provides insight into the national trends and factors predictive of opioid dependence following surgical procedures for DS in the United States.

Conclusions

The majority of patients underwent fusion for DS. Surgical decompression with fusion was associated with decreased postsurgery opioid dependence in patients with DS. Prior opioid dependence is associated with increased risk and increasing age is associated with decreased risk of opioid dependence following surgery for DS. Patients who underwent surgery for DS were twice as likely to become opioid independent as they were to become opioid dependent.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Sharma. Acquisition of data: Ugiliweneza. Analysis and interpretation of data: Sharma. Drafting the article: Sharma. Critically revising the article: Boakye, Sharma, Nuño, Drazin. Reviewed submitted version of manuscript: all authors. Statistical analysis: Ugiliweneza. Administrative/technical/material support: Boakye. Study supervision: Boakye.

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