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Commonly Used Opioids in the Orthopedic Operating Room: A Narrative Review

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Keywords: Orthopedic surgery, perioperative analgesia, postoperative pain management, opioids, multimodal analgesia, enhanced recovery after surgery, orthopedic anesthesia

<https://doi.org/10.52965/001c.158576>

Orthopedic Reviews

Vol. 18, 2026

Orthopedic surgical procedures are consistently associated with significant postoperative pain due to extensive tissue manipulation, osseous injury, and inflammatory responses. Effective perioperative analgesia is therefore fundamental to successful orthopedic outcomes, influencing early mobilization, complication rates, length of hospital stay, and patient satisfaction. Although opioid-sparing and enhanced recovery after surgery (ERAS) pathways have gained popularity, opioids remain central to analgesic management in orthopedic operating rooms. This narrative review examines the opioids most commonly used in orthopedic perioperative care, including fentanyl, morphine, remifentanyl, hydromorphone, oxycodone, sufentanil, and methadone. Emphasis is placed on pharmacologic properties, clinical indications, dosing considerations, adverse effects, and comparative evidence in orthopedic populations. In addition, the evolving role of opioids within multimodal analgesia frameworks is discussed, with attention to balancing effective pain control against opioid-related risks.

INTRODUCTION

Pain following orthopedic surgery is often severe and multifactorial, arising from bone trauma, periosteal disruption, soft tissue injury, and postoperative inflammation. Inadequate pain control has been associated with delayed ambulation, increased cardiopulmonary complications, prolonged hospitalization, impaired participation in physical therapy, and the development of chronic postsurgical pain syndromes.¹ Consequently, optimizing perioperative analgesia remains a primary goal in orthopedic care.

Opioids have long served an important role in perioperative pain management because of their potent analgesic effects mediated primarily through mu-opioid receptor activation in the central nervous system.² However, their widespread use has been accompanied by well-recognized adverse effects, including respiratory depression, postoperative nausea and vomiting (PONV), ileus, urinary retention, sedation, and pruritus.³ Moreover, increasing awareness of opioid misuse and dependence has prompted heightened scrutiny of perioperative opioid exposure, particularly in opioid-naïve patients.⁴

Despite these concerns, opioids remain indispensable in many orthopedic settings, particularly for procedures associated with high pain intensity such as total joint arthroplasty, spine surgery, and fracture fixation. Appropriate opioid selection and dosing, informed by pharmacologic principles and patient-specific factors, can optimize analgesia while minimizing harm. This narrative review dis-

cusses commonly used opioids in orthopedic operating rooms and their integration into contemporary multimodal analgesia strategies.

METHODS

A narrative literature review was performed using PubMed and MEDLINE databases. Search terms included combinations of “opioids,” “orthopedic surgery,” “perioperative analgesia,” “fentanyl,” “morphine,” “remifentanyl,” “hydromorphone,” “oxycodone,” “sufentanil,” and “methadone.” English-language clinical trials, observational studies, review articles, and professional society guidelines relevant to orthopedic perioperative care were included. Emphasis was placed on studies evaluating clinical efficacy, safety, and outcomes in orthopedic surgical populations. References are cited in the order in which they appear in the text.

OPIOID PHARMACOLOGY IN THE ORTHOPEDIC OPERATING ROOM

Opioids differ substantially in pharmacokinetic and pharmacodynamic characteristics, which directly influence their suitability for intraoperative versus postoperative use. Variables such as lipid solubility, receptor affinity, hepatic metabolism, active metabolites, and context-sensitive half-time determine onset of analgesia, duration of effect, and adverse event profiles.⁵ In orthopedic surgery, these differ-

ences are clinically relevant given the need for both rapid-onset intraoperative analgesia and sustained postoperative pain control.

Highly lipophilic opioids such as fentanyl, remifentanyl and sufentanil rapidly cross the blood-brain barrier and are favored intraoperatively for their fast onset and predictable hemodynamic effects. In contrast, longer-acting opioids such as morphine and methadone provide extended analgesia and are more commonly used in the postoperative period. Semi-synthetic opioids including hydromorphone and oxycodone occupy an intermediate role and are frequently incorporated into postoperative pain pathways.⁶

FENTANYL

Fentanyl is a synthetic phenylpiperidine opioid approximately 100 times more potent than morphine. Its high lipid solubility allows for rapid central nervous system penetration, resulting in analgesic onset within minutes following intravenous administration.⁷ These properties make fentanyl a mainstay of intraoperative analgesia in orthopedic anesthesia.

In orthopedic operating rooms, fentanyl is commonly administered during induction of anesthesia and in response to acute nociceptive stimuli such as incision, reaming, or tourniquet inflation. Compared with morphine, fentanyl produces minimal histamine release and is associated with greater cardiovascular stability, which is particularly advantageous in elderly patients undergoing joint arthroplasty.⁸ However, its short duration of action necessitates repeated dosing or continuous infusion, and accumulation may occur with prolonged administration, increasing the context-sensitive half-time.

In clinical practice, fentanyl is used almost exclusively via the intravenous route for acute perioperative analgesia. Although a transdermal formulation exists, it is intended for the management of chronic, stable pain in opioid-tolerant patients and is not appropriate for acute postoperative pain or intraoperative use due to its delayed onset, prolonged duration, and inability to rapidly titrate analgesic effect. As such, intravenous fentanyl remains the preferred formulation in orthopedic anesthesia, offering rapid, predictable analgesia that can be precisely titrated to procedural stimuli while maintaining hemodynamic stability.

MORPHINE

Morphine remains one of the most widely used opioids in perioperative medicine and serves as the reference standard for opioid comparison. It has a slower onset but longer duration of action than fentanyl, making it well suited for postoperative analgesia.⁹ Morphine undergoes hepatic metabolism to active metabolites, including morphine-6-glucuronide, which contributes to prolonged analgesia but may accumulate in patients with renal impairment.

In orthopedic practice, morphine is frequently administered intravenously in the post-anesthesia care unit or via patient-controlled analgesia (PCA). It is also used neuraxially, particularly as intrathecal morphine during spinal

anesthesia for joint replacement, where it provides extended postoperative pain relief.¹⁰ Despite its efficacy, morphine is associated with higher rates of PONV and pruritus compared with more lipophilic opioids.

Although oral formulations of morphine are available in both immediate-release and extended-release preparations, these are not routinely used in the acute perioperative or immediate postoperative setting. The intravenous route remains the preferred method for perioperative administration due to its predictable pharmacokinetics, titratability, and reliability in managing acute postoperative pain following orthopedic surgery.

REMIFENTANYL

Remifentanyl is an ultra-short-acting synthetic opioid with potency comparable to fentanyl and approximately 100 times that of morphine.^{2,6} It is uniquely metabolized by nonspecific plasma and tissue esterases, producing rapid hydrolysis independent of hepatic or renal function.^{5,6} This results in a fixed context-sensitive half-time of 3 to 6 minutes regardless of infusion duration, even after prolonged infusions.⁶ Its primary carboxylic acid metabolite is essentially inactive, and metabolism does not involve plasma cholinesterase, making remifentanyl safe in pseudocholinesterase deficiency.^{5,6}

A low pKa allows rapid blood-brain barrier penetration and fast plasma-effect site equilibration, with pharmacokinetics minimally affected by age or organ dysfunction.^{5,6} These properties enable precise titration and rapid, predictable emergence for cases prioritizing early neurologic assessment and mobilization.¹⁰ Remifentanyl-based TIVA provides stable hemodynamics and reduces volatile anesthetic requirements.^{6,10}

However, because remifentanyl's analgesic effects dissipate abruptly upon discontinuation, a transition to longer-acting analgesics must be established before the infusion is stopped. Failure to do so may result in severe rebound pain and increased postoperative opioid requirements.¹ In addition, remifentanyl has been associated with opioid-induced hyperalgesia (OIH), a phenomenon characterized by heightened pain sensitivity following opioid exposure. Importantly, clinicians should avoid misattributing postoperative pain solely to OIH, as inadequate intraoperative dosing, insufficient multimodal analgesia, or abrupt cessation without appropriate analgesic bridging can produce a similar clinical picture. Careful analgesic planning, multimodal strategies, and appropriate opioid transition are essential to distinguish true OIH from undertreated pain and to optimize postoperative outcomes.

HYDROMORPHONE

Hydromorphone is a semi-synthetic opioid derived from morphine and is approximately four to seven times more potent on a milligram basis. It has a relatively rapid onset and intermediate duration of action, characteristics that have contributed to its widespread use for postoperative pain management in orthopedic patients.¹¹ Hydromor-

phone produces less histamine release than morphine, which may result in improved tolerability.

In orthopedic practice, hydromorphone is commonly administered intravenously intraoperatively and in the immediate postoperative period to provide effective analgesia following major surgical procedures. It is frequently incorporated into patient-controlled analgesia (PCA) regimens after operations such as total knee arthroplasty and spine surgery. Comparative studies have demonstrated analgesic efficacy similar to morphine, with some evidence of reduced pruritus and nausea.¹² Due to its higher potency, careful dosing and monitoring are essential for minimizing respiratory depression.

Although an oral formulation of hydromorphone is available, it is less commonly used in routine postoperative pain management compared with other short-acting oral opioids such as hydrocodone. As a result, hydromorphone is most frequently utilized in the perioperative setting via the intravenous route, where its predictable onset, potency, and titratability make it a valuable option for managing moderate to severe acute postoperative pain.

OXYCODONE

Oxycodone is a semi-synthetic opioid frequently used in oral formulations for postoperative pain control. Its relatively high oral bioavailability makes it particularly useful for transitioning patients from intravenous to oral analgesia following orthopedic surgery.¹³ Oxycodone provides effective analgesia for moderate to severe pain and is commonly included in standardized postoperative pathways.

Clinical comparisons between oral oxycodone and oral morphine in orthopedic populations have demonstrated similar pain control, with some studies reporting higher patient satisfaction with oxycodone, potentially due to more predictable absorption and fewer gastrointestinal adverse effects.¹⁴ Nevertheless, oxycodone shares class-specific opioid risks and requires judicious prescribing.

SUFENTANIL

Sufentanil is a highly potent synthetic opioid, estimated to be five to ten times more potent than fentanyl. Its rapid onset and short context-sensitive half-time make it suitable for prolonged and complex orthopedic procedures requiring consistent intraoperative analgesia.¹⁵ Sufentanil is most commonly administered as a continuous infusion under close anesthetic supervision.

In major orthopedic surgeries, including revision arthroplasty and complex spine procedures, sufentanil-based regimens have been associated with reduced intraoperative opioid requirements and stable hemodynamics when compared with fentanyl-based techniques.¹⁶ The drug's potency necessitates careful titration and vigilant monitoring.

In clinical practice, sufentanil is used almost exclusively via the intravenous route for intraoperative analgesia and is not routinely employed for postoperative pain management. Its role is primarily limited to the operating room, where its rapid onset, potency, and infusion-based admin-

istration allow for precise titration during periods of intense surgical stimulation.

METHADONE

Methadone is a long-acting synthetic opioid with unique pharmacologic properties, including N-methyl-D-aspartate (NMDA) receptor antagonism and inhibition of serotonin and norepinephrine reuptake. These additional mechanisms may confer advantages in managing severe and opioid-tolerant pain states.¹⁷ Methadone's long and variable half-life allows for prolonged analgesia but also introduces the risk of delayed respiratory depression.

In orthopedic anesthesia, interest in methadone has increased due to evidence that a single intraoperative dose administered at induction can provide extended postoperative analgesia. Studies in spine and joint replacement surgery have demonstrated reduced postoperative opioid consumption and improved pain scores compared with short-acting opioid regimens.¹⁸ QT interval prolongation remains a concern, underscoring the importance of appropriate patient selection and monitoring.

Although methadone is available in oral formulations, these are primarily used in the outpatient setting for chronic pain management or opioid use disorder and are not routinely recommended for acute perioperative analgesia.¹⁷ Initiation of oral methadone requires specialized knowledge of its complex pharmacokinetics, drug-drug interactions, and cardiac risks, and patients should not be started on methadone unless managed by a pain management specialist or clinician with expertise in methadone dosing and monitoring.

INTRAOPERATIVE VERSUS POSTOPERATIVE OPIOID USE

Opioid selection in orthopedic surgery varies according to the perioperative phase. Intraoperatively, rapid onset, ease of titration, and hemodynamic stability are prioritized, favoring agents such as fentanyl and sufentanil. Postoperatively, longer-acting opioids including morphine, hydromorphone, oxycodone, and methadone are used to provide sustained analgesia and facilitate participation in rehabilitation.¹⁹

ADVERSE EFFECTS OF OPIOIDS IN ORTHOPEDIC PATIENTS

Opioid-related adverse effects remain a major limitation in orthopedic populations. Respiratory depression is the most serious complication and requires vigilant monitoring, particularly in elderly patients and those with obstructive sleep apnea.²⁰ PONV, pruritus, ileus, urinary retention, and sedation are also common and may delay recovery and discharge.

Table 1. Pharmacologic Characteristics of Commonly Used Opioids

Opioid	Relative Potency	Onset	Duration	Typical Role
Fentanyl	~100× morphine	Rapid	Short	Intraoperative
Morphine	1×	Moderate	Long	Postoperative
Remifentanyl	~100× morphine	Rapid	Ultra-Short	Intraoperative
Hydromorphone	4–7×	Moderate	Intermediate	Postoperative
Oxycodone	1–1.5× (oral)	Moderate	Intermediate	Postoperative oral
Sufentanil	~500×	Rapid	Short	Intraoperative
Methadone	Variable	Moderate	Very long	Extended analgesia

Table 2. Common Opioid-Related Adverse Effects and Mitigation Strategies

Adverse Effect	Clinical Impact	Management
Respiratory depression	Life-threatening	Naloxone, monitoring
PONV	Delayed recovery	Antiemetics
Pruritus	Patient discomfort	Antihistamines
Ileus	Delayed feeding	Early mobilization
Sedation	Fall risk	Dose adjustment

Table 3. Common Components of Multimodal Analgesia in Orthopedic Surgery

Adjunct	Mechanism	Clinical Benefit
Acetaminophen	Central COX inhibition	Reduced opioid use
NSAIDs	Anti-inflammatory	Improved pain scores
Gabapentinoids	Neuromodulation	Reduced hyperalgesia
Regional anesthesia	Nerve blockade	Targeted analgesia
Ketamine	NMDA antagonism	Opioid sparing

MULTIMODAL ANALGESIA AND OPIOID-SPARING STRATEGIES

Contemporary orthopedic anesthesia increasingly emphasizes multimodal analgesia, combining opioids with non-opioid medications and regional techniques to enhance analgesia while reducing opioid exposure.²¹ This approach has been shown to improve pain control, reduce opioid-related adverse effects, and facilitate early mobilization. See [Table 3](#) for list of commonly used multimodal analgesic agents, their mechanisms, and the clinical benefits.

DISCUSSION

Effective perioperative pain management in orthopedic surgery requires a careful balance between achieving adequate analgesia and minimizing opioid-related adverse ef-

Table 4. Factors Influencing Opioid Selection in Orthopedic Surgery

Factor	Clinical Relevance
Patient age	Altered pharmacokinetics
Renal function	Metabolite accumulation
Opioid tolerance	Higher dosing needs
Procedure duration	Choice of short vs long acting
Comorbidities	Risk of adverse effects

fects. While opioids remain indispensable for managing moderate to severe postoperative pain, increasing awareness of their risks has shifted clinical practice toward more judicious and individualized use. Contemporary orthopedic anesthesia therefore emphasizes thoughtful opioid selection, dose minimization, and integration with multimodal analgesic strategies.

One important consideration is the variety and complexity of orthopedic patient populations. Elderly patients undergoing joint arthroplasty often exhibit altered pharmacokinetics, increased sensitivity to opioids, and higher prevalence of comorbidities such as obstructive sleep apnea and renal dysfunction. These factors increase susceptibility to respiratory depression and delirium, underscoring the importance of selecting agents with predictable profiles and careful titration.²² Conversely, younger trauma patients and those with pre-existing opioid exposure may require higher doses or longer-acting agents to achieve adequate analgesia, highlighting the need for individualized regimens rather than standardized dosing. See [Table 4](#) for various factors influencing the choice of opioids in the orthopedic operating rooms as well as their clinical relevance.

Procedure-specific pain trajectories further influence opioid utilization. Total knee arthroplasty and spine surgery are consistently associated with high postoperative pain intensity and prolonged analgesic requirements, whereas minimally invasive orthopedic procedures may require only short-term opioid therapy. Evidence suggests that aligning opioid choice with anticipated pain duration improves patient comfort while reducing unnecessary exposure.²³ For example, the intraoperative use of methadone in spine surgery has demonstrated sustained postoperative analgesia and reduced opioid consumption,

suggesting that longer-acting opioids may be advantageous in select high-pain procedures when used appropriately.¹⁸

Another evolving aspect of orthopedic opioid use is the recognition of opioid-induced hyperalgesia, particularly with high-dose or prolonged administration of short-acting opioids such as fentanyl and remifentanyl. This phenomenon may contribute to increased postoperative pain and opioid requirements, complicating recovery.²⁴ Agents with NMDA receptor antagonism, such as methadone and ketamine, may mitigate this effect and represent an area of growing interest in orthopedic anesthesia practice.

The role of multimodal analgesia cannot be overstated. Numerous studies have demonstrated that combining opioids with non-opioid analgesics and regional anesthesia techniques reduces total opioid consumption, improves pain scores, and facilitates earlier mobilization.^{1,21} Peripheral nerve blocks, periarticular injections, and neuraxial techniques are particularly effective in orthopedic surgery and may substantially reduce reliance on systemic opioids.²⁵ Importantly, multimodal strategies also align with broader public health efforts aimed at reducing postoperative opioid prescribing and subsequent risk of long-term use.²⁶

Despite these advances, variability in opioid prescribing practices remains substantial across institutions and providers. This variability reflects differences in training, institutional culture, and patient expectations. Standardized, evidence-based pathways tailored to specific orthopedic procedures have been shown to reduce opioid use without compromising pain control and may serve as an effective strategy for improving consistency and safety.²⁷ Continued education of clinicians and patients regarding realistic postoperative pain expectations and safe opioid use is equally essential.

Future research should focus on identifying optimal opioid selection and dosing strategies for specific orthopedic procedures, evaluating long-term outcomes associated with perioperative opioid exposure, and refining multimodal protocols.

CONCLUSIONS

Opioids continue to play a central role in perioperative pain management within orthopedic operating rooms, reflecting the substantial pain burden associated with many orthopedic procedures. A detailed understanding of the pharmacologic properties, clinical applications, and limitations of commonly used opioids including fentanyl, morphine, remifentanyl, hydromorphone, oxycodone, sufentanyl, and methadone is essential for optimizing analgesic care.

Modern orthopedic anesthesia increasingly favors individualized opioid use integrated within multimodal analgesia frameworks. Such approaches allow clinicians to achieve effective pain control while minimizing opioid-related adverse effects and reducing overall opioid exposure.

Ultimately, improving perioperative pain management in orthopedic surgery requires a balanced, evidence-based approach that incorporates opioid stewardship principles, procedure-specific strategies, and patient-centered care. Ongoing research, standardized clinical pathways, and interdisciplinary collaboration will be essential to further refine opioid use and enhance recovery for orthopedic patients.

Submitted: February 09, 2026 EDT. Accepted: February 16, 2026 EDT. Published: March 12, 2026 EDT.

REFERENCES

1. Kehlet H, Dahl JB. The value of “multimodal” or “balanced analgesia” in postoperative pain treatment. *Anesth Analg*. 1993;77(5):1048-1056. doi:[10.1213/0000539-199311000-00030](https://doi.org/10.1213/0000539-199311000-00030). PMID:8105724
2. Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. *Pain Physician*. 2008;11(2 Suppl):S133-53. doi:[10.36076/ppj.2008/11/S133](https://doi.org/10.36076/ppj.2008/11/S133). PMID:18443637
3. Dahan A, Aarts L, Smith TW. Incidence, Reversal, and Prevention of Opioid-induced Respiratory Depression. *Anesthesiology*. 2010;112(1):226-238. doi:[10.1097/ALN.0b013e3181c38c25](https://doi.org/10.1097/ALN.0b013e3181c38c25). PMID:20010421
4. Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies--tackling the opioid-overdose epidemic. *N Engl J Med*. 2014;370(22):2063-2066. doi:[10.1056/NEJMp1402780](https://doi.org/10.1056/NEJMp1402780). PMID:24758595
5. Smith HS. Opioid metabolism. *Mayo Clin Proc*. 2009;84(7):613-624. doi:[10.1016/S0025-6196\(11\)60750-7](https://doi.org/10.1016/S0025-6196(11)60750-7). PMID:19567715
6. Inturrisi CE. Clinical pharmacology of opioids for pain. *Clin J Pain*. 2002;18(4 Suppl):S3-13. doi:[10.1097/00002508-200207001-00002](https://doi.org/10.1097/00002508-200207001-00002). PMID:12479250
7. Scholz J, Steinfath M, Schulz M. Clinical pharmacokinetics of alfentanil, fentanyl and sufentanil. An update. *Clin Pharmacokinet*. 1996;31(4):275-292. doi:[10.2165/00003088-199631040-00004](https://doi.org/10.2165/00003088-199631040-00004). PMID:8896944
8. Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesth Analg*. 2006;102(6):1884-1898. doi:[10.1213/01.ANE.0000219597.16143.4D](https://doi.org/10.1213/01.ANE.0000219597.16143.4D). PMID:16717343
9. Glare PA, Walsh TD. Clinical pharmacokinetics of morphine. *Ther Drug Monit*. 1991;13(1):1-23. doi:[10.1097/00007691-199101000-00001](https://doi.org/10.1097/00007691-199101000-00001). PMID:2057987
10. Rawal N. Current issues in postoperative pain management. *Eur J Anaesthesiol*. 2016;33(3):160-171. doi:[10.1097/EJA.0000000000000366](https://doi.org/10.1097/EJA.0000000000000366). PMID:26509324
11. Gulur P, Koury K, Arnstein P, et al. Morphine versus Hydromorphone: Does Choice of Opioid Influence Outcomes? *Pain Res Treat*. 2015;2015:482081. doi:[10.1155/2015/482081](https://doi.org/10.1155/2015/482081). PMID:26609431
12. DiGiusto M, Bhalla T, Martin D, Foerschler D, Jones MJ, Tobias JD. Patient-controlled analgesia in the pediatric population: morphine versus hydromorphone. *J Pain Res*. 2014;7:471-475. doi:[10.2147/JPR.S64497](https://doi.org/10.2147/JPR.S64497). PMID:25152630
13. Cheung CW, Ching Wong SS, Qiu Q, Wang X. Oral Oxycodone for Acute Postoperative Pain: A Review of Clinical Trials. *Pain Physician*. 2017;20(2S):SE33-SE52. doi:[10.36076/ppj.2017.sE52](https://doi.org/10.36076/ppj.2017.sE52). PMID:28226340
14. Guo KK, Deng CQ, Lu GJ, Zhao GL. Comparison of analgesic effect of oxycodone and morphine on patients with moderate and advanced cancer pain: a meta-analysis. *BMC Anesthesiol*. 2018;18(1):132. doi:[10.1186/s12871-018-0583-8](https://doi.org/10.1186/s12871-018-0583-8). PMID:30249205
15. Ilfeld BM. Continuous peripheral nerve blocks: a review of the published evidence. *Anesth Analg*. 2011;113(4):904-925. doi:[10.1213/ANE.0b013e3182285e01](https://doi.org/10.1213/ANE.0b013e3182285e01). PMID:21821511
16. Hassani V, Movassaghi G, Safaian R, et al. Bupivacaine-sufentanil versus bupivacaine-fentanyl in spinal anesthesia of patients undergoing lower extremity surgery. *Anesth Pain Med*. 2014;4(2):e12091. doi:[10.5812/aapm.12091](https://doi.org/10.5812/aapm.12091). PMID:24829809
17. Brown P, Ryder A, Robinson C, Valenti K, Phung K, Hasoon J. Methadone for Chronic Pain: A Review of Pharmacology, Efficacy, and Safety Concerns. *Health Psychol Res*. 2025;13:129552. doi:[10.52965/001c.129552](https://doi.org/10.52965/001c.129552). PMID:40041687
18. Murphy GS, Szokol JW, Avram MJ, et al. Clinical Effectiveness and Safety of Intraoperative Methadone in Patients Undergoing Posterior Spinal Fusion Surgery: A Randomized, Double-blinded, Controlled Trial. *Anesthesiology*. 2017;126(5):822-833. doi:[10.1097/ALN.0000000000001609](https://doi.org/10.1097/ALN.0000000000001609). PMID:28418966
19. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116(2):248-273. doi:[10.1097/ALN.0b013e31823c1030](https://doi.org/10.1097/ALN.0b013e31823c1030). PMID:22227789
20. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ*. 2000;321(7275):1493. doi:[10.1136/bmj.321.7275.1493](https://doi.org/10.1136/bmj.321.7275.1493). PMID:11118174

21. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg*. 2002;183(6):630-641. doi:[10.1016/S0002-9610\(02\)00866-8](https://doi.org/10.1016/S0002-9610(02)00866-8). PMID:12095591
22. Marcantonio ER. Delirium in Hospitalized Older Adults. *N Engl J Med*. 2017;377(15):1456-1466. doi:[10.1056/NEJMcp1605501](https://doi.org/10.1056/NEJMcp1605501). PMID:29020579
23. Lavand'homme P. Transition from acute to chronic pain after surgery. *Pain*. 2017;158(Suppl 1):S50-S54. doi:[10.1097/j.pain.0000000000000809](https://doi.org/10.1097/j.pain.0000000000000809). PMID:28134653
24. Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. *Anesthesiology*. 2006;104(3):570-587. doi:[10.1097/00000542-200603000-00025](https://doi.org/10.1097/00000542-200603000-00025). PMID:16508405
25. Hasoon J, Nguyen A. Regional Anesthesia for Orthopedic Surgeries: A Guide for Upper and Lower Extremity Procedures. *Orthop Rev (Pavia)*. 2025;17:133570. doi:[10.52965/001c.133570](https://doi.org/10.52965/001c.133570). PMID:40176923
26. 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(6):e170504. doi:[10.1001/jamasurg.2017.0504](https://doi.org/10.1001/jamasurg.2017.0504). PMID:28403427
27. Goesling J, Moser SE, Zaidi B, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. *Pain*. 2016;157(6):1259-1265. doi:[10.1097/j.pain.0000000000000516](https://doi.org/10.1097/j.pain.0000000000000516). PMID:26871536