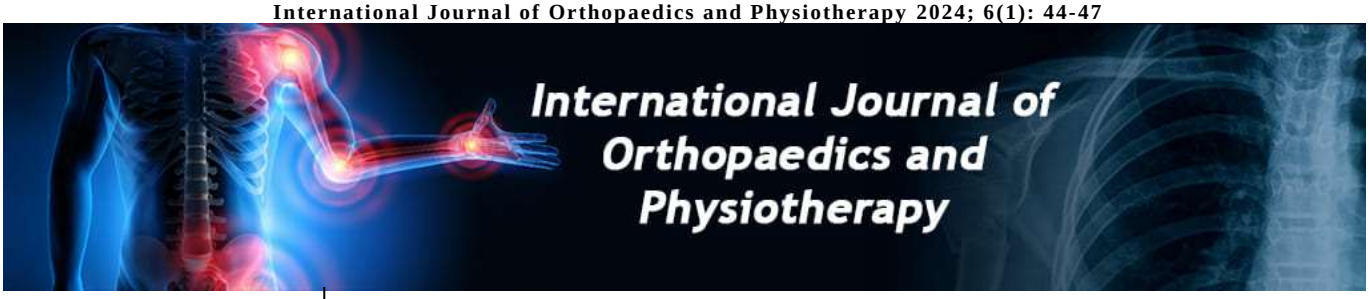

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Opioid use and its impact on long term functional outcomes in total knee arthroplasties

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Abstract
Background: With the current opioid epidemic, it is important for surgeons to be aware of how long-term opioid use affects post-operative outcomes and pain. This study aims to follow the long-term functional outcomes in a cohort of patients undergoing elective total knee arthroplasty (TKA) who were recipients of an established multimodal analgesia (MMA) pathway.
Methods: Patients who had undergone unilateral TKA with a standardized MMA at our health system were identified. A total of 150 patients were contacted via telephone for formal consent prior to acquisition to the following outcomes: Knee Injury and Osteoarthritis Outcome Scores (KOOS), analog pain scores, and opioid consumption. Outcomes were collected at three time points postoperatively: 3, 6, and 12 months.
Results: There was an improvement in KOOS scores and a decrease in persistent opioid use over time. There was not a significant difference in pain scores between opioid and non-opioid users at each of the three time points. There was a statistically significant difference with respect to KOOS scores at 3 and 6 months between opioid and non-opioid users.
Conclusion: Our study demonstrates that patients who underwent TKA with a standardized MMA who also had continued opioid use post-operatively were more likely to have lower functional outcomes compared to non-opioid users.

Keywords: Total joint arthroplasty, total knee arthroplasty, opioids, multimodal analgesia, outcomes

Introduction
Opioid overdose continues to be a public health crisis, accounting for almost 500,000 deaths in the United States since 1999 and 70% of all drug overdose deaths in 2019 alone [1]. A proportion of these opioid related deaths stem from prescription opioids [2]. For many patients, management of post-surgical pain is often their first experience with opioid analgesia, with a subset of patients going on to have persistent opioid use [3]. This has been observed in patients who have undergone orthopaedic surgery [4]. Opioid dependence after total knee arthroplasty has also been previously reported [5]. Aside from the risks associated with developing opioid dependance, long-term opioid use is an indicator for poorer patient outcomes with regards to both post-operative functional scores and pain reduction [6-8]. With the goal of decreasing perioperative opioid consumption and improving recovery, multimodal analgesia (MMA) pathways are becoming commonplace in many surgical disciplines [9-10]. To date, few studies have observed the association of perioperative multimodal analgesia and long-term patient functional outcomes after total knee arthroplasty. In this study, we aimed to follow long-term functional outcomes in a cohort of patients undergoing elective total knee arthroplasty (TKA) who were recipients of an established MMA pathway. Patient outcomes were objectively assessed using KOOS scores and opioid use was noted prior to surgery and followed for up to 12 months.

Materials and Methods
Following IRB approval, patients who had undergone a primary, unilateral TKA with standardized MMA at the University of Virginia Health System (Charlottesville, VA) were identified. Patients were then contacted via telephone for formal consent prior to the acquisition of the following outcomes:

Knee Injury and Osteoarthritis Outcomes Score (mini-KOOS) scores, analog pain scores, and opioid consumption. All outcomes were collected at three time points postoperatively: 3, 6, and 12 months. Fifty patients were surveyed at each of these time points, for a total of 150 patients. Baseline demographics, opioid use and pre-operative mini-KOOS were then obtained from the electronic medical record (EMR). The inclusion criteria for this study included patients who have undergone elective unilateral primary knee arthroplasty, age > 18, and willingness to consent. The exclusion criteria was refusal to participate.

Results

Demographic data is summarized in Table 1. BMIs and age were not significantly different among the time points. On average, female patients included a larger proportions of patient surveyed. There was a demonstrated improvement in KOOS scores (Table 2) and a reduction in persistent opioid use (Table 3) over time. There were not significant differences in analog pain scores (rest and with activity) between opioid and non-opioid users at each of the three time points. There was a statistically significant difference with respect to mini-KOOS Scores at 3 and 6 months between opioid and non-opioid users (Table 4).

Table 1: Patient Demographics (mean and standard deviation)

Cohort	Average Age	BMI	Male (%)
3 month follow-up	67.4 (10.0)	32.8 (5.6)	46
6 month follow-up	68.5 (8.3)	31.7 (5.5)	48
12 month follow-up	68.7 (9.0)	31.5 (5.1)	37.25

Table 2: Pre-op vs. follow-up mini KOOS score (mean and standard deviation shown; t-test for deference

Cohort	Pre-op Mini KOOS	Follow-Up Mini KOOS	Delta	P-value
3 month follow-up	45.4 (12.1)	73.0 (13.1)	27.6	0.0001
6 month follow-up	44.1 (12.1)	78.5 (13.5)	33.9	0.0001
12 month follow up	48.2 (16.5)	81.0 (15.3)	32.8	0.0001

Table 3: KOOS score between opioid and non-opioid users with morphine equivalents

Cohort	Continued Opioid Use	Morphine Equivalents	Opioid Use (%)	Post Op KOOS Scores (Mean, SD)	p-value
3 month follow-up	Y	14.83	18	64.4 (12.8)	0.046
	N	-	82	75 (12.5)	
6 month follow-up	Y	24	6	64.57 (4.3)	0.039
	N	-	94	79 (13.3)	
12 month follow-up	Y	19	6	54.4 (11.0)	0.051
	N	-	94	82.7 (13.9)	

Table 4: Pre-operative opioid use and post-operative KOOS scores

Cohort	Pre-Op Opioid Use	N	Mean KOOS	P Value
3	No	41	74.4	0.055
	Yes	9	66.88	
6	No	43	77.9	0.536
	Yes	7	81.8	
12	No	41	83.7	0.052
	Yes	10	69.9	

Discussion

The objective of the current study was to track long-term functional patient outcomes (mini-KOOS), pain, and opioid consumption trends for patients undergoing unilateral TKA who received a standardized peri-operative multimodal analgesia regimen. The results demonstrated a decrease in opioid use with respect to time from 3 (18%) to 6 (6%) months, with no change in opioid use noted between 6 and 12 months (6%).

Additionally, our results demonstrated a significant increase in functional scores compared to preoperative scores at each of the time points, with an improvement between 3 and 6 months, and a plateau between 6 and 12 months. This was comparable to the results shown by Nilsdotter *et al*., which found improvements in KOOS scores at 6 months and even greater improvements at 12 months [11].

Our data found similar rates of pre-operative opioid use as compared to a large, national database study, which found 24% (17.3%) of patients utilizing opioid pain medications prior to TKA, with 17% (12%) using opioids use at 12 months after TKA [12]. Opioid use prior to TKA has been found to be associated with a greater risk of complications and painful prolonged recoveries [13]. In addition, previous data suggests opioid use prior to TKA is associated with inferior outcomes, particularly subjective pain scores, hospital length of stay, and increased opioid usage in the postoperative period [8, 14]. The deleterious effects of pre-operative opioid use are supported by additional arthroplasty literature [15]. Similarly, our data demonstrates that patients with pre-operative opioid use were noted to have lower overall mini-KOOS scores in each cohort post-operatively, although this did not show statistical significance.

Furthermore, patients with continued opioid use post-operatively were also found to have lower functional outcomes as measured by the mini-KOOS scores with statistically significant differences in the 3 and 6 month cohorts. Persistent opioid use has been found to be associated with inferior postoperative outcomes in the literature. For example, persistent opioid use following TKA after the initial 90-day postoperative period has higher adjusted risk of 1 year revision compared to those patients not taking opioids at that time point [16]. Interestingly, in a

retrospective study by Cancienne *et al*. including over 100,000 patients preoperative opioid use was independently associated with increased risk of emergency room visits, readmission, infection, stiffness, and aseptic revision. Prolonged post-operative use of opioids was found to be associated with significantly higher rates of infections, stiffness, and aseptic revisions [17].

Overall, this data supports that pre/post-op opioid use is associated with poorer patient reported outcomes measures (PROM) as they relate to function following TKA. There are numerous studies looking at the negative impact on quality metrics associated with opioid use, however the results from this study add to the limited body of literature on the PROM with regards to TKA and its relationship with opioid use [18].

Due to the detrimental effects of opioids on outcomes and rehabilitation following orthopaedic procedures, multimodal analgesics in enhanced recovery (ERAS) protocols are used at our institution to reduce the need for opioid analgesics. Targeting a variety of pain pathways with multimodal analgesia facilitates early discharge from the hospital while minimizing the side effects related to opioid use [19]. Preoperatively, spinal anesthesia was administered in 85% of patients compared to general anesthesia. Neuraxial/spinal anesthesia is associated with fewer complications and adverse side effects such as nausea/vomiting, hypotension, urinary retention, respiratory depression compared to general anesthesia [20]. Beyond general or spinal anesthesia, peripheral nerve blocks are also used frequently in TKA. An adductor canal block was administered in 100% of the patients studied. A study by Venditolli *et al*. reported that patients who received a perioperative local anesthetic with morphine compared to morphine alone had significantly lower morphine consumption in the immediate post-operative and significantly less opioid related side effects [21].

This study does have limitations given its retrospective design. Another limitation is that this subset of patients represents a fraction of all patients that have had total knee arthroplasty at our institution. Furthermore, this study is prone both response and nonresponse bias as the data collection was dependent on patients answering the telephone surveys. Historically, a variety of questionnaire have been utilized to measure outcomes after TKA including Lysholm knee scoring scales, which focuses on short-term outcomes, and the WOMAC Osteoarthritis Index, which focused on long-term outcomes. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was developed as an extension of WOMAC Osteoarthritis Index to evaluate both short-term and long-term outcomes, and has been validated for TKA [22]. The mini-KOOS, a subset of the questions of the KOOS, was used for comparing preoperative and postoperative outcomes. Comparing preoperative KOOS to postoperative KOOS was preferable, but complete preoperative KOOS were not available upon chart review.

The data presented demonstrates several important trends and relationships between peri-operative opioid use and quantified functional outcomes surrounding TKA. Future studies can use these data to identify the effect of interventions on long-term functional outcomes with a goal of decreasing post-operative opioid use.

Conclusion

This study highlights the impact of continued opioid use on long-term functional outcomes following total knee arthroplasty (TKA) in patients managed with a standardized multimodal analgesia (MMA) pathway. Our findings demonstrate that despite improvements in Knee Injury and Osteoarthritis Outcome Scores (KOOS) over time, patients who continued to use opioids post-operatively exhibited lower functional outcomes compared to non-opioid users. This underscores the importance of minimizing opioid use in the post-operative period to optimize patient recovery and satisfaction following TKA.

Conflict of Interest

Not available.

Financial Support

Not available.

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