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CORR Insights®: How Does Perioperative Ketorolac Affect Opioid Consumption and Pain Management After Ankle Fracture Surgery?

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Where Are We Now?

Ankle fractures are one of the most-common fractures of the lower extremity, with a reported incidence of about 190 per 100,000 persons per year. Up to 25% of all patients with ankle fractures undergo surgery (most commonly, open reduction and internal fixation), which may help to avoid post-operative long-term sequelae including post-traumatic ankle osteoarthritis [8].

Post-operative pain is inevitable, and physicians who manage it must be mindful of the opioid epidemic in the United States. Although less than 5% of the world's population, Americans consume more than 80% of the world's prescribed opioids [13]. Beyond the serious nature of opioid abuse and dependence, physicians must also consider that post-operative opioid administration may inhibit bone healing. One animal model showed that post-operative use of opioid pain medication resulted in weaker and slower callus formation compared with controls [6]. One study demonstrated that patients with surgical fracture treatment who take more opioids reported greater pain intensity and less satisfaction with pain relief [4]. Another clinical study of 9995 humeral shaft fractures found that post-operative use of opioids was associated with fracture nonunion [3].

In the last two decades, post-operative opioid monotherapy gained prominence both because of aggressive marketing by pharmaceutical companies, and concerns about side effects of non-steroidal anti-inflammatory drugs (NSAIDs), including evidence associating them with delayed union or nonunion [13]. Multimodal analgesia typically includes several classes of analgesics and anti-inflammatory drugs (such as NSAIDs, selective cyclooxygenase-2 inhibitors, acetaminophen, paracetamol, neuromodulatory medications, opioid agonists, glucocorticoids, N-Methyl D-Aspartate antagonists) as well as local anesthetic techniques (wound infiltration and intra-articular injections), and sometimes peripheral nerve blocks [9]. One study found that multimodal analgesia substantially reduced the length of hospitalization in patients who underwent fusion surgery of the ankle and hindfoot [12]. However, this study has several limitations including retrospective character of the study, small number of patients included into this study, and the heavy selections bias as the selection for receiving the pain protocol was solely left to the surgeon's discretion [12]. Therefore, the results of this study should be interpreted with great caution [10].

In the current study, McDonald and colleagues [11] found that perioperative ketorolac administration may help to reduce the post-operative opioid consumption. This study is important because it demonstrates a simple protocol how to reduce opioid consumption and to improve pain management in patients who had ankle fracture surgery. Surgical treatment of the ankle is one of the most common surgical procedures in foot and ankle as well as in general traumatology. It is our "daily

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bread" and dealing with post-operative pain might be quite challenging, especially in the first two post-operative days. This study might indeed change our routine and improve the pain management of our patients in the first post-operative days.

Where Do We Need to Go?

Multimodal analgesia is not a single entity; it combines a variety of drugs, medication classes, and interventions. It is therefore reasonable to assume that the different multimodal protocols might not be similarly effective (or safe), and the protocols that have been demonstrated in other orthopaedic subspecialties—such as arthroplasty surgery—might deserve exploration in patients undergoing foot and ankle surgery.

In the current investigation, the authors found that adding an NSAID reduced opioid consumption [11]; future studies should build on that by evaluating whether the differences were large enough to influence patients' satisfaction with the intervention.

Finally, studies large enough to assess differences in the likelihood of union are needed, given that prior studies have associated NSAID use with delayed union and non-union [2, 3, 5].

How Do We Get There?

Further randomized trials should look beyond how to avoid opioids and concentrate on the question of how to improve the peri-operative and post-operative pain management for patients who undergo foot and ankle surgery. Randomized controlled studies are needed to compare different multimodal analgesia protocols in patients who have foot and ankle surgery. One good approach would be to test efficacy and safety of combined post-operative medication, such as NSAIDs, opioids, and peripheral nerve blocks.

Furthermore, we need to understand the meaning of pain from our patients' prospective. "More opioids equal less pain" sounds reasonable and simple, but it is not always valid [4] and we need to know why this is the case. Psychosocial factors may play an important role similar to how biomedical factors play a role in response to nociception. Patient-reported outcomes measurement instrumentation system including pain interference may help to predict and to assess post-operative success in foot and ankle patients from their own perspectives [1].

Finally, multi-center studies are most likely the solution to achieve sufficiently large comparative cohort studies. Large studies are needed to evaluate less-common endpoints like complications and non-union, which almost certainly will be missed or underestimated in small and single-center randomized trials. Multi-center studies inevitably require enormous time and man-power efforts and often associated with high financial burdens. Ideally, those studies can be performed using data from nation-wide registry settings. Unfortunately, there are no such registries in foot and ankle surgery areas. Therefore, by planning of such multi-center studies a realistic questions should be asked, as to detect small differences such studies can be simply too small.

References

1. Anderson MR, Houck JR, Saltzman CL, Hung M, Nickisch F, Barg A, Beals T, Baumhauer JF. Validation and generalizability of preoperative PROMIS scores to predict postoperative success in foot and ankle patients. *Foot Ankle Int*. 2018; 39:763-770.
2. Bhandari M, Tornetta P 3rd, Sprague S, Najibi S, Petrisor B, Griffith L, Guyatt GH. Predictors of reoperation following operative management of fractures of the tibial shaft. *J Orthop Trauma*. 2003;17: 353-361.
3. Bhattacharyya T, Levin R, Vrahas MS, Solomon DH. Nonsteroidal antiinflammatory drugs and nonunion of humeral shaft fractures. *Arthritis Rheum*. 2005;53:364-367.
4. Bot AG, Bekkers S, Arnstein PM, Smith RM, Ring D. Opioid use after fracture surgery correlates with pain intensity and satisfaction with pain relief. *Clin Orthop Relat Res*. 2014;472:2542-2549.
5. Burd TA, Hughes MS, Anglen JO. Heterotopic ossification prophylaxis with indomethacin increases the risk of long-bone nonunion. *J Bone Joint Surg Br*. 2003;85:700-705.
6. Chrastil J, Sampson C, Jones KB, Higgins TF. Postoperative opioid administration inhibits bone healing in an animal model. *Clin Orthop Relat Res*. 2013;471: 4076-4081.
7. Henry JK, Roney A, Cody EA, Hummel A, Mancuso CA, Ellis S. Fulfillment of expectations after orthopedic foot and ankle surgery. *Foot Ankle Int*. 2019: 1071100719864354.
8. Horisberger M, Valderrabano V, Hintermann B. Posttraumatic ankle osteoarthritis after ankle-related fractures. *J Orthop Trauma*. 2009;23:60-67.
9. Kohring JM, Orgain NG. Multimodal analgesia in foot and ankle surgery. *Orthop Clin North Am*. 2017;48: 495-505.
10. Leopold SS. Editorial: When "safe and effective" becomes dangerous. *Clin Orthop Relat Res*. 2014;472:1999–2001.
11. McDonald EL, Daniel JN, Rogero RG, Shakked RJ, Nicholson K, Pedowitz DI, Raikin SM, Bilolikar V, Winters BS. How does perioperative ketorolac affect opioid consumption and pain management after ankle fracture surgery? *Clin Orthop Relat Res*. [Published online ahead of print September 24, 2019]. DOI: 10.1097/CORR.0000000000000978.
12. Michelson JD, Addante RA, Charlson MD. Multimodal analgesia therapy reduces length of hospitalization in patients undergoing fusions of the ankle and hindfoot. *Foot & ankle international*. 2013;34:1526-1534.
13. Seymour RB, Ring D, Higgins T, Hsu JR. Leading the way to solutions to the opioid epidemic: AOA critical issues. *J Bone Joint Surg Am*. 2017;99:e113.