Published in final edited form as:

J Orthop Trauma. 2019 April ; 33(4): e131–e136. doi:10.1097/BOT.0000000000001392.

Using historical variation in opioid prescribing immediately after fracture surgery to guide maximum initial prescriptions

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Abstract

Objectives: Recent studies have advocated for prescription opioid maximums (based on percentage reductions from historical amounts) to reduce excess prescribing.⁽¹⁾ Implementing this in orthopaedic trauma has been difficult given injury variety and limited historical data on post-operative prescribing. We report on the initial opioid prescriptions for a large cohort of post-operative, opiate-naïve fracture patients and hypothesize that prescribing was associated with fracture location and morphology.

Design: Retrospective cohort analysis

Setting: Two ACS level I trauma centers

Patients: 6,879 orthopaedic trauma patients treated between 2002–2015. Only patients who had a single operatively-treated injury and were opiate-naïve (had not received an opioid prescription in the 6 months prior to presentation) were included.

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No conflicts of interest exist for any authors regarding this paper. One or more of the authors (MB) has received funding through a pre-doctoral Fellowship in Aging and Health Economics (NIA T32 AG 51108) from the National Institute on Aging. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Aging or the National Institutes of Health.

Presented as a poster at the Annual Meeting of the American Academy of Orthopaedic Surgeons, 2018, New Orleans, Louisiana.

Intervention: Post-operative opioid discharge prescription

Outcomes: We analyzed the quantity of initial opioids prescribed in morphine milligram equivalents (MME, a standardized unit of opioid dosage used for comparison across opioid types). Fracture location and morphology were classified using the AO/OTA classification.⁽²⁾

Results—Fracture location was an independent predictor of the MME prescribed ($p < 0.001$). All other fracture locations were prescribed significantly higher MME than distal radius fractures (control group, 150 MME⁽³⁾, $p < 0.01$). There was no difference in MMEs prescribed by articular involvement or degree of comminution.

Conclusions—We demonstrate significant variation in initial post-operative opioid prescribing to opiate-naïve orthopaedic trauma patients by fracture location, but not by fracture morphology. We use this data to propose a guideline based on the AO-OTA fracture classification for the maximum initial prescription of opioids.

Keywords

opioid; musculoskeletal trauma; pain; fracture classification

INTRODUCTION

Prescription opioids are among the most prescribed medicines in the United States and American use of opioids accounts for at least 80% of the global opioid use.⁽⁴⁾ While prescription opiates are commonly the mainstay of initial post-operative pain control in orthopaedic trauma patients, training on opioid prescribing for orthopaedic surgeons and trainees has historically been based on individual physician experience. Little is known about factors associated with physician prescribing and it is unclear if opioid prescribing varies for similar injuries.

Recent studies have demonstrated wide variation in opioid prescribing following injury or surgery.^(5–7) Based on these reports, some have advocated for prescription opioid “maximums” based on 20–40% reductions from historical discharge prescriptions to avoid excess prescribing.⁽¹⁾ This strategy has been effective in arthroplasty,⁽⁸⁾ but is particularly difficult in orthopaedic trauma given the wide variety of injuries and limited published data on historical prescribing following fracture surgery.^(9–12) This is especially important since a common belief is that the initial exposure to opioids is a major factor in the risk of long-term opioid use by patients.^(7,13,14) Our study explored this topic with respect to post-operative orthopaedic fracture care since it is unknown if orthopaedic providers consider fracture characteristics, like fracture location or morphology, when providing prescription opioids to patients after fracture surgery.^(4,15,16)

We report on the initial opioid prescriptions for a cohort of post-operative, opiate-naïve fracture patients. We examined whether post-operative opioid prescribing at discharge for opiate-naïve patients who had sustained a fracture varied by fracture characteristics. We hypothesized that initial opioid dosing at discharge varies significantly based on fracture location, articular involvement and degree of comminution (as reflected in the AO/OTA fracture classification⁽²⁾). Based on historical discharge prescriptions, we then propose a

heuristic based on the AO-OTA fracture classification for the maximum initial prescription of opioids.⁽¹⁾

METHODS

Ethics:

This study was approved by our institutional review board and they determined that individual patient and prescriber consent was not required.

Study Design:

Retrospective cohort study

Setting:

We identified operatively treated orthopaedic trauma patients at our two American College of Surgeons (ACS) Level 1 Trauma Centers using a prospectively collected billing database from 2002–2015. Detailed demographic and clinical data, including initial opioid prescription morphine milligram equivalents (MME) on hospital discharge, were matched to each patient using our institutions' Enterprise Data Warehouse (EDW) and Research Patient Data Registry (RPDR). The initial opioid prescription at hospital discharge was defined as the first opioid outpatient prescription received after surgery by this patient cohort.

Participants:

We restricted our study population to individuals who had an acute single fracture that was definitively treated with surgery (6879 operative cases; 6879 patients; 1 case per patient). We excluded patients with multiple fractures. To identify opiate naive patients, we excluded patients who were prescribed an opioid analgesic or opioid medication-assisted treatment in the 180 days prior to presentation, or those who had a documented opioid use history in their medical record.

Variables:

All fractures were classified using the AO/OTA fracture classification system to describe fracture location and morphology. In our cohort, all patients received a prescription for opioids to treat their pain after fracture surgery. We defined the discharge prescription as the first outpatient prescription registered in the electronic medical record immediately after the index procedure for the identified fracture. During the time period of our study, there was no institutional standardized prescribing guideline. Discharge prescriptions were then converted to total morphine milligram equivalent units per prescription (MME, a standardized unit of opioid dosage that allows for comparison across different opioid types) by multiplying quantity and dose, and applying standard conversion tables.⁽¹³⁾ MME units were summed across prescriptions in cases where more than one opioid prescription was prescribed on the same day. Patient comorbidity was defined using the count of unique medications for chronic conditions (hypertension, diabetes, etc.) in the prior 180 days, which is an accurate summary measure of patient co-morbidity in trauma settings.⁽¹⁷⁾ Use of adjunct pain medications such as acetaminophen, NSAIDs, and regional anesthetic blocks were utilized

at the discretion of the treating physicians and were not controlled in this retrospective study since we could not control for over-the-counter use of acetaminophen and NSAIDS, or the variety of blocks used within and between fracture types.^(3,5) Other physical or cognitive modalities for pain management may have been recommended, but were not formally recorded within the RPDR/EDW.

Statistics:

We compared fracture characteristics using multivariate linear regression, adjusting for patient age, gender and comorbidity. Extra-articular distal radius fracture was used as the control for fracture type as this was the most common injury in our database and previous studies have already shown that twenty 5 milligram oxycodone tablets (150 MME) at time of discharge is the recommended prescription maximum.⁽³⁾ The average MME for extra-articular distal radius fractures in our cohort was similar. We report regression coefficients for each fracture, which represents the amount of opioids prescribed above that given for extra-articular distal radius fractures.

We used a mathematical model to estimate the maximum initial opioid prescriptions based on historical prescribing data and existing literature.⁽¹⁾ We used prior prescribing data to estimate the difference in pain requirement for different fractures since it is generally believed that some injuries are more painful than others.⁽³⁾ We compared all fractures against extra-articular distal radius fractures (our control group) because this was the most common injury in our cohort and existing literature on physician prescribing and patient use in this setting has already found that an initial dose of 20 tablets of 5 mg oxycodone (150 MME) was an appropriate maximum prescription for a majority of opiate-naïve patients.⁽³⁾ In general, if the patient cohort is large enough, the average MMEs prescribed for an injury will generally reflect how painful that injury is on average.^(18,19) Thus, since our study looked at over 6700 patients/cases who were prescribed an opioid over 14 years, the regression coefficients we report estimate the average difference in MME for other fractures in relation to distal radius fractures.⁽¹⁸⁾ Since the regression coefficients reflect the additional MME needed over the maximum 150 MME recommended for distal radius fractures,⁽³⁾ the maximum initial MME for other fracture locations was calculated as 150 MME plus the regression coefficient for that injury.^(4,16)

Two-sided p-values less than 0.05 were considered statistically significant. Stata software, version 14 (StataCorp), was used for all analyses.

RESULTS

Characteristics of Patient Population

Our sample consisted of 6879 opiate-naïve orthopaedic trauma patients. The mean age of our study cohort was 50.8 years, 55% were women, 82% self-classified as white, and 20% of patients were over 70 years of age. Average ($\pm$ standard deviation) number of comorbidities was 0.54 (± 0.77). By broad anatomical location, 52 % of fractures were lower extremity, 42% were upper extremity, and 6% were pelvic/acetabular. Table 1 reflects demographic and clinical information for our patient sample that were used as patient-level

controls. Figure 1 depicts the distribution of operative injuries among patients using the fracture location portion of the AO/OTA fracture classification.

Prescribing by Fracture Location

We found significant variation in initial opioid prescribing patterns by AO/OTA classification ($p < 0.001$) for all fracture types. In general, operatively treated pelvic and lower extremity fractures were prescribed higher quantity of MMEs than operatively treated upper extremity fractures (Figure, Supplemental Digital Content 1). Compared to patients with operative distal radius fractures (control group, 150 MME), patients with operatively treated pelvic/acetabulum (405–445 MME, $p < 0.001$), femur (388–473 MME, $p < 0.001$), and tibia (coefficient 286–392 MME, $p < 0.001$) fractures were prescribed significantly higher quantity of MMEs at the time of discharge after controlling for patient age, gender, race, comorbidity, and fracture morphology (Table 2). For these fractures, the increased amount corresponded to at least 200 MME (approximately 27 tablets of 5 mg oxycodone). Figure, Supplemental Digital Content 2, demonstrates MME on discharge in increasing order by fracture location.

Prescribing by Fracture Morphology

Among patients who sustained non-diaphyseal long bone fractures, there was no statistical difference in the quantity of initially prescribed MMEs between operatively treated extra-articular and intra-articular fractures. Similarly, for patients with operatively treated diaphyseal (shaft) fractures, there was no statistical difference in prescribed MMEs by degree of comminution (Figure 2).

Maximum initial opioid prescriptions by AO/OTA Classification

Using the modeling technique described in the Statistical Methods section, Table 3 presents a summary of the proposed prescription maximums at hospital discharge for prescription opioids by fracture location, in terms of MME and 5 mg oxycodone tablets.

DISCUSSION

Opioid medications are the mainstay of initial pain management in orthopaedic trauma; however, it has become increasingly apparent that these medications pose a significant long-term risk of addiction to patients with musculoskeletal injuries.^(7,11,16) Formal validated training modules on opioid prescribing for orthopaedic surgeons are limited and there is little published data to guide post-operative prescribing following fracture surgery.^(9–12) In this cohort of opiate-naïve orthopaedic trauma patients, we identified fracture location as an independent predictor of post-operative opioid prescribing at hospital discharge, but not articular involvement or degree of comminution. We then used this data to propose maximum opioid prescriptions by AO-OTA fracture classification.

Our results contribute to the existing literature on pain control in orthopaedic trauma surgery by using an institutional historical dataset with sufficient size and injury-level detail to address how fracture characteristics are associated with variation in initial opioid prescribing behavior.⁽²⁰⁾ This level of detail about fracture characteristics is not available in existing

national and state databases. Similar to prior studies, we also found that pain and initial prescription MME dosing was greater for operatively treated lower extremity and pelvic/acetabular fractures as compared to upper extremity fractures.^(11,21) We further demonstrated that fracture location at the detailed level of the AO/OTA classification (beyond just upper, lower, pelvic/acetabulum fracture) is a significant independent predictor of opioid prescribing and should be considered by providers when counseling patients on post-operative pain.

Our finding that opioid prescribing was not associated with intra-articular involvement or comminution was surprising. Recent literature has suggested that the severity of injury has a significant effect on post-operative outcomes.^(22,23) As a result, we expected that fracture morphology would be a significant factor in opioid prescribing. However, our results suggest that influence of fracture morphology is likely dwarfed by fracture location and demographic factors.

Major national and state opioid prescribing guidelines advocate starting at a low and “effective” initial dose of opioids and titrating up if needed. However, there is limited guidance for what constitutes a reasonable start point after fracture surgery and how painful some fractures are in relation to others.^(4,13,24,25) As a result, there has been increased push to use prescription opioid maximums based on reductions from historical discharge prescriptions.⁽¹⁾ This has been challenging to implement in orthopaedic trauma given the wide variety of injuries. In this study, we were able to use historical injury-level data to explore the variation in prescribing by fracture characteristics, and then used this information to propose prescription maximums by fracture location without modifications for fracture morphology (Table 3).^(4,26) Our technique predicts a similar opioid comparison to that recently described for orthopaedic upper extremity injuries and for five common procedures in the general surgery literature based on physician prescribing and patient-reported use.⁽²⁷⁾ This information is useful to prescribers to balance excess prescribing with appropriate patient-specific pain-management.

Limitations

Our study has several limitations. Our investigation was limited to two academic ACS level I trauma centers that are regionally close to each other, but other work suggests that our results are likely to be similar across different locations.⁽²⁸⁾ Our results apply only to those who are opiate-naïve as we excluded those with prior opioid use within 180 days of fracture in this study. Prescribing guidelines for those with prior opioid use remains challenging and requires further study.⁽²⁹⁾ Our method for identifying prior opioid use and opioid naïve patients may be an underestimate since our data spans a time period not completely covered by the Massachusetts Prescription Monitoring Program, but our incidence rate is consistent with prior reports.⁽¹¹⁾ Opioid prescribing data for multi-system trauma or those with multiple fractures also requires further research. Another limitation in our cohort is that discharge prescribing was completed by junior residents, physician assistants, or nurse practitioners under the direction of attending physicians as this is reflective of the common practice at academic medical centers. A similar study using only experienced providers may lead to a different conclusion, but the current literature is unclear on the effect of provider

experience on opioid prescribing behavior. Some studies suggest that more experienced providers are more conservative in prescribing, while others have found them to be more liberal.^(30,31) Utilizing this data in aggregate, we believe that our results are more reflective of the injury type rather than the effect of any single physician.⁽¹⁸⁾ In addition, our technique reproduced and continues to build on findings from the upper extremity and general surgery literature.⁽²⁷⁾

We were unable to directly examine the effects of complimentary regional blocks or newer multi-modal anesthetic techniques with acetaminophen or ibuprofen given the variety of block techniques and potential unobserved over-the-counter use of other analgesics. However, we do not anticipate that this would significantly impact our results. Our goal (using Table 3) was to provide “maximum” amounts that should raise concern. While NSAIDs and regional blocks may reduce opioid use in the peri-operative period, their efficacy at later time points is an active area of study.^(32,33) Two recent studies noted similar limitations and could not accurately control by adjunctive pain medication or anesthesia type.^(3,5) Patients discharged on adjunctive pain medication or who received a block should still receive a personalized prescription of opioids, likely below the maximum amounts we calculated in Table 3. We lacked sample size to detect if a specific technique of fracture fixation was associated with differential prescribing patterns (i.e. plate versus intramedullary fixation), but do not anticipate this to have a major effect given prior literature.⁽³⁴⁾

Conclusion

Our results are of relevance to physicians who care for patients following fracture surgery. A common belief is that the initial exposure to opioids is a major influential factor in the risk of long-term opioid use by patients.^(7,13,14) However, we know very little about how opioid prescribing varies after fracture surgery, and this has made it difficult to determine appropriate dosing recommendations.^(11,27,35) We demonstrated that injury location was a significant factor in initial opioid dosing after fracture surgery and quantified how prescribing has historically differed for various fractures. We showed that articular involvement and degree of comminution were not significant factors. Lastly, we proposed maximum discharge prescription opioid amounts, based on fractional reductions of historical prescribing, using the AO/OTA fracture classification as a simple heuristic that can be used by clinicians to help guide opioid prescribing while the orthopaedic and trauma community continue to develop a better understanding of how to personalize opioid prescribing to individual patients based on their injury characteristics, pain perception, and coping abilities.^(18,26)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

We thank Alan Xie, Jacqueline You, Nick Seymour for research assistance; David Cutler for advice in economic and statistical analysis; Mark Vrahas, Michael McTague for discussions on study design, data acquisition, and interpretation of results; Rupa Bhashyam for assistance in figure design.

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Figure 1:
Distribution of injuries among patients by fracture location portion of AO/OTA fracture classification

Figure 2:
 (2a) Opioid Quantity (MME) by fracture morphology: extra-articular versus intra-articular for non-diaphyseal fractures; p=NS (2b) Opioid Quantity (MME) by diaphyseal fracture morphology: simple versus wedge versus complex; p=NS (NS=non-significant)

Table 1:

Characteristics of Patient Population; *Medication count is a medical co-morbidity measure that uses the count of unique medications prescribed for chronic medical conditions

Characteristic	Percent or Mean $\pm$ SD
Age	50.8 $\pm$ 20.2
70 years	19.8%
White Race	81.7%
Female Gender	54.8%
Medicaid	10.1%
Self-pay	5.4%
Medication Count	0.54 $\pm$ 0.77
Injury	
Upper Extremity Fracture	42.0%
Lower Extremity Fracture	51.8%
Pelvic/Acetabular Fracture	6.2%

Table 2:

Additional opioid quantity prescribed at discharge (as compared to 23-distal radius fracture) by AO/OTA fracture classification; (1) Without patient level controls, (2) With patient level controls; *p<0.05, **p<0.01, ***p<0.001

AO/OTA Fracture Classification	Additional MME Prescribed over 23-Distal Radius fracture	
	(1)	(2)
11 - Proximal Humerus	63.21*** (17.64)	55.86** (18.84)
12 - Diaphyseal Humerus	126.1** (44.15)	97.73* (46.11)
13 - Distal Humerus	162.0*** (27.75)	104.3*** (25.43)
21 - Proximal Radius/Ulna	112.8*** (21.87)	68.41** (22.30)
22 - Diaphyseal Radius/Ulna	277.4*** (59.59)	209.0*** (58.74)
31 - Proximal Femur	242.0*** (19.223)	238.4*** (23.89)
32 - Diaphyseal Femur	386.0*** (47.01)	327.8*** (48.93)
33 - Distal Femur	334.3*** (57.59)	255.3*** (57.71)
41 - Proximal Tibia	248.0*** (29.13)	154.4*** (29.24)
42 - Diaphyseal Tibia	349.3*** (30.70)	242.3*** (32.82)
43 - Distal Tibia	211.2*** (25.69)	136.1*** (26.64)
44 - Malleolar/Ankle	89.99*** (19.36)	54.04** (20.29)
61 - Pelvis	301.3*** (42.14)	255.4*** (44.67)
62 - Acetabulum	425.1*** (51.80)	295.0*** (50.93)
Patient Level Controls		Included
Fracture Morphology	Included	Included
N	6879	6462
R ²	0.0585	0.0909

Table 3:

Potential initial opioid prescribing maximums by fracture type

Fracture location	MME on discharge [†]	Additional MME (over 150 MME) +	Number of additional 5 mg oxycodone tablets [*]	Example of initial prescription for opioids on discharge
Radius/ulna - Distal	<i>150 MME base case[‡]</i>	---	---	20 tablets of 5 mg oxycodone
Ankle/Malleolar	204	54	7	25 tablets of 5 mg oxycodone
Humerus - Proximal	206	56	7	25 tablets of 5 mg oxycodone
Radius/ulna - Proximal	218	68	9	30 tablets of 5 mg oxycodone
Humerus-Diaphyseal	248	98	13	30 tablets of 5 mg oxycodone
Humerus - Distal	254	104	14	35 tablets of 5 mg oxycodone
Tibia - Proximal	304	154	21	40 tablets of 5 mg oxycodone
Radius/ulna - Diaphyseal	359	209	28	50 tablets of 5 mg oxycodone
Femur - Proximal	388	238	32	50 tablets of 5 mg oxycodone
Tibia - Diaphyseal	392	242	32	50 tablets of 5 mg oxycodone
Tibia - Distal	405	255	34	55 tablets of 5 mg oxycodone
Pelvic ring	405	255	34	55 tablets of 5 mg oxycodone
Femur - Distal	405	255	34	55 tablets of 5 mg oxycodone
Acetabulum	445	295	39	60 tablets of 5 mg oxycodone
Femur - Shaft	478	328	44	65 tablets of 5 mg oxycodone

MME = morphine milligram equivalents;

[†]From Table 2 regression results;[‡]From Table 2;^{*}Calculation of tablets = (Additional MME)/(mg/pill)/(conversion factor¹³)