



# Multimodal analgesia following microvascular free flap reconstruction of the oral cavity—the safety and benefits of supplemental regional anesthesia

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## Background

Acute pain management following head and neck surgery is no simple task. The type and extent of procedures performed are varied, occurring in a region of the body rich with special neurovascular organs, providing humans with unique sensory perception, and facial animation. Patients undergoing major head and neck microvascular reconstructive surgery require pain management to help control pre-, peri, and/or post-surgical pain. Opioid analgesics, even in short-term administration, can lead to long-term use and dependence. Despite short-term benefits of early mobilization and decreased length of hospitalization, opioid use is not without serious risks (1,2), including dependence and death from overdose. Other, less severe risks include constipation, respiratory depression, nausea, drowsiness, confusion, and euphoria (3).

Unfortunately, opioid addiction is an international problem with more than 564,000 United States (US) citizens suffering a fatal overdose from 1999–2020 (4), and 36.3 million individuals suffering from drug use disorders in 2019 (5). In addition, treatment for opioid-related complications consumes tens of billions of dollars in health care costs alone in the US. This excludes greater than \$100 billion associated with lost productivity and criminal justice costs annually (6).

## Study summary

In a recent study performed by Weyh *et al.*, opioid consumption was compared between 5 different institutions across 4 countries for patients undergoing microvascular free flap reconstruction of the mandible (7), a complex procedure with considerable postoperative pain management requirements. The purpose of this study was to first identify and quantify the differences in opioid use across five international centers, and then to determine the best practices for managing postoperative pain while minimizing opioid utilization following microvascular reconstructive surgery of the mandible. To address this, the authors designed a retrospective multi-institution cohort study that was approved by the Institutional Review Board (IRB) at the primary study institution of the University of Florida Jacksonville, and at each participating institution. Patients included in this study underwent primary fibula free flap (FFF) reconstruction for a mandibular defect between the years 2009 and 2019. Etiology of the mandibular defect included benign pathology and malignant pathology, infection, trauma, craniofacial deformity and excluded osteoradionecrosis (ORN) and medication-related osteonecrosis (MRON). The primary outcome was the total amount of oral morphine equivalent (OME) units consumed in the first 72 hours postoperatively. In addition,

secondary outcomes included the length of hospitalization stay (LOS, days), intensive care unit (ICU) admission, use of multimodal pain management, average pain score within 72 hours postoperatively, and total OME prescribed at the time of discharge.

A total of 185 patients from 5 institutions met the criteria for analysis. With regards to the primary outcome, both institutions in the US (University of Florida Jacksonville and University of Maryland) had the highest mean OME utilized within the first 72 hours postoperatively compared to their counterparts from Italy, Argentina, and India. The greatest difference was between the University of Maryland (US) having a mean OME of 306 (range, 183–592) and Sapienza University of Rome (Italy), 43.5 (range, 31–51). Mean LOS was generally longer in the non-US countries with the greatest occurring in Tata Medical Center (India) (13 days) and the shortest in the University of Florida Jacksonville, USA (6 days). Due to variations between institutional policies regarding postoperative care, ICU admissions also differed. For example, all patients at Tata Medical Center (India) went to the ICU while all patients at the University of Florida Jacksonville (US) went to a progressive care unit. The use of multimodal analgesia was mostly comparable between institutions with acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) commonly used as adjuncts. However, the use of NSAIDs varied to a greater degree among institutions due primarily to its antiplatelet effect and concern for postoperative bleeding. Pain scores are often subjective and were not consistently measured across all participating institutions. US centers were significantly more likely to discharge patients with opioids compared to their international counterparts.

Overall, this study revealed that postoperative opioid utilization following microvascular reconstruction of the mandible with the FFF varied among international centers with the US demonstrating the greatest usage compared to Italy, Argentina, and India. The difference in opioid utilization reflected in this study highlights the variation in prescribing habits as well as patient management ideologies both within and between countries.

## Commentary

This retrospective study emphasizes a key challenge in the current international “opioid crisis”; despite relative uniformity in surgical treatment, postoperative pain management varies widely worldwide. To address this

challenge, we must consider the evidence for multimodal analgesia in this specific subgroup of patients.

Most notably, a recently published systematic review by Go *et al.* provided evidence for the use of adjunct non-opioid analgesics, citing many challenges in developing a standardized postoperative pain management protocol (8). These include significant variability in the type of drug, dosage, route and timing of administration. Subjective pain outcome measurements were also highly variable. Overall, multimodal analgesia was shown to decrease perioperative opioid utilization without increased surgical or medical complications in free flap patients. Cramer *et al.* further provided commentary on Go *et al.*'s work by highlighting the strengths and weaknesses of a multimodal analgesia protocol for head and neck surgery patients (9). These include the benefit of safely adding non-opioid adjuncts such as ibuprofen and acetaminophen, when not contraindicated, and point out the limited efficacy of gabapentin for postoperative pain. Although selective COX-2 inhibitors do not increase the risk of bleeding and have been studied as a non-opioid adjunct for postoperative pain, additional prospective studies are needed to demonstrate its superior efficacy to non-selective NSAIDs following free flap surgery. While the risk for perioperative bleeding and hematoma may exist with nonselective NSAIDs, it remains infrequent and posed no significant risk when compared to a placebo in a systematic review consisting of 3,064 patients (10). Finally, preoperative opioid consumption is a common finding among patients with head and neck cancer, increasing the need for peri- and postoperative opioids (11-13).

In our opinion, the Weyh *et al.* paper selected an ideal study population: individuals undergoing major head and neck resection and fibula free flap reconstruction, with multiple operative sites, long operations, and featuring a long hospital course where immediate-acting intravenous opioids for acute pain are readily available. For patients undergoing free flap reconstruction, the addition of a second surgical site (flap donor site) augments the perception of pain that the patient experiences.

Current evidence supports the use of multimodal analgesia following major head and neck surgery as it has been shown to reduce both opioid utilization and length of hospitalization (8). However, due to the heterogeneity of current multimodal analgesic protocols, there currently does not exist a standardized universal protocol. While multiple adjuvant analgesics such as NSAIDs, acetaminophen, gabapentin, neuromuscular relaxants, corticosteroids, and

extremity nerve blocks have been described, only NSAID and acetaminophen-based regimens have been shown to provide a reliable and consistent outcome regarding acute pain control and decreased need for opioid utilization (14,15). Despite their simplicity, these inexpensive and widely available medications may provide a pathway forward, where more complex solutions have failed to gain wide acceptance.

The invitation to contribute to JOMA on this topic could not have come at a more critical time in the evolution of improved pain management in major open surgery. Regional supplemental anesthesia via extremity nerve blocks for patients undergoing free flap reconstruction of the head and neck has recently been shown to be associated with decreased hospitalization and opioid utilization (16-19). Regional anesthesia was first incorporated into enhanced recovery after surgery (ERAS) protocols for colorectal surgery but is now commonly performed in gynecologic, thoracic, breast, orthopedic, and spine surgery (20-23). Meanwhile, in head and neck surgery, several studies have shown its use was associated with decreased opioid utilization, decreased pain perception, and improved patient satisfaction postoperatively. Park *et al.* performed a retrospective study of 148 patients who underwent microvascular reconstructive surgery of the head and neck and showed that patients who received supplemental regional anesthesia at the donor graft harvest site had shorter hospitalization stay and a trend toward lower opioid utilization (16). More recently, Le *et al.* executed a prospective randomized controlled trial that analyzed the impact of supplemental regional anesthesia and opioid utilization following microvascular free flap reconstruction of the oral cavity. Patients who received regional anesthesia at the donor site utilized a lower number of opioids in the first five days postoperatively, however, length of hospitalization was comparable between the study groups (17). Zhang *et al.* performed a prospective randomized, double-blinded study evaluating the efficacy and safety of combined femoral and peroneal nerve blocks for free fibular flap reconstruction of mandibular defects and showed that the block intervention was associated with a reduction in sufentanyl use and improved postoperative analgesia at the donor site (18). In addition, Persson *et al.* performed a randomized, double-blinded, placebo-controlled study evaluating the effect of the popliteal nerve block for fibular free flap reconstruction of the head and neck and showed that patients in the treatment group

experienced fewer episodes of breakthrough pain, consumed lower number of opioids in the first postoperative week, and did not have any complications related to the block (19).

## Conclusions

Head and neck surgical patients remain among the most medically complex patients, requiring a multidisciplinary team approach to optimize patient satisfaction and long-term survival outcomes. Perioperative pain management remains a challenging task and important component addressed in the head and neck ERAS protocol (24). While completely eliminating opioid analgesics for postoperative pain management in this patient population does not appear imminent, opioid-sparing multimodal analgesia with an emphasis on non-opioid adjuncts such as NSAIDs, acetaminophen and regional anesthesia (i.e., nerve block), serve to limit opioid consumption in the early postoperative period and decrease the risk for long-term dependence. This is especially important to consider and incorporate in the higher opioid-prescribing in Western countries, such as the United States.

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## References

- Izumi Y, Amaya F, Hosokawa K, et al. Five-day pain management regimen using patient-controlled analgesia facilitates early ambulation after cardiac surgery. *J Anesth* 2010;24:187-91.
- Golladay GJ, Balch KR, Dalury DF, et al. Oral Multimodal Analgesia for Total Joint Arthroplasty. *J Arthroplasty* 2017;32:S69-73.
- Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician* 2008;11:S105-20.
- Wide-ranging online data for epidemiologic research (WONDER). Atlanta, GA: CDC, National Center for Health Statistics; 2021. Available online: <http://wonder.cdc.gov>
- UNODC (2021). World Drug Report 2021. Available online: <https://www.unodc.org/unodc/data-and-analysis/wdr2021.html>
- Florence C, Luo F, Rice K. The economic burden of opioid use disorder and fatal opioid overdose in the United States, 2017. *Drug Alcohol Depend* 2021;218:108350.
- Weyh AM, Pucci R, Busby E, et al. Contrasting opioid use for pain management in microvascular head and neck reconstruction: an international study. *Int J Oral Maxillofac Surg* 2022;51:1412-9.
- Go BC, Go CC, Chorath K, et al. Multimodal Analgesia in Head and Neck Free Flap Reconstruction: A Systematic Review. *Otolaryngol Head Neck Surg* 2022;166:820-31.
- Cramer JD, Brummett CM, Brenner MJ. Opioid prescribing and consumption after head and neck free flap reconstruction: what is the evidence for multimodal analgesia? *J Oral Maxillofac Anesth* 2022;1:17.
- Walker NJ, Jones VM, Kratky L, et al. Hematoma Risks of Nonsteroidal Anti-inflammatory Drugs Used in Plastic Surgery Procedures: A Systematic Review and Meta-analysis. *Ann Plast Surg* 2019;82:S437-45.
- Hinther A, Abdel-Rahman O, Cheung WY, et al. Chronic Postoperative Opioid Use: A Systematic Review. *World J Surg* 2019;43:2164-74.
- Hinther A, Nakoneshny SC, Chandarana SP, et al. Efficacy of Multimodal Analgesia for Postoperative Pain Management in Head and Neck Cancer Patients. *Cancers (Basel)* 2021.
- Zayed S, Lin C, Boldt RG, et al. Risk of Chronic Opioid Use After Radiation for Head and Neck Cancer: A Systematic Review and Meta-Analysis. *Adv Radiat Oncol* 2021;6:100583.
- Moore RA, Derry S, Aldington D, et al. Adverse events associated with single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2015;2015:CD011407.
- Moore RA, Derry S, Aldington D, et al. Single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database Syst Rev* 2015;2015:CD008659.
- Park EP, Le JM, Gigliotti J, et al. Does Supplemental Regional Anesthesia Decrease Length of Stay and Opioid Use for Patients Undergoing Head and Neck Microvascular Reconstruction? *J Oral Maxillofac Surg* 2021;79:712-21.
- Le JM, Gigliotti J, Sayre KS, et al. Supplemental Regional Block Anesthesia Reduces Opioid Utilization Following Free Flap Reconstruction of the Oral Cavity: A Prospective, Randomized Clinical Trial. *J Oral Maxillofac Surg* 2022. [Epub ahead of print]. pii: S0278-2391(22)00980-6. doi: 10.1016/j.joms.2022.10.015.
- Zhang X, Sun C, Bai X, et al. Efficacy and safety of lower extremity nerve blocks for postoperative analgesia at free fibular flap donor sites. *Head Neck* 2018;40:2670-6.
- Persson K, Sjövall J, Kander T, et al. Pain management with popliteal block for fibular graft harvesting in head and neck reconstruction; a randomised double-blind placebo-controlled study. *Oral Oncol* 2022;128:105833.
- Carli F, Kehlet H, Baldini G, et al. Evidence basis for regional anesthesia in multidisciplinary fast-track surgical care pathways. *Reg Anesth Pain Med* 2011;36:63-72.
- O'Donnell BD, Iohom G. Regional anesthesia techniques for ambulatory orthopedic surgery. *Curr Opin Anaesthesiol* 2008;21:723-8.
- Gilbertson L, Datta S. Regional anesthesia and analgesia in obstetrics. *Curr Opin Obstet Gynecol* 1993;5:652-6.
- Wheatley GH 3rd, Rosenbaum DH, Paul MC, et al. Improved pain management outcomes with continuous infusion of a local anesthetic after thoracotomy. *J Thorac Cardiovasc Surg* 2005;130:464-8.

24. Dort JC, Farwell DG, Findlay M, et al. Optimal Perioperative Care in Major Head and Neck Cancer Surgery With Free Flap Reconstruction: A Consensus

Review and Recommendations From the Enhanced Recovery After Surgery Society. *JAMA Otolaryngol Head Neck Surg* 2017;143:292-303.

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