Characterizing the risk and outcome profiles of lumbar fusion procedures in patients with opioid use disorders: a step toward improving enhanced recovery protocols for a unique patient population

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OBJECTIVE The authors set out to conduct the first national-level study assessing the risks and outcomes for different lumbar fusion procedures in patients with opioid use disorders (OUDs) to help guide the future development of targeted enhanced recovery after surgery (ERAS) protocols for this unique population.

METHODS Data for patients with or without OUDs who underwent an anterior lumbar interbody fusion (ALIF), posterior lumbar interbody fusion (PLIF), or lateral transverse lumbar interbody fusion (LLIF) for lumbar disc degeneration (LDD) were collected from the 2013–2014 National (Nationwide) Inpatient Sample database. Multivariable logistic regression was implemented to analyze how OUD status impacted in-hospital complications, length of hospital stay, discharge disposition, and total charges by procedure type.

RESULTS A total of 139,995 patients with LDD were identified, with 1280 patients (0.91%) also having a concurrent OUD diagnosis. Overall complication rates were higher in OUD patients (48.44% vs 31.01%, $p < 0.0001$). OUD patients had higher odds of pulmonary ($p = 0.0006$), infectious ($p < 0.0001$), and hematological ($p = 0.0009$) complications. Multivariate regression modeling of outcomes by procedure type showed that after ALIF, OUD patients had higher odds of nonhome discharge ($p = 0.0007$), extended hospitalization ($p = 0.0002$), and greater total charges ($p = 0.0054$). This analysis also revealed that OUD patients faced higher odds of complication ($p = 0.0149$ and $p = 0.0471$), extended hospitalization ($p = 0.0439$ and $p = 0.0001$), and higher total charges ($p < 0.0001$ and $p < 0.0001$) after PLIF and LLIF procedures, respectively.

CONCLUSIONS Obtaining a better understanding of the risks and outcomes that OUD patients face perioperatively is a necessary step toward developing more effective ERAS protocols for this vulnerable population. This study, which sought to characterize the outcome profiles for lumbar fusion procedures in OUD patients on a national level, found that this population tended to experience increased odds of complications, extended hospitalization, nonhome discharge, and higher total costs. Results from this study warrant future prospective studies to better the understanding of these associations and to further the development of better ERAS programs that may improve patient care and reduce cost burden.

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KEYWORDS opioid use disorders; lumbar disc degeneration; enhanced recovery; spine surgery; National Inpatient Sample

RECOVERY after spine surgery can be a complex process involving postoperative pain, mobilization, return to work, quality of life, and overall patient outcome. One of the challenges of recovery after surgery is the large dependence that both providers and patients

have for opioid analgesics. Recently, providers have been moving toward enhanced recovery after surgery (ERAS) multimodal systems that emphasize the importance of a multidisciplinary approach, improvement in outcomes, and reduction in cost. ERAS emphasizes the reduction of

ABBREVIATIONS ALIF = anterior lumbar interbody fusion; APR-DRG = All Patient Refined Diagnosis-Related Groups; ERAS = enhanced recovery after surgery; HCUP = Healthcare Cost and Utilization Project; ICD-9-CM = *International Classification of Diseases, Ninth Edition, Clinical Modification*; LLIF = lateral transverse lumbar interbody fusion; LDD = lumbar disc degeneration; NIS = National (Nationwide) Inpatient Sample; OUD = opioid use disorder; PLIF = posterior lumbar interbody fusion.

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opioid analgesics for a number of reasons, including reduction in opioid dependence, reduced length of stay, improved postoperative pain, and reduction in postoperative ileus.¹⁷

Since the founding of the ERAS society in the early 2000s, numerous studies have been published with efforts to improve postoperative outcomes by reducing opioid analgesic use. The development of new pain medication regimens and recovery pathways found a reduction in postoperative opioid use, earlier ambulation, and lower instances of nausea, sedation, and dizziness.^{9,22,35} Preoperative chronic opioid use has a clear influence on postoperative outcomes and is a growing problem that must be addressed when developing new ERAS systems.

Patients with opioid use disorders (OUDs) display problematic patterns of opioid consumption and represent a population that is particularly susceptible to opioid misuse after discharge. Patients with OUDs require additional considerations in preoperative planning and in developing new ERAS protocols for effective management in the perioperative period, which must inherently account for the unique risks and adverse outcomes faced by this population during their hospitalizations. Unfortunately, the perioperative period is a very vulnerable time for OUD patients, and there is a dearth of knowledge pertaining to the specific risks and outcomes they face during this time.³⁶ This has, to an extent, limited the ability of ERAS protocols to provide optimal care for this patient population.

Increased preoperative opioid consumption is associated with worse patient-reported outcomes in cervical, thoracolumbar, and lumbar spine surgery to treat structural disease.¹⁶ Increased opioid dependence, morbidity, and mortality in patients with preoperative opioid use was found across a number of studies for both spine and orthopedic procedures.^{1,24,37} For several years, the use of surgical fusion procedures to treat lumbar stenosis and degenerative disease has been steadily increasing.^{18,19} These procedures are performed anteriorly (anterior lumbar interbody fusion [ALIF]), posteriorly (posterior lumbar interbody fusion [PLIF]), laterally (lateral transverse lumbar interbody fusion [LLIF]), and transforaminally (transforaminal lumbar interbody fusion). While previous studies have examined the influence of preoperative chronic opioid use on the complications and outcomes in PLIF procedures,¹⁴ none have comprehensively assessed and compared the influence of OUDs on outcomes for various approaches of lumbar fusion procedures. Furthermore, no study has determined outcome profiles for these procedures on a national level for the purpose of influencing new enhanced recovery protocols in spine surgery for patients with OUDs.

Methods

Data Source

Data from 2013 to 2014 were obtained from the National (Nationwide) Inpatient Sample (NIS) of the Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality. The NIS has data for over 7 million hospitalizations per year, making it the largest all-payer national database. The NIS consists of a stratified sample of 20% of nonfederal hospitals in the United

States. To obtain regional and national estimates, an encoded weighting variable was applied that accounts for the stratified clustered sampling of the database, as specified by HCUP (<https://www.hcup-us.ahrq.gov/nisoverview.jsp>). Our institutional review board has exempted studies involving the NIS from individual review.

Inclusion Criteria and Patient Stratification

Patients were included if they had an *International Classification of Diseases, Ninth Edition, Clinical Modification* (ICD-9-CM) diagnosis code of lumbar disc degeneration (LDD; ICD-9-CM code 722.52). Patients were included in the OUD population if they had a diagnosis code for opioid dependence (304.00–304.03, 304.70–304.73) or nondependent opioid abuse (305.50–305.53) along with the code for LDD. In some analyses, patients were stratified based on the procedure type performed for lumbar spinal correction. This was done using procedure codes for primary or repeat ALIF (81.06, 81.36), PLIF (81.07, 81.37), or LLIF (81.08, 81.38).

Covariates

Data were obtained on patients' age, sex, race, hospital division, admission type, comorbidities, primary payer status, discharge status, median income by ZIP code, and All Patient Refined Diagnosis-Related Groups (APR-DRG) scores for severity of illness and mortality risk. The treatment modality employed to treat LDD was also considered as a covariate, particularly when assessing overall complication rates.

Outcomes

Primary outcomes included in-hospital mortality rate, overall complication rate, complication rate by organ system, and certain pertinent perioperative complications. Secondary outcome measures included discharge disposition, mean length of hospital stay, and total charges for the hospital visit. Any discharge that was not to home was considered a nonhome discharge. Hospitalization lengths greater than the 75th percentile for the entire study population were considered to be extended hospitalizations.

Organ system complications were determined for cardiac (410.xx or 785.xx), pulmonary (514, 518.xx, or 512.xx), neurological (stroke 433.x or 434.x, transient cerebral ischemia 435.x, and seizures 345.xx, and neurological complications after procedure 997.01 or 997.09), infectious (041.xx, 38.xx, 320.xx, 324.1, 481–486, 507.0, 595.0, 790.7, 995.9x, 996.64, 997.31, 998.59, 999.31), renal (584.x), hematological (285.xx or 998.1x, or red blood cell transfusion 99.04), gastrointestinal (578.x, 560.1, or 00845), and peripheral vascular (venous thromboembolic 453.xx or 415.xx) systems. Sodium disturbance events (253.5, 253.6, 276.0, or 276.1) as well as the proportion of patients who also underwent a gastrojejunostomy (43.1, 43.11, 43.19, or 46.32) or tracheostomy (31.1, 31.2, 31.21, or 31.29) were also examined.

Statistical Analysis

Statistical analysis was conducted using SAS (version 9.4, SAS Institute), wherein the survey procedures were

implemented to account for the special survey design of the NIS. The NIS now comprises a sampling of all discharges from HCUP-participating hospitals in the country rather than a sampling of hospitals from which all discharge records were obtained. Thus, each patient discharge was used as the sampling unit, discharge weight used as the sampling-weight variable, and NIS stratum as the stratum. Chi-square tests analyzed categorical baseline characteristics between the 2 populations. Fisher's exact test was used for contingency tables with expected counts less than 1 under the null hypothesis of independence. The means of any continuous variables between the 2 groups were assessed with a 2-sided, 2-sample t-test. Individual primary and secondary outcomes based on OUD status were first examined using univariate regression models. Multivariable regression models were later constructed using predictor variables previously identified as differing significantly between patients in the 2 cohorts as covariates. A Morel adjustment was applied to logistic regression analyses pertaining to rare conditions to reduce any small sample bias that may exist. A p value < 0.05 was set a priori as a threshold for statistical significance. All figures were produced using Prism 7 (GraphPad).

Results

Demographics

A weighted total of 139,995 patients undergoing an ALIF, PLIF, or LLIF procedure for LDD were included in this study, of whom 1280 patients (0.91%) also carried a concurrent OUD diagnosis. Table 1 displays the baseline characteristics of the patient populations based on OUD status. Of note, the patient populations differed significantly in their distributions for age ($p < 0.0001$), primary insurance payer ($p < 0.0001$), median income by ZIP code ($p = 0.0002$), discharge status ($p = 0.0008$), and hospital geographic division ($p < 0.0001$; Table 1). LDD patients with OUDs also had a significantly greater number of diagnoses on record ($p < 0.0001$), number of procedures on record ($p = 0.0003$), number of chronic conditions ($p < 0.0001$), mean APR-DRG risk of mortality scores ($p = 0.0065$), and mean APR-DRG severity of illness scores ($p < 0.0001$; Table 2). This patient population also had significantly higher frequencies of certain comorbidities, including alcohol abuse ($p < 0.0001$), deficiency anemia ($p = 0.0063$), arthritis ($p = 0.0024$), anemia due to chronic blood loss ($p = 0.0198$), chronic lung disease ($p = 0.0003$), depression ($p < 0.0001$), fluid and electrolyte disorders ($p = 0.0049$), obesity ($p = 0.0424$), peripheral vascular disease ($p = 0.0341$), psychosis ($p < 0.0001$), weight loss ($p < 0.0001$), and other neurological disorders ($p = 0.0040$; Fig. 1). Of note, the LDD population with OUD had a significantly lower rate of hypertension ($p = 0.0080$).

Outcomes

Despite the higher mean APR-DRG risk of mortality scores in the group with OUDs, none of these patients experienced an in-hospital mortality after their procedure. Patients with concurrent OUDs did, however, experience significantly higher overall rates of complication (48.44%) than those without OUDs (31.01%) ($p < 0.0001$). Univari-

TABLE 1. Demographics of the study population by OUD status

	OUD Status*		p Value
	LDD (n = 138,715)	LDD + OUD (n = 1280)	
Age, yrs			<0.0001
0–44	27,565 (20.1)	325 (25.5)	
45–64	65,630 (48.0)	745 (58.4)	
65–74	32,790 (24.0)	175 (13.7)	
≥75	10,810 (7.9)	30 (2.4)	
Sex			0.2282
Male	63,725 (45.96)	540 (42.19)	
Female	74,935 (54.04)	740 (57.81)	
Race			0.8210
White	109,955 (84.14)	850 (84.58)	
Black	9555 (7.31)	65 (6.47)	
Hispanic	6225 (4.76)	100 (4.98)	
Asian	635 (0.49)	5 (0.50)	
Other	3900 (4.00)	35 (3.48)	
Insurance			<0.0001
Medicare	53,355 (38.52)	530 (41.41)	
Medicaid	9040 (6.53)	170 (13.28)	
Private	61,110 (44.12)	465 (36.33)	
Other	15,000 (10.83)	115 (4.95)	
Median income by ZIP code			0.0002
0–25th percentile	31,700 (23.29)	215 (17.06)	
26–50th percentile	39,345 (28.91)	295 (23.41)	
51–75th percentile	35,650 (26.19)	340 (26.98)	
76–100th percentile	29,415 (21.61)	410 (32.54)	
Discharge status			0.0008
Home (routine)	117,035 (84.4)	955 (74.6)	
Short-term care	470 (0.3)	5 (0.4)	
Skilled nursing facility	25 (0)	0 (0)	
Died in hospital	95 (0.1)	0 (0)	
Designated cancer center or other	21,090 (15.2)	320 (25.0)	
Hospital division			<0.0001
New England	4865 (3.5)	60 (4.7)	
Middle Atlantic	14,465 (10.5)	120 (9.4)	
East North Central	23,550 (17.0)	165 (12.9)	
West North Central	10,145 (7.3)	265 (20.7)	
South Atlantic	30,070 (21.7)	240 (18.8)	
East South Central	11,155 (8.0)	30 (2.3)	
West South Central	20,405 (14.7)	45 (3.5)	
Mountain	15,160 (10.9)	190 (14.8)	
Pacific	8900 (6.4)	165 (12.9)	
Admission type			0.1534
Elective	130,220 (94.3)	1180 (92.2)	
Nonelective (urgent or emergency)	7919 (5.7)	100 (7.8)	

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TABLE 1. Demographics of the study population by OUD status

	OUD Status*		p Value
	LDD (n = 138,715)	LDD + OUD (n = 1280)	
APR-DRG risk of mortality score			0.0014
Minor likelihood of dying	119,525 (86.2)	1000 (78.1)	
Moderate likelihood of dying	14,695 (10.6)	190 (14.8)	
Major likelihood of dying	3650 (2.6)	70 (5.5)	
Extreme likelihood of dying	840 (0.6)	20 (1.6)	
APR-DRG severity of illness score			<0.0001
Minor loss of function	73,410 (52.9)	225 (17.6)	
Moderate loss of function	54,155 (39.0)	795 (62.1)	
Major loss of function	10,335 (7.5)	220 (17.2)	
Extreme loss of function	810 (0.6)	40 (3.1)	

p < 0.05 was used as a threshold for statistical significance.

* Values given as weighted count (%).

ate regression revealed that patients with OUDs faced significantly higher odds of complications after all 3 of the procedure types examined, including ALIFs (OR 2.707, 95% CI 1.725–4.248; $p < 0.0001$), PLIFs (OR 2.251, 95% CI 1.392–3.641; $p = 0.0009$), and LLIFs (OR 1.696, 95% CI 1.165–2.468; $p = 0.0059$) (Table 3).

Univariate regressions were applied to a selected set of pertinent complications related to specific organ systems (Fig. 2). Patients with OUDs faced significantly increased odds of complication in certain organ systems, including pulmonary complications (OR 2.295, 95% CI 1.425–3.696; $p = 0.0006$), infectious complications (OR 3.716, 95% CI 2.097–6.584; $p < 0.0001$), and hematological complications (OR 1.648, 95% CI 1.226–2.215; $p = 0.0009$). Of note, patients with OUDs did not experience significantly higher odds of neurological complications (OR 2.015, 95% CI 0.989–4.106; $p = 0.0537$).

We examined several specific complications with known relevance in spinal fusion procedures to more thoroughly examine the unique complication profiles of patients with OUDs after these procedures (Table 4). We found that patients with OUDs had significantly higher odds of pneumonia (OR 3.059, 95% CI 1.285–7.283; $p = 0.0115$), venous thromboembolism (OR 4.165, 95% CI 1.851–9.372; $p = 0.0006$), pulmonary embolism (OR 4.973, 95% CI 1.499–16.500; $p < 0.0088$), postoperative anemia (OR 1.957, 95% CI 1.406–2.722; $p < 0.0001$), wound infection (OR 9.387, 95% CI 3.357–26.249; $p < 0.0001$), systemic inflammatory response syndrome (OR 9.664, 95% CI 2.846–32.810; $p < 0.0001$), urinary tract infection (OR 2.626, 95% CI 1.407–4.901; $p = 0.0024$), or requiring a tracheostomy (OR 18.130, 95% CI 2.130–154.300; $p = 0.0080$).

TABLE 2. Differences in baseline characteristics in the study population by OUD status

	OUD Status		p Value
	LDD (n = 138,715)	LDD + OUD (n = 1280)	
APR-DRG risk of mortality			
Mean (95% CI)	1.18 (1.17–1.18)	1.305 (1.21–1.40)	0.0065
SEM	0.004	0.046	
APR-DRG severity of illness			
Mean (95% CI)	1.56 (1.54–1.57)	2.06 (1.97–2.15)	<0.0001
SEM	0.007	0.045	
Age, yrs			
Mean (95% CI)	56.8 (56.6–57.1)	52.7 (51.4–54.0)	<0.0001
SEM	0.127	0.679	
No. of diagnoses on record			
Mean (95% CI)	9.00 (8.87–9.12)	13.32 (12.48–14.16)	<0.0001
SEM	0.064	0.429	
No. of chronic conditions on record			
Mean (95% CI)	4.95 (4.89–5.01)	7.43 (7.04–7.83)	<0.0001
SEM	0.031	0.202	
No. of procedures on record			
Mean (95% CI)	5.80 (5.73–5.88)	6.40 (6.08–6.71)	0.0003
SEM	0.037	0.161	

p < 0.05 was used as a threshold for statistical significance.

FIG. 1. Comorbidity landscape of patients undergoing lumbar fusion procedures by OUD status. A p value < 0.05 was used as a threshold for establishing statistical significance. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.0001$. DM = diabetes mellitus.

Table 5 displays the results of univariate regression analysis examining the impact of OUDs on secondary outcome measures for resource utilization following fu-

sion procedures for lumbar disc degeneration. We found that LDD patients with concurrent OUDs experienced significantly longer mean hospitalization lengths of stay (p

TABLE 3. Univariate regression models evaluating the impact of OUD status on in-hospital mortality and complications by procedure type

	OUD Status*		OR (95% CI)	p Value
	LDD	LDD + OUD		
In-hospital mortality rate	95/138,715 (0.10)	0/1280 (0)	NA	NA
All complications	43,010/138,715 (31.01)	620/1280 (48.44)	2.090 (1.640–2.665)	<0.0001
ALIF complications	11,205/35,790 (31.15)	190/345 (55.07)	2.707 (1.725–4.248)	<0.0001
PLIF complications	12,770/44,130 (28.94)	165/345 (47.83)	2.251 (1.392–3.641)	0.0009
LLIF complications	19,035/58,615 (32.47)	265/590 (45.00)	1.696 (1.165–2.468)	0.0059

NA = not applicable.

$p < 0.05$ was used as a threshold for statistical significance.

* Values given as weighted count/total (%).

FIG. 2. Forest plot depicting the impact of OUD status on the odds of organ system complications following lumbar fusion procedures. Odds ratios obtained through univariate logistic regressions. ** $p < 0.01$; *** $p < 0.0001$.

< 0.0001) and higher total charges for their hospital stay ($p = 0.0076$). This analysis also indicated that this patient population experienced significantly increased odds of a nonhome discharge after their hospital stay ($p < 0.0001$),

with 25.39% of patients discharged not to home compared with 15.63% of patients in the population without an OUD.

Multiple regression analyses were performed for each procedure type to better examine how OUDs impact

TABLE 4. Univariate regression models evaluating the impact of OUD status on certain surgical complications across organ systems

	OUD Status*		OR (95% CI)	p Value
	LDD (n = 138,715)	LDD + OUD (n = 1280)		
Myocardial infarction	230 (0.17)	0 (0)	NA	NA
Cardiac arrest	575 (0.41)	10 (0.78)	1.892 (0.452–7.925)	0.3828
Renal failure	2520 (1.82)	35 (2.73)	1.519 (0.674–3.423)	0.3127
Pneumonia	1080 (0.78)	30 (2.34)	3.059 (1.285–7.283)	0.0115
Deep venous thrombosis	160 (0.12)	0 (0)	NA	NA
Venous thromboembolism	795 (0.57)	30 (2.34)	4.165 (1.851–9.372)	0.0006
Acute respiratory failure	685 (0.49)	10 (0.78)	1.587 (0.383–6.571)	0.5243
Pulmonary embolism	330 (0.24)	15 (1.17)	4.973 (1.499–16.500)	0.0088
Postop anemia	19,120 (13.78)	305 (23.83)	1.957 (1.406–2.722)	< 0.0001
Oliguria/anuria	155 (0.11)	0 (0)	NA	NA
Urinary complication	910 (0.66)	10 (0.78)	1.193 (0.289–4.919)	0.8076
Wound dehiscence	65 (0.05)	0 (0)	NA	NA
Wound infection	175 (0.13)	15 (1.17)	9.387 (3.357–26.249)	< 0.0001
Systemic inflammatory response syndrome	170 (0.12)	15 (1.17)	9.664 (2.846–32.810)	< 0.0001
Severe sepsis	140 (0.10)	5 (0.39)	3.882 (0.516–29.221)	0.1878
Septic shock	45 (0.03)	0 (0)	NA	NA
Urinary tract infection	2770 (2.00)	65 (5.08)	2.626 (1.407–4.901)	0.0024
Sodium disturbance complication	4480 (3.23)	40 (3.13)	0.967 (0.478–1.955)	0.9257
Tracheostomy	30 (0.02)	5 (0.39)	18.130 (2.130–154.300)	0.0080
Gastrojejunostomy	20 (0.01)	0 (0)	NA	NA

$p < 0.05$ was used as a threshold for statistical significance.

* Values given as weighted count (%).

TABLE 5. Univariate regression models evaluating the impact of OUD status on resource utilization and secondary clinical outcomes

	OUD Status		p Value
	LDD	LDD + OUD	
Mean length of stay, days	n = 138,715	n = 1280	
Mean (95% CI)	3.465 (3.407–3.522)	4.977 (4.499–5.454)	<0.0001
SEM	0.029	0.244	
Nonhome discharge	n = 138,715	n = 1280	
Weighted count (%)	21,680 (15.63)	325 (25.39)	<0.0001
OR (95% CI)	1.837 (1.361–2.481)		
Total charges	n = 137,630	n = 1270	
Mean (95% CI)	120,664 (117,458–123,870)	150,895 (128,511–173,280)	0.0076
SEM	1635	11,416	

p < 0.05 was used as a threshold for statistical significance.

large-scale primary and secondary clinical outcomes in these patient populations while controlling for important demographic and comorbidity variables (Table 6). The models in these analyses specifically examined the odds of a complication, a nonhome discharge, and an extended hospitalization, in addition to providing an estimate as to how much extra a patient with an OUD will be charged for the hospital stay for each procedure type. All of the models specifically controlled for demographic variables, including age, sex, race, primary payer status, hospital geographic division, and income quartile, as well as comorbidity variables, including alcohol use, deficiency anemia, anemia due to chronic blood loss, chronic lung disease, depression, hypertension, electrolyte and fluid disorders, obesity, peripheral vascular disease, psychosis, weight loss, and other neurological disorders.

In our model describing the effects of OUDs on ALIF outcomes, the odds of a nonhome discharge (OR 3.135, 95% CI 1.620–6.064; p = 0.0007) and extended hospitalization (OR 3.275, 95% CI 1.770–6.060; p = 0.0002) were significantly higher for patients with an OUD, while the odds of experiencing a complication were not significant (OR 1.535, 95% CI 0.692–3.406; p = 0.2915). In contrast, our model for PLIF outcomes indicated that the odds of a complication (OR 2.436, 95% CI 1.190–4.989; p = 0.0149) and an extended hospitalization (OR 1.941, 95% CI 1.018–3.698; p = 0.0439), but not nonhome discharge (OR 1.973, 95% CI 0.910–4.278; p = 0.0853), were significantly greater for patients with OUDs. Finally, in our model for LLIF outcomes, all of these variables differed significantly by OUD status. In addition, our models also indicated that patients with OUDs had significantly higher total charges for their hospital visits regardless of procedure technique. On average, this patient population was charged \$17,926 more for ALIFs (p = 0.0054), \$25,440 more for PLIFs (p < 0.0001), and \$37,228 more for LLIFs (p < 0.0001).

Discussion

Opioid use in the United States has markedly increased over the past 2 decades as prescription opioid therapies are one of the most common treatments for chronic back pain. Numerous studies have suggested that postoperative

outcomes may be improved by reducing opioid analgesic use.^{9,22,35} As such, ERAS protocols often emphasize reduction of opioid analgesics. However, patients with OUDs display problematic patterns of opioid consumption and are particularly difficult to manage with traditional ERAS

TABLE 6. Multivariate regression models evaluating the impact of OUD status on relevant primary and secondary outcome measures

Outcome	OR (95% CI)	Estimate (SE)	p Value
ALIF			
Complication	1.535 (0.692–3.406)		0.2915
Nonhome discharge	3.135 (1.620–6.064)		0.0007
Extended hospitalization	3.275 (1.770–6.060)		0.0002
Total charges		\$17,926 (6428)	0.0054
PLIF			
Complication	2.436 (1.190–4.989)		0.0149
Nonhome discharge	1.973 (0.910–4.278)		0.0853
Extended hospitalization	1.941 (1.018–3.698)		0.0439
Total charges		\$25,440 (248)	<0.0001
LLIF			
Complication	1.668 (1.007–2.763)		0.0471
Nonhome discharge	2.206 (1.317–3.695)		0.0027
Extended hospitalization	2.446 (1.558–3.839)		0.0001
Total charges		\$37,228 (3886)	<0.0001

Models control for demographic variables, such as age, sex, race, primary payer status, hospital census division, and income quartile, as well as comorbidities, including alcohol use, deficiency anemia, anemia due to chronic blood loss, chronic lung disease, depression, hypertension, electrolyte and fluid disorders, obesity, peripheral vascular disease, psychosis, weight loss, and other neurological disorders. p < 0.05 was used as a threshold for statistical significance.

protocols. More focused ERAS systems should be developed for OUD patients and must account for the unique risks and adverse outcomes faced by this population during their hospitalizations. In this study, we identified unique risk and outcome profiles that pertain to OUD patients that have not previously been discussed in the literature. This has limited the ability of ERAS protocols to provide optimal care in this population.

Demographics and Comorbidities

We observed several important differences between the demographics of the OUD and non-OUD patient populations. First, these groups showed statistically significant differences in the distributions of their ages, primary insurance payer, median income by ZIP code, discharge disposition, geographic hospital division, APR-DRG risk of mortality and severity of illness scores, and frequency of surgically relevant comorbidities such as alcohol abuse, deficiency anemia, arthritis, anemia due to chronic blood loss, chronic lung disease, depression, hypertension, fluid and electrolyte disorders, obesity, peripheral vascular disease, psychosis, and weight loss. Recognizing that these observed demographic differences could significantly impact measures of perioperative outcome and resource utilization, we constructed multivariate logistic regression models that controlled for these variables to better characterize how OUD status interacts with key perioperative variables to impact clinical outcome by the surgical approach taken to treat LDD.

Complications

Preoperative opioid use is known to be associated with increased rates of complication after a variety of surgical procedures.^{5,14,16} This study carefully assessed procedure-related complications from a variety of perspectives. Patient populations differing in their OUD status were examined for postprocedural complications according to which surgically relevant complications occurred, which organ systems were involved, and which surgical approach was used for the procedure.

Studies have shown that patients with chronic opioid use may have an increased risk of wound complications postoperatively.¹⁴ For example, systemic opioid levels have been associated with decreased angiogenesis and fewer myofibroblasts and macrophages at the wound site, which ultimately impairs wound healing.^{15,20,21} Importantly, results from this present study provide further support to this notion on an even larger scale. Based on our univariate regression models, we found that patients with OUDs were significantly more likely to experience wound infections after their procedures than patients without OUDs.

When examined from an organ systems perspective, we found that patients with OUDs had significantly higher odds of experiencing pulmonary, hematological, and infectious complications perioperatively (Fig. 2). Previous work has found that chronic opioid use is associated with higher levels of infectious complications,² such as pneumonia, particularly in elderly patients.⁷ This may be due to the broader immunosuppressive effects that some opioid medications exert by directly acting on the mu-opioid receptors found on immune cells as well as by indirectly

affecting glucocorticoid levels by acting on the sympathetic nervous system.^{29,30} In this study, we observed that OUD patients experienced significantly higher odds of infectious complications, and, more specifically, pneumonia and urinary tract infections.

Recent studies have also found that patients with OUDs have an increased risk of developing pulmonary complications, including the need for extended mechanical intubation or reintubation.³¹ In this study, OUD patients had 2.3-fold higher odds of developing pulmonary complications than non-OUD patients and faced higher odds of experiencing pneumonia and pulmonary embolism, but not acute respiratory failure. Taken together, our results are consistent with those previously reported in the literature, suggesting that OUD patients face higher odds of pulmonary complications postoperatively.

When examining the complication profiles of patients based on their procedure type, we found differences in the odds of complication for OUD patients depending on surgical approach. Results from our multivariate analysis suggest that, after controlling for demographic and comorbidity variables, the odds of complication for OUD patients were only significant for PLIF and LLIF (Table 6). Accordingly, previous studies described differences in the types and frequencies of complications after lumbar fusion procedures that depend on the surgical approach.⁸ However, there is debate in the literature comparing the complication rates across different lumbar fusion approaches. Smaller, single-institution studies have found that an anterior approach offers a lower incidence of complication rates,^{3,27,32} while large cohort analyses have found that patients with anterior lumbar spinal surgery have higher rates of postoperative complications and pain medication usage than patients who undergo posterior lumbar surgery, independent of opioid use status.^{13,23}

Mortality

We did not observe any significant increases in the odds of mortality for OUD patients in this study. Previous studies have identified age, sex, and certain comorbidities as risk factors that are most often associated with mortality during lumbar spine procedures.^{4,23,28,33,34} Despite these reported risk factors, it is also recognized that mortality rates in lumbar spine surgeries are historically low overall, with one large-scale study estimating an overall mortality rate of 0.13% across all lumbar surgical patients in the United States between 2003 and 2012.²⁶ This same study identified older age, black race, male sex, liver disease, and congestive heart failure to be significantly associated with increased mortality rates.²⁶ The OUD patients in this study tended to be younger and were not significantly different from non-OUD patients regarding sex, race, or congestive heart failure status, which may partially explain why mortality risk was not increased in this study.

Resource Utilization and Secondary Outcomes

Preoperative opioid use has been shown to independently influence costs, length of stay, and complication rates in surgical patients.^{5,14} Previous studies have also shown that patients with greater levels of preoperative opioid use also tend to have increased pain and pain perception compared

with opioid-naïve populations.^{10,12} Dagal et al. looked at a unique patient population in which more than half of the patients were on chronic opioid therapy.⁶ In this population, they developed a perioperative enhanced recovery care pathway for major spine surgery to improve postoperative outcomes in patients and found that patients with chronic opioid use prior to surgery reported more time in severe pain. In separate studies, there is increasing evidence that perioperative opioid consumption is associated with increased acute pain after surgeries and increased postoperative opioid use prior to discharge.^{10,25} This, in turn, can lead to prolonged hospitalizations, higher total costs, and increased readmission rates.¹¹ Accordingly, in the present study, patients with OUDs tended to perform more poorly in terms of resource utilization metrics, including extended hospitalization, nonhome discharge, and higher total costs of hospitalization. As such, the development of a more individualized ERAS model for this patient population may allow for novel cost-saving and resource utilization measures that have been previously unexplored.

Limitations

This study was inherently limited by its retrospective design, which makes it challenging to examine temporal relationships and makes selection bias a potential concern. The NIS database also possesses certain intrinsic limitations. First, NIS data are encoded by ICD-9-CM codes, which means that certain measures not represented by an ICD-9-CM code could not be examined. These may include various measures of opioid use and pain. Of note, it was not possible to stratify opioid-using patients by their daily morphine equivalent doses, track patients over time, or assess other meaningful variables such as the level and extent of lumbar compression, blood loss, surgery duration, mobilization time, or anesthesia. Additionally, because the NIS does not track mortality outside the hospital, patient mortality may not be fully represented. Rare conditions may also not reflect their true value in the population due to the study's relatively short time window. Finally, these data represent cases performed under various circumstances, with individual-level differences in surgical approach. While this introduces a certain degree of heterogeneity in the underlying data set, it also perhaps improves the generalizability to practices across the nation given the smaller influences of the specific practices and policies of individual surgical teams.

Conclusions

This is the first study to characterize the outcome profiles for lumbar fusion procedures in patients with OUDs on a national level as a step toward developing new ERAS protocols in spine surgery for this unique patient population. Patients face particularly difficult recoveries after spine surgery, and OUD patients are an especially vulnerable population in the perioperative period for whom traditional ERAS protocols may not be the most effective. Developing more effective ERAS protocols for OUD patients will require a more detailed understanding of the unique problems this population may face in the perioperative period. This study examined how OUD status influenced

primary outcomes, such as complications and mortality, as well as secondary outcomes and resource utilization metrics following a variety of lumbar fusion procedures.

Taken together, the results from this study suggest that OUD status is an important determinant of primary and secondary clinical outcomes after lumbar fusion procedures and poses certain perioperative risks that physicians, surgeons, and policymakers must be aware of when designing and implementing new enhanced recovery protocols to more optimally care for this patient population. These results warrant prospective studies to further the development of better ERAS programs that may improve patient care and reduce cost burden.

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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: Caridi, Martini. Acquisition of data: Caridi, Martini, Deutsch. Analysis and interpretation of data: all authors. Drafting the article: Martini, Nistal. Critically revising the article: Caridi, Martini, Nistal. Reviewed submitted version of manuscript: Caridi, Martini, Nistal. Statistical analysis: Martini, Deutsch. Study supervision: Caridi, Martini.

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