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Persistent Opioid Use Following Total Knee Arthroplasty: A Signal for Close Surveillance

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ABSTRACT

Background: Prolonged opioid use following total knee arthroplasty (TKA) has not been extensively studied.
Methods: A cohort study of primary TKA for osteoarthritis using an integrated healthcare system and Total Joint Replacement Registry (January 2008-December 2011) was conducted. Opioid use during the first year after TKA was the exposure of interest and cumulative daily oral morphine equivalent (OME) amounts were calculated. Total postsurgical OME per 90-day exposure periods were categorized into quartiles. The end point was aseptic revision surgery. Survival analyses were conducted and hazard ratios (HRs) were adjusted for age, gender, prior analgesic use, opioid-related comorbidities, and chronic pain diagnoses.
Results: A total of 24,105 patients were studied. After the initial 90-day postoperative period, 41.5% (N = 9914) continued to use opioids. Also, 155 (0.6%) revisions occurred within 1 year and 377 (1.6%) within 5 years. Compared to patients not taking any opioids, patients using medium-low to high OME after the initial 90-day period had a higher adjusted risk of 1-year revision, ranging from HR = 2.4 (95% confidence interval, 1.3-4.5) to HR = 33 (95% confidence interval, 10-110) depending on the OME and time period.
Conclusion: Patients who require opioids beyond 90 days after TKA warrant close follow-up.

Total knee arthroplasty (TKA) is an effective treatment for the management of end-stage knee arthritis, but it is recognized that a proportion of patients are not satisfied with the procedure. As the volume of total joint procedures rises, the growing pool of patients who require follow-up challenges many orthopedic practices. Follow-up compliance after TKA was 63% at the 1-year visit and 38% at 2 years in study where 1- and 2-year follow-up was considered mandatory [1]. There is no consensus regarding ideal follow-up after TKA with 45% of surveyed total joint surgeons recommending annual visits and 40% preferring biennial visits [2]. Persistent pain has been identified as one of the main factors leading to patient dissatisfaction after TKA [3]. Patient-reported outcome measures (PROMs), specifically Oxford Knee Scores (OKS), were found to be predictive of TKA revision risk [4]. However, considerable resources in time, labor, and costs preclude routine collection of PROMs in most clinical practices.

Opioids remain a major constituent of postoperative TKA pain management, despite development of perioperative multimodal protocols [5]. Electronic medical records and statewide narcotic prescription databases have made opioid prescription information more available to clinicians [6]. It was hypothesized that opioid prescriptions may serve as a surrogate for pain after TKA surgery providing early identification of patients who are at risk of failure.

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In a previous study, postoperative opioid use was associated with total hip arthroplasty (THA) revision risk [7,8]. It was hypothesized that the quantity, and duration, of narcotic use after TKA would also be associated with revision surgery. The purpose of this study was to evaluate the risk of 1-year and 5-year revision with the prolonged use of opioids in the year immediately after TKA surgery.

Methods

Study Design and Setting

A retrospective cohort study of patients who underwent primary TKA procedures at Kaiser Permanente was conducted. Kaiser Permanente is an integrated healthcare system with over 10 million members throughout the United States [9]. Three regions, Southern California, Northern California, and Hawaii, which account for 8.2 million members, were covered in this study. They were selected due to complete data availability. The Kaiser Permanente patient population has been shown to be demographically and socioeconomically representative of the geographical region it covers [10,11].

Data Sources

A Total Joint Replacement Registry (TJRR) was used to identify patients with TKAs and their specific characteristics, surgical indication, and surgical outcomes. Detailed information on this data source's coverage, processes, validation rules, and available data has been previously published [12,13]. In brief, the registry was established in 2001 and reported a 95% voluntary participation in 2011 [13]. The integrated healthcare system's electronic medical record was also used for this study. This Epic-based product was rolled out in 2004 and was fully implemented in all regions in 2008. The electronic medical records pharmacy module was used to identify medication utilization for the study subjects and inpatient and outpatient encounter modules were used to identify specific patient characteristics and history. International Classifications of Disease, ninth revision, codes were used to identify patient characteristics and disease history. Unique patient identifiers used by the integrated healthcare system linked data sources.

Study Sample

The study sample included unilateral primary TKA cases registered between January 1, 2008, and December 31, 2011. Only adult patients (age $\geq$18), without other elective arthroplasty procedures (knee or hip) within 365 days, with a surgical indication of osteoarthritis, and without history of cancer (identified using International Classifications of Disease, ninth revision, codes 140.*-208.*, except 173.* for pain related to cancer [14] and the specific Elixhauser comorbidities [15] of lymphoma, metastatic cancer, solid tumor without metastasis) were included. Patients without complete 1-year follow-up (3% of cases because they died or were lost to follow-up before the end of the study period), those with revisions for infection or any surgical site infections after their procedure, and those who had opioid amounts on the 99th percentile who were considered medication use outliers were not included in the final sample.

Outcomes of Interest

Aseptic revision surgery within 1 and 5 years of the TKA was the main end point of this study. Revision surgery was obtained from the TJRR, which monitors and validates (ie, events are adjudicated using manual chart review) all revision surgeries of primary procedures in the registry. Revision surgery was defined as any surgery where a component was removed or replaced.

Exposure of Interest

The cumulative daily amount, calculated as oral morphine equivalent (OME) [16], of oral and transdermal opioid medication was calculated over the 360 days postdischarge from the TKA procedure. OMEs were calculated using a standard conversion table to translate the dose and type of each opioid a patient received into OME dose for overall comparison of analgesic dose [17]. Total post-TKA OMEs per 90-day exposure periods categorized into quartiles were the exposure of interest. If a patient had a revision or died during the 360-day postoperative period, the amount of opioid exposure was calculated until the day before the event occurred. The cumulative OME daily dose was calculated by summing the total dose per day based on quantity of supply. The total OME for a 90-day exposure time was the sum of all OME daily doses for that period.

Covariates/Confounders

Patient gender, age at the time of surgery, opioid-related comorbidities, history of chronic pain, as well as 1-year prior opioid use, and 1-year preoperative and postoperative nonsteroidal anti-inflammatory drug use were evaluated as possible confounders. Opioid related comorbidities and history of pain reported in the year before and up to the surgery were defined and identified using Raebel et al's algorithm [14]. The opioid related comorbidities included anxiety, bipolar disease, depression, opioid dependency, post-traumatic stress disorder, and substance abuse. History of chronic pain was categorized into (1) nonspecific chronic pain, which included general chronic pain, migraines, tension headache, abdominal pain, hernia, kidney/gall stones, menstrual pain, neuropathy, and temporomandibular pain; and (2) chronic musculoskeletal pain, which included back pain, neck pain, fibromyalgia, arthritis, carpal tunnel, limb-extremity pain, pain in joint, "other" chronic musculoskeletal pain, fractures and contusions, costochrondritis and intracostal muscle injury.

Statistical Analysis

Descriptive statistics described the study sample and OME use per 90-day postoperative period. Cox-proportional regression models evaluated the risk of 1- and 5-year revision association with total amount of OME per 90-day postoperative period. Hazard ratios (HRs), 95% confidence intervals (CI), and Wald chi-square *P* values are reported. Because the amount of opioid intake naturally varied over time in the post-TKA rehabilitation period and in order to evaluate the independent effect of the amount of opioid throughout different periods postsurgery, a model for each specific postoperative 90-day period was created. In the first 90 days postsurgery (days 1-90), the entire sample was included in the model (N = 24,105); in the second 90-day (days 91-180) period, all survivors and nonrevised cases from the first period were included (N = 23,914); in the third 90-day (days 181-270) period, all survivors and nonrevised cases from the second period were included (N = 23,688); and in the fourth period (days 271-360), all survivors and nonrevised cases from the third period were included (N = 23,482). The categories of OME total amount evaluated included no opioids (reference category), low (less than the lowest quartile of the total dose in that period), medium-low (between lowest quartile and median dose), medium-high (between the median dose and third quartile dose), and high (those taking more than the highest quartile of opioids). Due to the limiting number of events,