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Long-term opioid use after inpatient surgery - A retrospective cohort study

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Abstract

Background—Knowledge of incidence and risk factors for long-term opioid prescribing is critical for surgical patients. In this retrospective cohort study, we linked information available at the time of surgery with prescription data to ascertain characteristics associated with prolonged opioid therapy.

Methods—Patients (n=6,003) with claims in the Colorado All Payer Claims Database (APCD) were matched with 20,501 encounters in a clinical database. Rates of prescription filling were defined by at least one monthly opioid claim relative to the date of surgery. Associations of variables with claims during months 2-6 post-operatively ("long-term prescription filling") were evaluated, and significant variables were jointly modeled using binomial regression.

Results—Rates of patients filling opioid prescriptions preoperatively [month (M) relative to date of surgery] were 22%(-3M), 24%(-2M), and 27%(-1M); after surgery, opioid fill rates were 62%(1M), 28%(2M), 24%(3), 24%(4M), 23%(5M), and 22%(6M). The majority, 71-76%, of

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patients filling prescriptions in months 2-6 after surgery had also filled before surgery. In the binomial regression model, long-term opioid use was associated with prior opioid use ($p<0.0001$), age ≥26 to <65 relative to age ≥ 65 ($p<0.0001$), orthopedic surgery ($p=0.001$), colorectal surgery ($p=0.003$), multiple procedures ($p<0.0001$), and worse physical status classification ($p<0.0001$).

Conclusions—Patients who had filled opioid prescriptions preoperatively comprised the majority of the group who filled long-term prescriptions. Surgical procedures were associated with discontinuation of previous opioid prescribing in some patients. For others, surgery marked the initiation of prolonged opioid therapy. Surgical encounters should include interventions aimed to reduce long-term opioid use.

Keywords

Opioid Use; Surgery; Opioid Prescribing; Claims Data

1. Introduction

Hospital admissions for surgical procedures exceed 14 million per year in the United States alone (Semel et al., 2012). Since pain was coined “the fifth vital sign” in the late 1990s (McCaffery and Pasero, 1997) there has been a marked rise in the sales of prescription opioids, which has been linked to the rapid increase in nationwide opioid-related morbidity and mortality (Dart et al., 2015; Olsen et al., 2006; Volkow et al., 2014). However, the recent guidelines on opioid prescribing by the United States Centers for Disease Control and Prevention do not include specific information on how to address persistent pain after surgery (Dowell et al., 2016). Detailed knowledge on incidence and factors associated with long-term opioid prescribing in patients undergoing various types of surgery is required for the development of targeted interventions to improve pain therapy and reduce rates of long-term opioid use in at-risk patients.

When clinicians prescribe opioids after hospital discharge following surgery, actual patient requirements for pain medications need to be estimated. Over-prescription of opioid analgesic medications after a surgical procedure is common and has been identified as a potential source of opioid prescription-induced morbidity (Bartels et al., 2016). However, with increasing institutional and legislative efforts to curb over-prescription of postoperative opioids, patients requiring intensive long-term pain treatment may now be at risk for inadequate therapy. Current prescribing practices appear to occur following a “one-size-fits-all” pattern and not in a patient-specific manner (Chen et al., 2017).

Long-term-opioid use after surgery appears to vary greatly depending on the population studied: in specific groups, such as bariatric surgery patients, who took opioids prior to surgery, chronic opioid use after surgery occurred in up to 77% of patients (Raebel et al., 2013). In retrospective cohort studies using administrative data from Canada, long-term opioid use was observed in 3-7.7% of previously opioid-naïve patients (Alam et al., 2012; Clarke et al., 2014). The addiction and pain research communities have been called upon to provide more evidence supporting non-opioid analgesic strategies for patients with chronic pain (Tompkins et al., 2017). In the context of surgery, early identification of patients likely to continue taking post-operative opioids in excess of one month is paramount to addressing

this issue. Providers may then develop a comprehensive pain plan that includes non-pharmacologic approaches, non-opioid analgesics, and patient and family education on opioid safety, safe storage, and substance use disorders.

The objective of this study was to link patient information that is available at the time of surgery with long-term post-operative opioid prescription patterns in a cohort of patients undergoing inpatient procedures at a U.S. academic medical center. To achieve our objective, we tested the hypothesis that there are important patient and procedural characteristics which predict long-term opioid therapy after surgery. Our approach included harmonizing and mining both a clinical (Epic) and a claims-based database, the Colorado All Payer Claims Database (APCD).

2. Material and methods

2.1 Study design and study population

This study was designed as a retrospective cohort study according to the STROBE guidelines (von Elm et al., 2008). Ethics approval was obtained prior to initiation of this study from the Colorado Multi-Institutional Review Board. All adult patients who underwent a procedure requiring anesthesia services at the University of Colorado Hospital within a two-year time frame from 10/01/2011-09/30/2013 were screened for inclusion using the University of Colorado Hospital electronic health record database. Only procedures that required at least overnight hospitalization were included. Exclusion criteria included patients aged less than 18 years and patients with American Society of Anesthesiology (ASA) physical status classification 6 (cadaveric organ donors).

2.2 Data extraction from electronic health record

Epic (Epic Systems Co, Verona, WI, USA) is the electronic health record and order entry system used at the study site. We queried Epic for detailed records from each patient's hospitalization. Patient characteristics acquired from Epic included age, gender, race, and physical status classification characterized by ASA status: 1, normal healthy patient; 2, patient with mild systemic disease; 3, patient with severe systemic disease; 4, patient with severe systemic disease that is a constant threat to life; 5, moribund patient who is not expected to survive without the operation; 6, cadaveric organ donor (Hurwitz et al., 2017). Age groups were chosen based on detailed age categories found in the 2016 National Survey on Drug Use and Health (NSDUH, 2017). The date of surgery was defined from the medical record. Opioid prescriptions filled within 90-days prior to surgery and within 180-days after surgery were defined according to the date of surgery. These were grouped in monthly (i.e., 30-day) increments.

2.3 Data matching with the Colorado All Payer Claims Database (APCD)

Data from the Epic query were matched with the Colorado APCD using the following unique patient identifiers: first name, last name, date of birth, and date of surgery. In a first step, duplicate records were detected and eliminated. Next, APCD matched “person keys”, which identified records as being associated with unique persons. Then, APCD queried their database for claims associated with these persons. In a stepwise fashion, we were able to

match 6,003 unique patients with claims in APCD and complete records from an initial dataset containing 20,501 clinical patient encounters in Epic (Figure 1).

2.4 Data analysis

Potential predictor variables of long-term opioid use (operationalized as filling an opioid prescription during the days 31-180 following surgery) were chosen based on the prior literature (Alam et al., 2012; Clarke et al., 2014) and our own hypothesized pathways. We evaluated associations between long-term opioid use and each independent variable with separate chi-square tests. We then jointly evaluated those significant variables in a binomial regression to estimate adjusted risk ratios for predicting long-term opioid prescription filling.

2.5 power analysis

Following preliminary matching of the two databases, we estimated that a sample size of 6000 patients provides 90% power to detect an odds ratio of 1.21 or higher as statistically significant at a time point, assuming 20% of patients are long-term opioid users (i.e., filled a prescription at the 31-180 day interval), and assuming a multiple correlation between the independent variables of 0.75 or less (Hsieh, 1989). Because of the large sample size, we conservatively set significance at a two-tailed alpha-level=0.01, and statistically significant results were further judged by evaluating the clinical relevance of the actual differences detected.

3. Results

Demographic characteristics of the study cohort are summarized in Table 1 along with comparisons on each variable between patients with and without long-term opioid prescription filling (any prescription filled month 2-6). Percent of patients filling opioid prescriptions according to the Colorado All Payers Claims Database relative to the date of surgery are depicted in Figure 2. Number and percent of patients filling Opioid prescriptions following surgery, dichotomized according to whether patients had an opioid prescription claim in the three months prior to surgery, are depicted in Table 2.

Significant variables from Table 1 were jointly evaluated in a binomial regression to estimate adjusted risk ratios for predicting long-term opioid prescription filling (Table 3). Patients who were between 26 and 64 years had 1.2 times greater risk of long-term opioid prescription filling than older patients. In comparison to patients with non-surgical procedures, those having the following procedures had significantly greater risk of long-term opioid prescription filling: colorectal surgery (1.3 times), orthopedic surgery (1.2 times), and multiple procedures (1.2 times); those having obstetric surgery had significantly lower risk (0.56 times) of long-term opioid prescription filling. A worsening level of ASA physical status classification was associated with 1.1 times greater risk of long-term opioid prescription filling.

4. Discussion

Our findings indicate that surgical encounters may serve as a crossroads for long-term opioid use. In this retrospective cohort study of 6,003 patients undergoing inpatient procedures

requiring at least over-night hospitalization, we found that opioid prescription filling beyond the first month after surgery occurred frequently, in 22-28% of cases. Although preoperative opioid prescription filling was highly associated with prolonged postoperative opioid use, 24-29% of patients taking opioids for an extended period after surgery did not fill a prescription before surgery.

Development of persistent post-surgical pain is multifactorial and mostly coincides with chronic pain from other causes (Johansen et al., 2014). Also, some surgical procedures are not intended to be curative, and care must be taken not to withhold indicated long-term opioid therapy, e.g., to hospice patients (Glod, 2017). Such considerations should be made prior to surgery to determine appropriateness of persistent post-operative opioid prescribing. Here, we defined readily identifiable patient and surgical characteristics that are associated with long-term opioid therapy after surgery and may be used to guide pain therapy.

The prevalence of long-term opioid use after surgery reported in other studies varies depending on the definition of long-term use, patient population, and procedural characteristics. Alam and colleagues, in a Canadian cohort of patients aged 66 years and older found a rate of 7.7% of opioid prescriptions filled one year after minor surgery (cataract surgery, laparoscopic cholecystectomy, transurethral resection of the prostate, or varicose vein stripping) (Alam et al., 2012). In a United States study based on insurance claims data, 36,177 previously opioid-naïve patients aged 18-64 years-old that underwent minor and major surgery and filled at least one perioperative opioid prescription, long-term opioid use was defined as having an opioid prescription filled between 90 and 180 days after surgery (Brummett et al., 2017). In the sub-cohort of patients that had major surgery, 6.5% were found to be new long-term opioid users. Although we did not require a perioperative opioid prescription for inclusion into our study, about 10% of patients who had no opioid prescription claim in APCD in the 3 months prior to surgery filled opioid prescriptions each month during post-operative days 91-180. Given that the aforementioned study included the major surgeries “ventral incisional hernia repair, colectomy, reflux surgery, bariatric surgery, and hysterectomy”, the higher rates of patients with new long-term prescription filling may have been due to a greater breadth of surgical procedures and higher overall patient morbidity.

In the past, definitions of long-term opioid use after surgery have been highly variable. More conservatively, Sun et al. used a definition of ten or more prescriptions or more than 120 days' supply of an opioid in the first year after surgery (Sun et al., 2016). Others used a much less stringent definition, such as any ongoing outpatient prescriptions for opioids for more than 90 days after surgery (Clarke et al., 2014). As shown in Figure 2, little decrease occurred in the rates of patients filling opioid prescription beyond the first month after surgery. Our data suggest that most of the post-operative healing should be completed within 30 days. Approximately half of patients who filled opioids during the three months prior to surgery no longer filled in months 2-6, possibly reflecting success of the procedure in regards to alleviating pain (Table 2). However, it should be acknowledged that persistent post-surgical pain might be present even after presumably curative surgery. For example, in a study of 887 patients undergoing ventral hernia repair, 50.3% reported pain at 1 month and 26.5% at 6 months after surgery (Cox et al., 2016). The rate of new persistent opioid use

(90-180 days postoperatively) in ventral incisional hernia patients is approximately 7.6% (Brummett et al., 2017). Ongoing opioid use beyond the first month of the initial prescription should trigger clinicians to comprehensively evaluate the causes of chronic pain and consider non-opioid based therapy when appropriate.

4.1 Limitations

Principal weaknesses of our study include its retrospective design, which inherently predisposes our results to unaccounted confounders. However, by combining a clinical database with a claims-based database, we attempted to attenuate some of the limitations that accompany claims and registry data sets such as data quality and residual confounding (Evans et al., 2010). Furthermore, there is no standard definition of our chosen primary outcome variable, long-term opioid use. However, given the distribution of patients with post-operative prescription filling observed in the months following surgery, we believe that our choice of using a cut off of >30 days is justified. Lastly, opioid prescriptions may have been filled but not submitted to the insurance for payment, or patients may have filled prescriptions but not taken any medications. Indeed, a study comparing claims data with survey data for diabetes has shown claims-based findings may differ from self-reported diagnosis in up to 6% of cases (Sakshaug et al., 2014). However, healthcare utilization and spending were similar in both groups.

5. Conclusion

Patients known to take opioids prior to surgery filled the majority of long-term prescriptions, yet surgery often marked the initiation of prolonged opioid therapy in patients not known to take opioids prior to the procedure. Perioperative care should aim to identify patients at risk for long-term opioid use so non-pharmacologic approaches, non-opioid analgesics, and education on opioid safety can be made available to these patients. Future research should aim to develop interventions to reduce the need for opioid prescriptions exceeding 30 days after surgery.

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Highlights

- Most patients with long term opioid prescriptions had prescriptions before surgery.
- Surgery can mark the beginning of long-term opioid prescribing.
- Some patients taking opioids prior to surgery discontinue these after surgery.
- Surgical encounters should be leveraged to reduce long-term opioid use.

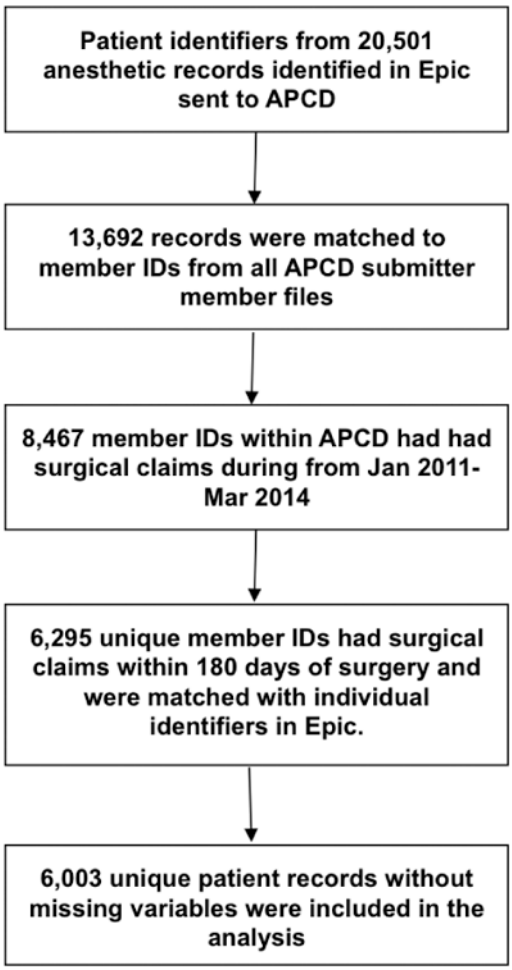

Figure 1.

Study flow diagram. CO APCD: Colorado All Payers Claims Database. For missing American Society of Anesthesiology (ASA) physical status classification, 292 member IDs were excluded from the final analysis.

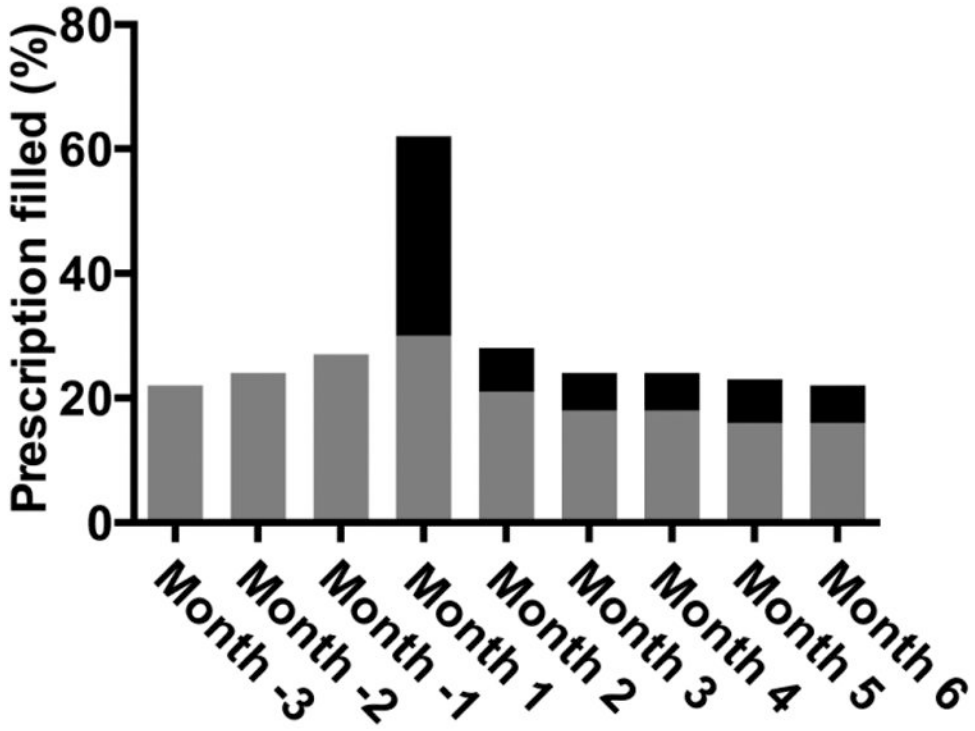

Figure 2.

Percent of patients filling opioid prescriptions according to the Colorado All Payers Claims Database relative to the date of surgery. Depicted in gray are patients that filled in the three months prior to surgery so that the proportion of post-operative prescriptions that were filled by patients that had also filled prior to surgery is gray. In black are patients filling opioid prescriptions after surgery that were not known to have filled opioid prescriptions prior to surgery (i.e., no opioid claims in Month-3 to Month -1).

Table 1

Patient demographics. Pre-operative opioid use was defined as opioid prescription filled in the 90 days preceding surgery. ASA status 4 and 5 were grouped together, as only 16 patients had ASA status 5. P-values obtained using Chi-square tests.

	All	No long-term opioid prescription	Any opioid prescription month 2-6	P-value
N	6003 (100%)	3385 (56.4%)	2618 (43.6%)	
Age				
> 18 and < 26	517 (8.6%)	363 (6.1%)	154 (2.6%)	<0.0001
≥26 and < 65	3828 (63.8%)	1989 (33.1%)	1839 (30.6%)	
≥65	1658 (27.6%)	1033 (17.2%)	625 (10.4%)	
Pre-operative opioid prescription	2278 (38.0%)	660 (11.0%)	1618 (27.0%)	<0.0001
Gender				
Female	3733 (62.2%)	2117 (35.3%)	1616 (26.9%)	0.5189
Male	2270 (37.8%)	1268 (21.1%)	1002 (16.7%)	
Race				
White or Caucasian	3914 (65.2%)	2156 (35.9%)	1758 (29.3%)	0.0003
Black or African American	754 (12.6%)	409 (6.8%)	345 (5.8%)	
Asian, Native Hawaiian, or Pacific Islander	157 (2.6%)	103 (1.7%)	54 (0.9%)	
Other or unknown	1178 (19.6%)	717 (11.9%)	461 (7.7%)	
Type of surgery				
Not specified	5 (0.1%)	3 (0.1%)	2 (0.0%)	<0.0001
General Surgery	1044 (17.4%)	643 (10.7%)	401 (6.7%)	
Thoracic Surgery	315 (5.3%)	195 (3.3%)	120 (2.0%)	
Colorectal Surgery	81 (1.4%)	39 (0.7%)	42 (0.7%)	
Obstetric Surgery	632 (10.5%)	524 (8.7%)	108 (1.8%)	
Gynecologic Surgery	484 (8.1%)	327 (5.5%)	157 (2.6%)	
Neurological Surgery	542 (9.0%)	315 (5.3%)	227 (3.8%)	
Orthopedic Surgery	731 (12.2%)	330 (5.5%)	401 (6.7%)	
Urologic Surgery	316 (5.3%)	195 (3.3%)	121 (2.0%)	
Vascular Surgery	117 (2.0%)	76 (1.3%)	41 (0.7%)	
Ophthalmic OMF ENT or Plastic Surgery	292 (4.9%)	152 (2.5%)	140 (2.3%)	
Non-surgical procedure	570 (9.5%)	322 (5.4%)	248 (4.1%)	
Multiple procedures	874 (14.6%)	264 (4.4%)	610 (10.2%)	
ASA status				
1	267 (4.5%)	183 (3.1%)	84 (1.4%)	<0.0001
2	2404 (40.1%)	1512 (25.2%)	892 (14.9%)	
3	2749 (45.8%)	1396 (23.3%)	1353 (22.5%)	
4 or 5	583 (9.7%)	294 (4.9%)	289 (4.8%)	

Table 2

Number and percent of patients filling opioid prescription (Rx) by post-operative month based on whether an opioid Rx was filled during any of the three months prior to surgery. Percentages are in ( ) relative to the sub cohort.

Post-operative month	1	2	3	4	5	6
Number (%) patients filling opioid Rx posteroperatively of patients who did not fill opioid Rx prior to surgery (n=3,725)	1,940 (52)	414 (11)	349 (9)	369 (10)	370 (10)	388 (10)
Number (%) patients filling opioid Rx posteroperatively of patients who filled opioid Rx prior to surgery (n=2,278)	1,806 (79)	1,243 (55)	1,097 (48)	1,056 (46)	986 (43)	955 (42)

Table 3

Binomial regression to estimate adjusted relative risks of patient and procedural characteristics for long-term opioid use (any opioid prescription filled beyond 30 days until 180 days after surgery). 95% Likelihood Ratio confidence limits are reported. OMF: Oral and maxillofacial, ENT: Ear nose and throat.

Characteristic	Relative Risk Estimate	95% confidence limits		p-value
Pre-operative opioid prescription	**2.199**	**2.067**	**2.338**	**<0.0001**
Age > 18 and < 26 vs. age ≥65	1.111	0.983	1.254	0.091
Age ≥26 and < 65 vs. age ≥65	**1.244**	**1.171**	**1.320**	**<0.0001**
Not specified vs. non-surgical procedure	1.308	0.433	3.956	0.634
General Surgery vs. non-surgical procedure	0.917	0.826	1.017	0.101
Thoracic Surgery vs. non-surgical procedure	0.948	0.820	1.097	0.475
Colorectal Surgery vs. non-surgical procedure	**1.298**	**1.096**	**1.538**	**0.003**
Obstetric Surgery vs. non-surgical procedure	**0.562**	**0.467**	**0.676**	**<0.0001**
Gynecologic Surgery vs. non-surgical procedure	0.835	0.725	0.963	0.013
Neurological Surgery vs. non-surgical procedure	0.978	0.870	1.010	0.711
Orthopedic Surgery vs. non-surgical procedure	**1.168**	**1.065**	**1.282**	**0.001**
Urologic Surgery vs. non-surgical procedure	0.905	0.781	1.048	0.182
Vascular Surgery vs. non-surgical procedure	0.887	0.699	1.124	0.320
Ophthalmic, OMF, ENT, or plastic surgery vs. non-surgical procedure	1.091	0.961	1.238	0.118
Multiple procedures vs. non-surgical procedure	**1.233**	**1.131**	**1.344**	**<0.0001**
Black or African American vs. White or Caucasian	1.025	0.976	1.077	0.318
Asian, Native Hawaiian, or Pacific Islander vs. White or Caucasian	0.933	0.787	1.107	0.427
Other or unknown vs. White or Caucasian	0.969	0.914	1.026	0.278
ASA status	**1.057**	**1.028**	**1.086**	**<0.0001**