

The use of Opioids in Total Knee Arthroplasty Patient: Main Characteristics, Risk Factors and Adverse Events

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ABSTRACT

Opioids are frequently used for the treatment of preoperative and postoperative pain among patients undergoing total knee arthroplasty (TKA) and revision TKA (RTKA). The greatest risk for prolonged opioid use after TKA is preoperative opioid use. Despite the effectiveness of multimodal postoperative pain protocols, younger patients with preoperative history of narcotic use require additional opioids and are at a higher risk for complications and a greater length of stay. At 90 days, respiratory complications were the most common opioid-related adverse events (TKA: 6%; RTKA: 8%), followed by postoperative nausea and vomiting (TKA: 3%; RTKA: 4%), and urinary retention complications (TKA: 3%; RTKA: 3%). For TKA, risk factors for respiratory complications included older age, lower socioeconomic status, more comorbidities, obesity, chronic obstructive pulmonary disease, white race, and patients in the Mid-

west and West (vs. South). The average Medicare payment for treating complications within 90 days of a TKA was \$6206 and \$6222 following RTKA. Avoidance or weaning of preoperative opioids should be considered.

Key words: Knee arthroplasty; Pain; Opioids

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INTRODUCTION

Opioids are frequently used for the treatment of pre-operative and post-operative pain among patients undergoing total knee arthroplasty (TKA)^[1]. Chronic opioid users pose a unique challenge for orthopaedic surgeons, as they often report suboptimal results after TKA^[2]. Preoperative opioid use has been suggested to augment postoperative pain and opioid consumption following TKA^[3].

Patients undergoing TKA may be at risk for prolonged post-operative opioid use due to a high rate of persistent post-surgical pain (20%) and high rates of pre-operative opioid use^[4]. Post-operative analgesia following primary TKA and revision TKA (RTKA) can be reliant on the use of opioids and may cause opioid-related adverse events^[5].

The purpose of this article is to investigate the current characteristics of the use of opioids in TKA patients before and after surgery and risk factors of chronic opioid use; and adverse events of opioid use before and after primary TKA and RTKA.

THE USE OF OPIOIDS IN TKA AND RTKA PATIENT

Table 1 summarizes the main characteristics of the use of opioids in TKA patients before and after surgery, risk factors of chronic opioid use and the main adverse events of opioid use before and after TKA^[1-21].

Table 1 Summary of characteristics, risk factors and adverse events of opioid use in total knee arthroplasty (TKA) and revision TKA (RTKA).

Authors	Year	Findings	Comments
Goeslin <i>et al</i> [6]	2016	Preoperatively, 574 TKA and total hip arthroplasty (THA) patients completed validated, self-report measures of pain, functioning, and mood and were longitudinally assessed for 6 months after surgery. Among patients who were opioid naive the day of surgery, 8.2% of TKA and 4.3% of THA patients were using opioids at 6 months. In comparison, 53.3% of TKA and 34.7% of THA patients who reported opioid use the day of surgery continued to use opioids at 6 months. Patients taking > 60 mg oral morphine equivalents preoperatively had an 80% likelihood of persistent use postoperatively. Day of surgery predictors for 6-month opioid use by opioid-naive patients included greater overall body pain, greater affected joint pain (knee/hip), and greater catastrophizing. For both opioid-naive and opioid users on the day of surgery, decreases in overall body pain from baseline to 6 months were associated with decreased odds of being on opioids at 6 months; however, change in affected joint pain (knee/hip) was not predictive of opioid use.	Many patients taking opioids before surgery continue to use opioids after arthroplasty and some opioid-naive patients remained on opioids; however, persistent opioid use was not associated with change in joint pain.
Aasvang <i>et al</i> [3]	2016	In a prospective observational study, we investigated the effect of > 4 weeks pre-operative opioid use [none vs. low dose (< 30 mg morphine equivalents (eq.)) vs. high dose (> 30 mg morphine eq.)] in patients scheduled for primary, unilateral TKA. All patients had well-defined multimodal opioid-sparing perioperative analgesic therapy, and continued any pre-operative opioid medication. The primary outcome was differences between groups in pain at rest and during walk for the first 6 post-operative days. Among 123 patients included, 115 were available for final analysis (93% follow-up rate). Post-operative pain during walk was significantly increased in both opioid-treated groups vs. non-opioid-treated patients. Secondary analysis of combining all pre-operatively opioid-treated patients vs. opioid-free patients, showed significantly increased pain at rest and walk and increased postoperative opioid requirement - excluding preoperative dosage - during the first postoperative week in opioid-treated patients.	Pre-operative opioid use increases the risk for postoperative pain at rest and walk, and increased opioid consumption after TKA.
Hansen <i>et al</i> [1]	2016	Opioid use among 15,020 patients undergoing TKA was examined. Generalized estimating equations assessed change in total oral morphine equivalents pre-TKA and post-TKA, and logistic regression estimated risk factors of chronic opioid use. Of the total sample, 7782 (52.0%) patients had at least 1 opioid (38.6% pre-TKA and 34.4% post-TKA). The most commonly prescribed opioids were oxycodone, codeine + acetaminophen, and tramadol. Pre-TKA, 720 (4.8%) patients were chronic opioid users, of which 241 (33.5%) stopped being chronic users after surgery and 479 (66.5%) continued but had a 16% reduction in total oral morphine equivalents. Of the 5077 (33.8%) occasional opioid user pre-TKA, 2407 (47.4%) stopped after surgery. Compared to nonopioid users, chronic users were younger, were female, had more comorbidity, and had longer hospital stays. Older age was associated with ceasing chronic opioid use post-TKA.	There was a reduction in opioid use following TKA. Almost 50% of occasional users and more than 30% of chronic users pre-TKA ceased opioids postoperatively. There was a reduction in use for those chronic users who continued to take opioids postsurgery.
Hernandez <i>et al</i> [7]	2017	These authors reviewed 105 primary TKAs performed with at least 1 year of follow-up. Exclusion criteria included bilateral TKA, preoperative opioid use, or reoperation within the first 3 months. Data collected included opioid refills, Knee Society Score, and total and daily morphine equivalent dose (MED) prescribed. Patients were most commonly discharged on oxycodone (90%), hydromorphone (5%), and hydrocodone/acetaminophen (1%). The average total prescribed MED was 1405 mg. Patients requiring refills did not differ in the total prescribed MED (1521 vs 1349 mg), daily prescribed MED (153 vs 155 mg), or preoperative Knee Society Score (63 vs 60). Average follow-up time was 2.4 years.	The quantity of opioids prescribed after TKA varied widely, ranging from a total MED of 273-3250 mg. The refill rate did not differ between large prescriptions (≥1400 mg) and smaller prescriptions. Excessive opioid prescriptions should be avoided as they did not decrease the number of refills and pose the risk of divergence and subsequent abuse.
Bedard <i>et al</i> [8]	2018	Patients who underwent primary TKA from 2007-2014 were identified within the Humana database. Postoperative opioid use was measured by monthly prescription refill rates. A preoperative opioid user (OU) was defined by history of opioid prescription within 3 months prior to TKA and a non-opioid user (NOU) was defined by no history of prior opioid use. Rates of opioid use were trended monthly for one year postoperatively for all cohorts. 73,959 TKA patients were analyzed and 23,532 patients (31.2%) were OU. OU increased from 30.1% in 2007 to 39.3% in 2014. Preoperative opioid use was the strongest predictor for prolonged opioid use following TKA, with OU filling significantly more opioid prescriptions than NOU at every time point analyzed. Younger age, female sex and other intrinsic factors were found to significantly increase the rate of opioid refilling following TKA throughout the postoperative year.	Approximately one-third of TKA patients use opioids within 3 months prior to surgery and this percentage has increased over 9% during the years included in this study. Preoperative opioid use was most predictive of increased refills of opioids following TKA. However, other intrinsic patient characteristics were also predictive of prolonged opioid use.
Rozell <i>et al</i> [9]	2017	These authors evaluated a consecutive series of 802 patients undergoing elective primary THA and TKA over a 9-month period. All patients were managed using a multimodal pain protocol. Data on medical comorbidities and history of preoperative narcotic use were collected and correlated with deviations from the protocol. Of the 802 patients, 266 (33%) required intravenous narcotic rescue. Patients aged < 75 years and with preoperative narcotic use were more likely to require rescue. Multivariate logistic regression analysis demonstrated that preoperative narcotic use was the largest independent predictor of increased postoperative opioid requirements. These patients developed more in-hospital complications. This was associated with an increased length of stay and a 2.5-times risk of requiring oral narcotics at 3 months postoperatively.	Despite the effectiveness of multimodal postoperative pain protocols, younger patients with preoperative history of narcotic use require additional opioids and are at a higher risk for complications and a greater length of stay.

Authors	Year	Findings	Comments
Kim <i>et al</i> [2]	2018	All preoperative chronic opioid users among 338 consecutive TKA cases performed at our institution between February and June 2016 were identified and divided into 2 cohorts: patients who (1) persistently used opioids and (2) discontinued use by the 6-month time point following surgery. Baseline characteristics were compared between cohorts in order to determine risk factors for persistent opioid use following TKA. Of the 338 patients, 53 (15.7%) were identified as preoperative chronic opioid users. Of these, 23 (43.4%) continued chronic opioid use 6 months following surgery, whereas 14 (4.9%) previously nonchronic users were identified as new chronic users at 6 months. Characteristics that were predictive of persistent opioid use included male gender, prior injury or surgery to the ipsilateral knee, current tobacco smoking status, and a history of psychiatric disorder. Opioid dose consumption of ≥ 12 mg/d morphine-equivalents over the 3 months leading up to surgery had an increased risk of persistent chronic opioid use by a factor of 6.	TKA candidates who have complicated medical, social, and surgical histories are at an increased risk of chronic opioid abuse postoperatively.
Starr <i>et al</i> [11]	2018	These authors analyzed medical records of Veterans Affairs patients who underwent TKA. Chronic opioid use was defined as opioid use for ≥ 3 months preoperatively. A cross-validated Cox proportional hazards model was created to predict revision TKA (RTKA) before initial TKA. Model performance was evaluated by the mean absolute error at 1 and 5 years. Totally, 32,297 patients were included. A risk calculator was generated with a mean absolute error of 0.1% at 1 year and 3.6% at 5 years. Chronic opioid use was a significant predictor of RTKA. Other model variables were age, female sex, body mass index, diabetes, chronic kidney disease, and nonchronic opioid.	Preoperative chronic opioid use is a predictor of RTKA. Using this association and others, a TKA revision risk calculator was generated at http://www.bit.do/tka .
Namba <i>et al</i> [12]	2018	A cohort study of primary TKA for osteoarthritis using an integrated healthcare system and Total Joint Replacement Registry 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. 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 to HR = 33 depending on the OME and time period.	Patients who require opioids beyond 90 days after TKA warrant close follow-up.
Dwyer <i>et al</i> [13]	2018	Using online prescription information, we calculated the number of filled prescriptions, total morphine equivalent dose (MED) and quantity of pills, and date of last opioid prescription (days) for 197 TKA and 186 total hip arthroplasty (THA) patients. Patients were classified based on refill status. Opioid data were compared between TKA and THA patients. Relationships between comorbidities and refill status were examined. Number of prescriptions, total quantity and MED, and days on opioids were greater for TKA patients. TKA patients required more refills for a greater quantity of pills. The presence of a comorbidity or anxiety/depression were correlated with refills for TKA patients only. A comorbidity increased the risk of refills by 3.1 times, while anxiety/depression had a 2.5 times greater risk of refills.	Compared to THA patients, TKA patients were twice as likely to require refill opioid prescriptions and were prescribed a greater total MED for a longer period of time post-operatively. Patients undergoing TKA who present with a comorbidity or are currently being treated for anxiety or depression are more likely to require a refill.
Politzer <i>et al</i> [14]	2018	A review of the prescription-tracking database of a large private payer from 2007 to 2013 was performed using International Classification of Diseases, Ninth Revision and Current Procedural Terminology codes. Chronic opioid use was defined as opioid prescriptions over 6 contiguous months postoperatively. The authors identified 66,950 patients who underwent TKA with minimum 2-year follow-up and medication codes. Of those taking opioids preoperatively (n = 36,668), 34.8% became chronic users postoperatively compared to only 5.0% of the opioid-naïve cohort (n = 30,282). Major risk factors for chronic postoperative opioid use included preoperative opioid use, female gender, and younger age. From 2007 to 2013, there was a significant linear increase in opioid use preoperatively and postoperatively, but chronic postoperative opioid use increased only marginally.	The greatest risk factors for chronic postoperative opioid use were preoperative use, younger age, female gender, greater length of stay, and worse health status. Although the use of opioids continues to grow significantly preoperatively and postoperatively, chronic opioid use post-TKA has remained clinically unchanged.
Hernandez <i>et al</i> [15]	2018	A retrospective review identified 53 patients on preoperative opioids who were matched 1:2 to 106 opioid-naïve patients undergoing primary TKA with at least 2-year follow-up. Opioid refills, Knee Society Score (preoperative and follow-up), morphine equivalent dose (MED) prescribed, and persistent opioid use were compared between groups. The average total MED prescribed at discharge was 1248 mg, ranging from 0 to 5600 mg. The average daily MED used before discharge was greater in the preoperative opioid group compared to the opioid-naïve group (90 \pm 75 mg vs 54 \pm 42 mg). The preoperative opioid group and opioid-naïve group differed in terms of refills (1.3 vs 0.4), persistent opioid use (21 [39%] vs 5 [4%]), postoperative KSS (85 vs 90), and manipulations under anesthesia (4 [8%] vs 1 [1%]). Preoperative tramadol users had the same risk of refills, persistent opioid use, reduced KSS, and manipulation under anesthesia as those taking other opioids.	Preoperative opioid users were discharged with less opioids, required more refills, were more likely to remain on opioids, and required more manipulations under anesthesia than opioid-naïve patients. These risks extended to preoperative tramadol users.
Namba <i>et al</i> [16]	2018	A retrospective cohort study of TKAs in an integrated health-care system was conducted. The number of opioid prescriptions per 90-day period after TKA (up to 1 year), was the outcome of interest. Patient risk factors that were evaluated included demographics, pain prescriptions, comorbidities, and chronic pain conditions. Multivariable Poisson regression models were employed. The median age for 23,726 patients was 67 years. Before surgery, 60.0% used opioids. Three months after surgery, 41.2% of patients continued using opioids. Factors associated with greater opioid use included: younger age, liver disease, preoperative nonsteroidal anti-inflammatory drug use, anxiety, substance abuse, diabetes mellitus, preoperative opioid use, back pain, congestive heart failure, depression, fibromyalgia, hypertension, nonspecific chronic pain, black race, and chronic lung disease.	Several preoperative factors were associated with prolonged opioid use after TKA. Avoidance or weaning of preoperative opioids should be considered.

Authors	Year	Findings	Comments
Kheir <i>et al</i> [17]	2018	A retrospective study of 203 primary unilateral cemented TKAs consecutively performed with or without tourniquet was performed. Identical perioperative pain and blood loss protocols were used in all cases. In tourniquetless TKAs, the tourniquet was not inflated at any time, and sterile CO ₂ gas compression maximized cement interdigitation. After exclusions for scientific confounds, 184 TKAs (93 with tourniquet; 91 tourniquetless) were analyzed. Controlling for multiple covariates, females with a tourniquet reported significantly more pain and opioid consumption the first 24 hours after surgery compared to females without a tourniquet. There were no differences in pain or amount of opioids consumed among males with and without a tourniquet. Tourniquet use resulted in a significant reduction in blood loss for both females and males, although the total blood savings of approximately 200 mL is of unknown clinical significance.	Avoiding tourniquet use during TKA for females may be a relatively risk-free adjunct to minimize opioid consumption during hospitalization.
Ben-Ari <i>et al</i> [10]	2017	These authors performed an analysis of patients who had had TKA within the U.S. Veterans Affairs (VA) system over a 6-year period and had been followed for 1 year postoperatively. The length of time for which an opioid had been prescribed and the morphine equivalent dose were calculated for each patient. Patients for whom opioids had been prescribed for >3 months in the year prior to the TKA were assigned to the long-term opioid group. A natural language processing-based machine-learning classifier was developed to classify revisions due to infectious and non-infectious causes on the basis of the postoperative note. Survival curves for the time to knee revision or manipulation were used to compare the long-term opioid group with the patients who did not take opioids long-term. Hazard and odds ratios for knee revision and manipulation were obtained as well. Of 32,636 patients (94.4% male; mean age 64 years) who underwent TKA, 12,772 (39.1%) were in the long-term opioid group and 734 (2.2%) had a revision within a year after the TKA. Chronic kidney disease, diabetes, and long-term opioid use were associated with revision within 1 year and were also the leading factors associated with a revision at any time after the index TKA. Long-term opioid use had a hazard ratio of 1.19 in the analysis of its relationship with knee revision, but the hazard was not significant in the analysis of its association with knee manipulation. The accuracy of the text classifier was 0.94, with the area under the receiver operating characteristic curve being 0.99. There was no association between long-term use of opioids and the specific cause for knee revision.	
Roche <i>et al</i> [18]	2018	This study assessed the effects of drug abuse in TKA patients. Specifically, these authors identified RTKA: (1) incidence, (2) causes, (3) time to revision, and (4) patient demographics in patients with a history of drug abuse. The Medicare database within the PearlDiver Supercomputer (Warsaw, IN) was queried to identify 2,159,221 TKAs performed between 2005 and 2012. Drug abuse was subdivided into cocaine, cannabis, opioid, SHIA, amphetamine, and alcohol users. Amphetamine users had the fastest mean time to revision (691 days). At 30-, 90-day, and 6-month postoperative, cocaine had the highest proportion of patients requiring RTKA (7, 12, and 20%, respectively), and at 1-year alcohol abusers. Infection was the most common cause of revision in all drug abuse/dependent cohorts. Age distributions varied significantly by group for primary TKA. Comorbidity status was similar in all RTKA patients as determined by comparison of the mean Charlson comorbidity index scores.	Based on these results, drug abuse patients are at increased risk for RTKA. These high-risk patients should be appropriately risk stratified and receive comprehensive postoperative pain management.
Hadlandsmyth <i>et al</i> [4]	2018	This study used a Veterans Health Administration sample of 6653 Veterans who underwent TKA in the fiscal year 2014 that did not require surgical revision during the subsequent year. Sixty percent of the sample had used an opioid in the year prior to surgery, including 20% who were on long-term opioid use at the time of surgery (defined as 90+ days of continuous use) and 40% with any other opioid use in the year prior to surgery. In patients on long-term opioids at the time of surgery, 69% received opioids for at least 6 months and 57% for at least 12 months after TKA. In patients not on long-term opioids at the time of TKA, only 4% received opioids for at least 6 months and 2% for at least 12 months after TKA. Differing risk factors for prolonged opioid use 12 months after TKA were identified in these 2 cohorts (ie, those who were and were not receiving long-term opioids at TKA).	These findings suggest that the greatest risk for prolonged opioid use after TKA is preoperative opioid use.
Gonzalez <i>et al</i> [5]	2018	This study evaluated the risk of opioid-related adverse events (ORAEs) following TKA and RTKA using the 5% Medicare claims (2010-2013) database. There were 41,702 TKA and 3817 RTKA patients who met the inclusion criteria. At 90 days, respiratory complications were the most common complication (TKA: 6.12%; RTKA: 8.01%), followed by postoperative nausea and vomiting (TKA: 2.86%; RTKA: 3.95%), and urinary retention complications (TKA: 2.79%; RTKA: 3.20%). For TKA, risk factors for respiratory complications included older age, lower socioeconomic status, more comorbidities, obesity, chronic obstructive pulmonary disease, white race, and patients in the Midwest and West (vs. South). The average Medicare payment for treating complications within 90 days of a TKA was \$6206 and \$6222 following RTKA.	Awareness risks for ORAEs in select patients can assist in developing a multimodal postoperative pain control and patient education protocols.
Manalo <i>et al</i> [19]	2018	Patient-reported outcome measures (PROMs) collected from patients undergoing TKA were reviewed. These authors identified two matched groups: (1) 30 patients who used opioids preoperatively and (2) 137 patients who did not use opioids preoperatively. The non-opioid group was carefully selected to match the opioid cohort. Statistical analyses were performed to determine the difference in demographics, PROMs, length of stay, disposition and co-morbidities between the two groups. The non-opioid users had significant improvement in both EuroQol5D (EQ-5D) PROMs and visual analogy scale (VAS) scores postoperatively; however, preoperative opioid users did not show improvement in either measure. University of California Los Angeles (UCLA) scores were significantly improved for both non-opioid users and opioid users. Non-opioid users had higher preoperative EQ-5D scores than opioid users. There was no difference in range of motion, length of stay, or disposition between cohorts.	The results demonstrated that TKA patients with preoperative opioid use had significantly lower VAS scores and trends of lower UCLA and EQ-5D scores postoperatively compared to non-opioid patients, suggesting the use of opioid medications prior to TKA negatively affects patient reported outcomes following surgery.

Authors	Year	Findings	Comments
Rodriguez-Merchan <i>et al</i> [20]	2019	This review article showed that local infiltration analgesia (LIA) is a good option for reducing the use of post-operative opioids. Multimodal blood-loss prevention is sometimes advised in combination with opioid-free analgesia.	In most studies, however, no differences were reported or contradictory outcomes existed. Post-operative pain management protocols vary so much that it was difficult to strongly favor a determined pathway.
Waldman <i>et al</i> [21]	2019	This “consensus statement: toward opioid-free arthroplasty: A leadership forum” recommended a checklist for prescribers of opioid analgesia after TKA.	The authors acknowledged that pain management amid the opioid epidemic is a shifting landscape. They offered it with the understanding that determining the best care for each patient requires ethical decision-making – weighing the risks and benefits of various pain-management strategies, including opioids.

In 2016 Goeslin *et al* reported the trends and predictors of opioid use after TKA. They found that many patients taking opioids prior to surgery continue to use opioids after TKA and some opioid-naïve patients remained on opioids; however, persistent opioid use was not associated with change in knee pain^[6]. Aasvang *et al* investigated the effect of > 4 weeks pre-operative opioid use [none vs. low dose [< 30 mg morphine equivalents (eq.)] vs. high dose (> 30 mg morphine eq.)] in patients scheduled for primary, unilateral TKA. They found that pre-operative opioid use augmented the risk for post-operative pain at rest and walk, and increased opioid consumption after TKA^[3].

In 2017 Hansen *et al* reported a retrospective cohort study on the chronic use of opioids before and after TKA. They encountered that there was a reduction in opioid use following TKA. Almost 50% of occasional users and more than 30% of chronic users pre-TKA ceased opioids post-operatively. There was a reduction in use for those chronic users who continued to take opioids post-surgery^[1]. Hernandez *et al* analyzed if patients discharged with greater quantities of opioids following TKA were more likely to request refills. They found that the refill rate did not differ between large prescriptions (≥ 1400 mg) and smaller prescriptions^[7]. Bedard *et al* encountered that about one-third of TKA patients used opioids within 3 months before surgery and this percentage augmented over 9% during the years included in this study. Preoperative opioid use was most predictive of augmented refills of opioids following TKA. However, other patient characteristics (younger age, female sex) were also predictive of prolonged opioid use^[8]. Rozell *et al* observed that younger patients with preoperative history of narcotic use required additional opioids and were at a higher risk for complications and a greater length of stay^[9]. Ben-Ari *et al* reported that pre-operative opioid use was associated with early revision after TKA. Long-term opioid use prior to TKA was associated with augmented risk of knee revision during the first year after TKA among predominantly male patients^[10].

In 2018 Kim *et al* analysed the risk factors associated with patients who were pre-operative chronic opioid users and continued to use 6 months after TKA. They encountered that TKA candidates who have complicated medical, social, and surgical histories were at an augmented risk of chronic opioid abuse post-operatively. Characteristics that were predictive of persistent opioid use included male gender, prior injury or surgery to the ipsilateral knee, current tobacco smoking status, and a history of psychiatric disorder^[2]. Starr *et al* reported that chronic opioid use was a significant predictor of RTKA. Other variables were age, female sex, body mass index, diabetes, chronic kidney disease, and non-chronic opioid^[11]. Namba *et al* studied prolonged opioid use following TKA. They observed that after the

initial 90-day post-operative period, 41.5% continued to use opioids. Also, 0.6% revisions occurred within 1 year and 1.6% within 5 years. Compared to patients not taking any opioids, patients using medium-low to high oral morphine equivalent (OME) after the initial 90-day period had a higher adjusted risk of 1-year revision, ranging from Hazard Ratio (HR) = 2.4 to HR = 33 depending on the OME and time period^[12]. Dwyer *et al* examined post-operative opioid use in TKA patients and described factors associated with the need for refill prescriptions. They observed that patients undergoing TKA who presented with a comorbidity or were being treated for anxiety or depression were more likely to need a refill^[13].

In 2018 Politzer *et al* encountered that the greatest risk factors for chronic postoperative opioid use were preoperative use, younger age, female gender, greater length of stay, and worse health status. Although the use of opioids continued to grow significantly pre-operatively and post-operatively, chronic opioid use post-TKA remained clinically unchanged^[14]. Hernandez *et al* reported that pre-operative opioid use affected opioid prescribing, refills, and results after TKA. They encountered that pre-operative opioid users were discharged with less opioids, needed more refills, were more likely to remain on opioids, and required more manipulations under anaesthesia than opioid-naïve patients. These risks extended to preoperative tramadol users^[15]. Namba *et al* reported patient factors associated with prolonged post-operative opioid use after TKA. Compared to patients not taking any opioids, patients using medium-low to high oral morphine equivalent (OME) after the initial 90-day period had a higher adjusted risk of 1-year revision, ranging from HR = 2.4 to HR = 33 depending on the OME and time period^[16]. Kheir *et al* reported that tourniquetless TKA with modern perioperative protocols decreased pain and opioid consumption in women. They stated that avoiding tourniquet use during TKA for females may be a relatively risk-free adjunct to minimise opioid consumption during hospitalization^[17]. Roche *et al* analysed the incidence of drug abuse in RTKA. The authors stated that drug abuse patients were at augmented risk for RTKA. They observed a significant increase in the number of primary TKAs in cocaine, cannabis, opioid, sedatives/hypnotics/anxiolytics (SHA), amphetamine, and alcohol users. Amphetamine users had the fastest mean time to revision (691 days). At 30-, 90-day, and 6-month postoperative, cocaine had the highest proportion of patients requiring RTKA (7, 12, and 20%, respectively), and at 1-year alcohol abusers (38%). Infection was the most common cause of revision in all drug abuse/dependent cohorts. Age distributions varied significantly by group for primary TKA. Comorbidity status was similar in all RTKA patients as determined by comparison of the mean Charlson comorbidity index scores^[18].

In 2018 Hadlandsmlyth *et al* observed that the greatest risk for prolonged opioid use following TKA was pre-operative opioid use^[4]. Gonzales *et al* reported the risk of opioid-related adverse events after primary TKA and RTKA. At 90 days, respiratory complications were the most common complication (TKA: 6.12%; RTKA: 8.01%), followed by post-operative nausea and vomiting (TKA: 2.86%; RTKA: 3.95%), and urinary retention complications (TKA: 2.79%; RTKA: 3.20%). For TKA, risk factors for respiratory complications included older age, lower socio-economic status, more comorbidities, obesity, chronic obstructive pulmonary disease, white race, and patients in the Midwest and West (vs. South). The average Medicare payment for treating complications within 90 days of a TKA was \$6206 and \$6222 following RTKA^[5]. Manalo *et al* observed that preoperative opioid medication use negatively affected health related quality of life after TKA. TKA patients with preoperative opioid use had significantly lower visual analogy scale (VAS) scores and trends of lower University of California Los Angeles (UCLA) and EuroQol5D (EQ-5D) scores postoperatively compared to non-opioid patients, suggesting the use of opioid medications prior to TKA negatively affects patient reported results after surgery^[19].

Rodriguez-Merchan *et al* have recently published that local infiltration analgesia (LIA) is a good option for reducing the use of post-operative opioids. Multimodal blood-loss prevention was recommended in combination with opioid-free analgesia^[20].

In 2019 Waldman *et al* have reported a consensus statement entitled "toward opioid-free arthroplasty: a leadership forum", recommending a checklist for prescribers of opioid analgesia after TKA, and some important guidelines shown in Table 2^[21].

CONCLUSIONS

It is advisable to avoid or eliminate the use of pre-operative opioids. The greatest risk of prolonged use of opioids after a TKA is the pre-operative use of opioids. Despite the efficacy of existing multimodal postoperative pain protocols, younger patients with a pre-operative history of narcotic use require additional opioids and have a higher risk of complications and higher lengths of stay. At 90 days, the most common complications related to the use of opioids were respiratory (TKA: about 6%, RTKA: 8%), followed by post-operative nausea and vomiting (TKA: around 3%, RTKA: about 4%) and urinary retention (TKA: around 3%; RTKA: about 3%). For TKA, risk factors for respiratory complications included advanced age, lower socio-economic status, more comorbidities, obesity, chronic obstructive pulmonary disease, white race. The average cost of treating complications within the first 90 days was \$ 6206 after a TKA and \$ 6,222 following a RTKA.

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Table 2 Guidelines toward opioid-free total knee arthroplasty (TKA) [21].

Clinicians must identify at-risk patients
Clinicians must establish opioid-responsible prescribing and education
Centres should ensure non-opioid-based comprehensive pain management
Clinicians and centres must address risk stratification and mitigation
Centres should align communications among patients and clinicians
Next steps: Advance understanding of novel analgesics, techniques, and care of the opioid-tolerant patient

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