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Perioperative Opioid Analgesia: Finding the Right Balance

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Opioids have served a primary role in surgical pain control since the isolation of morphine in the 19th century through the development of synthetic agonists used in modern anesthesia. While opioids offer potent analgesia, there are considerable downsides for patients perioperatively and long-term. The broader adverse impacts of opioids as well as scrutiny around their appropriate use intraoperatively has intensified. Advances in multimodal analgesia have reduced reliance on opioids, allowing for opioid-sparing and even opioid-free anesthesia. This effort has further expanded to providing effective pain control while minimizing opioids as part of enhanced recovery after surgery (ERAS). This article will explore differences and outcomes of these approaches and discuss the positive outcomes of culture change with implementation of ERAS protocols.

Over 50 million surgeries are performed annually in the United States with around 60–80% of opioid-naïve patients prescribed opioids postoperatively.[1,2] Patients who already take opioids prior to surgery face poorer outcomes, worse pain control measures, and higher costs.[3] For many surgical patients, perioperative opioid exposure can lead to continued use, with rates of new persistent opioid use 90 days after surgery around 6%,[4] despite the consensus that extended opioid use for chronic, noncancer pain has marginal benefit and considerable risk.[5] The opioid epidemic varies by country with many lower income populations facing considerable inadequate access to opioid medication.[6] Anesthesia professionals are in a unique position to intervene at this juncture, using expertise in pain management to investigate alternative options to achieve optimal analgesia in the perioperative period that are affordable and accessible worldwide.

Opioid-based anesthesia refers to the standard treatment of pain through opioid receptor agonists, such as morphine or fentanyl, or an agonist-antagonist, like buprenorphine. Opioids are historically prioritized perioperatively due to their quick onset, high efficacy in relieving somatic pain, predictability, and widespread availability. However, opioids also contribute to postoperative nausea and vomiting (PONV), respiratory depression, bowel hypomotility or ileus, delirium, tolerance, and even increased pain through opioid-induced hyperalgesia.[7] Opioids, particularly in high doses, may also increase postoperative complications, extend hospital stays, and lead to readmissions.[7] While

complete elimination of opioid-based analgesia appears to be a solution, simply reducing intraoperative opioid administration can result in worse postoperative pain and increased opioid consumption.[8] This can be detrimental for patients as uncontrolled pain after surgery itself contributes to postoperative complications and increases the risk of chronic postsurgical pain, suggesting effective and timely pain control is paramount to successful recovery.[9]

Clinicians leverage multimodal analgesia to minimize opioids, a combinatorial approach to pain control by acting on multiple pathways pharmacologically in addition to incorporating regional anesthesia. Regional techniques include single-shot injections (e.g., upper and lower extremity nerve blocks, paravertebral blocks, and field blocks), continuous nerve catheters, and neuraxial anesthesia. Medications include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, ketamine, dexmedetomidine, gabapentinoids, and local anesthetics.[10] Each has advantages and risks. Ketamine, an NMDA receptor antagonist, has direct analgesic effects and reduces central sensitization, but higher doses cause dissociation and hallucinations. NSAIDs decrease inflammation and pain through COX inhibition, while higher doses can lead to gastrointestinal bleeding or renal injury. Dexmedetomidine, an α_2-agonist, enhances inhibitory pain pathways and blunts the sympathetic response to pain; however, higher doses contribute to excess sedation, bradycardia, and hypotension. The recently FDA-approved medication suzetrigine is part of a promising new nonopioid class that acts through voltage-gated sodium channel 1.8 (NaV1.8) inhibition, stopping nociceptive signals in peripheral neurons.[11] The combination of multiple analgesics may reduce the effective dose of each individual medication and their associated side effects.

Opioid-free anesthesia (OFA) is a strategy that avoids intraoperative opioid administration. High quality, robust research in the effectiveness of OFA is limited, although there are some noteworthy studies. One randomized controlled trial of women undergoing gynecologic laparoscopic surgery compared intraoperative ketamine and dexmedetomidine vs. sufentanil and found no significant differences in PONV, pain scores, or opioid consumption, while the OFA group had a delayed discharge effect from excess sedation.[12] Another study on patients undergoing laparoscopic hiatal hernia repair showed no difference in postoperative pain requirements in the OFA group, though they were significantly more likely to be discharged the same day (the primary endpoint).[13] A study on patients undergoing video-assisted thoracoscopic surgery compared OFA with a paravertebral block to opioid-based anesthesia without a block and demonstrated significantly

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Studies Have Not Demonstrated Convincing Evidence to Support Broad Use of Opioid-Free Anesthesia

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decreased pain scores and 24-hour opioid consumption in the OFA group.[14] When broadening our scope to meta-analyses, OFA cohorts have demonstrated advantages with decreased PONV and time to normal bowel function, but increased chance of bradycardia and overall similar postoperative pain scores and opioid consumption.[15,16] In other words, there is not clear evidence to broadly espouse OFA outside of specific considerations, and therefore more research is warranted.

Opioid-sparing anesthesia, on the other hand, minimizes, while not eliminating, the use of intraoperative opioids, seeking a balanced approach. There are numerous studies on individual adjuvant medications and regional techniques, which demonstrate reduced opioid requirements and improvements in recovery by incorporating an opioid-sparing strategy. One small randomized controlled trial compared dexmedetomidine infusion to placebo during laparoscopic cholecystectomy, with the treatment group showing decreased postoperative morphine use, decreased incidence of severe pain, and longer time to first rescue analgesic.[17] In cardiac surgery patients, an opioid-sparing regimen incorporating a parasternal block and intravenous ketamine for the first 24-hours postoperatively in the ICU demonstrated similar visual analog scales (VAS) pain scores, but significantly lower opioid consumption as well as reduction in rates of ileus, delirium, mechanical ventilation time, and bronchopneumonia.[18]

These studies provide evidence for strategies to be incorporated into formalized ERAS protocols, which can vary by surgery type and institution, but which focus on opioid-sparing comprehensive patient recovery and pain control strategies. The implementation of ERAS protocols may address opioid overuse through a multidisciplinary cultural shift in approaches to perioperative care. At our institution (a multihospital, community-based health system), ERAS protocols were implemented across seven surgical specialties, each with a unique set of interventions to enhance patient education and recovery.[19] Following the establishment of these ERAS protocols, the length of hospital stay decreased by approximately one day, patients were more likely to be discharged in fewer than three days, in-hospital opioid consumption decreased by 50%, and pain scores were more commonly mild compared to the moderate/severe pain scores observed prior.[19] We are also performing a double-blinded randomized controlled trial (ClinicalTrials.gov number NCT05953428) building upon the prior mentioned study on laparoscopic hernia repair,[13] investigating the potential benefits of an opioid sparing anesthesia regimen in this population of patients with respect to reducing discharge opioid consumption, pain scores, PONV incidence, and hospital length of stay. Implementing these changes requires a cultural shift in how perioperative clinicians approach patient education and treatment at each phase of care, which includes provider education, stakeholder buy-in, and resource availability.

Opioid-sparing anesthesia strategies emphasizing multimodal analgesia have been shown to improve outcomes and mitigate risks associated with perioperative opioid use. Implementing this framework through evidence-based ERAS protocols can have institutional and logistical barriers, but ultimately enhances care on a hospital system level to improve patient safety, recovery, and satisfaction. Studies have not demonstrated convincing evidence to support broad use of OFA, although particular patients and types of surgeries may certainly benefit. It remains to be demonstrated whether opioid-reducing strategies decrease the risk of chronic postsurgical pain or new persistent opioid use, as many of the patients receiving OFA were still prescribed opioids at discharge. The anesthesia professional plays an integral role in helping further bridge the gap and avert adverse events from inadequate or inappropriate analgesic practices in the perioperative period.

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REFERENCES

1. Wunsch H, Wijeysundera DN, Passarella MA, et al. Opioids prescribed after low-risk surgical procedures in the United States, 2004–2012. *JAMA.* 2016;315:1654–1657. PMID: 26978756.
2. Brat GA, Agniel D, Beam A, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study. *The BMJ*. 2018;360:j5790. PMID: 29343479.
3. Cron DC, Englesbe MJ, Bolton CJ, et al. Preoperative opioid use is independently associated with increased costs and worse outcomes after major abdominal surgery. *Ann Surg.* 2017;265:695–701. PMID: 27429021.
4. Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg.* 2017;152:e170504. PMID: 28403427.
5. Els C, Jackson TD, Hagtvedt R, et al. High-dose opioids for chronic non-cancer pain: an overview of Cochrane Reviews. *Cochrane Db Syst Rev*. 2023;3:CD012299. PMID: 36961252.
6. Hadjiat Y, Toufiq J, Ntizimira C, et al. Analysis of opioid analgesics consumption in Africa: a longitudinal study from a 20-year continental perspective. *Lancet Glob Health*. 2024;12:e1120-e1128. PMID: 38876759.
7. Long DR, Lihn AL, Friedrich S, et al. Association between intraoperative opioid administration and 30-day readmission: a pre-specified analysis of registry data from a healthcare network in New England. *Br J Anaesth*. 2018;120:1090–1102. PMID: 29661386.
8. Mercado LASC, Liu R, Bharadwaj KM, et al. Association of intraoperative opioid administration with postoperative pain and opioid use. *JAMA Surg*. 2023;158:854. PMID: 37314800.
9. Van Boekel RLM, Warlé MC, Nielen RGC, et al. Relationship between postoperative pain and overall 30-day complications in a broad surgical population: an observational study. *Ann Surg.* 2019;269:856–865. PMID: 29135493.
10. Siu EY, Moon TS. Opioid-free and opioid-sparing anesthesia. *Int Anesthesiol Clin*. 2020;58:34–41. PMID: 32004171.
11. Jones J, Correll DJ, Lechner SM, et al. Selective inhibition of NaV 1.8 with VX-548 for acute pain. *N Engl J Med*. 2023;389:393–405. PMID: 37530822.
12. Massoth C, Schwellenbach J, Saadat-Gilani K, et al. Impact of opioid-free anaesthesia on postoperative nausea, vomiting and pain after gynaecological laparoscopy—a randomised controlled trial. *J Clin Anesth*. 2021;75:110437. PMID: 34229292.
13. Hoffman C, Buddha M, Mai M, et al. Opioid-free anesthesia and same-day surgery laparoscopic hiatal hernia repair. *J Am Coll Surg.* 2022;235:86–98. PMID: 35703966.
14. Copik MM, Sadowska D, Smereka J, et al. Assessment of feasibility of opioid-free anesthesia combined with preoperative thoracic paravertebral block and postoperative intravenous patient-controlled analgesia oxycodone with non-opioid analgesics in the perioperative anesthetic management for video-assisted thoracic surgery. *Anaesthesiol Intensive Ther.* 2024;56:98–107. PMID: 39166501.
15. Feenstra ML, Jansen S, Eshuis WJ, et al. Opioid-free anesthesia: a systematic review and meta-analysis. *J Clin Anesth*. 2023;90:111215. PMID: 37515877.
16. Salomé A, Harkouk H, Fletcher D, Martinez V. Opioid-free anesthesia benefit–risk balance: a systematic review and meta-analysis of randomized controlled trials. *J Clin Med.* 2021;10:2069. PMID: 34065937. .
17. Bielka K, Kuchyn I, Babych V, et al. Dexmedetomidine infusion as an analgesic adjuvant during laparoscopic cholecystectomy: a randomized controlled study. *BMC Anesthesiol.* 2018;18:44. PMID: 29678158.
18. Darras M, Schneider C, Marguerite S, et al. Multimodal analgesia with parasternal plane block protocol within an enhanced recovery after cardiac surgery program decreases opioid use. *JTCVS Open.* 2024;22:25–35. PMID: 39780824.
19. Blumenthal RN, Locke AR, Ben-Isvy N, et al. A retrospective comparison trial investigating aggregate length of stay post implementation of seven enhanced recovery after surgery (ERAS) protocols between 2015 and 2022. *J Clin Med.* 2024;13:5847. PMID: 39407911.