Editorial Commentary

Global variation in opioid prescribing after head and neck reconstruction: understanding the United States' outlier status

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Introduction

W. Edwards Deming, widely acknowledged as the Father of Quality Management, observed that "Uncontrolled variation is the enemy of quality" and much of the progress in improving the quality of patient care can be attributed to standardization (1). Yet few aspects of healthcare exhibit more global variation than the administration of opioids for head and neck cancer. For example, one study of pain management practices after major head and neck surgery found that 87% of American patients received opioids in contrast to <1% in Hong Kong (2). The United States' (U.S.) outlier status in opioid prescribing behavior is well-documented (3), and these patterns might reflect not only different cultural perceptions but also different beliefs regarding the safety, efficacy, and risks of opioid medications (4).

Weyh and colleagues recently reported the results of an international retrospective study in which the authors contrasted practices around opioid use for pain management in patients undergoing fibula microvascular free flap reconstruction (5). Their primary outcome measure was oral morphine equivalent (OME) units administered during the first 72 hours after surgery, and secondary outcomes assessed included length of inpatient stay (LOS), use of multimodal pain management strategy, mean pain score during the first 72 literature. These findings afford a stepping-off point for understanding the current state of the opioid epidemic in the U.S. hours, need for admission to an ICU, and the OME of opioids prescribed at discharge. Data were collected from two U.S. centers and three international centers, including India, Argentina, and Italy. Consistent with other literature on global opioid usage, the U.S. had the highest opioid utilization, corresponding to approximately twice that of India, four times that of Argentina, and six times that of Italy. The U.S. was also an outlier in opioids prescribed at discharge, underscoring patterns documented in prior

Painmanagement in the United States

Opioid use disorder is a global problem, with over 35 million people suffering from drug dependence worldwide (5). In the U.S., a campaign identifying pain as "The Fifth Vital Sign" spurred over-prescribing, which was exacerbated by misinformation directed to health professionals on the risk of opioids. In ensuing years, opioids in circulation progressively increased, and the economic costs of opioid prescription-related overdose, abuse, and dependence now exceed 75 billion dollars annually (5). In 2016, the Centers for Disease Control and Prevention (CDC) issued its *Guideline for Prescribing Opioids*; its release was

associated with rapid reductions in opioid prescribing and corresponding increases in prescribing of nonopioid pain medications. The results varied as new laws, regulations, and policies were enacted. States that implemented opioid duration limits showed a more marked reduction in opioid prescribing (6). However, there was also evidence of patient harm, including untreated and undertreated pain, inappropriate rapid opioid tapers, and abrupt discontinuation of maintenance opioids.

The serious harmful effects resulted in a public backlash that underscored the need for more individualized, patient-centered approaches to opioid prescribing, opioid tapering, and treatment of complex pain (7). The recently released 2022 CDC Clinical Practice Guideline provides guidance for clinicians based on five systematic reviews, noting that nonopioid therapies are at least as effective as opioids for many types of acute pain, although this guideline excluded cancer-related pain. The guideline recommends that clinicians maximize the use of nonopioid therapies and prescribe opioids to treat acute pain only when the benefits are anticipated to outweigh the risks. The guideline highlights the role es are contraindicated or ineffective. When opioids, non-steroidal ant-inflammatory drugs (NSAIDs) or other analgesics are needed for pain, they should be prescribed at the lowest effective dose and for only the expected duration of pain for which they are necessary. Even in the U.S., where opioids use rates are higher than in other parts of the world, patients may encounter barriers to accessing evidence-based pain treatment. Therefore, shared decision-making by patients and clinicians is necessary; abruptly discontinuing opioids after extended use is potentially harmful. The goal is equitable access to effective, individualized, and safe pain management while reducing the risks arising from opioid use.

Despite recent progress in pain management, including the promotion of multimodal regimens (4), calls for effective and equitable pain management (7), and rollout of enhanced recovery after surgery protocols (8), optimal pain management remains a challenge worldwide. The findings of Wyeth *et al.* are consistent with prior data showing that while the U.S. has high rates of opioid utilization, Italy is among the lowest (5). Patient reluctance to receive opioids might be an important factor in this lower utilization; the association of opioids with dependence, overdose, or death might contributes to opioid aversion (5). Although cultural mores will continue to shape expectations for pain control and perpetuate higher opioid utilization in U.S. for the foreseeable future, improved education of patients and practitioners might have a role in moderating opioid utilization (9).

Challenges in managing pain in head and neck surgery patients

Patients undergoing head and neck ablative surgery and microvascular reconstruction present a dilemma for clinicians aspiring to standardize perioperative opioid-sparing analgesic regimens. Amid the opioid crisis, multimodal analgesic regimens have emerged as a potentially promising strategy to improve outcomes in this population. Still, the evidence base is fraught with complexity, arising from inconsistent protocols, practices, and outcome measures. The evidence demonstrates that when combined with acetaminophen, NSAIDs provide safe, highly effective analgesia for postoperative pain and reduce the need for opioid analgesia. Gabapentin affords only modest analgesic or antiemetic benefits and has notable side effects. These observations provide the basis for practical guidance on initiating multimodal analgesic therapy after free flap surgery.

Although it might seem impractical to reconcile the opposing goals of the standardized practice and tailored care, a patient-centered lens allows for both objectives to be achieved. Health professionals can begin by understanding factors that may influence pain, such as prior exposure to opioids for cancer or chronic pain; presence of benign versus malignant disorders; prior history of chemoradiation; extent of disease, including considerations of site and stage; expectations for pain management; and perceptions regarding opioid or multimodal analgesia (10-12). Opioid administration is also influenced by differences in clinician attitudes towards pain management, practices or regulations at their institutions, and structural differences in hospital capacity, services, or extended care options that influence the LOS and discharge planning.

Any duration of opioid treatment is associated with a risk of dependence, opioid use disorder, or overdose (13), but these risks increase roughly in proportion to the amount and duration of opioids consumed (14). Weyh *et al.* found that fibula microvascular reconstruction for malignancy was associated with increased OME, although prescribing in India (where 97% of patients were treated for a malignant pathology) was still at half the level observed for the U.S. For patients with advanced head and neck cancer requiring extirpative surgery and free tissue reconstruction, the risk of opioids is magnified by both the extent of surgery and the necessary duration of recovery. At three months after treatment of head and neck cancer, the rates of chronic

opioid use range from 41–64% (10,15). Many patients initiate opioid analgesia preoperatively for cancer-related pain, although some head and neck cancer patients have their initial exposure to opioids during or immediately after surgery. A key insight shared by Weyh *et al.* is that avoiding delays in performing cancer surgery not only reduces the risk of tumor extension of spread but also reduces the need for opioids preoperatively (5).

Importance of multimodal analgesia after microvascular reconstruction

Improving opioid stewardship in head and neck cancer patients undergoing microvascular reconstructions requires adopting an evidence-based approach while delivering individualized care. A 2017 systematic review recommended opioid-sparing, multimodal postoperative pain management using NSAIDs and acetaminophen for patients undergoing head and neck cancer surgery with free flap reconstruction. Effective opioid stewardship after head and neck surgery requires partnership across health professions, including anesthesiologists, surgeons, nurses, patients, families, and other interprofessional team members (16-22). Another recent systematic review by Go *et al.* investigated multimodal analgesia in head and neck microvascular reconstructive surgery (23). The review incorporated ten studies with 1,253 patients, and the multimodal analgesia strategies included acetaminophen, NSAIDs, Gabapentin, corticosteroids, ketamine, and (rarely) lower extremity nerve blocks; preoperative analgesia was also used in some cases (23). Multimodal analgesia reduced perioperative opioid consumption in 8 of 10 studies and reduced hospital LOS in one study (24).

A similar pattern emerged in the study by Weyh *et al.*, with relatively frequent use of multimodal approaches but rare use of nerve blocks. Because head and neck primary sites are less amenable to regional anesthesia techniques, their utility in head and neck surgery is low; however, managing donor site-related pain may represent an untapped opportunity to reduce opioid utilization. Nonopioid regional block can provide excellent anesthesia for up to 72 hours postoperatively with a popliteal nerve block administered by an indwelling catheter. Liposomal bupivacaine has been shown to reduce acute postoperative pain and limit opioid doses for various procedures in the head and neck (25). Regional anesthesia also alleviates systemic stress responses, reduces LOS, and might reduce the risk of thromboembolic complications if patients can ambulate sooner with adequate pain control (26). Pain at the donor site can be worse than at the head and neck surgical site but can be reduced to nearly zero with the placement of popliteal nerve blocks (27). No centers in the retrospective study by Weyh used this method.

Prior work on multimodal analgesia specific to microvascular surgery remains limited, with a paucity of randomized studies in the literature, but available evidence suggests benefit (23); more prospective investigations on multimodal analgesia in head and neck cancer are needed. NSAIDs are often a component of multimodal analgesia strategies for head and neck microvascular reconstruction. Combining acetaminophen and NSAIDs is among the safest and most effective approaches for acute postoperative pain (28,29). A meta-analysis of randomized trials shows that combining ibuprofen 400 mg with acetaminophen 1,000 mg provides significantly more effective pain control than oxycodone 10mg and acetaminophen 650 mg across a wide range of procedures (4). NSAIDs appear to have no discernable effect on flap survival (30) and afford a marked reduction in the risk of adverse events (12,17,19). Nonetheless, thrombosis and bleeding risk are concerns for head and neck surgeons. NSAIDs include nonselective cyclooxygenases (COX-1 and COX-2) inhibitors (e.g., ibuprofen); preferential COX-2 inhibitors (e.g., meloxicam); and selective COX-2 inhibitors (e.g., celecoxib). Although studies of NSAIDs have not identified an increased risk of bleeding/hematoma or flap failure (23), most data are based on selective COX-2 inhibitors. Selective COX-2 inhibitors do not impair platelet function or otherwise increase the risk of bleeding and, therefore, have an intuitive appeal (4). Weyh *et al.* highlight multimodal regimens, including celecoxib, in their consensus recommendations for perioperative analgesia for head and neck free flap surgery (5).

Gabapentin has been extensively studied in the postoperative setting, including investigations of multimodal analgesia after head and neck microvascular surgery (23) and is included in the sample regimens described by Weyh *et al.* (5); however, recent evidence suggests limited benefit and significant tradeoff with this approach. A meta-analysis of 281 randomized controlled trials of Gabapentin in the postoperative setting (24,682 patients) (31) prompted a reappraisal of the risk-benefit tradeoffs of Gabapentin. Although Gabapentin led to a reduction in opioid consumption, the effect size for differences in acute pain was not clinically significant, nor for a reduction in chronic post-surgical pain. In addition, Gabapentin is associated with increased visual disturbance, dizziness, sedation, and

risk of addiction (31).

Reducing variation in analgesic practices

Weyh *et al.* offer consensus recommendations categorized into preoperative care, day of surgery, postoperative, and discharge that support evidence-based, multimodal analgesia. For the preoperative period, they recommend gathering a thorough pain history, avoiding delays in surgery, identifying alternatives to opioid analgesia, and having candid discussions about pain management goals. On the day of surgery, the recommendations emphasize using preoperative multimodal pain management and considering regional anesthesia to alleviate donor site pain, including indwelling catheter-based blocks. In the postoperative period, principal goals include expediting the transition to oral or enteric delivery of analgesia, monitoring pain with validated pain assessment tools (recalibrating pain regimen as needed), and consulting pain management services early in cases of complex pain. Finally, discharge considerations include assessing whether alternatives to opioids can be used (avoiding routine opioid prescribing) and counseling regarding disposing unused opioids.

These recommendations are consistent with a recent clinical practice guideline focusing on opioid prescribing for common head and neck procedures (12). Broad stakeholder engagement is another critical element of successful opioid stewardship, relevant to the inpatient setting and after hospital discharge. Although Weyh *et al.* focused primarily on opioid management during the first 72 hours after surgery, their data suggest opportunities for reducing variation during the entire postoperative period. A mindful approach to pain management might also reduce the number of patients transitioning from acute to chronic pain. Practical strategies include collecting data on patient opioid consumption, tracking clinician prescribing practices, and identifying risk factors for opioid use disorder or inadequate analgesia (12,21). Such measures can help connect high-risk patients to a pain management specialist when appropriate.

Expert consensus is emerging regarding the optimal head and neck anesthesia for patients undergoing microvascular reconstruction (32). Multidisciplinary approaches are valuable in patients with free flap reconstruction involving the oral cavity or aerodigestive anatomy because of the complex interplay of airway management, including the risk of hypoxia or aspiration (33,34). Opioids affect the level of consciousness and can place patients with microvascular surgery at risk for respiratory compromise, particularly in patients with tracheostomy and complex airway needs (35,36). Reducing variation has been associated with improved outcomes (37), and quality improvement initiatives involve iterative cycles of tracking data and improving practices (38). Engaging interprofessional learners supports quality improvement initiatives and creates an opportunity for growing future leaders (16,39), who in turn can champion effective opioid stewardship.

Conclusions

Understanding the United States' outlier status in opioid utilization after complex head and neck reconstruction is instructive for practitioners around the world, underscoring the need for teamwork across disciplines to implement opioid-sparing multimodal analgesic regimens. Multimodal analgesic regimens incorporating acetaminophen and NSAIDS can reduce opioid consumption without worsening pain or increasing complications after head and neck microvascular reconstruction. In addition, a patient-centered approach that aligns individualized care with evidence from international practice can improve the safety and quality of head and neck care.

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