Preoperative Opioid Use and Readmissions Following Surgery

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Objective: To assess the association between preoperative opioid exposure and readmissions following common surgery.

Summary Background Data: Preoperative opioid use is common, but its effect on opioid-related, pain-related, respiratory-related, and all-cause readmissions following surgery is unknown.

Methods: We analyzed claims data from a 20% national Medicare sample of patients ages ≥ 65 with Medicare Part D claims undergoing surgery between January 1, 2009 and November 30, 2016. We grouped patients by the dose, duration, recency, and continuity of preoperative opioid prescription fills. We used logistic regression to examine the association between prior opioid exposure and 30-day readmissions, adjusted for patient risk factors and procedure type.

Results: Of 373,991 patients, 168,579 (45%) filled a preoperative opioid prescription within 12 months of surgery, ranging from minimal to chronic high use. Preoperative opioid exposure was associated with higher rate of opioid-related readmissions, compared with naive patients [low: aOR=1.63, 95% CI=1.26–2.12; high: aOR=3.70, 95% CI=2.71–5.04]. Preoperative opioid exposure was also associated with higher risk of pain-related readmissions [low: aOR=1.27, 95% CI=1.23–1.32; high: aOR=1.62, 95% CI=1.53–1.71] and respiratory-related readmissions [low: aOR=1.10, 95% CI=1.05–1.16; high: aOR=1.44, 95% CI=1.34–1.55]. Low, moderate, and high chronic preoperative opioid exposures were predictive of all-cause readmissions (low: OR 1.09, 95% CI: 1.06–1.12); high: OR 1.23, 95% CI: 1.18–1.29).

Conclusions: Higher levels of preoperative opioid exposure are associated with increased risk of readmissions after surgery. These findings emphasize the importance of screening patients for preoperative opioid exposure and creating risk mitigation strategies for patients.

Keywords: opioid, opioid prescribing, opioid use, postoperative complication, postoperative pain management, preoperative opioid use, readmission, surgery

In 2017, the United States accounted for 99.2% of global consumption of hydrocodone, and was the main consumer country for hydromorphone and oxycodone.[1] According to a national survey in 2015, 37.8% of US adults used prescription opioids in the previous 12 months, most commonly for pain relief.[2] Opioid use is common among older patients, with 1 in 3 Medicare Part D beneficiaries receiving a prescription opioid in 2016.[3] Troublingly, older individuals also experienced the largest increase in opioid-related deaths between 2001 and 2016.[4] In addition to risk of overdose, opioid analgesics have serious side effects including respiratory depression, bladder dysfunction, and hyperalgesia.[5–7]

Patients with pre-existing opioid use present a particular challenge to surgeons, who strive to balance appropriate pain control with avoiding adverse effects of postoperative opioids. Previous studies have found that postoperative pain is predictive of subsequent emergency department visits and increased healthcare utilization.[8,9] Chronic opioid exposure is also associated with increased postoperative complications, readmission rates, and healthcare costs.[10,11] However, it is unknown whether the degree of preoperative opioid exposure changes the risk of adverse events after surgery, such as readmissions. Moreover, preoperative opioid exposure is heterogeneous,[12,13] and practical strategies to define risk based on clinically meaningful groups of preoperative opioid exposure are not well described. Understanding this relationship could help identify high-risk patients and potentially prevent adverse events. To date, there is little information regarding the nuances of preoperative opioid exposure, and their effect on postoperative outcomes, including details of dosage, timing, and continuity in preoperative opioid exposure.

Readmission rates are key quality metrics for stakeholders interested in optimizing the value of surgical care, as preventable readmissions represent missed care opportunities for interventions and the need for better preoperative screening. For example, one study found that 48% of readmissions after laparoscopic bariatric surgery were preventable, indicating a need for quality improvement.[14] Recently, the Centers of Medicare and Medicaid Services have provided financial incentives to decrease readmissions, improve quality of care, and lower costs.[15–17] To better understand the effect of preoperative opioid exposure on postoperative readmissions, we used the previously described opioid exposure classifications to study the risk of 30-day hospital readmissions among Medicare beneficiaries 65 years and older undergoing common major or minor surgery.[18] We hypothesized that preoperative opioid exposure would be associated with increased risk of opioid-related, pain-related, respiratory-related, and all-cause hospital readmissions 30 days after surgery.

METHODS

Data Source and Patient Cohort

In this retrospective observational study, we examined a 20% national sample of Medicare claims data to examine patients 65 years and older who underwent a surgical procedure from January 1, 2009 to November 30, 2016. This study was deemed exempt by the University of Michigan Human Research Protections Office.

As age has shown to increase risk of adverse effects from opioids,[19,20] our cohort included patients aged 65 years and older who were continuously enrolled in Medicare Parts A, B, and D for 12 months before and 6 months after their surgical date. We selected 15 common procedures based on Current Procedural Terminology Fourth Edition codes (Appendix I, http://links.lww.com/SLA/C23) and categorized them as major or minor procedures. Minor procedures included varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral prostate surgery, parathyroidectomy, and carpal tunnel. Major procedures included ventral incisional hernia repair, colectomy, reflux surgery, bariatric surgery, hysterectomy, total hip arthroplasty, and total knee arthroplasty. We excluded patients who had a length of stay greater than 30 days, and patients who were not discharged home.

Outcomes

We examined four outcomes: (1) 30-day opioid-related readmissions (eg., adverse effects of opioids, opioid abuse, and opioid poisoning), (2) 30-day pain-related readmissions (eg., postoperative pain, abdominal and bowel pain, and fibromyalgia), (3) 30-day respiratory-readmissions (eg., acute respiratory failure, upper respiratory drug-induced interstitial lung disorders, and apnea), and (4) 30-day all-cause readmissions. We queried claims data for inpatient and emergency department claims with a readmission date within 30 days after discharge. We identified opioid-related readmissions by matching diagnosis codes in the claims with the list in Appendix II, http://links.lww.com/SLA/C23.[21] We identified pain-related readmissions using a previously described algorithm.[22] For respiratory-readmissions, we reviewed related ICD-9 and ICD-10 diagnosis codes as described in Appendix III, http://links.lww.com/SLA/C23.

Explanatory Variable and Other Patient Characteristics

The main explanatory variable was preoperative opioid exposure. Medicare Part D pharmacy claims were used to identify patients with preoperative opioid exposure, defined as filling at least 1 prescription during the year before surgery. Opioid prescriptions were selected based on generic name matched with National Drug Code. Total amount prescribed was calculated by taking the product of strength, quantity and a factor for converting different types of opioid to oral morphine equivalents (OMEs).[23] For the ease of interpretation, prescription size was also reported as number of tablets of 5/325 mg hydrocodone-acetaminophen (one 5 mg hydrocodone tablet = 5 OME).

Preoperative opioid exposure was described using four attributes: dose, duration, recency, and continuity of use.[18] Dose was defined as total OMEs of prescriptions filled in the year before the operation. Duration was the total number of months during which a patient filled an opioid prescription. Recency was defined as the number of months since the last opioid filled before the operation. Continuity was defined as the longest "streak" of months that a patient consecutively filled a prescription. We used previously described clustering analysis, a machine learning algorithm, to classify patients into groups of preoperative exposure.[24,18]

Patient demographic characteristics were age, sex, race/ethnicity, region of residence, and Medicaid eligibility. Patients were grouped into 5 age groups (65–69, 70–74, 75–79, 80–84, and 85+). Race/ethnicity included White, Black, Hispanic, and Others. There were 9 geographic regions of residences including East North Central, East South Central, Middle Atlantic, Mountain, New England, Pacific, South Atlantic, West North Central, and West South Central. Medicaid eligibility was based on the dual eligibility status in the month of surgery.

Charlson Comorbidity index (CCI), tobacco use, mental health disorders, and pain disorders were based on diagnosis codes in the claims during the year before surgery. CCI was categorized into different categories: 0, 1–2, 3–4, and ≥5. Patients who had a diagnosis of tobacco use (ICD-9-CM: 305.1, V15.82; ICD-10-CM: F17.***, Z87.891, Z72.0) were defined as smoker or history of smoking. Mental health disorders (adjustment, anxiety, mood, suicide or self-harm, disruptive, personality, psychosis, alcohol or other substance abuse disorders, and other mental health disorders) were based on the Clinical Classifications Software for ICD-9-CM and ICD-10-CM.[25] History of pain disorders (arthritis, back, neck, and other pain) were identified by ICD-9 and ICD-10 diagnosis codes (see Appendix IV, http://links.lww.com/SLA/C23). Additionally, we adjusted for any hospitalization and skilled nursing facility stay within 1 year before the patient's surgical date. We also identified patients who concurrently filled a benzodiazepine and opioid prescription in the perioperative period, defined as 30 days prior to and 14 days after surgery.

Statistical Analysis

We used descriptive statistics to present demographic and clinical characteristics of the study cohort. We then used logistic regression models to estimate preoperative opioid exposure and the other factors associated with opioid-related readmissions, pain-related readmissions, respiratory-related readmissions, and all-cause readmissions within 30 days after discharge. Multicollinearity was tested among all covariate. The model fit was evaluated using c-statistics. Cluster analysis was performed using R version 3.6.1, and all other analyses were performed using SAS version 9.4 and Stata version 15.1. Statistical significance was defined as $P < 0.05$ with 2-sided tests.

RESULTS

We identified 373,991 patients who underwent common major or minor surgical procedures during the study period. The demographic and clinical profiles of the overall patient cohort are summarized in Table 1. In this cohort, 223,541 (60%) underwent a major procedure, and 150,449 (40%) underwent a minor procedure. In addition, 231,563 (62%) were female, 320,694 (86%) were Caucasian, and 20,950 (6%) were African-American. There were 14,771 (4%) patients who filled a benzodiazepine concurrently with their opioid prescription during the preoperative period. Finally, 205,412 (55%) patients were opioid-naive, while 168,579 (45%) had filled an opioid prescription in the 12 months before surgery.

Patterns of Preoperative Opioid Exposure

We classified preoperative opioid exposure into 5 distinct groups based on dose, recency, duration, and continuity. The attributes of groups 1 to 4 are summarized in Table 2. Group 1 patients (n = 50,495) had remote, low-dose use of opioids within 1 month before surgery. Median [interquartile range] prescription amount was 250 (400) OME, received at a median of 8 (4) months before surgery. Group 2 patients (n = 70,024) were characterized by recent (within 2 months), moderate dose use of low duration. Patients in this group

TABLE 1. Patient Characteristics

Characteristics	n	%
Total cases	373,991	
Age, yr		
65–69	109,094	29.17
70–74	108,156	28.92
75–79	78,288	20.93
80–84	48,741	13.03
≥85	29,712	7.94
Sex		
Male	142,428	38.08
Female	231,563	61.92
Race/ethnicity		
White	320,694	85.75
Black	20,950	5.6
Hispanic	20,633	5.52
Other	9855	2.64
Missing	1859	0.5
Resided in Metropolitan County		
Yes	278,266	74.4
No	95,318	25.49
Missing	407	0.11
Division		
East North Central	39,005	10.43
East South Central	18,757	5.02
Middle Atlantic	34,378	9.19
Mountain	30,912	8.27
New England	51,773	13.84
Pacific	16,997	4.54
South Atlantic	77,765	20.79
West North Central	29,195	7.81
West South Central	36,851	9.85
Unknown	38,358	10.26
Charlson Comorbidity Index		
None (CCI 0)	94,751	25.34
Mild (CCI 1, 2)	141,481	37.83
Moderate (CCI 3, 4)	77,217	20.65
Severe (CCI ≥5)	60,542	16.19
Medicaid eligibility	56,628	15.14
Any hospitalization in previous year	78,201	20.91
Skilled nursing facility stay in previous year	12,483	3.34
History of tobacco use	56,317	15.06
Surgery type		
Major surgery	223,542	59.77
Minor surgery	150,449	40.23
Mental health disorders		
Adjustment	6579	1.76
Anxiety	46,862	12.53
Mood	56,450	15.09
Suicide or self-harm	590	0.16
Disruptive	1393	0.37
Personality	678	0.18
Psychosis	7183	1.92
Alcohol or other substance use disorders	9507	2.54
Other mental health disorders	10,101	2.7
Pain disorders		
Arthritis	311,507	83.29
Back	149,225	39.9
Neck	57,661	15.42
Other pain	149,055	39.86
Opioid filled during preop period (365 to 31 d prior to admission)		
Yes	168,579	45.08
No (Opioid naive)	205,412	54.92
Opioid filled during periop period (30 d before admission to 14 d after discharge)	266,444	71.24
Benzo and Opioid filled concurrently during periop period	14,771	3.95

received a median equivalent of 540 (975) OME over a 2-month duration. Group 3 patients (n = 30,108) received a higher dose of 4050 (4640) OME over a longer duration of 7 months. They had more recent preoperative opioid exposure and some discontinuity of fills (median continuity 4 months). Group 4 patients (n = 17,952) had the highest dose use (''high chronic''), receiving a median equivalent of 11,964 (15,460) OME over 11 months. Patients in this group had sustained use (median continuity 11 months), and had filled 1 month before surgery.

Overall readmission rates stratified by preoperative opioid exposure are summarized in Table 3. Among minimal preoperative opioid users, there were 58 (0.11%) opioid-related readmissions, 3259 (6.45%) pain-related readmissions, 1622 (3.21%) respiratory-related readmissions, and 6305 (12.49%) all-cause readmissions. Among patients with low preoperative opioid exposure, there were 102 (0.15%) opioid-related readmissions, 5261 (7.51%) pain-related readmissions, 2526 (3.61%) respiratory-related readmissions, and 9602 (13.71%) all-cause readmissions. Patients with moderate opioid exposure before surgery were at greater risk of readmissions with 63 (0.21%) opioid-related readmissions, 2908 (9.66%) pain-related readmissions, 1474 (4.90%) respiratory-related readmissions, and 4885 (16.22%) all-cause readmissions. Patients with high chronic opioid exposures experienced the highest risk of readmissions, with 82 (0.46%) opioid-related readmissions, 2072 (11.54%) pain-related readmissions, 1065 (5.93%) respiratory-related readmissions, and 3167 (17.64%) all-cause readmissions.

Association of Preoperative Opioid Exposure and Postoperative Readmissions

After multivariable risk adjustment, preoperative opioid exposure was significantly associated with increased risk of readmission (Fig. 1). Compared with the opioid-naive group (0.08%), patients with minimal and low levels of opioid exposure had increased adjusted rate of opioid-related readmissions (0.11% and 0.13%, respectively). Likelihood of opioid-related readmissions for moderate level users was double (0.16%) that of opioid-naive patients, and individuals with high chronic exposure experienced the greatest risk of readmissions (0.30%).

We observed similar associations between preoperative opioid exposure and pain-related readmissions. Risk of pain-related readmissions after discharge was higher (8.67%) in patients with high chronic opioid exposure, compared with their opioid-naive counterparts (5.58%). Minimal, low, and moderate levels of exposure were also associated with increased risk of pain-related readmissions (6.18%, 6.96%, 7.61%, respectively).

Compared with baseline (3.06%), high chronic exposure was predictive of increased respiratory-related readmissions (4.31%). Patients with low and moderate levels of opioid exposure also experienced greater risk of respiratory-related readmissions relative to the opioid-naive group (3.34% and 3.73%, respectively).

We observed a similar risk of all-cause readmissions in patients with minimal preoperative opioid exposures (12.08%) compared with baseline (12.10%). However, patients with low, moderate, and chronic high exposure to opioids within 12 months of surgery were at higher risk of all-cause readmissions (13.05%, 13.69%, and 14.45%, respectively).

Opioid-related Readmissions

The results of our multivariate logistic regression for preoperative opioid exposures are summarized in Table 4. High chronic exposure was the most influential predictor of opioid-related readmission, with high chronic users 3.7-fold more likely to have opioid-related readmissions compared with opioid-naive patients (high: OR 3.70, 95% CI: 2.71–5.04). Other variables significantly associated

TABLE 2. Patient Groups and Attributes of Preoperative Opioid Exposure Within One Year of Surgery

| Group | Group Name | n | % | Total Oral Morphine Equivalent (OME) Filled During Preop | | Duration in Month | | Continuity in Month | | Recency in Month | |
				Median	IQR	Median	IQR	Median	IQR	Median	IQR
1	Minimal	50,495	29.95	250	400	1	0	1	0	8	4
2	Low	70,024	41.54	540	975	2	2	1	1	2	1
3	Moderate	30,108	17.86	4050	4640	7	2	4	2	2	1
4	High Chronic	17,952	10.65	11964.4	15,460	11	1	11	2	1	1

5 OME indicates one 5 mg hydrocodone tablet; IQR, interquartile range.

TABLE 3. Association Between Preoperative Opioid Exposure and Readmissions

| Group | Group Name | Total n | Opioid-related Readmissions | | Pain-related Readmissions | | Respiratory-related Readmissions | | All-cause Readmissions | |
			n	%	n	%	n	%	n	%
0	Opioid-naive	205,412	147	0.07	10,205	4.97	5529	2.69	23,017	11.21
1	Minimal	50,495	58	0.11	3259	6.45	1622	3.21	6305	12.49
2	Low	70,024	102	0.15	5261	7.51	2526	3.61	9602	13.71
3	Moderate	30,108	63	0.21	2908	9.66	1474	4.9	4885	16.22
4	High chronic	17,952	82	0.46	2072	11.54	1065	5.93	3167	17.64
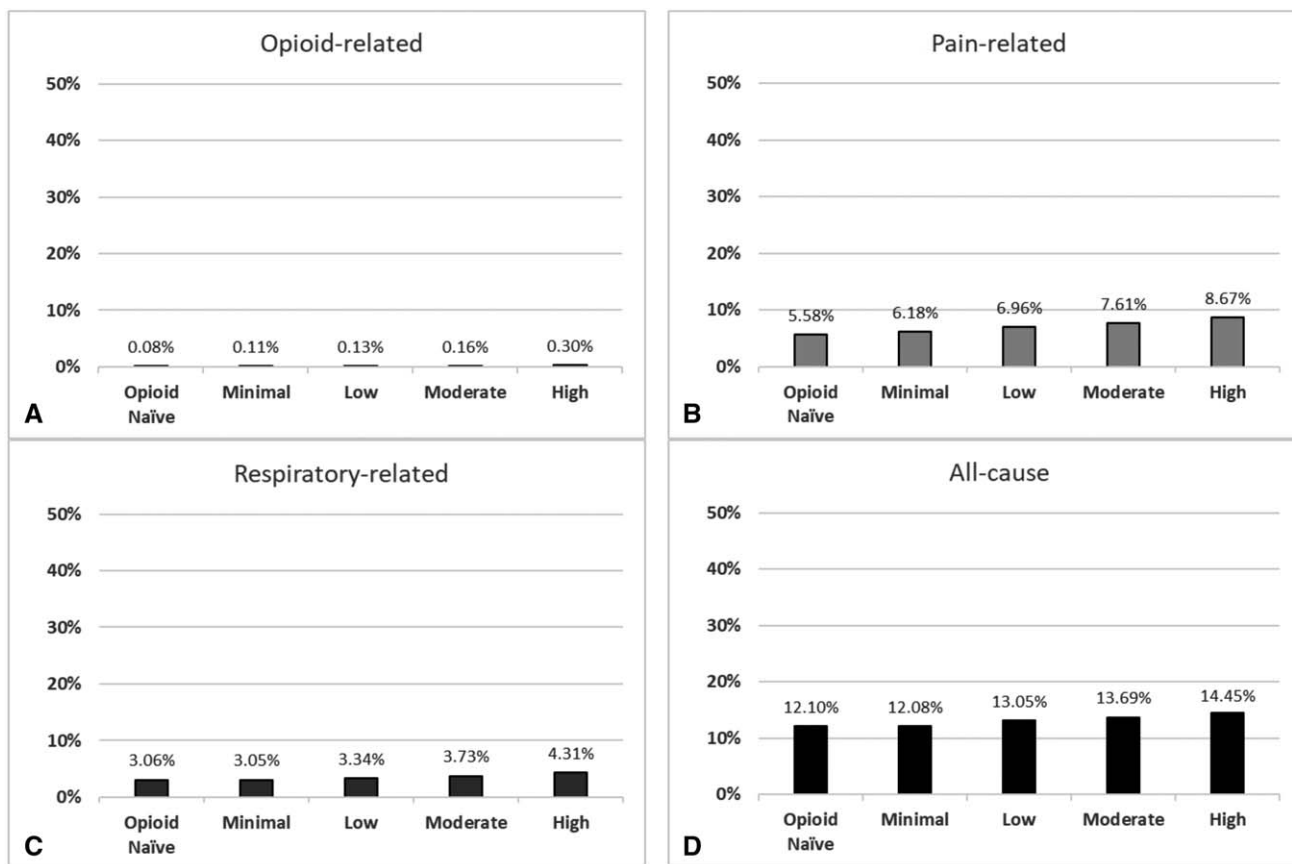
FIGURE 1. Adjusted rates of opioid-related, pain-related, respiratory-related, and all-cause readmissions (%) by preoperative use (opioid-naive, minimal, low, moderate, and high chronic).

TABLE 4. Association Between Preoperative Opioid Exposure and Respiratory-related Complications, Opioid-related Complications, Pain-related Complications, and All-Cause Readmissions Within 30 Days After Discharge

	Opioid-related Readmissions		Pain-related Readmissions		Respiratory-related Readmissions		All-Cause Readmissions	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Preop opioid exposure group (Ref: Opioid-naive)								
Minimal	1.36 (1.00 1.85)	0.052	1.12 (1.07 1.16)	<0.001	1.00 (0.94 1.06)	0.974	1.00 (0.97 1.03)	0.931
Low	1.63 (1.26 2.12)	<0.001	1.27 (1.23 1.32)	<0.001	1.10 (1.05 1.16)	<0.001	1.09 (1.06 1.12)	<0.001
Moderate	1.90 (1.38 2.61)	<0.001	1.40 (1.34 1.47)	<0.001	1.24 (1.16 1.32)	<0.001	1.16 (1.12 1.20)	<0.001
High	3.70 (2.71 5.04)	<0.001	1.62 (1.53 1.71)	<0.001	1.44 (1.34 1.55)	<0.001	1.23 (1.18 1.29)	<0.001
Age, yr (Ref: 65–69)								
70–74	0.84 (0.66 1.09)	0.188	1.06 (1.02 1.10)	0.002	1.11 (1.05 1.17)	<0.001	1.08 (1.06 1.11)	<0.001
75–79	1.08 (0.83 1.41)	0.577	1.17 (1.12 1.22)	<0.001	1.37 (1.30 1.44)	<0.001	1.23 (1.20 1.27)	<0.001
80–84	1.16 (0.85 1.58)	0.343	1.32 (1.26 1.38)	<0.001	1.51 (1.43 1.61)	<0.001	1.41 (1.36 1.46)	<0.001
≥85	1.40 (0.98 1.99)	0.065	1.55 (1.47 1.63)	<0.001	1.92 (1.79 2.05)	<0.001	1.64 (1.58 1.71)	<0.001
Female (Ref: Male)	1.14 (0.93 1.41)	0.204	1.00 (0.97 1.02)	0.714	0.92 (0.88 0.96)	<0.001	0.82 (0.81 0.84)	<0.001
Race (Ref: White)								
Black	0.92 (0.60 1.40)	0.696	1.27 (1.20 1.33)	<0.001	1.05 (0.97 1.12)	0.229	1.28 (1.23 1.33)	<0.001
Hispanic	0.98 (0.61 1.55)	0.919	0.92 (0.86 0.97)	0.005	0.69 (0.63 0.75)	<0.001	0.96 (0.92 1.01)	0.084
Other	1.24 (0.67 2.26)	0.495	0.97 (0.89 1.05)	0.421	0.74 (0.66 0.84)	<0.001	0.98 (0.92 1.04)	0.439
Missing	2.33 (0.95 5.71)	0.065	0.86 (0.69 1.07)	0.177	0.68 (0.48 0.97)	0.036	0.83 (0.70 0.97)	0.021
Medicaid eligibility (Ref: No)	0.68 (0.51 0.91)	0.009	1.29 (1.24 1.34)	<0.001	1.64 (1.56 1.71)	<0.001	1.33 (1.29 1.36)	<0.001
Charlson Comorbidity Index (Ref: None (CCI 0))								
Mild (CCI 1, 2)	0.88 (0.68 1.15)	0.342	1.19 (1.15 1.24)	<0.001	1.50 (1.41 1.60)	<0.001	1.20 (1.17 1.24)	<0.001
Moderate (CCI 3, 4)	0.96 (0.72 1.30)	0.802	1.37 (1.31 1.43)	<0.001	1.98 (1.85 2.11)	<0.001	1.42 (1.38 1.47)	<0.001
Severe (CCI ≥5)	1.22 (0.90 1.66)	0.205	1.71 (1.63 1.79)	<0.001	2.65 (2.48 2.84)	<0.001	1.84 (1.78 1.90)	<0.001
History of tobacco use (Ref: Nonsmoker)	1.26 (1.00 1.60)	0.052	1.13 (1.09 1.17)	<0.001	1.49 (1.43 1.56)	<0.001	1.12 (1.09 1.15)	<0.001
Surgery type (Ref: Minor)								
Major	1.90 (1.53 2.36)	<0.001	1.21 (1.17 1.24)	<0.001	1.19 (1.15 1.24)	<0.001	1.20 (1.17 1.22)	<0.001
Mental health disorders								
Adjustment (Ref: No)	1.60 (1.03 2.50)	0.037	1.01 (0.92 1.10)	0.878	0.94 (0.83 1.06)	0.327	1.02 (0.95 1.09)	0.554
Anxiety	1.20 (0.94 1.54)	0.147	1.16 (1.12 1.21)	<0.001	1.14 (1.08 1.20)	<0.001	1.13 (1.10 1.17)	<0.001
Mood	1.15 (0.90 1.46)	0.267	1.19 (1.15 1.23)	<0.001	1.19 (1.13 1.25)	<0.001	1.17 (1.14 1.20)	<0.001
Suicide or self-harm	1.24 (0.43 3.55)	0.687	1.43 (1.15 1.78)	0.001	1.03 (0.76 1.39)	0.838	1.38 (1.15 1.66)	0.001
Disruptive	1.83 (0.84 3.98)	0.128	1.00 (0.83 1.20)	0.960	0.86 (0.67 1.12)	0.264	1.05 (0.91 1.21)	0.532
Personality	1.38 (0.48 3.94)	0.551	1.12 (0.88 1.41)	0.362	0.95 (0.69 1.30)	0.745	1.21 (1.01 1.46)	0.042
Psychosis	1.41 (0.90 2.22)	0.132	1.16 (1.08 1.25)	<0.001	1.33 (1.21 1.45)	<0.001	1.19 (1.12 1.27)	<0.001
Alcohol or other substance use disorders	2.44 (1.77 3.37)	<0.001	1.20 (1.12 1.29)	<0.001	0.99 (0.90 1.09)	0.860	1.19 (1.12 1.25)	<0.001
Other mental disorders	1.55 (1.06 2.27)	0.023	1.18 (1.10 1.27)	<0.001	1.10 (1.00 1.21)	0.057	1.12 (1.06 1.18)	<0.001
Pain disorders								
Arthritis (Ref: No)	1.38 (0.96 1.97)	0.083	1.16 (1.11 1.21)	<0.001	0.89 (0.84 0.94)	<0.001	0.89 (0.87 0.92)	<0.001
Back	1.04 (0.85 1.28)	0.696	1.14 (1.11 1.18)	<0.001	1.01 (0.97 1.06)	0.528	1.06 (1.04 1.08)	<0.001
Neck	1.11 (0.87 1.40)	0.403	1.02 (0.98 1.06)	0.299	0.96 (0.91 1.01)	0.112	0.98 (0.95 1.00)	0.087
Other pain	1.14 (0.93 1.39)	0.203	1.22 (1.19 1.26)	<0.001	1.18 (1.13 1.22)	<0.001	1.15 (1.13 1.18)	<0.001
Any hospitalization in previous year (Ref: No)	1.12 (0.88 1.43)	0.367	1.28 (1.24 1.32)	<0.001	1.46 (1.40 1.53)	<0.001	1.36 (1.33 1.40)	<0.001
Skilled nursing facility stay in previous year (Ref: No)	1.32 (0.91 1.91)	0.151	0.99 (0.94 1.06)	0.853	1.15 (1.06 1.23)	<0.001	1.02 (0.98 1.08)	0.323
Benzo and Opioid filled concurrently during periop period (Ref: No)	2.08 (1.55 2.78)	<0.001	1.19 (1.12 1.26)	<0.001	1.01 (0.93 1.11)	0.774	1.13 (1.08 1.19)	<0.001

with opioid-related readmissions included diagnoses of alcohol and substance use disorder (OR 2.44, 95% CI: 1.77–3.37) and concurrent fills of benzodiazepines during the perioperative period (OR 2.08, 95% CI: 1.55–2.78). Patients with low and moderate preoperative exposure were also at significantly higher risk of opioid-related readmissions (low: OR 1.63, 95% CI: 1.26–2.12; moderate: OR 1.90, 95% CI: 1.38–2.61).

Pain-related Readmissions

Higher preoperative opioid exposure was also associated with increased risk of pain-related readmissions. Increased likelihood of pain-related readmissions was found to be significant even for patients with minimal preoperative opioid exposure compared to opioid-naive patients (minimal: OR 1.12, 95% CI: 1.07–1.16; low: OR 1.27, 95% CI: 1.23–1.32; moderate: OR 1.40, 95% CI: 1.34–1.47; high: OR 1.62, 95% CI: 1.53–1.71). Patients with a Charlson Comorbidity Index > = 5 had the highest risk of pain-related readmissions (OR 1.71, 95% CI: 1.63–1.79). Mental health disorders, including suicidality (OR 1.43, 95% CI: 1.15–1.78) and alcohol or substance abuse disorders (OR 1.20, 95% CI: 1.12–1.29), were also predictive of pain-related readmissions.

Respiratory-related Readmissions

Preoperative opioid exposure was significantly associated with an increased risk of respiratory-related readmissions compared to patients who were opioid-naive (low: OR 1.10, 95% CI: 1.05–1.16); moderate: OR 1.24, 95% CI: 1.16–1.32; high: OR 1.44, 95% CI: 1.34–1.55). A high Charlson Comorbidity Index score (> = 5) was the most significant predictor of respiratory-related readmissions (OR 2.65, 95% CI: 2.48–2.84). Other attributes correlating with higher risk of respiratory-related readmissions include history of tobacco use (OR 1.49, 95% CI: 1.43–1.56) and hospitalization in the previous year (OR 1.46, 95% CI: 1.40–1.53).

All-cause Readmissions

While minimal preoperative opioid exposure was not significantly associated with higher all-cause readmissions (OR 1.00, 95% CI: 1.40–1.53), low, moderate, and high chronic preoperative opioid exposures were predictive of all-cause readmissions (low: OR 1.09, 95% CI: 1.06–1.12); moderate: OR 1.16, 95% CI: 1.12–1.20; high: OR 1.23, 95% CI: 1.18–1.29). A high Charlson Comorbidity Index score (> = 5) was the most significant predictor of all-cause readmissions (OR 1.84, 95% CI: 1.78–1.90), followed by age of 85 years or older (OR 1.64, 95% CI: 1.58–1.71).

DISCUSSION

In this national cohort of Medicare beneficiaries undergoing common surgery, we observed that nearly 1 of every 2 patients (45%) presenting for surgery filled an opioid prescription in the previous 12 months, a relatively higher preoperative opioid use rate compared with younger cohorts described in previous studies.[10,18,26] To capture intermittent use, this study's definition of preoperative opioid exposure includes any fills in the year prior to surgery. While likelihood of readmissions rose with higher preoperative opioid exposure, we found that even remote, minimal exposure increased the risk of readmissions compared with opioid-naive patients. For patients with recent, moderate-dose exposure of low duration—which accounted for 41.5% of the preoperative opioid users—our results indicated a significantly higher risk of opioid-related, pain-related, respiratory-related, and all-cause readmissions. Taken together, these findings highlight the importance of preoperative risk screening and optimization for patients already using opioids prior to undergoing common surgery.

Our research aligns with prior studies examining the association between preoperative opioid exposure and increased postoperative healthcare utilization[9,27,28] and further describes the nuanced effect of varying degrees of opioid exposure. Among studies examining the association between preoperative opioid exposure and health outcomes, many have stratified groups based on the duration of preoperative opioid use alone.[29–32] Incorporating the granular details of dosage, timing, and continuity allows for identification of the highest risk groups, specifically among patients with a high degree of preoperative opioid exposure. Increased pain-related complications in patients with preoperative opioid exposure have been well documented,[33,34] and may relate to analgesic tolerance and opioid-induced hyperalgesia, along with other pathophysiologic effects of opioids.[35] In this context, patients with preoperative opioid exposure could require additional opioid prescriptions after discharge or larger prescriptions,[8] which may be challenging in light of a growing number of policies restricting opioid prescribing for acute pain. Notably, in this cohort, even patients with relatively minimal preoperative opioid exposure were more likely to experience pain-related readmissions.

Surprisingly, few studies have described the relationship between preoperative opioid exposure and respiratory-related readmissions after discharge. In one study, opioid abuse and dependence in patients undergoing elective orthopedic surgery was associated with postoperative morbidity and mortality, including respiratory failure.[36] This may be due to the challenging nature of managing postoperative pain in patients with high opioid tolerance, whose higher opioid exposure may cause nocturnal hypoxemia and increase morbidity risk in patients with preexisting obstructive sleep apnea.[37,38] Consistent with these reported outcomes, our analysis found that high chronic opioid exposure significantly increased the likelihood of respiratory-related readmissions even when controlling for other comorbidities. Even patients with relatively low and moderate levels of preoperative opioid exposures had greater risk of respiratory readmissions after discharge.

Opioid-related readmissions in patients with preoperative opioid exposure have previously been contextualized under discharge planning for patients in remission from opioid use disorder.[39] In such patients, poorly controlled pain and access to prescription opioids can lead to both craving and relapse.[40,41] Overdose prevention education and nasal naloxone prescription have been suggested as part of their relapse mitigation strategy. While there are distinct differences between high chronic exposure and opioid use disorder, our data shows significantly greater risk of opioid-related readmissions after surgery in high chronic users. With high chronic exposure as the most influential predictor of opioid-related readmissions, providing naloxone prescriptions at discharge may be warranted for some high-risk patients as part of their safe postoperative pain management plan.

Our study has several notable limitations. First, this is a retrospective analysis of Medicare claims data, and we could only account for opioid prescriptions that patients filled rather than the amount consumed. We also could not account for prescription opioids obtained outside of active insurance, medications that were filled prior to the restricted 12-month window, and opioids obtained from diverted prescriptions or other illicit opioid use (eg., heroin use). Analysis of administrative claims data depends on coding methodology and accuracy, which may lead to underestimation or overestimation of readmissions data. Additionally, although we did account for comorbid conditions, this may not fully capture patient frailty, which may affect risk of readmission after discharge. Finally, this study may not be generalizable to other age groups.

Despite these limitations, our findings have important implications for practitioners and policy makers. As standard practice, surgeons can set expectations by discussing postoperative pain and duration of opioid use with patients. For patients expected to need ongoing opioid prescriptions after surgery, surgeons may consider strategies like multimodal pain management therapy that have shown to significantly reduce follow-up pain scores and readmissions after discharge.[42] One study of patients undergoing total joint arthroplasty also reported improved pain and functional outcomes after preoperative opioid reductions, providing further rationale for preoperative opioid weaning to minimize risk after surgery.[43,44] Multidisciplinary programs that cater to individual pain management needs, which may include preoperative opioid weaning if appropriate, have the potential to reduce complications after surgery among patients with preoperative opioid exposure.[45,46] These results complement our findings and highlight the importance of preoperative screening, which may facilitate disclosing risk to patients, coordinating care with their usual prescriber, and allocating resources effectively. Future clinical studies should assess postoperative outcomes of opioid-weaning protocols optimized for different surgical procedures, the results from which may better inform strategies for practical implementation.

As preoperative opioid exposure has shown to be predictive of readmissions, surgeons can benefit from routinely screening for preoperative opioid exposure as part of surgical risk assessment. This is particularly relevant to patients with relatively low and

moderate levels of preoperative opioid exposure, whose remote or infrequent prescription filling may exclude them from being routinely queried. A prior study of patients undergoing major abdominal surgery found preoperative opioid exposure, which was quantified as a binary variable, to be predictive of increased costs and worse postoperative outcomes.[10] By adding granularity to the levels of preoperative opioid exposure, our study validates thresholds of clinically meaningful risk by demonstrating that even minimal or low levels of opioid exposures can increase readmission rates, thereby contributing to higher healthcare costs. Future studies may consider incorporating details of dose, duration, recency, and continuity of use to better quantify cost burden associated with varying levels of preoperative opioid exposure.

In addition to optimizing preoperative counseling regarding pain expectations, our finding that high chronic exposure accounted for 10% of our cohort underscores the importance of identifying risk factors and screening patients prior to surgery. However, all surgical patients receiving postoperative opioids can benefit from a more coordinated transitioning of care after discharge. In a cross-sectional survey of primary care physicians, most respondents reported deficiencies (poor communication, unclear postoperative plan, and unspecified provider roles in postsurgical care) in the transfer of care process for postsurgical patients and perceived these inadequate transitions to have contributed to adverse events.[47] Developing guidelines for transitions of care for postoperative opioid prescribing and incentivizing multidisciplinary care coordination may promote a more patient-centered care, while minimizing suboptimal outcomes.[48]

CONCLUSION

Among Medicare beneficiaries 65 years and older, higher levels of preoperative opioid exposure were associated with increased opioid-related, pain-related, respiratory-related, and all-cause readmissions after common surgery. Even minimal preoperative opioid exposure was predictive of readmissions. Our findings emphasize the importance of screening patients prior to surgery and tailoring safe postoperative pain management plans for patients with varying levels of preoperative opioid exposure.

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