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Postoperative opioid utilization associated with revision risk following primary shoulder arthroplasty

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Introduction: With a substantial increase in utilization of primary shoulder arthroplasty, it is important to understand risk factors that may signal early failure and need for revision. Recent studies have reported that sustained postoperative opioid use is associated with a higher revision risk after total hip or knee arthroplasty. In this study, we evaluated postoperative opioid utilization as a risk factor for revision after primary shoulder arthroplasty.

Methods: We conducted a cohort study using data from a United States integrated health care system's Shoulder Arthroplasty Registry. Patients who had a primary elective shoulder arthroplasty were identified (2009-2017); those with cancer or who underwent other arthroplasty procedures (either shoulder, hip, or knee) within the preceding year were excluded. Cumulative daily opioid utilization during the first year postoperative, calculated as oral morphine equivalents (OME), was categorized into 3 exposure groups: high user ($\geq$15 mg OME daily), moderate user (<15 mg OME daily), and no opioid use (reference group). The exposure window was stratified into 2 time periods: postoperative days 1-90 and postoperative days 91-360. Multivariable Cox proportional-hazards regression was used to evaluate the association between postoperative opioid use and aseptic revision risk.

Results: The final study sample included 8325 shoulder arthroplasty procedures. Of these individuals, 3707 (45%) received some opioid within the 1 year before the index procedure. We failed to observe a difference in aseptic revision risk between opioid utilization in the first 90 days postoperatively, regardless of dose. After the first 90 days, a higher revision risk was observed for high opioid users compared with nonusers (hazard ratio = 1.62, 95% confidence interval = 1.10-2.41), and no association was observed for moderate users (hazard ratio = 1.25, 95% confidence interval = 0.82-1.91).

Conclusions: We found a positive association between opioid consumption and aseptic revision risk after primary shoulder arthroplasty. This study cannot determine if opioids have a direct physiological cause that increases the risk of revision; rather it is likely that opioid consumption is a marker of chronic pain, poor function, and/or poor coping mechanisms. Further study is needed to determine if programs designed to decrease opioid use may impact revision risk after shoulder arthroplasty.

Level of evidence: Level III; Retrospective Case-Control Design; Prognosis Study

Keywords: Shoulder arthroplasty; opioid utilization; oral morphine equivalent; revision; registry; risk factors

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This study was approved by the Kaiser Permanente institutional review board (IRB #5527).

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Utilization of primary total shoulder arthroplasty (TSA) in the United States has increased by nearly 10% annually,[13] with a 2.7-fold increase in procedures from 2005 to 2013.[15] Revision surgery has also increased from 4.5% in 1993 to 7% in 2007.[13] Revision shoulder arthroplasty is an undesirable outcome, associated with prolonged treatment, inferior outcomes, and surgical challenges at significant expense to the health care system. Therefore, it is important for providers to be aware of risk factors for failure to allow for timely and effective treatment of an unsatisfactory shoulder arthroplasty.

The United States is in the midst of an opioid epidemic, with the Centers for Disease Control and Prevention reporting approximately 33,000 deaths in 2015 and the White House Council of Economic Advisors estimating an economic burden of 393.9 billion US dollars the same year.[21] Opioids are commonly used to treat pain not related to cancer; however, opioid use after surgical procedures is associated with risk of chronic opioid dependence.[8,42] This may result from high level of or prolonged opioid consumption, but may also occur at regular prescribed doses.[19]

It is well established in the arthroplasty literature that preoperative opioid usage is associated with more postoperative utilization,[5-7,18,20,23,24,31,34,39,40] and poorer outcomes in terms of revision risk and patient-reported outcome measures (PROM).[2-4,6,28,43,46] Recent publications also support close surveillance of individuals who use opioids persistently after total knee or total hip arthroplasty as this may be an early indicator for pain requiring revision surgery.[7,9,22,29,30,44] In contrast, the association of postoperative opioid utilization on revision risk after primary shoulder arthroplasty is not established.

We postulate that opioid prescriptions are a more readily tracked surrogate for pain that might be used to identify shoulder arthroplasty patients who are at risk for failure requiring revision surgery. The objective of this study was to determine the association of sustained postoperative opioid use on revision risk after elective TSA, stratified by patients who were opioid naïve and patients who used opioids within 1 year before primary shoulder arthroplasty. We hypothesized that revision risk would differ depending on postoperative opioid utilization and that preoperative opioid use may be an effect modifier.

Materials and methods

Study design, setting, and data sources

We conducted a cohort study using our integrated health care system's Shoulder Arthroplasty Registry (SAR). The integrated health care system covers over 12.2 million lives throughout 8 geographical regions (ie, Colorado, Georgia, Hawaii, Mid-Atlantic, Northern California, Northwest, Southern California, and Washington) in the United States.

A detailed summary of data collection procedures, geographic coverage, demographics, and participation rates for the SAR has been published previously.[14,33] Briefly, this surveillance tool for all shoulder arthroplasty procedures performed within the integrated health care system collects patient, procedure, implant, surgeon, and hospital information using electronic intraoperative forms that are completed at the point of care by the operating surgeon. Information is then supplemented using data from the electronic health record (EHR), administrative claims data, membership data, and mortality records. Outcomes are prospectively monitored using electronic screening algorithms and validated by trained clinical content experts using the EHR. Our integrated health care system's EHR was the second data source for this study. This Epic-based platform (Verona, Wisconsin) was introduced in 2004 and was fully implemented in all regions in 2008. The EHR's pharmacy module was used to identify opioid medication prescription and dispensing.

Study sample

The study sample was selected using the SAR and comprised all primary elective shoulder arthroplasty procedures for nonfracture indications performed between January 1, 2009, and December 31, 2017. Hemiarthroplasty, reverse total shoulder arthroplasty, and TSA procedures were included. Because of availability of prescription data in the EHR (eg, supply days, daily dose, quantity per day, strength), only the Northern and Southern California regions of the health care system were included in the study. Patients with a history of cancer (identified using International Classifications of Disease, 9th Revision, Clinical Modification [ICD-9-CM] codes 140.xx-208.xx, except 173.xx for pain related to cancer[37] or the specific Elixhauser comorbidities[36] of lymphoma, metastatic cancer, solid tumor without metastasis), a history of another arthroplasty surgery (including hip, knee, or shoulder) in the 1 year preceding the index procedure, and procedures for the indication of fracture were excluded.

Exposure of interest

The exposure of interest was 1-year postoperative opioid prescription, calculated as daily oral morphine equivalents (OME) of oral or transdermal opioids (Table I).[45] Daily OME dose was calculated as cumulative dose over observation days. If a patient had a revision, died, or terminated health care plan membership during the first 360 days postoperatively, the amount of opioid exposure was calculated until the last observation day. For analysis, daily opioid amount was categorized into 3 exposure groups: high dose ($\geq$15 mg OME daily, equivalent to 3 tabs of Norco5/325 daily), moderate dose ($<$15 mg OME daily), and no opioid prescription (reference group).

The 1-year postoperative exposure window was also broken down into 90-day periods (days 0-90, days 91-180, days 181-270, and days 271-360). For the purposes of this study, days 0-90 was referred to as the early recovery period and days 91-360 was the later rehabilitation period. Daily opioid use during days 91-360 were studied together because prevalence and OME consumption patterns were similar across the 3 periods.

Table I Oral or transdermal opioids included in this study

Medication	Route	Oral morphine equivalent[44]
Acetaminophen with codeine	Oral	0.15
Buprenorphine	Transdermal	40 (ref)
Butalbital/acetaminophen/caffeine/codeine	Oral	0.15
Codeine/butalbital/aspirin/caffeine	Oral	0.15
Codeine phosphate/guaifenesin	Oral	0.15
Codeine sulfate	Oral	0.15
Fentanyl	Transdermal	2.4
Hydromorphone HCl	Oral	4.0
Methadone HCl	Oral	3.0
Morphine sulfate	Oral	1.0
Oxycodone HCl	Oral	1.5
Oxycodone HCl/acetaminophen	Oral	1.5
Oxycodone HCl/aspirin	Oral	1.5
Promethazine HCl/codeine	Oral	0.15
Promethazine/phenylephrine/codeine	Oral	0.15
Pseudoephedrine/codeine/guaifenesin	Oral	0.15
Tramadol HCl/acetaminophen	Oral	0.10
Tramadol HCl	Oral	0.10

Outcome of interest

Aseptic revision was the outcome of interest. Revision was defined as any reoperation performed after the index shoulder arthroplasty where an implant was exchanged, removed, or added for aseptic reasons. Revision reason was reported by the operating surgeon; cultures were taken at the discretion of the surgeon, not mandated. After the index shoulder arthroplasty procedure, each patient was continuously monitored for revision using validated surveillance algorithms and surgeon report until either death or membership termination (leaving our institution's health care plan). Identified revisions are then manually validated by trained research associates during quarterly quality control.

Confounders

Preoperative risk factors of postoperative opioid use identified in a prior study were considered as potential confounders in the present study.[39] Risk factors included preoperative opioid/nonsteroidal anti-inflammatory drug use (yes vs. no), patient age ($\geq$60 vs. $<$60 years old), sex (female vs. male), race/ethnicity (Hispanic vs. others), body mass index (BMI, $\geq$35 vs. $<$35 kg/m^2), American Society of Anesthesiologists (ASA) classification ($\geq$3 vs. 1-2), procedure type (hemiarthroplasty, reverse total shoulder arthroplasty, and TSA); other medical comorbidities (present vs. absent) including chronic pulmonary disease, depression, liver disease, neurodegenerative disorders, and rheumatoid arthritis/collagen vascular diseases; opioid use–related comorbidities (present vs. absent) including anxiety, dementia and psychosis, opioid dependence, post-traumatic stress disorder, and substance abuse; and history of chronic pain (present vs. absent) including back pain, fibromyalgia, kidney/gall stone pain, and migraines. Specific opioid use–related comorbidities and history of chronic pain were identified using an ICD-9-CM coding algorithm.[36] Other medical comorbidities were identified using the Elixhauser comorbidity algorithm.[17]

Effect modifier

Preoperative opioid use was considered as a potential effect modifier. Preoperative use was defined as at least 1 opioid prescription dispensed during the 1 year before the index procedure and opioid naïve defined as no opioid prescription dispensed during the 1 year before the index procedure.

Statistical analysis

Cox proportional hazard regression was used to evaluate the effect of postoperative opioid prescription on aseptic revision. The model included the exposure variable and all potential confounders listed above as fixed effects; the operating surgeon was included in the model as a random intercept to adjust for surgeon variability and procedure volume. Follow-up time was defined as the time from the exposure period of interest until the date of revision surgery, death, health care membership termination, or the date of final registry surveillance for the study (December 31, 2017), whichever came first. In this study, patients not experiencing the aseptic revision had survival follow-up times censored on the date septic revision, death, health care membership termination, or the date of final registry surveillance. We also calculated the completeness of follow-up as the sum of observed follow-up times divided by the sum of potential follow-up times.[10] For the exposure time windows evaluated, each model only included "at risk" patients who had follow-up time greater than or equal to the beginning of the exposure start time. For example, if a patient had 3 tabs of Norco5/325 daily since postoperative day 1 and then was died on postoperative day 60, that patient was classified as high dose ($\geq$15 mg OME daily) and was included in

the early recovery period model and censored at day 60, but the patient was not included in the later rehabilitation period model.

The proportional hazards assumption for the exposure variables was checked by the proportional hazards test; when the exposure of interest had a varying impact on the hazard over time (ie, nonproportional hazard), we modeled the effect using time-dependent variables. The same analysis was performed for the overall cohort and then after stratifying by preoperative opioid use. To account for missing values (sex = 1 [<1%], race = 19 [<1%], BMI = 6 [<1%], ASA = 1457 [17.5%], opioid use–related comorbidities = 3570 [42.9%], history of chronic pain = 3570 [42.9%], other medical comorbidities = 155 [1.9%]), fully conditional specification multiple imputations using the Markov chain Monte Carlo estimation method were performed to create 50 versions of the analytic dataset. Each dataset was separately analyzed using the same model, and the results were combined using Rubin's rules.[41] The imputation model included all variables and the baseline hazard function.[48] Analyses were performed using R version 3.3.0. Hazard ratios (HR) and 95% confidence intervals (CIs) are presented. All tests were 2-sided, and the alpha level was 0.05 for statistical significance for this study.

Results

The final study sample comprised 8325 primary elective shoulder arthroplasty procedures performed in 7355 patients. The procedures were performed by 185 surgeons at 37 health care centers in 2 regions. Of these shoulder arthroplasty patients, 86.6% were 60 years or older, 54.4% were female, 80.5% (n = 6688) were white, 18.5% had a BMI ≥35 kg/m^2, 47.3% had an ASA classification ≥3, and 57.8% underwent a TSA. Almost half (44.5%) of patients had at least 1 opioid prescription during the 1-year preoperative time window, whereas only 19.1% had at least 1 nonsteroidal anti-inflammatory drug prescription. Select comorbidities for the study sample are presented in Table II.

Postoperatively, 60.0% of patients used opioids (38.4% had a moderate daily dose [<15 mg] and 22.2% had a high daily dose [≥15 mg]) in the first 90 days (early recovery period) (Table III). Of patients who were opioid users during the early recovery period, the 25th percentile for daily consumption was 6.2 mg, and 50th and 75th percentiles were 10.0 mg and 20.8 mg, respectively. During the later rehabilitation period (days 91-360), 24% of patients used opioids (14.9%-13.8% moderate daily dose, 8.7%-8.2% high daily dose).

Overall follow-up was an average of 3.1 years and 9 years maximum; 95.8% of patients included in the study sample had complete follow-up. The overall 5-year cumulative incidence of aseptic revision was 4.2% (95% CI = 3.4%-4.4%). For the overall cohort, we failed to observe a difference in aseptic revision risk when comparing postoperative opioid use during the early recovery period with no use (<15 mg daily use: HR = 0.90, 95% CI = 0.72-1.13; ≥15 mg daily use: HR = 1.26, 95% CI = 0.94-1.68). Regarding opioid consumption in the later rehabilitation period, a higher revision risk was observed for patients who used at least 15 mg of opioids daily (HR = 1.62, 95% CI = 1.10-2.41) (Table IV); no association was observed for moderate daily dose compared with no opioid use (HR = 1.25, 95% CI = 0.82-1.91).

Table II Characteristics of 8325 primary elective shoulder arthroplasty patients

Characteristic	n (%)
Age ≥60 (yr)	7210 (86.6)
Median (interquartile range)	70 (64-77)
Female sex	4526 (54.4)
Race/ethnicity	
Asian	206 (2.5)
Black	411 (4.9)
Hispanic	923 (11.1)
Other	78 (0.9)
White	6688 (80.5)
Body mass index (kg/m^2)	
<20	151 (1.8)
20-24.9	1522 (18.3)
25-29.9	3042 (36.6)
30-34.9	2069 (24.9)
≥35	1535 (18.5)
ASA classification ≥3	3249 (47.3)
Surgery type	
Hemiarthroplasty	809 (9.7)
Reverse total shoulder arthroplasty	2705 (32.5)
Total shoulder arthroplasty	4811 (57.8)
Preoperative opioid use	3707 (44.5)
Preoperative NSAID use	1591 (19.1)
Other medical comorbidities	
Chronic pulmonary disease	1894 (23.2)
Depression	911 (11.2)
Liver disease	358 (4.4)
Neurodegenerative disorders	543 (6.6)
Rheumatoid arthritis/collagen vascular diseases	572 (7.0)
Opioid use-related comorbidities	
Anxiety	682 (14.3)
Dementia and psychosis	54 (1.1)
Opioid dependence/abuse	84 (1.8)
Post-traumatic stress disorder	27 (0.6)
Substance abuse	515 (10.8)
History of chronic pain comorbidities	
Back pain	621 (13.1)
Fibromyalgia	82 (1.7)
Kidney/gall stone pain	26 (0.5)
Migraines	62 (1.3)

ASA, American Society of Anesthesiologists; *NSAID*, nonsteroidal anti-inflammatory drug; *BMI*, body mass index.
Missing: sex = 1 (<1%), race = 19 (<1%), BMI = 6 (<1%), ASA = 1457 (17.5%), other medical comorbidities = 155 (1.9%), opioid use–related comorbidities = 3570 (42.9%), history of chronic pain = 3570 (42.9%).

Table III Postoperative opioid utilization (in OME) after primary elective shoulder arthroplasty (N = 8325), by 90-day postoperative window

	Exposure window			
	Days 1-90	Days 91-180	Days 181-270	Days 271-360
Total N at risk	8325	7895	7504	7085
Daily opioid user, n (%)				
No opioid use	3278 (39.4)	6026 (76.3)	5778 (77.0)	5528 (78.0)
<15 mg	3196 (38.4)	1180 (14.9)	1077 (14.4)	975 (13.8)
≥15 mg	1851 (22.2)	689 (8.7)	649 (8.6)	582 (8.2)
Daily OME* (mg)				
25th percentile	6.2	2.6	2.3	2.0
50th percentile	10.0	8.3	8.3	8.3
75th percentile	20.8	28.0	27.5	27.9

OME, oral morphine equivalent.
* Percentiles were calculated for opioid users only.

Results for patients who had at least 1 preoperative opioid prescription were similar to those found for the overall cohort (Table IV): no difference was observed in revision risk by opioid consumption during the early recovery period (<15 mg daily use: HR = 1.22, 95% CI = 0.81-1.82; ≥15 mg daily use: HR = 1.51, 95% CI = 0.99-2.29) or for moderate users during the later rehabilitation period (HR = 0.97, 95% CI = 0.59-1.59), but a higher revision risk during the first postoperative year was observed for preoperative opioid users who continued to use a high daily opioid dose during the later rehabilitation period (HR = 2.43, 95% CI = 1.22-4.85). No difference was observed in revision risk after the first postoperative year for patients who were preoperative opioid users who continued to use a high daily opioid dose during the later rehabilitation period (HR = 0.96, 95% CI = 0.57-1.63). For patients who were opioid naïve at the time of the shoulder arthroplasty procedure, those who took moderate dose during the early recovery period had a lower revision risk in the first postoperative year (HR = 0.37, 95% = 0.21-0.67), but no difference was observed in risk after the first postoperative year (HR = 1.26, 95% CI = 0.74-2.14). Preoperative opioid naïve patients who used opioids during the later rehabilitation period had a higher revision risk compared with nonusers, regardless of dose (<15 mg daily use: HR = 1.82, 95% CI = 1.14-2.91; ≥15 mg daily use: HR = 3.17, 95% CI = 1.31-7.66).

Discussion

This study evaluated aseptic revision risk for individuals with no, low (<15 mg morphine equivalents per day), and high (≥15 mg morphine equivalents per day) daily postoperative opioid prescription after primary elective shoulder arthroplasty. A higher aseptic revision risk was observed in patients who continued to have a high dose of opioids during the later rehabilitation period, both for patients who were opioid users at the time of the index procedure and for those who were opioid naïve. Further, opioid naïve patients who continued to use opioids after the 90-day postoperative period even at moderate doses also had a higher aseptic revision risk even though a lower revision risk was observed for this group of patients during the early recovery period.

Prior studies have described the relationship between postoperative opioid use and revision risk for hip and knee arthroplasty. Namba et al found that prolonged oral opioid utilization after both total hip[29] and knee arthroplasty[30] was associated with higher 1- and 5-year aseptic revision rates. These findings were confirmed by other US studies finding chronic postoperative opioid utilization to be associated with a higher revision risk using PearlDiver data,[7,9] as well as an Australian cohort of total hip arthroplasty patients.[22]

The present study moves beyond this work, also finding prolonged postoperative opioid prescription associated with revision risk in the setting of elective shoulder arthroplasty. We also stratified based on preoperative opioid use and found the strongest association to be for opioid naïve patients who continued to use opioids after the early recovery period with the strength of the association increasing as the average daily dose increased. Interestingly, an inverse lower revision risk was observed for opioid naïve patients who used opioids during the early recovery period. We hypothesize that opioid use may be a stronger indicator for "true" postsurgical pain during this time. Prolonged opioid use in the late recovery period in the opioid naïve population may be more prescient of revision risk in which a surgeon may want to monitor the patient's postsurgical progress and course with perhaps more heightened clinical concern, whereas preoperative opioid use may not be as reliable an indicator of pain given neurobiologic and physiological changes associated with chronic opioid use. Preoperative opioid users did have a higher revision risk but only for high dose usage after the first postoperative year.

As the present study is observational, the associations reported here between postoperative opioid prescription and higher revision risk cannot be interpreted as more opioid utilization directly causes implant problems necessitating

Table IV Crude and adjusted associations of postoperative opioid oral morphine equivalents consumption (in mg) and risk of aseptic revision after primary elective shoulder arthroplasty

Sample	Exposure window	Daily opioid use	Number revised	5-yr revision CIF (95% CI)	Adjusted* HR (95% CI)	*P* value
Overall (N = 8325)	Days 1-90	No opioid use	88	3.4% (2.7-4.1)	(ref)	–
		<15 mg	73	3.5% (2.6-4.3)	0.90 (0.72-1.13)	.350
		≥15 mg	72	5.6% (4.2-6.9)	1.26 (0.94-1.68)	.116
	Days 91-360	No opioid use	127	2.9% (2.4-3.4)	(ref)	–
		<15 mg	34	4.6% (2.9-6.2)	1.25 (0.82-1.91)	.298
		≥15 mg	29	5.6% (3.5-7.7)	**1.62 (1.10-2.41)**	**.016**
Preoperative opioid user (N = 3707)	Days 1-90	No opioid use	25	3.7% (2.2-5.2)	(ref)	–
		<15 mg	42	4.4% (3.0-5.7)	1.22 (0.81-1.82)	.341
		15+ mg	55	6.0% (4.3-7.6)	1.51 (0.99-2.29)	.054
	Days 91-360	No opioid use	57	3.9% (2.8-4.9)	(ref)	–
		<15 mg	20	4.4% (2.3-6.4)	0.97 (0.59-1.59)	.911
		15+ mg	25	5.3% (3.2-7.5)	**2.43 (1.22-4.85)**†	**.011**
					0.96 (0.57-1.63)‡	.884
Opioid naïve (N = 4618)	Days 1-90	No opioid use	63	3.3% (2.5-4.1)	(ref)	–
		<15 mg	31	2.7% (1.7-3.6)	**0.37 (0.21-0.67)**†	**.001**
					1.26 (0.74-2.14)‡	.394
		≥15 mg	17	4.5% (2.3-6.7)	1.17 (0.70-1.96)	.557
	Days 91-360	No opioid	70	2.4% (1.8-2.9)	(ref)	–
		<15 mg	14	4.9% (2.3-7.5)	**1.82 (1.14-2.91)**	**.012**
		15+ mg	4	8.5% (0.0-16.5)	**3.17 (1.31-7.66)**	**.011**

CIF, cumulative incidence function; *CI*, confidence intervals; *HR*, hazard ratio; *ASA*, American Society of Anesthesiologists; *BMI*, body mass index.

* Model adjusted for operating surgeon and patient risk factors: days 1-90 = age, gender, surgical procedure, ASA classification, BMI, opioid dependent, substance abuse, general chronic pain, anxiety, chronic pulmonary disease, migraines, liver disease, Hispanic, and depression; days 91-360 = age, gender, surgical procedure, ASA classification, BMI, opioid dependent, substance abuse, general chronic pain, anxiety, chronic lung disease, back pain, rheumatoid arthritis/collagen vascular diseases, neurodegenerative disorders, and depression.

† Revision risk within 1 year postoperatively, stratified due to varying impact on the hazard over time (nonproportional hazard).

‡ Revision risk after 1 year postoperatively, stratified due to varying impact on the hazard over time (nonproportional hazard).

Bold values are statistically significant ($P < .05$).

revision. Rather, more opioid utilization may be a marker for 1 or both of the following mechanisms: (1) ongoing nociceptive pain, which may result from implant-related or soft tissue complications that ultimately warrant revision surgery, and/or (2) a constellation of known risk factors (eg, anxiety, chronic pain, workers compensation) that also impact revision rates. Risk factors for prolonged opioid utilization after elective shoulder arthroplasty are well described. Rao et al[39] found that preoperative opioid use, chronic pain conditions, and psychiatric issues, such as anxiety, were associated with greater postoperative opioid utilization. Eads et al[16] similarly reported that patients with a history of depression, anxiety, or medication for a mood disorder were 4 times more likely to use narcotics after TSA. Other studies found preoperative opioid utilization to be the strongest risk factor for postoperative opioid utilization.[5,12,23,32] Preoperative opioid utilization, chronic pain, and mood disorders as important risk factors for postoperative narcotic utilization are consistent in the literature across orthopedic procedures including hip and knee arthroplasty,[6,18,20,24,31,34,40] anterior cruciate ligament (ACL) reconstruction,[1,38] rotator cuff repair,[47] and cervical spine surgery.[35]

Associations between preoperative opioid use and outcomes in shoulder arthroplasty have also been previously reported. Morris et al[28] noted that patients who were exposed to opioids preoperatively had lower baseline PROM and lower postoperative PROM after TSA compared with opioid naïve patients, even though improvements in scores from baseline to postoperative were observed. Thompson et al[43] recently added that pain and motion had significantly more improvement in the opioid-naive group compared with a group that had taken opioids for 3 months before primary total shoulder replacement.

This work has implications for further study. Evaluating the potential reduction of TSA revision rates by using multimodal pain management, reduction, or elimination of perioperative opioids and prospective monitoring of at-risk individuals are particular areas of interest.

Strengths and limitations

Study strengths include data that were obtained from an integrated health care system's registry, with 100% capture rate and prospective data collection methodologies, increasing

internal validity. Our study sample includes health care centers with different case volumes and surgeon training from 2 geographic regions, increasing generalizability. This study included a larger sample, allowing for robust statistical analysis of an outcome (revision) that is relatively uncommon.

There are several limitations to consider. First, opioid prescription and dispensing may not be a perfect marker for pain as individuals have variable pain tolerance.[27] Second, OME was calculated based on dispensed quantities and the intended prescribed frequency. Further, only oral and transdermal opioids dispensed postoperatively within the integrated health care system were captured via the EHR's outpatient encounter modules. It is acknowledged that a patient could take more or less than instructed and may not consume all dispensed quantities. Third, we lacked information on the reason for opioid prescriptions so patients may have been prescribed opioids for other indications. To reduce this confounding factor, we excluded patients who underwent other arthroplasties within 1 year of the index shoulder arthroplasty and patients with a history of cancer. Fourth, there were over 40% missing values in opioid-related comorbidities (eg, anxiety, dementia, chronic pain) due to conversion in 2016 of coding from ICD-9 to ICD-10. These data were considered missing at random because administrative coding changes were not directly related to patient status. Missing data as potential confounders were handled with imputation by chained equations; unbiased results can be obtained with missing imputation, even in the setting of up to 90% of missing data, provided the imputation model is properly specified and data are missing at random.[25] With this method, the uncertainties due to missing data were compensated with a larger standard error and wider CIs.[11,26] A sensitivity analysis excluding opioid-related comorbidities from the multivariable model was performed, and the same results regarding postoperative opioid use and revision risk were observed. Fifth, it is possible that individuals with chronic infections by low-virulence organisms with a negative workup were coded as aseptic loosening by the treating physician given the lack of mandatory intraoperative cultures. However, we do not expect this to depend on opioid use status. Finally, a direct mechanism or causation of opioid prescription and revision of shoulder arthroplasty cannot be inferred from this work.

Conclusions

Opioid utilization during the late rehabilitation period after elective primary shoulder arthroplasty was associated with a higher revision risk, a risk that was more pronounced in opioid naïve patients. It is prudent to counsel and monitor individuals with known risk factors for sustained opioid utilization. Shoulder arthroplasty patients who continue to use opioids after the early recovery period warrant close follow-up as it is an independent risk factor for revision.

Disclaimer

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References

1. Anthony CA, Westermann RW, Bedard N, Glass N, Bollier M, Hettrich CM, et al. Opioid demand before and after anterior cruciate ligament reconstruction. Am J Sports Med 2017;45:3098-103. https://doi.org/10.1177/0363546517719226
2. Bedard NA, DeMik DE, Dowdle SB, Owens JM, Liu SS, Callaghan JJ. Does preoperative opioid use increase the risk of early revision total hip arthroplasty? J Arthroplasty 2018;33:S154-6. https://doi.org/10.1016/j.arth.2018.01.018
3. Bedard NA, DeMik DE, Dowdle SB, Owens JM, Liu SS, Callaghan JJ. Preoperative opioid use and its association with early revision of total knee arthroplasty. J Arthroplasty 2018;33:3520-3. https://doi.org/10.1016/j.arth.2018.06.005
4. Ben-Ari A, Chansky H, Rozet I. Preoperative opioid use is associated with early revision after total knee arthroplasty: a study of male patients treated in the veterans affairs system. J Bone Joint Surg Am 2017;99:1-9. https://doi.org/10.2106/JBJS.16.00167
5. Berglund DD, Rosas S, Kurowicki J, Horn B, Mijic D, Levy JC. Preoperative opioid use among patients undergoing shoulder arthroplasty predicts prolonged postoperative opioid use. J Am Acad Orthop Surg 2018;27:e691-5. https://doi.org/10.5435/JAAOS-D-18-00008
6. Blevins Peratikos M, Weeks HL, Pisansky AJB, Yong RJ, Stringer EA. Effect of preoperative opioid use on adverse outcomes, medical spending, and persistent opioid use following elective total joint arthroplasty in the United States: a large retrospective cohort study of administrative claims data. Pain Med 2020;21:521-31. https://doi.org/10.1093/pm/pnz083
7. Bolarinwa SA, Casp AA, Cancienne JM, Werner BC, Browne JA. Narcotic use and total hip arthroplasty. Hip Int 2019;29:379-84. https://doi.org/10.1177/1120700018781759
8. Brummett CM, Waljee JF, Goesling J, Moser S, Lin P, Englesbe MJ, et al. New persistent opioid use after minor and major surgical procedures in us adults. JAMA Surg 2017;152:e170504. https://doi.org/10.1001/jamasurg.2017.0504
9. Cancienne JM, Patel KJ, Browne JA, Werner BC. Narcotic use and total knee arthroplasty. J Arthroplasty 2018;33:113-8. https://doi.org/10.1016/j.arth.2017.08.006
10. Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. Lancet 2002;359:1309-10. https://doi.org/10.1016/s0140-6736(02)08272-7
11. Collins LM, Schafer JL, Kam CM. A comparison of inclusive and restrictive strategies in modern missing data procedures. Psychol Methods 2001;6:330-51.
12. Curtis W, Rounds AD, Stone M, Vangsness CT Jr, Weber AE, Hatch GFR III, et al. Effect of preoperative opioid usage on pain after total shoulder arthroplasty. J Am Acad Orthop Surg 2019;27:e734-42. https://doi.org/10.5435/jaaos-d-18-00112
13. Day JS, Lau E, Ong KL, Williams GR, Ramsey ML, Kurtz SM. Prevalence and projections of total shoulder and elbow arthroplasty in the United States to 2015. J Shoulder Elbow Surg 2010;19:1115-20. https://doi.org/10.1016/j.jse.2010.02.009
14. Dillon MT, Ake CF, Burke MF, Singh A, Yian EH, Paxton EW, et al. The Kaiser Permanente Shoulder Arthroplasty Registry: results from

6,336 primary shoulder arthroplasties. Acta Orthop 2015;86:286-92. https://doi.org/10.3109/17453674.2015.1024565
15. Dillon MT, Chan PH, Inacio MCS, Singh A, Yian EH, Navarro RA. Yearly trends in elective shoulder arthroplasty, 2005-2013. Arthritis Care Res (Hoboken) 2017;69:1574-81. https://doi.org/10.1002/acr.23167
16. Eads RB, Brolin TJ, Smith RA, Azar FM, Throckmorton TW. Mood disorders are associated with inferior outcomes of anatomic total shoulder arthroplasty. Curr Orthop Pract 2019;30:142-6. https://doi.org/10.1097/BCO.0000000000000727
17. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.
18. Goesling J, Moser SE, Zaidi B, Hassett AL, Hilliard P, Hallstrom B, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. Pain 2016;157:1259-65. https://doi.org/10.1097/j.pain.0000000000000516
19. Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic opioid use after surgery: implications for perioperative management in the face of the opioid epidemic. Anesth Analg 2017;125:1733-40. https://doi.org/10.1213/ane.0000000000002458
20. Hernandez NM, Parry JA, Mabry TM, Taunton MJ. Patients at risk: preoperative opioid use affects opioid prescribing, refills, and outcomes after total knee arthroplasty. J Arthroplasty 2018;33:S142-6. https://doi.org/10.1016/j.arth.2018.01.004
21. The While House. Council of Economic Advisers report: the underestimated cost of the opioid crisis. Washington, DC. 2017. Available at: https://www.whitehouse.gov/briefings-statements/cea-report-underestimated-cost-opioid-crisis/. Accessed April 4, 2020
22. Inacio MCS, Pratt NL, Roughead EE, Paxton EW, Graves SE. Opioid use after total hip arthroplasty surgery is associated with revision surgery. BMC Musculoskelet Disord 2016;17:122. https://doi.org/10.1186/s12891-016-0970-6
23. Khazi ZM, Lu Y, Patel BH, Cancienne JM, Werner B, Forsythe B. Risk factors for opioid use after total shoulder arthroplasty. J Shoulder Elbow Surg 2020;29:235-43. https://doi.org/10.1016/j.jse.2019.06.020
24. Kim SC, Choudhry N, Franklin JM, Bykov K, Eikermann M, Lii J, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. Osteoarthritis Cartilage 2017;25:1399-406. https://doi.org/10.1016/j.joca.2017.04.002
25. Madley-Dowd P, Hughes R, Tilling K, Heron J. The proportion of missing data should not be used to guide decisions on multiple imputation. J Clin Epidemiol 2019;110:63-73. https://doi.org/10.1016/j.jclinepi.2019.02.016
26. Meng X-L. Multiple-imputation inferences with uncongenial sources of input. Statist Sci 1994;9:538-58.
27. Mogil JS. The genetic mediation of individual differences in sensitivity to pain and its inhibition. Proc Natl Acad Sci U S A 1999;96:7744-51.
28. Morris BJ, Sciascia AD, Jacobs CA, Edwards TB. Preoperative opioid use associated with worse outcomes after anatomic shoulder arthroplasty. J Shoulder Elbow Surg 2016;25:619-23. https://doi.org/10.1016/j.jse.2015.09.017
29. Namba RS, Inacio MCS, Pratt NL, Graves SE, Roughead EE, Craig Cheetham T, et al. Postoperative opioid use as an early indication of total hip arthroplasty failure. Acta Orthop 2016;87(Suppl. 1):37-43. https://doi.org/10.1080/17453674.2016.1181820
30. Namba RS, Inacio MCS, Pratt NL, Graves SE, Roughead EE, Paxton EW. Persistent opioid use following total knee arthroplasty: a signal for close surveillance. J Arthroplasty 2018;33:331-6. https://doi.org/10.1016/j.arth.2017.09.001
31. Namba RS, Singh A, Paxton EW, Inacio MCS. Patient factors associated with prolonged postoperative opioid use after total knee arthroplasty. J Arthroplasty 2018;33:2449-54. https://doi.org/10.1016/j.arth.2018.03.068
32. Nicholson AD, Kassam HF, Steele JL, Passarelli NR, Blaine TA, Kovacevic D. Development of a clinical risk calculator for prolonged opioid use after shoulder surgery. J Shoulder Elbow Surg 2019;28:2225-31. https://doi.org/10.1016/j.jse.2019.03.033
33. Paxton EW, Inacio MC, Kiley ML. The Kaiser Permanente implant registries: effect on patient safety, quality improvement, cost effectiveness, and research opportunities. Perm J 2012;16:36-44.
34. Prentice HA, Inacio MCS, Singh A, Namba RS, Paxton EW. Preoperative risk factors for opioid utilization after total hip arthroplasty. J Bone Joint Surg Am 2019;101:1670-8. https://doi.org/10.2106/JBJS.18.01005
35. Pugely AJ, Bedard NA, Kalakoti P, Hendrickson NR, Shillingford JN, Laratta JL, et al. Opioid use following cervical spine surgery: trends and factors associated with long-term use. Spine J 2018;18:1974-81. https://doi.org/10.1016/j.spinee.2018.03.018
36. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-cm and ICD-10 administrative data. Med Care 2005;43:1130-9. https://doi.org/10.1097/01.mlr.0000182534.19832.83
37. Raebel MA, Newcomer SR, Reifler LM, Boudreau D, Elliott TE, DeBar L, et al. Chronic use of opioid medications before and after bariatric surgery. JAMA 2013;310:1369-76. https://doi.org/10.1001/jama.2013.278344
38. Rao AG, Chan PH, Prentice HA, Paxton EW, Funahashi TT, Maletis GB. Risk factors for opioid use after anterior cruciate ligament reconstruction. Am J Sports Med 2019;47:2130-7. https://doi.org/10.1177/0363546519854754
39. Rao AG, Chan PH, Prentice HA, Paxton EW, Navarro RA, Dillon MT, et al. Risk factors for postoperative opioid use after elective shoulder arthroplasty. J Shoulder Elbow Surg 2018;27:1960-8. https://doi.org/10.1016/j.jse.2018.04.018
40. Rozell JC, Courtney PM, Dattilo JR, Wu CH, Lee G-C. Preoperative opiate use independently predicts narcotic consumption and complications after total joint arthroplasty. J Arthroplasty 2017;32:2658-62. https://doi.org/10.1016/j.arth.2017.04.002
41. Rubin DB. Multiple imputation for nonresponse in surveys. New York: Wiley; 1987.
42. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. JAMA Intern Med 2016;176:1286-93. https://doi.org/10.1001/jamainternmed.2016.3298
43. Thompson KM, Hallock JD, Smith RA, Brolin TJ, Azar FM, Throckmorton TW. Preoperative narcotic use and inferior outcomes after anatomic total shoulder arthroplasty: a clinical and radiographic analysis. J Am Acad Orthop Surg 2019;27:177-82. https://doi.org/10.5435/JAAOS-D-16-00808
44. Vakharia RM, Sabeh KG, Sodhi N, Naziri Q, Mont MA, Roche MW. Implant-related complications among patients with opioid use disorder following primary total hip arthroplasty: a matched-control analysis of 42,097 Medicare patients. J Arthroplasty 2020;35:178-81. https://doi.org/10.1016/j.arth.2019.08.003
45. Von Korff M, Saunders K, Thomas Ray G, Boudreau D, Campbell C, Merrill J, et al. De facto long-term opioid therapy for noncancer pain. Clin J Pain 2008;24:521-7. https://doi.org/10.1097/AJP.0b013e318169d03b
46. Weick J, Bawa H, Dirschl DR, Luu HH. Preoperative opioid use is associated with higher readmission and revision rates in total knee and total hip arthroplasty. J Bone Joint Surg Am 2018;100:1171-6. https://doi.org/10.2106/JBJS.17.01414
47. Westermann RW, Anthony CA, Bedard N, Glass N, Bollier M, Hettrich CM, et al. Opioid consumption after rotator cuff repair. Arthroscopy 2017;33:1467-72. https://doi.org/10.1016/j.arthro.2017.03.016
48. White IR, Royston P. Imputing missing covariate values for the cox model. Stat Med 2009;28:1982-98. https://doi.org/10.1002/sim.3618