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Review Article

The Role of Preoperative Opioid Use in Foot and Ankle Surgery: A Systematic Review

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ABSTRACT

Prescription opioids, particularly for treating musculoskeletal pain, are a significant contributor to the opioid epidemic in North America. There is also evidence to suggest that chronic use of opioids is associated with poor outcomes after orthopedic surgery. However, whether this association is relevant in foot and ankle surgery is still unclear. Accordingly, a systematic review of the literature was undertaken to assess the impact of preoperative opioid use in patients undergoing foot and ankle surgery concerning postoperative pain, complications, and postoperative opioid dependence. Four databases, including EMBASE, MEDLINE, PubMed, and CINAHL, were searched to March 2022 for studies reporting preoperative opioid use and its effect on postoperative outcomes or opioid use after foot and ankle surgery. A total of 22,092 patients were included in the final synthesis of 8 studies. Most of which were level 3 evidence (5 studies). Around 18% of the patients used opioids preoperatively. Preoperative opioid use was associated with more quantities and prolonged use of opioids postoperatively. Two studies showed an increased risk of complications postoperatively in patients who used opioids preoperatively compared to the nonopioid group. Preoperative opioid use in patients undergoing foot and ankle surgeries is associated with increased and prolonged use of opioids postoperatively and may therefore predict the potential for misuse.

The use of prescription opioid medication worldwide doubled from 2001 to 2013 (1). Unfortunately, opioid misuse has increased as well. The rate of drug overdose deaths involving opioids increased from 1 per 100,000 in 2013 to 6.2 per 100,000 in 2016 in the United States (2). In 2017, the federal government of the United States identified the current opioid crisis as a national health emergency (3).

Orthopedic surgeons play a critical role in the opioid epidemic. Collectively, orthopedic surgeons are responsible for 7.7% of all opioid prescriptions in the United States, more than any other surgical specialty (4). Such prescriptions are thought to be a major contributor to opioid use disorder and opioid-related fatalities (5,6). There has been substantial interest in recent years in reducing the utilization of opioids following orthopedic surgery (7).

The use of opioids preoperatively is increasingly prevalent in orthopedic patients (8). Orthopedic conditions are very painful, and opioids are liberally prescribed for nonoperative and peri-operative management of musculoskeletal pain (9). Orthopedic patients may also have concurrent chronic pain and other medical comorbidities associated with the chronic use of opioids. However, emerging evidence suggests that chronic preoperative opioid use is associated with adverse surgical outcomes and prolonged use of opioids postoperatively (10-12,13). For example, preoperative opioid users demonstrate worse outcome scores and higher rates of revision after total knee arthroplasty compared with opioid-naive patients (14).

Foot and ankle surgeons in particular among the orthopedic subspecialties manage patients with chronic pain disorders, multiple medical comorbidities, and painful orthopedic conditions (15). It is likely that the frequency of patients using opioids preoperatively is higher in foot and ankle surgery when compared with sports medicine, shoulder, or hand surgery (15). It remains unclear to what extent preoperative opioid use predicts revision surgery, readmission, and postoperative opioid

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use after foot and ankle surgery. Some studies show no link between preoperative opioid use and complications following foot and ankle surgery, while others show a positive association (16,17).

The purpose of this systematic review is to assess the data currently available on preoperative opioid usage in patients having foot and ankle surgery, along with its relation to postoperative clinical outcomes, complication rates, and postoperatively opioid use.

Materials and Methods

This systematic review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews (18).

Search Strategy

From the date of inception through March 30, 2022, the EMBASE, MEDLINE, PubMed, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases were searched. The database-specific search technique includes terms for preoperative opioid use and its relation to clinical outcome.

Subject heading terms were used in various combinations to increase the sensitivity of the search process. The reference lists of articles that fulfilled the eligibility criteria were manually reviewed. (Supplementary Material).

Eligibility Criteria

To maximize potentially eligible data, no restrictions were made on publication date or follow-up. The criteria for inclusion were: (1) studies on foot and ankle patients who underwent surgical interventions with perioperative use of opioids; (2) studies that reported at least 1 clinical, functional, or radiological outcome related to the procedures.

The exclusion criteria were: (1) Studies focused on surgery for acute fractures; (2) studies that did not report preoperative opioid use; (3) studies that did not report postoperative opioid use or outcomes; (3) studies that included less than 5 patients; (4) reviews, conference abstracts, and non-English studies.

Study Screening

Study selection was performed by 2 authors using Covidence (Veritas Health Innovation, Melbourne, Australia). The enrolment of studies was performed first by title and abstract, then full-text review. Discrepancies were resolved at each stage by a third senior researcher. The reference lists of included studies were manually screened for additional articles that may have missed the primary search strategy.

Data Collection

Data were extracted by 2 reviewers independently from one another into a predefined data abstraction spreadsheet. Extracted data included basic study characteristics (publication year, country, study design, sample size, diagnosis, period of follow-up), patient demographics (age, sex, co-morbid conditions), preoperative opioid use, outcome measures (pain, opioid use, satisfaction), and complications (infection, revision, nonunion). Whenever possible, opioid use was summarized as oral morphine equivalents (OME) and duration of use in months.

Risk of Bias and Quality Assessment

The Methodological Index for Non-Randomized Studies (MINORS) was used by 2 independent reviewers to assess risk of bias in the included studies (19). The MINORS scale assigns a score of 0, 1, or 2 for a list of 8 and 12 questions in noncomparative and comparative studies, respectively. A MINORS score of 16 and 24 represents the lowest risk of bias in noncomparative and comparative studies respectively (19).

Statistical Analysis

Descriptive statistics were calculated to reflect the frequency and percentage of abstracted study data. Using Cohen's Kappa (k) (20), inter-reviewer agreement at each stage of the screening process was calculated with a k value of 0.81 to 1.0 for near perfect agreement, 0.61 to 0.80 for substantial agreement, 0.41 to 0.60 for moderate agreement, and 0.21 to 0.40 as fair agreement (21). Using intraclass correlation coefficient (ICC), interobserver agreement for methodologic quality assessment was considered adequate if ICC of a value of $\geq$0.65 (22).

Results

Study Characteristics

Of the 276 studies retrieved using our search strategy, 26 underwent full-text review. Of these, eight studies fulfilled all inclusion criteria and were included in the subsequent qualitative analysis (Fig.) (16,17,23-27,28). Both title and abstract (k = 0.68) screening and full-text review (k = 0.64) demonstrated substantial agreement between assessors. Quality assessment scores using the MINORS criteria showed adequate agreement between assessors (ICC, 0.88). The mean MINORS score for included comparative studies was 13 $\pm$ 1.1.

The included studies were published between 2016 and 2021. Of the included studies, 2 (25%) presented Level 2 evidence (n = 352) and 6 (75%) presented Level 3 evidence (n = 21,883). Two studies analyzed an identical patient cohort but assessed discrete outcomes (16,17). Most studies (75%) were conducted in the United States.

In total, 22,235 patients were included. The median sample size was 188 patients. Six studies reported the ages of participants, with a mean age of 53.3 years. Of the included patients, 16.8% were male. The majority of patients underwent hallux valgus correction (20,770), total ankle arthroplasty (564), or ankle arthrodesis (49). Other procedures included Achilles tendon repair, ankle arthroscopy, bunion surgery, and pes deformity correction. One study included patients undergoing ORIF for acute fracture among other foot & ankle operations, though the precise number of patients with this diagnosis was not reported. Four studies did not report precise numbers of patients undergoing each procedure (n = 604). The follow-up period was reported in 7 studies, ranging from 2 weeks to 3.9 years. A detailed breakdown of study characteristics is presented in Table 1.

Opioid Use

Of the 22,235 patients included in analysis, 3873 (17%) were classified as preoperative users of opioids (Table 2). The precise opioid agents were not identified. Three studies quantified preoperative opioid exposure by conversion to oral morphine equivalents (OME). One study further stratified opioid users by daily and occasional use. One study differentiated patients using opioids in the 6 months prior to surgery from patients using opioids in the 12 months prior to surgery.

Six studies reported on postoperative opioid use. Two studies demonstrated that preoperative opioid users consumed greater quantities of opioids postoperatively, and 4 studies demonstrated in these patients an increased risk for prolonged postoperative use of opioids.

For example, DeMik et al (n = 544) found that 12 months following total ankle arthroplasty, 30.5% of patients with preoperative opioid use continued to take opioids, compared with only 6.9% of patients who were opioid naïve prior to surgery (OR 9.20, 95% confidence interval (CI), 4.98-17.72) (24). Bhashyam et al (n = 303) found that patients who used opioids in the 6 months preceding surgery consumed a greater quantity of prescribed postoperative opioid medication compared with patients who were opioid naïve prior to surgery (mean 25.7 5 mg oxycodone pills, SD 20.7, vs 17.3 (19.7), p = .014) (23). One study did not find prior chronic opioid use to be a risk factor for postoperative opioid use; however, only 16 patients with preoperative opioid use were included (26).

Comorbid Conditions

Two studies reported comorbidities stratified by the presence of preoperative opioid use. In these studies, a greater proportion of patients using opioids preoperatively were obese, used tobacco and alcohol, and had diabetes, hyperlipidemia, hypertension, peripheral vascular disease, congestive heart failure, coronary artery disease, chronic kidney, lung, or liver disease, thyroid disease, depression,

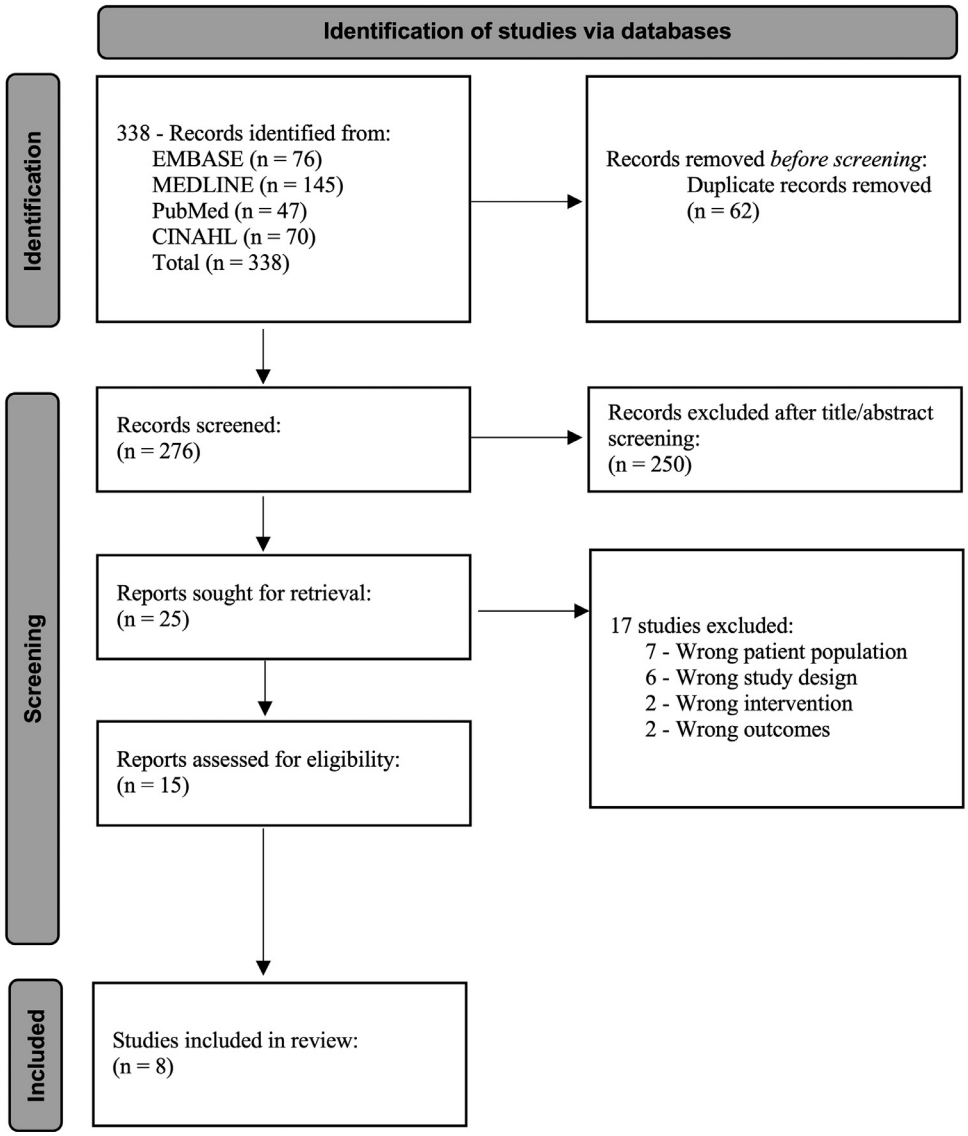

Fig. Prisma flow diagram.

migraine disorder, lumbago, and fibromyalgia. Variance and tests of significance were not reported.

Pain Reporting

Two studies reported on postoperative pain using a numeric rating scale or visual analog scale (Table 3). Both found that preoperative opioid use was associated with higher postoperative pain. Guichard et al found that preoperative opioid consumption was associated with a high acute pain trajectory (50% vs 19%, p = .04), defined as a pain intensity rating greater than 2/10 on at least 8 of 10 days postsurgery (25). Mulligan et al found an association with pain beyond 1 year after surgery (29). Other functional outcomes such as patient satisfaction, AOFAS score, range of motion, time to recovery, were not reported in any included study (27). Radiographic outcomes were likewise not reported.

Complications and Revision Surgery

Granadillo et al found that preoperative opioid use was associated with re-admission within 30 days of surgery (OR 1.59) but was not associated with emergency department visits during the same period, nor with infection within 6 months (Table 3) (16).

Mulligan et al found that preoperative opioid consumption was associated with overall rate of complications, including nonunion, infection, reoperation, and wound complications, with an OR 2.63 (95% CI, 1.21-5.75) in a multivariate analysis (17).

Only 2 studies explored the relationship between preoperative opioid use and reoperation, with 1 study finding an increased risk (OR 1.29) and 1 study finding no association.

Discussion

This review of the current literature suggests increased and prolonged use of opioids in patients undergoing foot and ankle surgery who reported using opioids preoperatively. In addition, the current literature suggests that preoperative use of opioids may be associated with higher postoperative pain, complications, and readmission to the hospital.

Perioperative opioid use for orthopedic conditions has been proposed to be a driver of the ongoing opioid crisis in North America (30).

Table 1
Study characteristics

Author	Year	Design	Level of evidence	Country	MINORS score	Age, mean (sd)	Sample size	Sex (female %)	BMI	Diagnosis	Operative procedure	Follow-up period
Bhashyam et al	2019	prospective cohort study	2	United States	13	50.5	303	64%	NR	NR	Bony procedures 142 (47%), nonbony procedures 157 (52%), not recorded 4 (1%)	6 wk
DeMik et al	2020	Retrospective cohort	3	United States	10	NR	544	51.80%	NR	NR	Total ankle arthroplasty	12 mo
Granadillo et al	2021	Retrospective cohort	3	United States	11	NR	20749	85%	NR	Hallux valgus	Hallux valgus correction	NR
Guichard et al	2019	prospective cohort study	2	France	14	60.2 ±13.2	49	51%	27.5	Osteoarthritis	Total ankle arthroplasty 20 (41%), ankle arthrodesis 29 (59%)	18-24 mo
Kvarda et al	2019	Retrospective cohort	3	United States	9 (noncomparative)	50 ±16.3	535 (244 included in analysis)	69%	29	NR	Minor procedures 18 (7%), Moderate soft tissue procedures 48 (20%), Moderate bony procedures 161 (66%), Major procedures 17 (7%)	2 wk
Mulligan et al	2016	Retrospective cohort	3	United States	15	55	139	54%	29.9	posttraumatic 61 (44%), degenerative 52 (37%), neurogenic 6 (4%), inflammatory 10 (7%), other 10 (7%)	Total ankle arthroplasty, ankle arthrodesis, hindfoot arthrodesis	2.7 y
Mulligan et al	2018	Retrospective cohort	3	United States	15	55.3	139	53%	30	posttraumatic 61 (44%), degenerative 52 (37%), neurogenic 6 (4%), inflammatory 10 (7%), other 10 (7%)	Total ankle arthroplasty, ankle arthrodesis, hindfoot arthrodesis	1.5 y
Verier et al	2021	prospective cohort study	3	Canada	10 (noncomparative)	63 ±10	116 (82 included in analysis)	56%	34.4	NR	Total ankle arthroplasty, ankle arthrodesis, hindfoot arthrodesis, pes planovalgus and cavovarus correction	6 mo

Legend: Minor procedures - ankle arthroscopy, excision of soft tissue lesion, wound debridement, single hammertoes correction. Moderate soft tissue procedures - gastrocnemius resection, achilles tendon repair, tendon transfer, posterior leg compartment decompression, other ligament reconstruction. Moderate pony procedures - hallux valgus correction, toe amputation, hardware removal, hammertoes correction in combination or multiple, corrective osteotomies, one bone ORIF, bimalleolar ORIF, exostectomy. Major procedures - TAA, ankle arthrodesis, trimalleolar or other complex fracture.

Table 2
Opioid use

Author	Year	Preoperative opioid use, n (%)	Opioid type	Opioid dose, OME	Postoperative opioid use
Bhashyam et al	2019	51 (17) with use in preceding 6 mo; 15 (5) with use in preceding year	NR	NR	Patients with preoperative opioid use had higher postoperative opioid consumption (p = .019). Number of 5 mg oxycodone pills used after surgery for patients who used opioids in last year (18.9, sd 16.64), in the last 6 mo (25.9, sd 20.7), and the opioid naïve (17.3, sd 19.71) differed. Percentage of prescribed pills consumed differed for patients using opioids in the last year (51.8%), in the last 6 mo (66.2%), and the opioid naïve (43.0%).
DeMik et al	2020	180 (33.1)	hydrocodone, oxycodone, hydromorphone, codeine, morphine, fentanyl, oxymorphone, methadone	NR	Preoperative opioid use was associated with continued opioid use 12 mo after surgery (OR 9.20, 95% CI 4.98-17.72)
Granadillo et al	2021	3464 (16.7)	oxycodone, oxycontin, hydrocodone, hydromorphone, morphine, fentanyl, oxymorphone, propoxyphene	NR	4339 (20.9%) of all patients had prolonged postoperative opioid use, (new prescription for opioids filled between 3 and 6 mo postoperatively). Preoperative opioid use was associated with increased risk for prolonged postoperative use (OR 8.02).
Guichard et al	2019	14 (28.6)	NR	25 mg daily	NR
Kvarda et al	2019	16 (6.5)	NR	NR	Prior chronic use of opioids was not found to be a risk factor for postoperative opioid use.
Mulligan et al	2016	50 (36)	NR	554 mg over 3 mo	Patients with preoperative opioid use were more likely to have continued use of opioids past postoperative day 90 (38 (76%), OR 7.67, 95% CI, 2.36-24.91) These patients also consumed >6X the quantity of postoperative opioids as opioid naïve patients (3769 mg vs 602 mg, $p < .01$)
Mulligan et al	2018	50 (36)	NR	NR	NR
Verier et al	2021	20 (24) with daily use; 13 (16) with occasional use	NR	<3 mg daily: 13 3-10 mg daily: 4 10-15 mg daily: 6 15-30 mg daily: 4 >30 mg daily: 6	Occasional (OR 16.6, 98.3% CI, 0.9-2379.8) and regular (OR 15.2, 98.3% CI, 1.1-1448.8) preoperative opioid users were more likely to use opioids at 6 mo postoperatively.

Given the enormous impact of opioid misuse worldwide and the association between opioid use and negative surgical outcomes, there is substantial interest in reducing the use of opioids in the orthopedic perioperative setting (30,31). Additionally, the preoperative use of opioids has been shown to increase the risk of poor surgical outcomes in arthroplasty, spine, and shoulder surgery (10,12). Menedez et al retrospectively analyzed 15901 opioid-dependent patients undergoing various arthroplasties or spinal fusions, compared to over 9 million controls (32). They noted that preoperative opioid dependence was associated with increased morbidity (OR 2.3, 95% CI, 2.2-2.4), mortality (OR 3.7, 95% CI, 2.7-5.1), increased hospital length of stay (OR 2.5, 95% CI, 2.4-2.5), and discharge to rehabilitation facilities (OR 2.2, 95% CI, 2.2-2.3). These relationships were evident even after adjusting for demographic, comorbidity, hospital, and operative variables. As well, a prospective series of 802 patients undergoing primary total hip arthroplasty (THA) and total knee arthroplasty (TKA) found that preoperative opioid users were more likely to require intravenous narcotics during their postoperative stay than opioid naïve patients (OR, 2.74; 95% CI, 2.01-3.75) (33). There have recently been calls to wean patients from chronic opioids prior to surgical intervention, both to reduce the risks of surgical complications as well as to minimize postoperative opioid misuse (31).

We found agreement amongst the studies included in this review that the use of opioids prior to foot and ankle surgery predicts continued opioid use after surgery and higher postoperative pain. The underlying mechanism is unclear. Likely, opioid use preoperatively produces both opioid tolerance and hyperalgesia which produce an increased reliance on opioids postoperatively (34). It is also possible that this relationship is confounded by the presence of chronic pain, psychiatric conditions, or other underlying patient characteristics. A large database study of 20,749 patients undergoing hallux valgus correction found that preoperative tobacco use, obesity, depression, back pain, and fibromyalgia were risk factors for prolonged postoperative opioid use (16). Most studies in this review attempted to control for confounding variables through the use of multivariate analysis. Nevertheless, the numbers of included patients were low, and more robust models with larger sample sizes would allow a clearer delineation of meaningful associations.

Our review found 2 studies reporting on complications after foot and ankle surgery. Both reported that preoperative opioid use was associated with readmission to the hospital, deep infection, nonunion, and overall complication rate (16,17). This is consistent with prior literature on patients undergoing spinal surgery demonstrating increased surgical site infection (OR 2.5, 95% CI, 2.0-3.0), prolonged length of stay (OR 2.5, 95% CI, 2.4-2.5), and aggregate morbidity (OR 2.3, 95% CI, 2.2-2.4) in preoperative opioid users (32).

We did not identify any studies evaluating the association between preoperative opioid use and functional foot and ankle outcome measures. However, this has been observed in other areas of orthopedic surgery. Evidence from patients undergoing hip and knee replacements supports a clinically and statistically significant association between preoperative opioid use and reduced hip and knee scores and range of motion postoperatively (35). Similarly, in a retrospective cohort of 253 patients undergoing anterior cruciate ligament reconstruction, patients with preoperative opioids demonstrated inferior patient-reported scores across all outcome measures, including International Knee

Table 3
Postoperative outcomes

Author	Year	Pain	Complications	Conclusions
Bhashyam et al	2019	NR	NR	Recent preoperative opioid use is an independent risk factor for increased postoperative opioid consumption.
DeMik et al	2020	NR	NR	Preoperative opioid use was strongly associated with prolonged postoperative opioid use after controlling for other known risk factors.
Granadillo et al	2021	NR	Preoperative opioid use was associated with admission to hospital within 30 d (OR 1.59 95% CI, 1.20-2.21 $p = .001$). Preoperative opioid use in general was not associated with ED visits within 30 d (OR 1.16 95% CI, 0.97-1.38, $p = .104$), although 3 narcotic prescriptions (OR 1.28 95% CI, 1.03-1.59, $p = .015$) and ≥4 prescriptions (OR 1.78 95% CI, 1.32-2.39, $p < .0001$) were. Preoperative opioid use was not found to be associated with infection within 6 mo.	Preoperative opioid use is a significant, dose-dependent risk factor for prolonged postoperative opioid use.
Guichard et al	2019	Preoperative opioid use was associated with a high acute pain trajectory (57% vs 24%, $p = .04$, but not with chronic pain.	NR	Preoperative pain and psychological distress are predictive factors of acute and persistent postoperative pain after ankle surgery.
Kvarda et al	2019	NR	NR	BMI, procedure type, and higher initial pill dispensation, but not chronic preoperative opioid use, correlated with a larger number of consumed pills during the postoperative period.
Mulligan et al	2016	Preoperative opioid use was associated with pain beyond 1 y postoperative (VAS 3 vs 2)	NR	Opioid use within 3 mo prior to surgery increases the risk for pain and extended opioid use after major ankle and hindfoot reconstruction
Mulligan et al	2018	NR	41 (28%) complications were identified, 9 of which considered major. Patients with opioid consumption before surgery more likely to have a complication (40%, OR 2.63 95%CI, 1.21-5.75)	Patients who consumed alcohol or had been prescribed any amount of narcotic within 3 mo preoperatively were at increased risk for complications. Surgeons should be aware of these factors and counsel patients before surgery.
Verier et al	2021	NR	NR	Regular preoperative opioid use is associated with persistent postsurgical opioid use

Documentation Committee and Knee Injury and Osteoarthritis Outcome Score (36).

There are several limitations in this review. First, the indications for preoperative opioid use were not mentioned in the included studies. It is therefore difficult to determine whether confounding variables, such as chronic pain, are present or adequately addressed. Similarly, there is a lack of Level 1 evidence in this review, and thus known and unknown confounders of postoperative outcomes may have been imbalanced between groups. Thus, a causal relationship could not be determined. Given the inclusion of noncomparative studies, and the lack of a clear and consistent comparative group, meta-analysis of the included studies was not possible. Second, our conclusions were limited by availability of published data. Only a few of the included studies included data on comorbidities, functional outcomes, or complications. These data, which would have been useful for the foot and ankle surgeon in counseling their patients on preoperative opioid use, were not included in our analyses. The inclusion of patients with acute fractures in some included studies may confound the interpretation of the effect of opioid use on elective surgical outcomes. Third, imprecise terminology in the included studies complicates a robust analysis. For example, the frequently-used term “opioid naïve” can alternately refer to patients who have never been exposed to opioids, or to patients who have been free from prescribed opioids for a particular period of time (e.g., 6 months before surgery). Patients who have profound prior opioid use may nevertheless be classified as opioid-naïve if the latter definition is used, though their prior history of opioid use may substantially influence perioperative outcomes. Finally, the risk of bias in the included studies was high, reflected by a mean MINORS score of 13 out of possible 24 for noncomparative studies. This must be taken into consideration when interpreting results.

Further research is required to better understand the influence that preoperative opioids have on postoperative outcomes in foot and ankle surgery, especially with respect to functional scores and patient-related outcome measures. Despite these limitations, our findings are consistent with those reported in other orthopedic studies (10-12,13,33,35,36). The studies included in this review have identified that preoperative opioid use increases the risk for postoperative complications, pain, and greater ongoing opioid use. These data are likely to guide clinical and surgical decision-making when planning orthopedic patient care protocols.

In conclusion, our review found that the current literature suggests an association between preoperative opioid use and increased and prolonged postoperative opioid consumption in patients undergoing foot and ankle surgery. The association of preoperative opioids with inferior clinical outcomes warrants further study.

IRB Approval

This review did not require Institutional Review Board (IRB) approval as the data reviewed are public.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1053/j.jfas.2023.10.003.

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