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The Management of Acute Pain for Musculoskeletal Conditions: The Challenges of Opioids and Opportunities for the Future

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Overview of the Opioid Epidemic

Opioids are commonly used for acute pain. Nonetheless, their associated risks have resulted in substantial increases in morbidity and mortality. The United States (US) specifically has experienced a steep increase in the rates and quantities of opioids prescribed in recent decades, with a peak in 2010.[1,2] Although prescribing is declining, the amount of opioids prescribed in 2015 in the US remained fourfold higher than in Europe at the time, and three times as high as they were in the US just fifteen years prior.[2] Additionally, recent evidence suggests that declines in opioid prescribing are uneven, and have remained high in surgical and procedural care.[3] Importantly, the rise in prescribing has paralleled a sharp rise in opioid-related overdoses, and despite prescribing decreases in recent years, the rate of opioidrelated deaths has continued to rise.[2]

Orthopaedic procedures are often associated with substantial perioperative pain, which can adversely affect recovery by increasing the risk of complications, length of stay, recovery time and cost.[4] For example, fear of acute postoperative pain has been cited as a main reason that patients delay arthroplasty surgery.[5] In addition, orthopaedic surgeons are the third most frequent prescribers of opioids among physicians in the United States, accounting for 7.7% of all opioid prescriptions nationwide.[6] In this review, we will highlight current evidence regarding opioid prescribing and use among patients undergoing orthopaedic surgical procedures, and opportunities for future strategies that allow for effective pain management, balanced with the risks and benefits of opioid analgesics.

Pain and Musculoskeletal Conditions

A widely accepted characterization of pain, first published in 1994 by the International Association for the Study of Pain (IASP), defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in

terms of such damage.[7] The differentiation of acute from chronic pain is primarily based on timing, with the understanding that the duration of acute pain reflects the mechanism and severity of the underlying inciting events; definitions consider acute pain as brief as 7 days, or as long as 3 months, according to the IASP.[8,9] Acute postoperative pain is expected to subside with the healing of tissue, typically within three months after the procedure.[10] Notably, acute and chronic pain often coexist, and the indication for surgery can be chronic pain, as in the example of symptomatic degenerative osteoarthritis. In addition, the presentation of both acute and chronic pain may be influenced by patient-level factors, such as prior opioid exposure or the presence of comorbid physical and mental health conditions. Broadly, musculoskeletal pain can be categorized in several ways, which can inform pain management strategies.

Degenerative joint pain related to osteoarthritis is one of the most prevalent conditions nationwide, with a clinical diagnosis of osteoarthritis occurring in greater than 12% of the US population, an estimated 27 million people.[11] Additionally, primary total hip arthroplasties (THA) and total knee arthroplasties (TKA) are among the most common surgical procedures performed in the United States, and are expected to continue to increase, given the aging population.[12] Spine-related pain encompasses neck and back pain, ranging from chronic, which often presents in the form of degenerative disease, to acute, which can present with or without radiculopathy. Low back pain specifically is the second most common symptom-related reason for physician visits in the United States, and although opioids are commonly prescribed, they may not be efficacious for chronic pain relief.[13,14] In one study, almost a fifth of initial back pain presentations to primary care providers, were found to result in a filled opioid prescription.[15] As such, it is not surprising that preoperative opioid use in this population is common, reported in 65% of patients presenting for orthopaedic spinal procedures, and 33% of patients presenting for joint arthroplasty.[16,17]

In addition to degenerative joint disease, musculoskeletal pain is also commonly related to trauma, and often managed with opioids. Trauma resulting in musculoskeletal injury and pain can present in a diverse patient population, encompassing accidents in younger age groups as well as falls in the elderly. For example, among patients prescribed an opioid in emergency care settings, the three most common pain-related diagnoses were: non-fracture injuries (29%), back pain (10.5%), fractures (9.5%).[18] In contrast to elective settings, such as primary care or elective surgical procedures, patients with traumatic injuries may have a greater risk of uncoordinated care. Emergency setting allows the time to evaluate an initial response to treatment, potentially permitting the time for a first line trial of nonopioid alternatives. However, longitudinal follow-up is difficult, limiting the ability of providers to titrate prescriptions to the patients' needs once discharged and ensuring coordinated hand-offs to other providers may be difficult. Therefore, it may be challenging to tailor prescribing, and prescribers may default to standard prescription sizes for each patient. Without prescribing guidelines based on normative data on patient use, opioid prescribing is often high and excessive, and tailoring prescribing to patient-specific factors such as pain response or risk of persistent use is difficult.[19]

Musculoskeletal pain is also common in children, particularly related to sports and traumatic injuries. Sport injuries occurring in young patients are often acute primary injuries,

including sprains, strains, ligament tears, and fractures. Treatment poses unique challenges for pediatric patients. In addition to the etiology of presenting pain, the developmental level of the child, and the child's previous experiences with pain, should inform management strategies.[20] Adolescents prescribed opioids after surgery are particularly vulnerable to subsequent misuse and substance use disorder.[21] Additionally, adolescents may have prior nonmedical prescription opioid use, often obtained from unused prescriptions, which substantially increases the risk of substance use disorder symptoms in exposed individuals later in life.[22]

Opportunities for Improvement

Acute postoperative pain, and its management, should be distinguished from the pain of acute musculoskeletal pain conditions that are sport or trauma related. For patients undergoing elective surgery, there is an opportunity for education regarding postoperative recovery, along with the likelihood and extent of postoperative pain. These factors provide an element of predictability to the postoperative course, as well as allow expectation setting with patients. Nonetheless, there are important opportunities for improvement in opioid prescribing after surgery, including minimizing unwarranted variation, adverse events, and prolonged use.

Variation in prescribing—While opioids provide effective and accessible analgesia postoperatively, prescribing patterns vary widely across procedures and prescribers, and are often in excess.[2,23,24] For example, among patients undergoing total joint arthroplasty, the median number of unused pills was 32 after total knee arthroplasty and 50 after total hip arthroplasty.[25] Similarly, a recent study on shoulder reconstruction procedures showed an excess of 20 pills on average[26]. In another report, 1month after a spine surgical procedure, 73% of patients reported having unused opioid pills, with most patients receiving no instructions on how to store them or dispose of them[27]. Among a cohort of patients undergoing a hand surgical procedure, almost one-half of all prescribed opioids were reported as unused[28]. Overprescribing may result in patients continuing opioid use or excess pills that can become diverted to others, posing a substantial risk to patients and communities[29].

Prescribing guidelines have emerged from single institutions with subsequent declines in the size of opioid prescriptions, the number of refills, and the overall dosage[30], as well as a decrease in the total number of prescribed pills and postoperative patient telephone encounters[31]. For example, at the Mayo Clinic, patient utilization data, along with predictors of opioid consumption, successfully informed the development of guidelines for postoperative prescribing[32]. The Rothman Institute at Thomas Jefferson University similarly showed that, by following anatomical and procedure-specific opioid prescribing guidelines, opioid prescribing could be reduced with retained patient satisfaction and low refill rates[33]. The successful implementation of these guidelines supports the growing evidence that opioid prescribing following orthopaedic procedures can typically be reduced without compromising pain control[34,35].

The American Academy of Orthopaedic Surgeons (AAOS) published *Surgical Management of Osteoarthritis of the Knee: Evidence-Based Clinical Practice Guideline* in 2015, which has since been endorsed by the American Association of Hip and Knee Surgeons, as well as several other professional societies. This guideline makes strong recommendations for inpatient use of alternative pain management techniques such as local anesthetics, nerve blockades, and neuraxial anesthesia to decrease opioid use when performing orthopaedic procedures[36]. A 2015 statement by the AAOS also supported the standardization of opioid prescribing protocols in all settings in order to control and limit opioid prescriptions, with several recommendations for providers for individual practice[37]. The Orthopaedic Trauma Association published the *Clinical Practice Guidelines for Pain Management in Acute Musculoskeletal Injury* and reinforced that the opioids prescribed for acute pain should be the lowest effective dose for the shortest period possible, in an immediate release formulation.[38]

Opioid-related Adverse Drug Events—Adverse drug events are common, occurring among >10% of opioid-exposed patients undergoing procedures. These patients had significantly prolonged hospital stays, as well as higher readmission rates, costs of care, and mortality[39–41]. A history of substance use disorder and prior opioid use were independently associated with adverse drug events. Moreover, risk may exist whenever an opioid is prescribed, regardless of the amount[39,42]. Opioid-related adverse drug events among patients undergoing joint arthroplasty are as high as 8.5% and are an independent risk factor for both increased length of stay and discharge to an extended care facility[43].

Prolonged Opioid Use—Prolonged opioid use among patients after surgical procedures has drawn scrutiny to the prescribing patterns, procedures, and patient characteristics that may contribute to it[44–47]. The definitions for prolonged opioid use vary, but all include an individual who was opioid-naive prior to the surgical procedure and continues to fill opioid prescriptions for an extended time after postoperative pain would be expected to have resolved[47–50]. Patients who are opioid-exposed, because of either ongoing opioid therapy or a history of opioid use disorder, may experience greater risk due to challenges of coordinating care and medication regimens. New, persistent opioid use is common following orthopaedic operations, such as total hip arthroplasty and total knee arthroplasty[48]. Persistent postoperative opioid use may also reflect the need to alleviate other nonoperative pain or symptoms, such as disordered sleep or affective distress[51].

Sports-related injuries comprise 6% of surgical procedures[52], and persistent opioid use has been observed after anterior cruciate ligament (ACL) reconstruction[53], rotator cuff repair[54], ankle sprains[55], and ankle fractures[56]. Notably, these are also common among adolescents, who are at particular risk[57]. One effective strategy for reducing opioid consumption following rotator cuff repair was a preoperative education intervention that resulted in an earlier cessation of opioid analgesia and decreased the number of opioid pills consumed[58]. Institutional policies could encourage the implementation of similar simple interventions, especially among pediatric and sports injury populations with high proportions of opioid-naive patients.

Despite provider-level factors, patient risk factors also contribute. Mental health conditions, overall body and surgical site pain, medical comorbidities, and tobacco or substance use are correlated with persistent opioid use following surgical procedures[59,60]. With regard to musculoskeletal conditions such as osteoarthritis, in which the indication for a surgical procedure is preoperative chronic pain, risk factors become more varied. Notably, chronic opioid use is common among patients undergoing arthroplasty, and preoperative opioid use has been identified as an independent risk factor for persistent opioid use after surgical procedures[51,61]. Characteristics including female sex, younger age, higher body mass index, preoperative anxiety, depressive symptoms, body pain, and functional impairment have been associated with persistent opioid use among patients undergoing joint arthroplasty[51,62,63].

Opioid Alternatives

Several alternative analgesic interventions should be considered in the management of acute musculoskeletal pain. Nonopioid analgesic options have been shown to reduce pain intensity and overall opioid requirements[64]. Multimodal pain management is an approach that has been proven to decrease complications and improve patient outcomes, as well as increase patient satisfaction after both hip and knee arthroplasty, and we believe that it should be implemented more broadly[4].

Anti-inflammatories—Nonsteroidal anti-inflammatory drug (NSAID) use has been under debate since early observations that they may delay osseous healing, in both animal[65] and human studies[66]. Although more recent studies have indicated that short-term NSAID use is not harmful for fracture-healing and may provide equivalent relief to opioids among patients with osteoarthritis and those undergoing arthroplasty, the use of NSAIDs remains controversial and further research is needed to define the extent of, and the mechanisms that underlie, their impact on osseous healing[67–69]. To minimize bleeding complications, it has been recommended for patients to discontinue NSAID use 7 days prior to elective arthroplasties[70]. Notably, for perioperative pain control, over-the-counter doses of commonly used NSAIDs are not sufficiently anti-inflammatory. For these drugs to optimally reduce postoperative pain, which has a strong inflammatory component, higher doses at the prescription dosage size are necessary (e.g., 2,400 to 3,000 mg of ibuprofen per day or 500 to 750 mg of naproxen daily). Clinicians should also be cognizant of the different half-lives of these drugs. NSAIDs with a duration of action of >8 hours (e.g., naproxen, celecoxib) are generally better to use for acute pain because a nighttime dose will still be effective the following morning, theoretically leading to less sleep impairment from pain, as well as less pain upon awakening.

Acetaminophen—In the inpatient setting, intravenous acetaminophen has helpedto reduce the patient length of stay, opioid-related adverse drug events, patient-reported pain scores, the need for rescue opioids, and overall opioid requirements[71,72]. In the outpatient setting, acetaminophen is often prescribed in combination with an opioid, but is underutilized as a standalone treatment for pain, as it is considered a weak analgesic. In the treatment of chronic low back pain and osteoarthritis, opioids were not more effective than either acetaminophen or NSAIDs individually[73]. Among patients undergoing total hip arthroplasty, acetaminophen in combination with ibuprofen reduced morphine consumption in the acute

postoperative period[74]. In this context, acetaminophen has a role in a multimodal pain management model.

Gabapentinoids—Gabapentinoids are known to be effective analgesic agents for immediate postoperative pain relief and may have utility as a component of a longer-term multimodal pain management strategy. Usage in the perioperative period reduces acute pain and has been found to promote opioid cessation after surgical procedures[49,75,76], along with decreasing the use of additional postoperative analgesic agents[77]. With regard to chronic postoperative pain, the data on the effect of gabapentinoids are mixed; however, the majority of studies have suggested that gabapentinoids may substantially reduce chronic pain[78]. Across studies, adverse effects were consistent with known neuromodulator side effects, including dizziness and visual disturbances. In summary, the routine use of perioperative gabapentinoids may be warranted. Optimal dosing in the context of specific orthopaedic operations should be a focus of further research to decrease prolonged opioid use.

Integrative Pain management

Nonpharmaceutical options are also an important component of effective and safe pain management. Enhanced Recovery After Surgery (ERAS) or prehabilitation pathways constitute an evidence-based, multidisciplinary approach to perioperative care - and represent an opportunity for opioid reduction.[79] These programs center on preoperative physical, medical, and social optimization of modifiable risk factors. The preoperative nature of the pathway increases patient engagement and allows for the individualization of perioperative pain management strategies, including intraoperative opioid-sparing techniques and opioid alternatives for pain management. The implementation of ERAS pathways among patients with osteoarthritis undergoing total knee arthroplasty and total hip arthroplasty resulted in lower complication rates, high patient satisfaction, and a decreased number of patients requiring opioids beyond their 1-week prescription[80]. Beyond promoting judicious prescribing, ERAS pathways may present an opportunity to identify patients currently using opioids to promote safer transitions of care to other physicians[81].

The Management of Opioid Exposed Patients During Surgical Care

Nearly one-third of surgical osteoarthritis patients have previously used prescription opioids[16]. With high numbers of opioid-exposed patients presenting for a surgical procedure, it is important to have appropriate protocols and recommendations for assessing patient risk and managing pain. Pain management requirements for opioid-exposed patients during recovery are often higher than those for opioid-naive patients[51,59,60]. In addition, preoperative opioid use has been found to be a risk factor for slower recovery, increased cost, and increased complications after total knee arthroplasty and total hip arthroplasty[82]. For example, prior data have demonstrated that a mean preoperative daily opioid dose of >60 oral morphine equivalents was independently associated with new, persistent opioid use[51]. A preoperative opioid taper to a lower dose may improve outcomes and has been found to return a patient’s postoperative recovery to one more closely resembling that of an opioid-naive patient[83].

Best Practices in Transitions of Care

A surgical procedure is episodic, and as such, often requires at least one transition of care to primary care providers (PCPs), as surgeons are not often involved in the long-term care of patients, and rarely manage the entirety of a patients' comorbidities. The coordination of postoperative opioid prescribing requires especially deliberate coordination in patients at high risk for chronic pain and chronic opioid use.[84] The high number of patients with preoperative opioid prescriptions necessitates clear communication of the plan for postoperative pain management to PCPs, who may bear the burden of postoperative pain management. Effective communication of a pain management plan that includes alternative analgesic options may help to prevent high-risk prescribing behaviors such as overlapping prescriptions and prescriptions from multiple providers, and it may help to shorten the quantity and duration of opioid use.

Conclusions

Although opioids are effective for the management of acute musculoskeletal pain, the morbidity and mortality related to opioid analgesics reinforce the need for evidence-based guidelines. Despite research on the effectiveness of opioid alternatives, such as NSAIDs, acetaminophen, and gabapentinoids, there is not a large body of evidence on the comparative effectiveness of these strategies, as they are often studied as part of a multimodal intervention. Even less research has addressed the comparative efficacy of pharmacologic and nonpharmacologic methods of pain management. Future studies could inform their role as opioid alternatives. Additionally, further research must address the association between prescription size and opioid use, as well as patient-reported pain control and functional ability.

Although there are efforts being made to limit overprescribing at both the institutional and societal levels, more research on procedure-specific pain management strategies and maximum recommended opioid dosages is needed. Providers should make an effort to evaluate patient risk preoperatively, should prescribe judiciously while incorporating multimodal pain management plans, and should integrate a preoperative discussion with patients about the opioid usage, mentioning both the risk to individual patients and the risk that excess opioids poses to their community. An acknowledgment that not all of the prescribed pills may be needed and clear instructions on how to store and dispose of the excess should be included in perioperative care protocols to inform and empower patients to mitigate risk.

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- Opioid use for chronic and acute musculoskeletal pain is common.
- Orthopaedic surgeons are frequent opioid prescribers.
- Opioids are commonly prescribed for acute pain, with high variation.
- Opioid alternatives for acute pain are effective, and the incorporation of multimodal pain management in the perioperative period can decrease opioid use.
- Although opioids are effective for the management of acute musculoskeletal pain, the morbidity and mortality related to opioid analgesics reinforce the need for robust, evidence-based guidelines.
- Providers should evaluate patient risk preoperatively, should prescribe judiciously with multimodal pain management plans, and should integrate a preoperative discussion on opioid usage.
- Future research should include procedure-specific pain management strategies, as well as the comparative efficacy of pharmacologic and nonpharmacologic methods of pain management.