



RESEARCH ARTICLE

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The Incidence of Opioid Use in Patients Undergoing Orthopaedic Oncology Surgery

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ABSTRACT

Objective: Primary or metastatic cancer can cause debilitating pain. Despite societal concerns regarding opioid use and abuse, opioid utilization patterns in orthopaedic oncology patients is not well-described. The purpose of this study is to determine patterns of opioid use in orthopaedic oncology patients and to identify factors associated with chronic use postoperatively.

Methods: A retrospective review of 119 orthopaedic oncology patients who underwent surgical treatment for a bone or soft tissue tumor at our institution between November 2017 and August 2018 was conducted. Opioid consumption was measured using the New Jersey Prescription Monitoring Program, a database that monitors when a controlled substance prescription is dispensed. Utilization rates at various perioperative timepoints were measured, and factors associated with chronic use were identified using single variable logistic regression.

Results: At the initial encounter with the orthopaedic oncologist, 18.1% of patients were using opioids, which increased to 51.3% at 2 weeks postoperatively. The prevalence declined to 25.2% by 6 weeks postoperatively, and 15.9% by 1 year postoperatively. The highest prevalence of chronic opioid use, defined as opioid use on most days for greater than 3 months, was 17.7% at 3 months postoperatively. Factors associated with chronic opioid use postoperatively included continued opioid use at 6 weeks postoperatively, chronic opioid use preoperatively, Charlson Comorbidity Index, diabetes, metastatic cancer, soft tissue tumors, and VAS scores.

Conclusions: By understanding opioid consumption habits, and the factors associated with chronic use postoperatively, orthopaedic oncologists can better counsel their patients on the potential for addiction and individual propensity for developing chronic use. Persistent opioid consumption at 6 weeks postoperatively was associated with the development of chronic use, suggesting that the 6 week mark should serve as a warning threshold, and providers should therefore attempt to wean patients from opioids by 6 weeks postoperatively.

Keywords: Opioid, Narcotic Pain Medication, Orthopaedic Oncology, Bone Tumor, Soft Tissue Tumor.

Introduction

In 2017, 191 million Americans were prescribed opioids; orthopaedic surgeons are the third most common prescriber. Because of the current opioid epidemic, many studies have investigated opioid consumption habits of patients undergoing various orthopaedic procedures, with preoperative utilization rates ranging from 16-52.4% [3-10]. Other studies have evaluated factors associated with chronic postoperative opioid use, which include preoperative opioid use, male gender, younger age, mental illness, and substance use disorders [1-11].

Despite numerous studies performed on this topic, there are few reports investigating opioid use in orthopaedic oncology patients.

This is not due to lack of consumption in this population: 50-55% of cancer patients report pain, and 43% of all cancer patients consume opioids throughout the course of their treatment. Patients with primary musculoskeletal tumors or metastatic bone disease experience severe pain that negatively affects their quality of life, and their symptoms are often exacerbated by complications, such as pathologic fracture. The World Health Organization (WHO) recommends a stepwise escalation from non-opioid analgesics and mild opioids to strong opioids until adequate pain relief is achieved [12-15]. Because opioids such as morphine, oxycodone, and fentanyl are commonly prescribed to orthopaedic oncology patients to manage pain, it is imperative that their physicians better understand utilization patterns in this population.

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The purposes of this retrospective study were to determine the prevalence of opioid use in orthopaedic oncology patients and to identify factors in this patient population that were associated with chronic opioid use postoperatively, defined by the Centers for Disease Control and Prevention (CDC) as opioid use on most days for greater than 3 months [16]. We investigated whether there is a timepoint postoperatively, at which if patients are still using opioids, they exhibit an increased tendency to develop chronic use. The study will also identify the prescribers of opioids to orthopaedic oncology patients, at various timepoints in their treatment.

Materials and Methods

Following Institutional Review Board approval, a retrospective review of opioid use amongst orthopaedic oncology surgical patients treated at our institution between November 2017 and August 2018 was conducted. The institutional orthopaedic oncology surgical database was used to identify patients over the age of 18 who underwent surgery for a soft tissue or bone tumor, at our institution by a fellowship-trained orthopaedic oncologist. Patients without a tumor diagnosis, treated outside of the study period or at an outside facility, under the age of 18, treated non-surgically, or pregnant at the time of surgery were excluded. The initial search yielded 149 patients, and 119 patients met final inclusion criteria (Figure: 1).

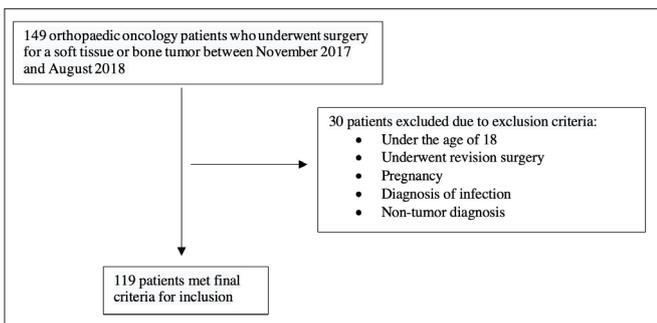


Figure 1: Flowchart depicts patient inclusion and exclusion criteria for the study

The hospital’s electronic medical record was used to extract demographic data, tobacco use, alcohol use, illicit drug use, body mass index (BMI), Visual Analogue Scale (VAS) pain scores at the initial encounter with the orthopaedic oncologist, and medical comorbidities as listed by the Charlson Comorbidity Index (CCI). CCI is a validated prognostic score that is utilized to assess patients’ overall health status at the time of surgery [17]. Operative and pathology notes were reviewed to identify tumor location, lesion size, and pathologic diagnosis.

Opioid use was measured by using opioid prescription data through a multi-state online database accessible to opioid

prescribers that records each prescription filled by a patient in the last two years. Search results display the date the prescription was filled, opioid name, dose, quantity dispensed, days prescribed, and prescriber’s name. The CDC’s “Opioid Oral Morphine Milligram Equivalent” (MME) table was used to convert each prescription to its MME to allow for consumption comparisons of various drugs with different potency [18]. We calculated the mean daily opioid consumption rate per user at various peri-operative timepoints. Non-users were excluded from this calculation.

Because the database only provides data for two years prior to the access date, prescription data could only be collected from July 2017 to July 2019. A power analysis was not performed as our study size was limited to the patients treated in that time frame. Opioid use data before the initial visit was not available for 25 patients due to date limitations.

Descriptive statistics, such as mean, range, and frequency were used to describe the demographic and medical data. SAS v9.4 (SAS Institute, Cary, NC) was used to perform the statistical analysis, and values were considered statistically significant if $p < 0.05$. Single and multiple variable logistic regression analyses were performed to determine if there was a relationship between study variables and chronic opioid use at 3 months postoperatively and includes odds ratios (OR) with 95% confidence intervals (CI).

Results

Cohort Characteristics

One hundred nineteen patients with a mean age of 52.9 years (range 19-88) who underwent surgery for a bone or soft tissue tumor at our institution were included (Table 1). The mean CCI of the study population was 3.6 (range=0-13). Figure 2 describes the pathologic diagnoses of the study population.

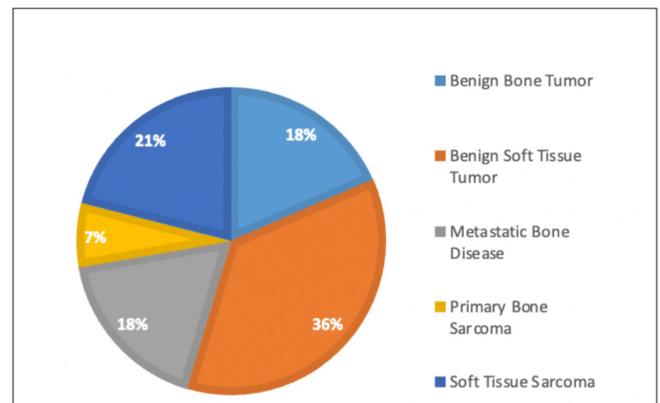


Figure 2: Pie chart depicts pathologic tumor diagnosis of 119 patients included in the study

Table 1: Demographic data and medical characteristics of 119 study patients

Demographic Variable	Number of Patients (%)
Total number of patients	119
MALE	55 (46.2%)
FEMALE	64 (53.8%)
Age	
Age <50	46 (38.7%)
Age 50-59	26 (21.8%)
Age 60-69	19 (16%)
Age 70-79	17 (14.3%)
Age >80	11 (9.2%)
Race	
White	94 (79%)
African American	5 (4.2%)
Asian	3 (2.5%)
Hispanic	11 (9.2%)
Native American	1 (0.8%)
Other	5 (4.2%)
Marital Status	
Single	43 (36.1%)
Relationship	69 (58%)
Unknown	7 (5.9%)
Employment Status	
Employed	40 (33.6%)
Unemployed	21 (17.6%)
Disability	1 (0.8%)
Retired	29 (25.2%)
Unknown	28 (23.5%)
Medical Factor	
Mental Illness	30 (25.2%)
Tobacco Use	15 CURRENT (12.6%) 46 FORMER (38.7%)
Alcohol Use	73 (61.3%)
Illicit Drug Use	10 (8.4%)
Mean Charlson Comorbidity Index (CCI) Score	3.6 (RANGE = 0-13)
Diabetes	20 (16.8%)
Liver Disease – Moderate to Severe	3 (2.5%)
Leukemia/Lymphoma/Localized Malignancy	37 (31.1%)
Metastatic Cancer	20 (16.8%)
Chronic Kidney Disease (CKD)	2 (1.7%)
Congestive Heart Failure (CHF)	3 (2.5%)
Myocardial Infarction (MI)	5 (4.2%)
Chronic Obstructive Pulmonary Disease (COPD)	11 (9.2%)
Peripheral Vascular Disease (PVD)	1 (0.8%)
Stroke/Transient Ischemic Attack (CVA/TIA)	2 (1.7%)

Dementia	1 (0.8%)
Hemiplegia	1 (0.8%)
Connective Tissue Disorder	1 (0.8%)
Peptic Ulcer Disease (PUD)	5 (4.2%)
Mean BMI	28.9 (range = 18.7-46.8)
Mean Lesion Size	6.4 cm (range= 0.1 cm - 25 cm)

Opioid Use

At the initial encounter with the orthopaedic oncologist, 17 patients (18.1%) were using opioids with a mean daily consumption of 55 MME (range=10-163 MME), and the number increased to 28 (24.6%) at the time of surgery (Figure 3 and 4). The highest prevalence was observed at 2 weeks postoperatively, 60 patients (51.3%), with a mean daily consumption rate of 55 MME (range=4-540 MME). By 6 weeks postoperatively, number opioid users declined to 30 patients (25.2%) and was 19 (15.9%) by 1 year postoperatively, which was lower than the prevalence at the initial visit. The mean opioid daily consumption at 6 weeks postoperatively was 68 MME (range=8-288 MME) and increased to 113 MME (range=10-1484 MME) by 3 months postoperatively, which was the greatest daily amount of opioid consumption observed. By one year postoperatively, opioid users consumed a mean of 39 MME/day (range=9-106 MME), which was less than the mean daily opioid consumption at the initial visit. Thirty-three patients (27.7%) never used opioids during the study period.

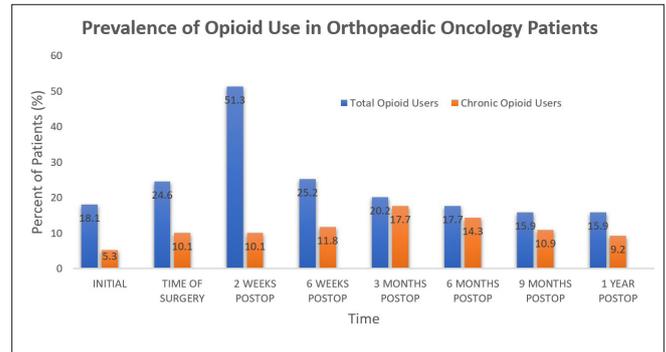


Figure 3: Bar graph depicts the percent of total opioid users (blue) and chronic opioid users (orange) in the study population

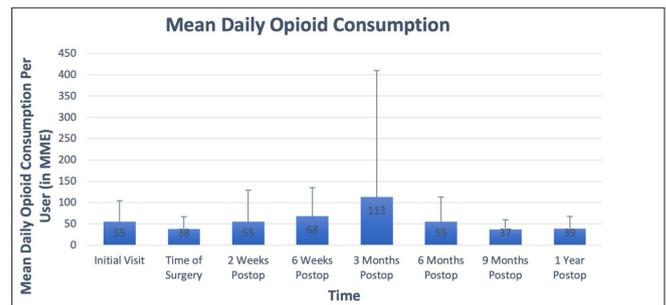


Figure 4: Mean daily opioid consumption

Chronic Opioid Use

At the initial visit, 5 patients (5.3%) were chronic opioid users. This number increased to 21 patients (17.7%) at 3 months postoperatively, which was the highest prevalence of chronic opioid use in this study. This rate decreased to 9.2%, or 11 patients, by 1 year postoperatively. Of the chronic opioid users identified at 1 year postoperatively, 4 patients (36.4%) were

already prescribed narcotics prior their initial visit with the orthopaedic oncologist; the remaining patients had developed the chronic use pattern during their postoperative experience.

Risk Factors

Factors with a statistically significant association with chronic opioid use postoperatively included opioid use preoperatively (OR=31.64, CI=9.38-106.74, p<0.0001), chronic use preoperatively (OR=105.6, CI=12.32-904.77, p<0.0001), CCI (OR=1.15, CI=1.02-1.30, p=0.02), malignancy (OR=2.34, CI=1.23-4.08, p=0.01), metastatic cancer (OR=3, CI=1.03-8.74, p=0.04), and VAS scores at the initial visit (OR=1.25, CI=1.05-1.48, p=0.01) (Table 2). Additionally, continued opioid use at 6 weeks postoperatively (OR=20.92, CI=6.55-66.84, p<0.0001) was associated with chronic use at 3 months postoperatively, suggesting that the 6-week mark is a critical timepoint threshold for predicting the development of a chronic consumption pattern. Multivariable analysis of predictors of chronic use at 3 months was performed including only the statistically significant variables from the univariate analysis; opioid use data at various timepoints were excluded from the multivariable analysis due to collinearity. Malignant tumors (p=0.02) and VAS scores at the initial encounter (p=0.02) were statistically significant in the multivariable analysis.

Table 2: Univariate Analysis of Risk Factors Associated with Chronic Opioid Use in 119 Patients

Factors	P-Value	Odds Ratio	95% Confidence Interval
Demographics			
Age:			
Age 50-59	0.40		
Age 60-69	0.08		
Age 70-79	0.08		
Age >80	0.86		
Gender	0.27		
BMI	0.45		
Race:			
African American	0.89		
Asian	0.98		
Hispanic	0.39		
Other	0.73		
Marital Status	0.57		
Employment Status	0.30		
Tumor Characteristics			
Bone Tumor	0.87		
Soft Tissue Tumor	0.15		
Malignant Tumor	0.01*	2.24	1.23-4.08
Metastatic Cancer	0.04*	3	1.03-8.74
Mean Lesion Size	0.74		
Medical Factors			
CCI Score	0.02*	1.15	1.02-1.30
Diabetes	0.08		
Liver Disease – Moderate to Severe	0.98		

CKD	0.27		
CHF	0.98		
MI	0.90		
COPD	0.45		
PVD	0.99		
CVA/TIA	0.27		
Dementia	0.99		
Hemiplegia	0.99		
Connective Tissue Disorder	0.99		
PUD	0.21		
Mental illness	0.48		
VAS Pain Score at Initial Visit	0.01*	1.25	1.05-1.48
Opioid Use at Preop	p<0.0001*	31.64	9.38-106.74
Continued Opioid Use at 6 Weeks Postop	p<0.0001*	20.92	6.55-66.84
Chronic Opioid Use at Preop	p<0.0001*	105.6	12.32-904.77
Social Factors			
Tobacco Use	0.42		
Alcohol Use	0.66		
Illicit Drug Use	0.07		

*Denotes statistical significance.

Bone and Soft Tissue Sarcomas

Thirty-three patients were diagnosed with a primary bone or soft tissue malignancy. At the time of surgery, 8 of these patients (24.2%) were opioid users and 3 (9.1%) were chronic users (Figure: 5). by 2 weeks postoperatively, 12 patients (36.4%) were using opioids, the highest prevalence of opioid use observed in this cohort, and decreased to 6 (18.2%) by 6 months postoperatively. Chronic opioid use had the highest prevalence, 8 patients (24.2%), at 3 months postoperatively and declined to 3 patients (9.1%) by 1 year postoperatively. Two of the 3 chronic users at 1 year postoperatively were chronic users prior to their initial encounter with the orthopaedic oncologist. Factors with a statistically significant association with chronic opioid use at 3 months postoperatively in this subset of patients included opioid use preoperatively (OR=168, CI=9.27->999.999, p=0.001), continued opioid use at 6 weeks postop (OR=36.74, CI=3.50-386.09, p=0.002), and pain at the initial visit (OR=1.32, CI=1.02-1.72, p=0.04) (Table 3). Preoperative opioid use was the only variable with a statistically significant association with chronic opioid use at 3 months postoperatively on multivariate analysis (p=0.001) among this subset of patients.

Table 3: Univariate Analysis of Risk Factors Associated with Chronic Opioid Use in 33 Bone and Soft Tissue Sarcoma Patients

Factors	P-Value	Odds Ratio	95% Confidence Interval
Demographics			
Age:			
Age 50-59	0.88		
Age 60-69	0.43		
Age 70-79	0.88		
Age >80	0.81		
Gender	0.14		
BMI	0.84		
Race:			
African American	0.98		
Asian	0.11		
Hispanic	0.12		
Other	0.97		
Marital Status	0.90		
Employment Status	.083		
Tumor Characteristics			
Bone Tumor	0.95		
Soft Tissue Tumor	0.95		
Mean Lesion Size	0.97		
Medical Factors			
CCI SCORE	0.92		
Diabetes	0.32		
Liver Disease	0.98		
Moderate to Severe			
CHF	0.98		
MI	1.00		
COPD	0.97		
CVA/TIA	0.40		
Dementia	0.98		
Hemiplegia	0.97		
PUD	0.70		
Mental illness	0.81		
VAS Pain Score at Initial Visit	0.04*	1.32	1.02-1.72
Opioid Use at Preop	0.001*	168	9.27->999.999
Continued Opioid Use at 6 Weeks Postop	0.002*	36.74	3.50-386.09

Chronic Opioid Use at Preop	0.97		
Social Factors			
Tobacco Use	0.57		
Alcohol Use	0.27		
Illicit Drug Use	0.81		

*Denotes statistical significance.

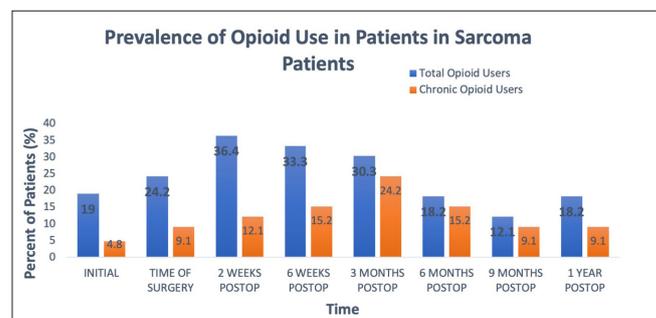


Figure 5: Bar graph depicts the percent of total opioid users (blue) and chronic opioid users (orange) in 33 patients with a bone or soft tissue sarcoma.

Opioid Prescribers

Orthopaedic oncologists prescribed opioids to 14 opioid users (50%) preoperatively and to 50 users (83.3%) by 2 weeks postoperatively. By 3 months postoperatively, only 6 opioid users (25%) obtained their prescription from an orthopaedic oncologist, which decreased to 3 users (15.8%) by 1 year postoperatively.

Discussion

This study evaluated the prevalence of opioid use in orthopaedic oncology patients during their perioperative course and factors associated with chronic postoperative use. To our knowledge, an investigation of this topic in this patient population has not been previously reported although cancer related pain is an indication for opioid prescription in the WHO’s ladder for approaching cancer pain [14, 15].

The results of this study showed that 18.1% of patients were using opioids prior to their initial evaluation by an orthopaedic oncologist, and this rate increased to 23.5% by the time of surgery. We found that the overall rate of opioid use dropped from 23.5% at time of surgery to 9.2% at 1 year postoperatively (although it rose acutely to 51.3% in the immediate postoperative phase). The vast majority of those patients using narcotics peri-operatively for acute pain achieved ablative pain relief from their surgery and were able to discontinue opioid use within a year. This finding supports the valuable role of orthopaedic oncology surgical intervention in the care of these patients. We observed that 5.3% of patients presenting to the orthopaedic oncologist were chronic opioid users, per the CDC definition, which is lower than the frequencies observed in other orthopaedic subspecialties [16, 19].

The highest rate of opioid use was found at 2 weeks postoperatively, which is consistent with other reports [11]. This finding is reasonable in the authors’ opinion because many of these patients are discharged with opioids to manage

acute postoperative pain. The majority of these narcotics were prescribed by the operative orthopaedic oncologist. The average daily opioid consumption during the first two weeks was 55 MME, which was relatively low compared to later timepoints, representing the fact that while many patients were using opioids for acute pain, they did so sparingly. This is also consistent with opioid use amongst surgical oncology patients in other fields, such as breast surgery. A study by Park et al. found that mean opioid use amongst breast surgical oncology patients was 54 oral morphine equivalents (OME) at 1 week postoperatively [20]. In contrast, the highest mean daily opioid consumption rate was reported at 3 months postoperatively, which is consistent with the highest prevalence of chronic use reported by our study. The patients who were still using these medications at 3 months postoperatively were doing so in relatively high doses; only 25% patients were receiving a prescription from an orthopaedic oncologist by that time.

One of our primary goals was to investigate chronic opioid use. Metastatic cancer and malignant lesions were associated with chronic opioid use. Metastatic bone disease tends to be associated with pain at multiple sites and is one of the few circumstances where chronic opioid use may be indicated. Therefore, these patients often have relationships with medical oncologists or pain management physicians who may have prescribed these medications prior to presentation to an orthopaedist [12]. Severe pain is also a common early symptom for bone sarcomas, and patients often report persistent pain even after curative sarcoma treatment [12, 21]. This is consistent with the findings of our study since there was a higher prevalence of chronic opioid users amongst patients with sarcomas between 2 weeks and 6 months postoperatively in comparison to the total study population. However, by 1 year postoperatively, the frequency of chronic opioid use is equivalent to that of the total study population, indicating that the frequency of opioid use amongst sarcoma patients aligns with that of the overall orthopaedic oncology population. In contrast, many patients with benign tumors should not need opioids at all, and our data found that 26.6% of them were able to recover in an opioid-free way. It would be ideal to identify these patients prior to surgery and not prescribe any opioids to those who reliably do not need them.

Additionally, our study found that continued opioid use at 6 weeks postoperatively was associated with chronic use after 3 months postoperatively. This is an important finding, as it could indicate that a patient is at an increased risk of developing a habit of chronic use if they are still consuming opioids 6 weeks postoperatively. This risk association has been consistently reported by studies of patients undergoing TKA, spine surgery, arthroscopic meniscal surgery, and anterior cruciate ligament reconstruction [3, 10, 19, 22, 23]. Based on these data and taking into consideration recent improvements in cancer survival rates along with the adverse events associated with chronic opioid use, we suggest that surgeons designate the 6 week postoperative timepoint as a goal for patients' termination of narcotic use.

It is also important to consider who the prescribers of these medications are. In this study, 50% of patients obtained an opioid prescription from an orthopaedic oncologist preoperatively, and the frequency increased to 82.8% by 2 weeks postoperatively. These data suggest that peri-operatively, pain control is a priority

of the treating orthopaedic oncologist, and he/she is comfortable prescribing narcotics around the time of surgery. Providers who continue to prescribe opioids in the chronic setting must consider the mental and social health opportunities available to counsel their chronic pain patients. Surgeons should clearly advise patients in the perioperative period that the optimal use of opioids is the least amount possible for the shortest duration possible. Lee et al. demonstrated that patient education and standardized guidelines statistically significant reduced opioid use in their cohort of patients who underwent breast cancer and melanoma procedures [24].

By 6 months postoperatively, only 9.5% of opioid users were obtaining a prescription from their orthopaedic oncology surgeon. This is consistent with a survey of orthopaedic surgeons of various specialties which found that 46% of orthopaedic surgeons stopped prescribing opioids by 4 weeks postoperatively and an additional 40% stopped by 8 weeks postoperatively [25]. The peri-operative prescribing practices of orthopaedic oncologists differ from those of arthroplasty surgeons, who only prescribed 23% of opiate prescriptions to their patients perioperatively [26]. However, since oncology patients are more likely to report severe pain because of the nature of their disease, and oncology-trained surgeons are trained to focus on pain control as a fundamental component of treatment, it is reasonable for orthopaedic oncologists to prescribe opioids at a higher frequency to their patients. By 1 year postoperatively, nearly all patients in our study who remained on opioids were obtaining them from someone other than their orthopaedic surgeon, such as a chronic pain management specialist, which the authors believe is the safest strategy for long-term narcotic prescribing.

Our study had several limitations. First, a power analysis was not performed to determine the required sample size because the database only provided patient data for up to 2 years prior to the access date. Due to the limited size of the study, it may have been underpowered to detect all significant associations when they truly did exist: for example, we did not find an association between mental illness and opioid use in orthopaedic oncology patients, while other studies have reported mental illness as a factor associated with chronic postoperative opioid use in orthopaedic patients [27-29]. This discrepancy may also be due to the fact that only 25% of our population had a mental illness. The same limitation can be applied to gender and several medical comorbidities, such as peripheral vascular disease, which were not common in our patient population and failed to achieve statistically significant associations with chronic opioid use. Second, opioid consumption was calculated based on opioid prescriptions filled by patients and reported by the multi-state database. The database does not provide information about how many pills the patient actually consumed, so it cannot provide rigorously granular data on opioid consumption. Our next step is to conduct a prospective study of opioid consumption, involving pill counts during follow-up evaluations, to overcome this limitation.

This study is timely and important in consideration of recent improvements in cancer survival rates, leading to more durable and functional outcomes, combined with consideration of the adverse medical and social effects associated with opioid use [1, 30-32]. By gaining a better understanding of the morbidity and

mortality associated with this public-health issue, and factors that can assist in identifying high-risk patients, orthopaedic oncologists can more effectively counsel patients about their risk of postoperative opioid dependency and tailor their prescribing practices. Future studies should be conducted to develop evidence-based guidelines for the prescription of opioids in patients with bone and soft tissue tumors.

Conflict of Interest

One of the co-authors is an unpaid consultant for Adler, Daiichi Sankyo.

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