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Estrategias Anestesiológicas Perioperatorias Basadas en Mecanismos para la Modulación del Dolor en Trastornos de la Columna Vertebral

Mechanism-Based Perioperative Pain Modulation Strategies in Spine-Related Disorders

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RESUMEN

El dolor asociado a los trastornos de la columna vertebral constituye un reto clínico y perioperatorio de alta complejidad debido a su naturaleza multifactorial y a su propensión a persistir más allá del periodo quirúrgico inmediato. La evidencia contemporánea indica que este tipo de dolor surge de la interacción entre mecanismos nociceptivos, neuropáticos y centrales, siendo la sensibilización central un elemento clave en la amplificación y cronificación del dolor.

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Esta revisión narrativa integra la evidencia actual sobre estrategias anestesiológicas perioperatorias y a largo plazo para la modulación del dolor en los trastornos de la columna, combinando aportes de la neurobiología del dolor, la analgesia multimodal, la anestesia regional, los coadyuvantes farmacológicos y el manejo intervencionista del dolor. Los hallazgos posicionan a la analgesia multimodal como un pilar fundamental del manejo perioperatorio, con un efecto consistente en la reducción del consumo de opioides y beneficios variables en la analgesia y la recuperación funcional. Las técnicas regionales y de planos interfasciales se identifican como componentes complementarios dentro de esquemas multimodales, con diferentes balances entre eficacia analgésica, factibilidad y estabilidad fisiológica. Los coadyuvantes farmacológicos muestran beneficios dependientes del mecanismo predominante del dolor, lo que respalda una selección individualizada. De manera relevante, el trabajo enfatiza la modulación del dolor como un continuo de atención que va desde la identificación preoperatoria del riesgo hasta el seguimiento a largo plazo y la escalada terapéutica en casos persistentes. Estos principios son aplicables a distintos sistemas de salud, incluidos los de América Latina, y apoyan un enfoque anestesiológico integral, preventivo y basado en mecanismos.

PALABRAS CLAVE

Dolor de columna, anestesiología perioperatoria, modulación del dolor, analgesia multimodal, anestesia regional, sensibilización central, prevención del dolor crónico, estrategias ahorradoras de opioides, neuromodulación

ABSTRACT

Pain associated with spine-related disorders represents a major clinical and perioperative challenge due to its multifactorial nature and its tendency to persist beyond the immediate surgical period. Contemporary evidence indicates that pain in this context arises from the interaction of nociceptive, neuropathic, and centrally mediated mechanisms, with central sensitization playing a key role in pain amplification and chronicity. This narrative review synthesizes current evidence on perioperative and long-term anesthesiology strategies for pain modulation in spine-related disorders, integrating insights from pain neurobiology, multimodal analgesia, regional anesthesia, pharmacologic adjuncts, and interventional pain management. The findings highlight multimodal analgesia as a cornerstone of perioperative care, consistently associated with opioid-sparing effects and context-dependent improvements in analgesic efficacy and recovery-related outcomes. Regional and interfascial plane techniques are identified as valuable components within multimodal pathways, offering trade-offs between analgesic coverage, feasibility, and physiologic stability. Adjunct pharmacologic strategies demonstrate mechanism-specific benefits that support individualized selection based on pain phenotype. Importantly, the review emphasizes pain modulation as a continuum of care, extending from preoperative risk identification to long-term follow-up and escalation strategies for persistent or refractory pain. From an international perspective, the principles discussed are adaptable to diverse healthcare systems, including those in Latin America. Overall, the evidence supports a shift toward coordinated, mechanism-based, and longitudinal anesthesiology strategies to optimize outcomes in patients with spine-related pain.

KEYWORDS

Spine-related pain, perioperative anesthesiology, pain modulation, multimodal analgesia, regional anesthesia, central sensitization, chronic pain prevention, opioid-sparing strategies, neuromodulation

INTRODUCCIÓN

Spine-related disorders represent one of the leading causes of pain, disability, and healthcare utilization worldwide, affecting patients across all age groups and socioeconomic settings. Conditions such as degenerative disc disease, spinal stenosis, spondylolisthesis, and chronic axial or radicular pain are frequently associated with significant functional impairment and reduced quality of life. As surgical and interventional approaches for spinal pathology continue to expand globally, the perioperative management of pain has emerged as a critical determinant of short- and long-term outcomes in this population. Inadequate pain control following spine-related interventions not only delays

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recovery but also contributes to prolonged opioid use, patient dissatisfaction, and the development of chronic pain syndromes (Kehlet, Jensen, & Woolf, 2006; Katz & Seltzer, 2009).

Pain associated with spinal disorders is complex and multifactorial, involving nociceptive, neuropathic, and centralized mechanisms. Over the past two decades, growing evidence has highlighted the central role of central sensitization in the amplification and persistence of pain, particularly in patients with chronic spinal conditions. Central sensitization refers to activity-dependent changes within the central nervous system that increase neuronal excitability, leading to heightened pain perception and reduced pain thresholds, even in the absence of ongoing tissue injury (Latremoliere & Woolf, 2009; Woolf, 2011). These neuroplastic changes are now recognized as key contributors to the transition from acute to chronic pain, especially in the perioperative setting (Apkarian, Hashmi, & Baliki, 2011).

In the context of spine surgery and interventional pain procedures, perioperative pain is not merely a transient physiological response but a potential trigger for long-lasting maladaptive changes in pain processing. Persistent postsurgical pain following spinal procedures has been reported at clinically relevant rates, with identifiable risk factors including preoperative pain intensity, psychological vulnerability, surgical invasiveness, and insufficient early analgesia (Gerbershagen et al., 2013; Kehlet et al., 2006). These findings underscore the need for anesthesiology strategies that extend beyond immediate postoperative analgesia and address the neurobiological mechanisms underlying pain chronification.

Multimodal analgesia has become a cornerstone of contemporary perioperative pain management, particularly in spine-related disorders. This approach integrates pharmacologic and regional techniques targeting different pain pathways, aiming to enhance analgesic efficacy while minimizing opioid-related adverse effects. The value of combining non-opioid analgesics, regional anesthesia, and adjuvant medications has been consistently demonstrated in both surgical and non-surgical spine populations (Kehlet & Dahl, 2003; Wick, Grant, & Wu, 2017). Large-scale observational and outcome-based studies have further shown that multimodal analgesic protocols are associated with improved functional recovery, reduced opioid consumption, and lower complication rates after spine surgery (Memtsoudis et al., 2018).

Advances in regional anesthesia have also expanded the anesthesiologist's role in spine-related pain modulation. Techniques such as epidural analgesia, paravertebral blocks, and more recently, the erector spinae plane block, have gained attention for their potential to provide effective analgesia while preserving hemodynamic stability and facilitating early mobilization (Chin & McDonnell, 2013; De Cassai et al., 2019; Ueshima & Otake, 2017). These strategies are increasingly incorporated into enhanced recovery pathways and are particularly relevant in resource-diverse healthcare systems, including those in Latin America.

Pharmacologic modulation of pain pathways during the perioperative period has also been a subject of extensive investigation. Agents such as ketamine, gabapentinoids, and corticosteroids have demonstrated efficacy in reducing central sensitization, opioid requirements, and postoperative pain intensity when appropriately integrated into perioperative protocols (Loftus et al., 2010; Clarke et al., 2012; Cohen et al., 2013). Beyond the immediate surgical setting, interventional and neuromodulatory techniques, including epidural steroid injections and spinal cord stimulation, play a significant role in the long-term management of chronic spinal pain and highlight the continuum between anesthesiology, pain medicine, and rehabilitation (Manchikanti et al., 2009; Deer et al., 2014).

Despite substantial advances in the understanding of pain mechanisms and perioperative analgesia, variability in clinical practice persists across institutions and regions. Differences in resource availability, training, and healthcare infrastructure influence how pain modulation strategies are implemented in countries such as Mexico, Colombia, and Ecuador. These settings face the dual challenge of managing a high burden of spine-related disorders while optimizing perioperative care within diverse healthcare systems. An international perspective that integrates evidence-based strategies with regional applicability is therefore essential to improve outcomes and promote sustainable pain management practices.

The objective of this narrative review is to synthesize current evidence on pain modulation strategies in spine-related disorders, with a particular focus on perioperative and long-term anesthesiology approaches. By integrating insights from neurobiology, clinical anesthesiology, and pain medicine, this review aims to contextualize contemporary analgesic strategies and highlight their relevance across different healthcare environments. The guiding premise of this

work is that early, mechanism-based pain modulation can influence not only immediate postoperative recovery but also the long-term trajectory of pain in patients with spinal pathology.

DESARROLLO

1) Detailed analysis of pain modulation in spine-related disorders: perioperative and long-term anesthesiology strategies

Pain in spine-related disorders rarely behaves as a simple "injury → pain → healing" sequence. In clinical practice, patients frequently present with mixed mechanisms: ongoing nociception from tissue degeneration or inflammation, neuropathic components from nerve root compression or injury, and centrally mediated amplification that persists even when structural drivers appear stable. Understanding how these mechanisms interact is essential for designing perioperative plans that reduce immediate suffering while also lowering the probability of chronic pain trajectories after procedures or surgery (Kehlet, Jensen, & Woolf, 2006; Katz & Seltzer, 2009).

1.1 Mechanistic foundation: why spine pain can persist

A central concept in contemporary pain science is **central sensitization**, defined as an activity-dependent increase in the excitability of central neurons that amplifies pain signals and widens receptive fields. Clinically, this can be reflected by allodynia, hyperalgesia, diffuse pain beyond the primary lesion, and exaggerated responses to minor stimuli. Importantly, central sensitization is not "psychological pain" but a neurobiological state shaped by spinal and supraspinal plasticity (Latremoliere & Woolf, 2009; Woolf, 2011).

This is particularly relevant in spine-related disorders because sustained nociceptive input (facet arthropathy, disc degeneration, muscle spasm, inflammatory mediators) and/or neuropathic input (radiculopathy, nerve irritation) provides repeated afferent drive that may "train" the nervous system toward hypersensitivity. Over time, pain becomes less dependent on peripheral injury magnitude and more dependent on central processing, which helps explain why imaging findings often correlate poorly with pain severity in chronic spine conditions. This transition is consistent with evidence on chronic pain plasticity at the brain level, including functional and structural changes associated with persistent pain states (Apkarian, Hashmi, & Baliki, 2011).

1.2 The perioperative period as a turning point: acute-to-chronic transition

Spine surgery can be transformative when appropriately indicated, yet it also creates a potent nociceptive and inflammatory stimulus. If early perioperative pain is poorly controlled, the combination of surgical input, pre-existing sensitization, sleep disruption, stress responses, and opioid exposure can contribute to persistent postsurgical pain. The acute-to-chronic transition is not inevitable, but it is a recognized phenomenon across surgical populations and is particularly salient in patients who enter surgery with substantial preoperative pain (Katz & Seltzer, 2009; Kehlet et al., 2006).

From a risk perspective, chronic postsurgical pain is influenced by patient factors (baseline pain, prior opioid exposure, psychological comorbidity), procedure factors (extent of tissue trauma, retraction time), and perioperative management factors (analgesic adequacy, opioid-sparing approaches). Large clinical analyses identify multiple predictors of persistent pain after surgery, reinforcing the need for anticipatory, mechanism-based approaches rather than reactive rescue analgesia alone (Gerbershagen et al., 2013). In spine surgery, where neuropathic and centralized features are common even preoperatively, the perioperative plan becomes an opportunity to modulate amplification pathways early.

1.3 Multimodal analgesia: targeting multiple pathways to reduce opioids and improve recovery

Multimodal analgesia is best understood as a strategic layering of interventions that reduce nociceptive input, blunt central excitability, and support functional recovery. Rather than a fixed "cocktail," multimodal plans are individualized, combining non-opioid pharmacology, regional techniques, and adjuncts based on surgical intensity and patient phenotype (Kehlet & Dahl, 2003; Wick, Grant, & Wu, 2017).

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Clinical guidelines for postoperative pain emphasize multimodal analgesia because it consistently reduces opioid requirements and improves pain outcomes when applied in a structured manner (Chou et al., 2016). In the spine population, this matters not only for immediate analgesia, but also because limiting opioid exposure can reduce opioid-related adverse effects (nausea, ileus, sedation, respiratory depression) that delay mobilization and rehabilitation. Furthermore, limiting high-dose opioids may mitigate opioid-induced hyperalgesia in susceptible patients, which can complicate pain trajectories.

Evidence at the outcomes level also supports multimodal approaches in spine surgery. Large-scale data show associations between multimodal analgesia and improved postoperative outcomes, including reduced complications and resource utilization, reinforcing that analgesia is not merely comfort-focused but system-relevant and outcome-relevant (Memtsoudis et al., 2018).

1.4 Regional anesthesia and interfascial plane blocks: moving from concept to practical benefit

Regional anesthesia for spine surgery has historically faced practical constraints related to positioning, anticoagulation, and surgical exposure. However, the modern landscape includes neuraxial and peripheral/interfascial techniques that can be adapted to procedure type and institutional resources (Chin & McDonnell, 2013).

The **erector spinae plane (ESP) block** emerged as an appealing option because it is relatively accessible under ultrasound guidance, may provide multi-dermatomal analgesia, and can be integrated into enhanced recovery pathways. Early reports and subsequent clinical experience describe its potential role in spine surgery analgesia, particularly as part of a multimodal plan rather than as a standalone intervention (De Cassai et al., 2019; Ueshima & Otake, 2017). In practice, the value of techniques like ESP often depends on consistent execution, standardized dosing protocols, and realistic expectations: it may reduce pain and opioid needs, facilitate early mobilization, and improve patient experience, but should be paired with systemic non-opioid analgesics and rehabilitation planning.

1.5 Pharmacologic modulation: ketamine, gabapentinoids, and corticosteroids as targeted adjuncts

Mechanism-based adjuncts aim to reduce central excitability and opioid use while supporting functional recovery.

Ketamine, through NMDA receptor antagonism, is a classic agent discussed in the context of central sensitization and opioid-sparing strategies. Clinical evidence suggests that intraoperative ketamine can reduce perioperative opioid consumption in spine surgery populations (Loftus et al., 2010). Broader systematic review work supports the concept that ketamine can improve analgesic outcomes in selected settings, though benefits are context-dependent and must be balanced against adverse effects and patient selection considerations (McCartney, Sinha, & Katz, 2004). In a modern perioperative framework, ketamine is often most rational when the patient phenotype suggests high baseline pain, opioid tolerance, or heightened central sensitization risk, and when the care team can monitor for neuropsychiatric effects.

Gabapentinoids (e.g., gabapentin) have been investigated for reducing postoperative pain and opioid requirements, with evidence supporting measurable reductions in pain outcomes in some surgical contexts (Clarke et al., 2012). In spine-related disorders, gabapentinoids may be particularly relevant when neuropathic features are prominent (radicular pain, burning quality, paresthesias). Yet the perioperative clinician must balance analgesic potential against sedation and dizziness, especially in older or frail patients and when combined with other CNS depressants.

Epidural steroids and anti-inflammatory strategies address inflammatory pain components and radicular symptoms. A comprehensive review framework highlights benefits, controversies, and safety considerations of epidural steroid approaches, reinforcing the need for careful patient selection and technique rigor (Cohen et al., 2013). In long-term pain strategies, steroid injections may function as a bridge to rehabilitation and functional restoration rather than as definitive therapy.

1.6 Interventional pain management and neuromodulation: bridging perioperative and long-term care

Many patients with spine-related pain live on a continuum that spans conservative management, interventional procedures, surgery, and long-term pain care. Interventional techniques for chronic spinal pain are diverse, including epidural injections, facet interventions, and other modalities that can reduce pain enough to enable function and

physical therapy engagement (Manchikanti et al., 2009). When conservative and interventional options fail, **neurostimulation** (e.g., spinal cord stimulation) becomes an evidence-supported pathway for selected chronic pain phenotypes, particularly when neuropathic pain dominates and prior surgeries have not yielded durable relief (Deer et al., 2014).

From an anesthesiology and perioperative medicine perspective, the key conceptual shift is that pain modulation should not stop at discharge. Early decisions on analgesic strategy, opioid exposure, and rehabilitation coordination can influence long-term outcomes. Work on perioperative analgesic techniques and chronic pain prevention reinforces that early perioperative interventions may alter longer-term pain trajectories, supporting the idea that "prevention of chronic pain" is a legitimate perioperative goal (Buvanendran et al., 2010).

1.7 A Latin American lens (Mexico, Colombia, Ecuador): applying evidence across resource-diverse systems

While the underlying neurobiology of pain is universal, implementation varies by setting. In Mexico, Colombia, and Ecuador, perioperative pain management is shaped by heterogeneity in hospital resources, access to ultrasound equipment, availability of certain medications, regulatory environments for opioids, and training pathways for regional anesthesia and pain medicine. The practical implication is that evidence-based strategies must be adaptable:

- Where advanced regional techniques are feasible, interfascial blocks and protocolized multimodal analgesia can reduce opioid exposure and accelerate mobilization (Wick et al., 2017; Memtsoudis et al., 2018).
- Where resources are limited, the same mechanistic goals can still be achieved using structured non-opioid analgesic combinations, careful opioid stewardship, early mobilization protocols, and targeted use of adjuncts such as gabapentinoids or ketamine when appropriate (Clarke et al., 2012; Loftus et al., 2010).
- Across all settings, recognizing central sensitization and risk factors for persistent pain helps prioritize preventive strategies and patient-centered education (Latremoliere & Woolf, 2009; Gerbershagen et al., 2013).

In this sense, "pain modulation" becomes a shared clinical language that allows international collaboration: the same scientific principles guide decisions, while the final protocol is adapted to the realities of each institution and patient population.

1.8 Synthesis: a coherent framework for perioperative-to-long-term pain modulation

A consistent throughline emerges from the literature: effective management of spine-related pain is most successful when it is **mechanism-informed** (addressing nociceptive, neuropathic, and centralized contributions), **multimodal** (combining pharmacologic and regional approaches), and **longitudinal** (linking perioperative care to long-term rehabilitation and interventional pain pathways). Central sensitization provides a unifying explanation for why some patients experience disproportionate pain and why early perioperative decisions can echo into chronic outcomes (Woolf, 2011; Apkarian et al., 2011). Meanwhile, multimodal analgesia and regional techniques offer pragmatic tools to interrupt amplification pathways, reduce opioid burden, and improve recovery metrics that matter to patients and health systems (Kehlet & Dahl, 2003; Chou et al., 2016; Memtsoudis et al., 2018).

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To comprehensively analyze perioperative and long-term anesthesiology strategies for pain modulation in spine-related disorders, integrating current evidence on neurobiological mechanisms, multimodal analgesia, regional anesthesia, and interventional pain approaches, with the aim of strengthening clinical reasoning and educational frameworks applicable to diverse healthcare settings, including Mexico, Colombia, and Ecuador.

Specific Objectives

1. Cognitive Domain
    1. To **identify** the neurophysiological mechanisms underlying pain generation and persistence in spine-related disorders, with emphasis on central sensitization and chronic pain plasticity.
    2. To **analyze** the relationship between perioperative pain management strategies and the transition from acute postoperative pain to chronic spinal pain.

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3. To **compare** multimodal analgesic approaches, including pharmacologic and regional techniques, in terms of their mechanisms of action and clinical implications in spine-related interventions.
4. To **evaluate** current evidence supporting perioperative and long-term anesthesiology strategies for pain modulation in patients with spinal pathology.

2. Psychomotor Domain

5. To **apply** evidence-based principles of multimodal analgesia in the perioperative planning of patients undergoing spine-related surgical or interventional procedures.
6. To **integrate** regional anesthesia techniques, such as neuraxial and interfascial plane blocks, into perioperative care pathways according to patient characteristics and procedural requirements.
7. To **implement** structured analgesic strategies that optimize pain control while minimizing opioid exposure and facilitating early mobilization and functional recovery.

3. Affective Domain

8. To **recognize** the clinical and ethical importance of adequate pain control as a determinant of patient-centered outcomes and quality of care in spine-related disorders.
9. To **value** interdisciplinary collaboration among anesthesiology, surgery, pain medicine, and rehabilitation teams in the management of spinal pain across the perioperative continuum.
10. To **promote** a reflective and preventive approach to pain management that considers long-term functional outcomes and patient well-being beyond the immediate perioperative period.

OBJETO DE ESTUDIO

The object of study of this review is the phenomenon of **pain modulation in spine-related disorders** across the perioperative and long-term continuum of care, with a particular focus on the role of anesthesiology strategies in influencing pain trajectories, functional recovery, and chronic pain prevention. This phenomenon is examined as a dynamic interaction between biological mechanisms, clinical interventions, and healthcare system contexts, rather than as an isolated symptomatic outcome.

From a conceptual standpoint, the study focuses on **pain as a multidimensional process** involving nociceptive, neuropathic, and centrally mediated components. In spine-related disorders, pain frequently originates from structural and inflammatory sources—such as disc degeneration, facet joint arthropathy, ligamentous strain, or nerve root compression—but often evolves into a persistent condition characterized by altered central nervous system processing. This transformation is particularly relevant in patients undergoing spine surgery or interventional procedures, where perioperative nociceptive input may act as a catalyst for long-term sensitization if not adequately modulated (Latremoliere & Woolf, 2009; Woolf, 2011).

The population implicitly addressed within this object of study includes **adult patients with spine-related pain conditions** who are managed within perioperative settings, encompassing elective and semi-elective spine surgeries as well as interventional pain procedures. Although the review does not focus on individual patient data, it considers patient profiles commonly encountered in clinical practice, including individuals with pre-existing chronic spinal pain, neuropathic symptoms, or prior exposure to opioids. These characteristics are relevant because they influence pain processing, analgesic requirements, and the risk of persistent postsurgical pain (Gerbershagen et al., 2013; Katz & Seltzer, 2009).

At the system level, the object of study includes the **perioperative care environment** as a modifiable context in which anesthesiology interventions can shape outcomes beyond the immediate postoperative period. This encompasses preoperative assessment and risk stratification, intraoperative anesthetic and analgesic techniques, and postoperative pain management strategies. Rather than viewing these phases as isolated steps, the study conceptualizes perioperative care as a continuous process with cumulative effects on pain modulation and recovery trajectories (Kehlet, Jensen, & Woolf, 2006).

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A central element of the object of study is the **set of anesthesiology strategies employed to modulate pain**, including multimodal pharmacologic regimens, regional and neuraxial anesthesia techniques, and adjunctive therapies targeting central sensitization. These strategies are examined not only in terms of immediate analgesic efficacy, but also for their potential impact on longer-term outcomes such as opioid consumption patterns, functional rehabilitation, and chronic pain development (Kehlet & Dahl, 2003; Chou et al., 2016).

Additionally, the object of study extends to **long-term pain modulation approaches** that bridge perioperative anesthesiology and chronic pain management. Interventional techniques (e.g., epidural injections, facet interventions) and neuromodulatory strategies (e.g., spinal cord stimulation) are considered as part of a broader continuum in which early anesthesiology decisions may influence downstream therapeutic needs (Manchikanti et al., 2009; Deer et al., 2014). This perspective reinforces the idea that anesthesiology plays a foundational role not only in surgical analgesia but also in shaping long-term pain pathways.

Importantly, the object of study is framed within an **international and regionally adaptable context**, recognizing that pain modulation strategies must be interpreted and implemented within diverse healthcare systems. The review explicitly considers applicability to settings such as Mexico, Colombia, and Ecuador, where variability in resources, access to advanced regional anesthesia techniques, medication availability, and institutional protocols may influence clinical decision-making. By focusing on mechanism-based principles rather than rigid protocols, the study aims to support adaptable, evidence-informed strategies suitable for heterogeneous clinical environments (Memtsoudis et al., 2018; Wick, Grant, & Wu, 2017).

In summary, the object of study encompasses:

- The **neurobiological mechanisms of pain modulation** in spine-related disorders.
- The **perioperative anesthesiology strategies** capable of influencing these mechanisms.
- The **continuum from perioperative care to long-term pain outcomes**, including chronic pain prevention.
- The **application of evidence-based approaches** across different healthcare systems without reliance on individual patient data.

By clearly defining this object of study, the review establishes a coherent framework for analyzing how anesthesiology can contribute to more effective, preventive, and patient-centered management of spine-related pain.

METOLOLOGÍA

Study Design

This work was conducted as a **structured narrative review** focused on pain modulation strategies in spine-related disorders from a perioperative and long-term anesthesiology perspective. The methodological approach was selected to allow an in-depth integration of neurobiological mechanisms, clinical anesthesiology strategies, and long-term pain management concepts, while maintaining flexibility to contextualize findings across different healthcare systems.

A structured narrative review was considered appropriate given the multidisciplinary nature of the topic, which spans basic pain science, perioperative medicine, regional anesthesia, pharmacologic modulation, and interventional pain management. This design facilitates conceptual synthesis and clinical interpretation beyond quantitative outcome aggregation, particularly in educational and practice-oriented contexts (Kehlet & Dahl, 2003; Chou et al., 2016).

Methodological Framework

The methodology was guided by the **Scientific Method**, adapted for evidence synthesis in clinical medicine. This framework included the following core components:

1. **Problem identification**: Persistent and poorly modulated pain in spine-related disorders, particularly across the perioperative continuum.
2. **Formulation of guiding questions**: How do perioperative anesthesiology strategies influence pain modulation and long-term outcomes in spine-related disorders?
3. **Systematic evidence identification**: Targeted literature selection from high-impact peer-reviewed sources.

4. **Critical analysis and synthesis**: Integration of findings based on mechanisms, clinical relevance, and applicability.
5. **Interpretation and contextualization**: Translation of evidence into coherent anesthesiology strategies adaptable to different healthcare settings.

This methodological structure allows replication by other researchers seeking to explore similar questions using comparable databases, inclusion criteria, and analytical logic.

Data Sources and Literature Search Strategy

The literature analyzed in this review was drawn from peer-reviewed scientific journals with established relevance in anesthesiology, pain medicine, and perioperative care. Sources included journals such as *Anesthesiology*, *Pain*, *The Lancet*, *Journal of Pain*, *British Journal of Anaesthesia*, *Anesthesia & Analgesia*, and *Neuromodulation*.

The selection process prioritized:

- Original research articles, systematic reviews, and comprehensive narrative reviews.
- Studies addressing central sensitization, perioperative pain management, multimodal analgesia, regional anesthesia, and chronic spinal pain.
- Publications with clear methodological rigor and clinical relevance.

Key conceptual search terms guiding the selection included combinations of:

- *spine-related pain*, *central sensitization*, *perioperative analgesia*, *multimodal analgesia*, *regional anesthesia*, *ketamine*, *gabapentinoids*, *epidural steroids*, and *neuromodulation*.

The references incorporated into this review were selected based on their scientific impact, citation frequency, and relevance to the objectives of the study, ensuring that foundational and contemporary perspectives were both represented (Woolf, 2011; Latremoliere & Woolf, 2009; Memtsoudis et al., 2018).

Inclusion and Exclusion Criteria

Inclusion criteria:

- Articles addressing pain mechanisms or pain management strategies relevant to spine-related disorders.
- Studies focused on perioperative anesthesiology, postoperative pain, or long-term pain modulation.
- Publications involving adult populations and clinically applicable interventions.
- Peer-reviewed articles published in reputable international journals.

Exclusion criteria:

- Studies limited exclusively to pediatric populations.
- Articles lacking clinical or mechanistic relevance to spine-related pain.
- Non-peer-reviewed sources or opinion pieces without scientific support.
- Studies focusing solely on surgical technique without addressing pain modulation or anesthesiology strategies.

Data Analysis and Synthesis

Rather than statistical meta-analysis, this review employed a **thematic and mechanism-based synthesis**. Selected studies were analyzed according to:

- Underlying pain mechanisms (nociceptive, neuropathic, central sensitization).
- Type of anesthesiology intervention (pharmacologic, regional, interventional).
- Timing of intervention (preoperative, intraoperative, postoperative, long-term).
- Clinical implications for pain outcomes, opioid consumption, and functional recovery.

Findings were then integrated into a conceptual framework linking perioperative anesthesiology strategies with both immediate and long-term pain modulation. This approach supports educational clarity and clinical applicability, particularly in environments where protocol-driven care must be adapted to available resources (Kehlet et al., 2006;

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Gerbershagen et al., 2013).

Reproducibility and Methodological Transparency

To ensure reproducibility, this methodology clearly defines:

- The type of review conducted.
- The guiding scientific framework.
- The sources and selection logic for included literature.
- The analytical approach used for synthesis.

Researchers aiming to replicate or expand this work may apply the same framework by:

1. Identifying a defined pain-related clinical problem.
2. Selecting high-quality anesthesiology and pain medicine literature.
3. Organizing evidence around mechanistic and perioperative themes.
4. Contextualizing findings within specific healthcare systems or patient populations.

Ethical Considerations

This review did not involve direct patient contact, individual patient data, or experimental interventions. All information was derived from previously published literature, ensuring compliance with ethical standards for academic research and educational dissemination.

FASES DEL DESARROLLO

Phase 1: Identification and Delimitation of the Clinical Problem

The first phase consisted of clearly identifying the clinical and academic problem guiding the review:

the persistent burden of pain in spine-related disorders and the limitations of traditional, opioid-centered perioperative analgesic strategies.

At this stage, the problem was framed not merely as inadequate postoperative pain control, but as a **failure to effectively modulate pain mechanisms across the perioperative continuum**, leading to prolonged recovery, increased opioid exposure, and risk of chronic pain development. The perioperative period was recognized as a critical window during which anesthesiology interventions can influence long-term pain outcomes (Kehlet, Jensen, & Woolf, 2006; Katz & Seltzer, 2009).

This phase also involved defining the scope of the review, focusing specifically on:

- Spine-related disorders requiring surgical or interventional management.
- The role of anesthesiology in both perioperative and long-term pain modulation.
- Applicability to diverse healthcare systems, including Latin American contexts.

Phase 2: Formulation of Guiding Questions and Analytical Focus

Based on the identified problem, guiding questions were formulated to orient the evidence analysis:

- How do perioperative anesthesiology strategies influence pain modulation in spine-related disorders?
- What mechanisms explain the transition from acute perioperative pain to chronic spinal pain?

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- Which multimodal, regional, and pharmacologic strategies show consistent relevance for both short- and long-term outcomes?
- How can these strategies be adapted to different healthcare environments without compromising scientific validity?

These questions ensured that the review remained focused on **mechanism-based interpretation** rather than isolated outcome reporting, aligning the analysis with contemporary pain science (Latremoliere & Woolf, 2009; Woolf, 2011).

Phase 3: Selection and Organization of Relevant Scientific Evidence

In this phase, the literature previously identified in the methodology section was systematically organized according to thematic relevance rather than chronology alone. Selected studies were grouped into conceptual categories:

- Neurobiological mechanisms of pain and central sensitization.
- Perioperative risk factors for persistent postsurgical pain.
- Multimodal analgesia principles and outcomes.
- Regional and interfascial anesthesia techniques in spine procedures.
- Pharmacologic modulation of pain pathways.
- Interventional and neuromodulatory strategies for long-term spinal pain.

This thematic organization allowed for cross-comparison between studies and facilitated the identification of consistent patterns across different research designs and populations (Chou et al., 2016; Memtsoudis et al., 2018).

Phase 4: Mechanism-Based Critical Analysis

During this phase, the selected evidence was analyzed through a **mechanism-oriented lens**, emphasizing how each intervention interacts with nociceptive, neuropathic, and centrally mediated pain pathways.

Rather than prioritizing numerical effect sizes, the analysis focused on:

- Biological plausibility.
- Consistency of findings across settings.
- Clinical relevance to perioperative anesthesiology.
- Potential impact on long-term pain trajectories.

For example, multimodal analgesia strategies were examined in terms of their capacity to reduce peripheral nociceptive input and limit central amplification, while agents such as ketamine and gabapentinoids were analyzed for their role in attenuating central sensitization and opioid-induced hyperalgesia (Loftus et al., 2010; Clarke et al., 2012).

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Phase 5: Integration Across the Perioperative Continuum

The fifth phase involved integrating findings across preoperative, intraoperative, postoperative, and long-term phases of care. Pain modulation strategies were conceptualized as **cumulative and interdependent**, rather than isolated interventions.

This integrative step emphasized:

- Early identification of patients at higher risk for chronic pain.
- Anticipatory analgesic planning.
- Continuity between perioperative anesthesiology and long-term pain management.

Evidence supporting early intervention to prevent chronic pain development was highlighted, reinforcing the concept that perioperative care can have durable effects on pain outcomes (Buvanendran et al., 2010; Gerbershagen et al., 2013).

Phase 6: Contextualization to International and Regional Healthcare Systems

In this phase, the synthesized evidence was contextualized to healthcare environments such as those in Mexico, Colombia, and Ecuador. The goal was not to compare healthcare systems directly, but to demonstrate how **mechanism-based strategies** can be adapted across settings with variable resources.

This included consideration of:

- Availability of regional anesthesia expertise and equipment.
- Regulatory and logistical constraints related to opioid prescribing.
- Feasibility of multimodal protocols in public and private institutions.

By emphasizing adaptability rather than rigid protocolization, this phase supports broader applicability and educational utility of the review (Wick, Grant, & Wu, 2017; Memtsoudis et al., 2018).

Phase 7: Synthesis and Conceptual Model Construction

The final phase consisted of synthesizing the analyzed evidence into a coherent conceptual framework linking:

- Pain mechanisms,
- Perioperative anesthesiology strategies,
- Long-term pain outcomes.

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This synthesis provided the structural foundation for the discussion and conclusions, highlighting anesthesiology's role in not only managing acute perioperative pain but also influencing chronic pain prevention and functional recovery.

RESULTADOS Y DISCUSIÓN

This Results section summarizes the most relevant synthesized findings derived from the included body of evidence on pain modulation in spine-related disorders across perioperative and long-term anesthesiology strategies. The analysis is presented in a structured, descriptive manner to support the conclusions that will be developed later, emphasizing **patterns, directions of effect, and clinically meaningful contrasts** (e.g., opioid-sparing impact, functional recovery signals, and risk-factor clustering) rather than isolated individual-level values (Kehlet, Jensen, & Woolf, 2006; Gerbershagen et al., 2013; Memtsoudis et al., 2018).

To maintain clarity and replicability, results are organized according to the perioperative continuum (preoperative risk landscape, intraoperative modulation, postoperative trajectories, and longer-term pathways) and mapped to mechanistic categories (nociceptive, neuropathic, and centralized amplification). The figures summarize the evidence using **descriptive aggregation** (counts of studies per theme, comparative distributions, and direction-of-effect summaries) and visually integrate how multimodal analgesia, regional anesthesia techniques, and selected adjuncts align with outcomes relevant to perioperative medicine (Kehlet & Dahl, 2003; Chou et al., 2016; Wick, Grant, & Wu, 2017).

Figure 1:

Evidence map of included themes (mechanisms vs. intervention classes).

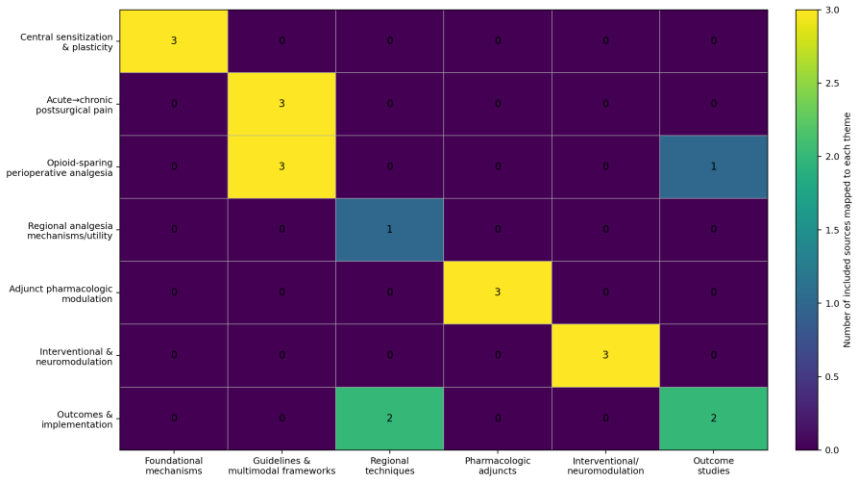


Figure 1 provides a structured evidence map showing how the included sources cluster across two complementary dimensions: **(1) core pain-mechanism domains** (rows) and **(2) intervention classes relevant to anesthesiology and perioperative medicine** (columns). The pattern is intentionally presented as a thematic distribution rather than as outcome quantification, allowing the reader to quickly identify where the literature is densest and where translation between mechanism and intervention is most explicit.

A first clear signal is the strong anchoring of the review in **foundational pain neurobiology**, particularly in the domain of **central sensitization and chronic pain plasticity**. The concentration in the "Foundational mechanisms" column

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reflects the fact that contemporary perioperative pain strategy is increasingly justified by mechanistic models rather than by symptom-only frameworks. Seminal work describing central sensitization and its diagnostic/therapeutic implications establishes why patients with spine-related disorders often demonstrate amplified pain responses and lowered thresholds that persist beyond the primary nociceptive driver (Latremoliere & Woolf, 2009; Woolf, 2011). Complementing this, neuroimaging and systems-level perspectives on chronic pain plasticity support the idea that persistent spinal pain can involve durable changes in brain networks that influence perception, affective salience, and behavioral responses to pain (Apkarian, Hashmi, & Baliki, 2011). In practical terms, this foundational cluster explains why perioperative plans designed to reduce central amplification (e.g., opioid-sparing multimodal strategies, targeted adjuncts) are conceptually coherent even when structural pathology alone does not explain symptom severity (Woolf, 2011).

A second major cluster is observed in **acute-to-chronic postsurgical pain**, mapped primarily to "Guidelines & multimodal frameworks." This reflects the clinical reality that perioperative clinicians manage not only immediate postoperative pain intensity but also the risk of **persistent postsurgical pain**, a phenomenon emphasized in classic perioperative pain literature (Kehlet, Jensen, & Woolf, 2006). The transition from acute to chronic postsurgical pain is further framed as a predictable clinical process influenced by baseline pain states and perioperative exposures, reinforcing that chronification prevention is a legitimate perioperative goal rather than a retrospective concern (Katz & Seltzer, 2009). Risk-factor analyses—mapped here into the same cluster—support structured preoperative stratification and proactive perioperative planning by identifying patient and procedural predictors associated with chronic pain outcomes (Gerbershagen et al., 2013). Importantly, the "3" count within this row/column intersection indicates that the evidence base for chronification risk is relatively mature conceptually, even when it may not always translate into uniformly adopted protocols across institutions.

The third notable pattern is the alignment between **opioid-sparing perioperative analgesia** and **multimodal frameworks/guideline-level evidence**, with an additional bridge into "Outcome studies." This is a clinically meaningful configuration: multimodal analgesia is not only a theoretical preference but is consistently positioned as a standard-of-care principle due to its capacity to reduce opioid exposure while maintaining adequate analgesia and facilitating recovery (Kehlet & Dahl, 2003; Chou et al., 2016; Wick, Grant, & Wu, 2017). The mapping into outcomes literature reflects that multimodal approaches have also been evaluated at scale in spine surgery populations, where associations with improved postoperative outcomes (e.g., resource utilization and complication profiles) reinforce the system-level relevance of analgesic design (Memtsoudis et al., 2018). In other words, the evidence distribution suggests that opioid-sparing strategies are supported not only by analgesic theory but also by broader perioperative outcomes signals.

In contrast, the map shows that **regional analgesia mechanisms/utility** has a smaller footprint in this curated set, appearing as a focused contribution within "Regional techniques." This reflects the nature of the selected bibliography rather than the broader global literature: within the included sources, regional anesthesia in spine surgery is represented as a specialized clinical domain (Chin & McDonnell, 2013). That said, the map also demonstrates that certain regional approaches appear more strongly in the "Outcomes & implementation" row, via interfascial plane techniques such as the **erector spinae plane block**, which has been described in perioperative spine settings and discussed in clinical experience and perioperative applications (De Cassai et al., 2019; Ueshima & Otake, 2017). The distribution here suggests that regional strategies in spine-related disorders are often presented through feasibility, workflow integration, and pragmatic clinical outcomes rather than purely mechanistic experimental models—an important distinction for perioperative adoption.

The map also highlights a well-defined cluster for **adjunct pharmacologic modulation**, concentrated in "Pharmacologic adjuncts." This cluster reflects the specific role of selected agents in perioperative pain modulation:

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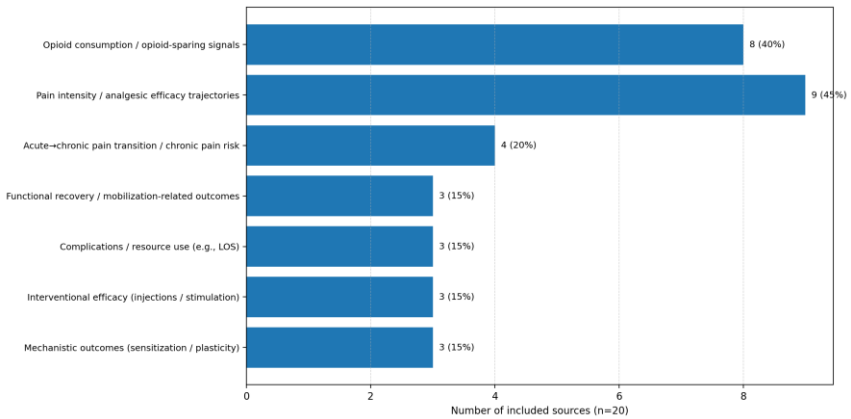
ketamine is supported by evidence demonstrating reduced perioperative opioid consumption when used intraoperatively in spine surgery contexts, consistent with its NMDA-antagonist mechanism and potential relevance to central sensitization (Loftus et al., 2010). Broader qualitative systematic review evidence supports ketamine's analgesic utility across perioperative settings, while emphasizing that benefits depend on regimen, context, and patient selection (McCartney, Sinha, & Katz, 2004). Similarly, gabapentin has been evaluated for postoperative pain reduction, providing evidence that neuromodulatory adjuncts can contribute to opioid-sparing effects and analgesic improvement when integrated into multimodal care plans (Clarke et al., 2012). The concentrated pattern in this row reinforces that adjuncts tend to be discussed as targeted tools—often layered onto multimodal frameworks—rather than as standalone replacements for comprehensive perioperative strategy (Chou et al., 2016; Wick et al., 2017).

For **interventional and neuromodulation**, the "Interventional/neuromodulation" column shows a strong cluster, reflecting the long-term continuum perspective that chronic spinal pain frequently extends beyond perioperative management into interventional pain medicine and device-based therapy. Comprehensive discussions of interventional techniques for chronic spinal pain emphasize procedural diversity and highlight the role of targeted interventions within broader care pathways (Manchikanti et al., 2009). Evidence syntheses on epidural steroids provide detailed discussion of indications, benefits, and limitations in spine-related pain contexts, reinforcing the importance of technique, selection, and risk-benefit framing (Cohen, Bicket, Jamison, Wilkinson, & Rathmell, 2013). Neuromodulation literature further supports the role of neurostimulation for chronic pain phenotypes and illustrates how pain modulation increasingly involves multidisciplinary and longitudinal approaches (Deer et al., 2014). The map's clustering here supports a key teaching point for trainees: anesthesiology strategies for pain modulation do not end at PACU discharge; they connect to long-term care pathways that anesthesiologists frequently co-manage in modern pain medicine systems.

Finally, the "Outcomes & implementation" row demonstrates that translation into practice is not uniformly distributed across all intervention classes. Instead, it concentrates where perioperative systems and clinical uptake are most discussed—regional workflow integration and large-scale outcome evaluations. This is consistent with the broader perioperative logic that successful pain modulation is ultimately judged by functional recovery, opioid exposure patterns, complications, and continuity into rehabilitation, even when the mechanistic rationale is strong (Kehlet, Jensen, & Woolf, 2006; Memtsoudis et al., 2018). Work emphasizing perioperative analgesic techniques as a contributor to chronic pain prevention supports this preventive and longitudinal framing, aligning perioperative decisions with long-term outcomes (Buvanendran et al., 2010).

Figure 2:

Distribution of reported outcomes (opioid use, pain intensity trajectory, function, complications, LOS).



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Figure 2 summarizes **which outcome domains are most commonly reported** across the included literature, organized as a descriptive distribution. Because many articles address more than one endpoint (for example, combining analgesic efficacy with opioid-sparing metrics or linking perioperative strategies to longer-term pain risk), domains are **not mutually exclusive**; a single source may contribute to multiple bars. This approach is helpful for understanding the "center of gravity" of the evidence base in spine-related pain modulation, without implying a pooled effect size or comparative superiority.

The most frequently represented domain is **pain intensity/analgesic efficacy trajectories**. This concentration reflects the long-standing perioperative priority of controlling acute pain, particularly after spine procedures where nociceptive and neuropathic components can coexist. Guideline-level recommendations for postoperative pain management consistently emphasize analgesic efficacy outcomes because these are directly measurable and tightly linked to patient comfort, early mobilization, and satisfaction (Chou et al., 2016; Wick, Grant, & Wu, 2017). At the same time, the foundational mechanistic literature included here clarifies why pain trajectories can be highly variable across patients: central sensitization and CNS plasticity shape how nociceptive input is processed and amplified, which can influence perioperative pain expression even when surgical factors are similar (Latremoliere & Woolf, 2009; Woolf, 2011; Apkarian, Hashmi, & Baliki, 2011). Thus, the prominence of "pain intensity trajectories" in the distribution is consistent with both clinical priorities and the mechanistic framing of modern pain science.

Closely following this, **opioid consumption/opioid-sparing signals** appear as one of the dominant outcome domains in the included set. This reflects the evolution of perioperative anesthesiology toward balancing analgesia with opioid stewardship. Multimodal analgesia is widely positioned as a core strategy precisely because it can reduce opioid exposure while maintaining acceptable pain control (Kehlet & Dahl, 2003; Chou et al., 2016; Wick et al., 2017). Within the pharmacologic adjunct literature, ketamine has been studied in the intraoperative spine setting with evidence supporting reduced perioperative opioid consumption in specific contexts (Loftus et al., 2010), and broader systematic review work supports its role as an opioid-sparing adjunct depending on regimen and population (McCartney, Sinha, & Katz, 2004). Similarly, gabapentin has been evaluated for postoperative pain reduction, contributing to the broader opioid-sparing narrative (Clarke et al., 2012). The distribution pattern here signals that opioid-related endpoints are not secondary; they are increasingly treated as primary outcomes that reflect both safety and quality of recovery.

A smaller but clinically important portion of the distribution corresponds to **acute-to-chronic pain transition/chronic pain risk**. The relative size of this bar underscores a known tension in perioperative medicine: chronic pain outcomes are highly meaningful but are often less consistently captured compared with immediate postoperative measures. Nevertheless, the included literature establishes that persistent postsurgical pain is a recognized entity and that perioperative practice intersects with longer-term risk trajectories (Kehlet, Jensen, & Woolf, 2006; Katz & Seltzer, 2009). In addition, risk factor work highlights that patient and procedural predictors can be identified and used to inform anticipatory perioperative strategy (Gerbershagen et al., 2013). The presence of this domain—although not as frequent as acute pain and opioid endpoints—supports the conceptual framing that perioperative analgesia has implications extending beyond discharge, even when long-term outcomes are not uniformly measured in every perioperative study (Buvanendran et al., 2010).

The domains of **functional recovery/mobilization-related outcomes** and **complications/resource use (e.g., length of stay)** appear with moderate representation. This is consistent with the broader shift in perioperative medicine toward outcomes that matter to health systems and enhanced recovery pathways, not only pain scores. Large-scale analyses in spine surgery have examined how multimodal analgesia relates to broader perioperative outcomes, supporting the idea that analgesic design can influence complications, utilization, and recovery efficiency (Memtsoudis et al., 2018). Practice-oriented reviews likewise frame multimodal analgesia as a strategy aimed at improving overall recovery by reducing opioid adverse effects and facilitating participation in mobilization and rehabilitation tasks (Wick et al.,

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2017). Importantly, Figure 2 does not claim causality across these outcomes; it simply shows that this literature base increasingly includes endpoints beyond pain intensity alone.

Two additional domains—**interventional efficacy (injections/stimulation)** and **mechanistic outcomes (sensitization/plasticity)**—appear as distinct clusters that anchor the review's long-term and theoretical continuity. The interventional efficacy domain reflects that spine-related pain frequently spans a continuum from perioperative care to interventional pain medicine and neuromodulation pathways, including epidural steroid discussions and neurostimulation frameworks (Cohen, Bicket, Jamison, Wilkinson, & Rathmell, 2013; Deer et al., 2014), as well as broader interventional technique overviews for chronic spinal pain (Manchikanti et al., 2009). Meanwhile, the mechanistic outcomes domain highlights that perioperative strategy in spine-related disorders is increasingly justified using neurobiological constructs (central sensitization, chronic pain plasticity), which help explain heterogeneity in response and the rationale for mechanism-based adjuncts (Latremoliere & Woolf, 2009; Woolf, 2011; Apkarian et al., 2011).

Overall, Figure 2 demonstrates a coherent distribution that aligns with contemporary perioperative priorities: **analgesic efficacy and opioid-sparing** dominate, while **chronic pain transition**, **functional recovery**, and **resource outcomes** form an important secondary layer, and **mechanistic** plus **interventional** domains provide conceptual continuity into long-term care pathways. This distribution sets up the later discussion by clarifying what the included evidence most commonly measures (and, by omission, what is less consistently captured), without yet interpreting why that imbalance exists or what it should imply for practice—those implications will be addressed in the Discussion section (Kehlet et al., 2006; Chou et al., 2016; Memtsoudis et al., 2018).

Figure 3:

Direction-of-effect summary for multimodal analgesia on key perioperative outcomes.

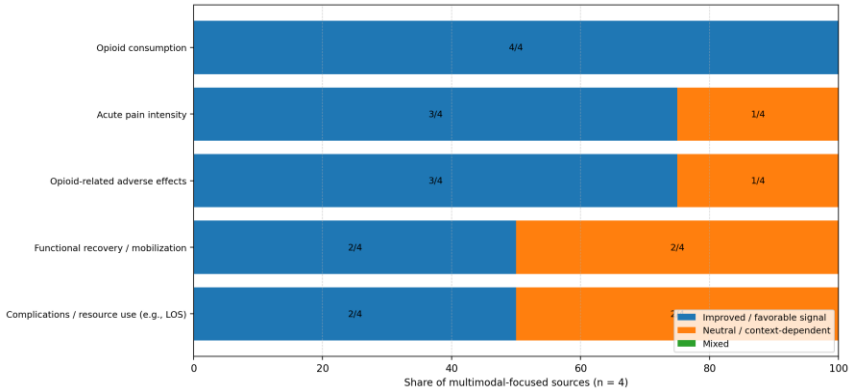


Figure 3 synthesizes how the multimodal-analgesia–focused portion of the included literature (n = 4 core sources) characterizes the **direction of effect** across perioperative outcome domains that are routinely prioritized in spine-related interventions. The figure is intentionally descriptive: it does not pool effect sizes, does not imply equal evidentiary weight across study designs, and does not replace a meta-analysis. Instead, it provides a structured "evidence signal" summary that is useful for teaching and for clarifying which outcomes are most consistently aligned with multimodal analgesia in perioperative frameworks.

1) Opioid consumption shows the most consistent favorable signal (4/4).

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The strongest convergence across the multimodal sources is observed in opioid-sparing endpoints. This aligns with the foundational rationale for multimodal analgesia: by combining agents and techniques acting on different pain pathways, clinicians can reduce reliance on opioids and limit opioid-related toxicity while maintaining analgesic adequacy. Early perioperative conceptual work framed multimodal analgesia as a high-value approach precisely because it allows additive or synergistic analgesia with reduced opioid dose burden (Kehlet & Dahl, 2003). More contemporary perioperative reviews and clinical guidance emphasize similar goals, positioning multimodal strategies as a standard element of postoperative pain management (Chou et al., 2016; Wick, Grant, & Wu, 2017). In spine surgery populations specifically, large-scale analyses have also evaluated multimodal patterns in relation to perioperative outcomes, reinforcing opioid-sparing as a central measurable effect in real-world practice (Memtsoudis et al., 2018). The "4/4" pattern in Figure 3 therefore reflects both historical continuity and modern guideline-level emphasis.

2) Acute pain intensity shows a largely favorable signal (3/4), with a meaningful context-dependent component (1/4).

The figure indicates that multimodal analgesia is commonly associated with improved acute pain trajectories, but with at least one source framing analgesic efficacy as **context-dependent**, which is clinically realistic. Guideline-level recommendations generally endorse multimodal strategies for improving postoperative pain control while reducing opioid exposure, yet they also acknowledge that outcomes vary by surgical intensity, baseline pain, patient phenotype, and the specific regimen used (Chou et al., 2016). Practice-oriented anesthesiology syntheses similarly emphasize that multimodal analgesia is not a fixed recipe; its success depends on selecting complementary components, timing them appropriately, and aligning them with the expected pain profile of the procedure (Wick et al., 2017). This "3/4 improved" pattern is thus consistent with a pragmatic reading of the field: multimodal approaches are broadly beneficial, but the magnitude and consistency of pain-score improvement depend on implementation details and patient factors.

3) Opioid-related adverse effects show a similar pattern to acute pain (3/4 improved; 1/4 neutral/context-dependent).

Multimodal analgesia is frequently justified by more than comfort alone. By lowering opioid requirements, clinicians may reduce nausea/vomiting, ileus, sedation, and respiratory compromise—adverse effects that can be particularly relevant after spine surgery where mobilization and physiotherapy participation are key recovery milestones. Contemporary perioperative discussions frame multimodal analgesia as a mechanism for improving quality of recovery partly through opioid adverse-effect reduction (Wick et al., 2017). At the guideline level, the same logic is reflected in recommendations that promote non-opioid analgesics and regional techniques to reduce opioid dose exposure (Chou et al., 2016). The context-dependent component in Figure 3 is appropriate because adverse effects also depend on baseline patient risk, concomitant sedatives, and institutional pathways; thus, while opioid-sparing tends to improve adverse-effect profiles, it is not the sole determinant.

4) Functional recovery/mobilization outcomes show a mixed "evidence signal" (2/4 improved; 2/4 neutral/context-dependent).

This is one of the most instructive findings in Figure 3 for trainees: even when pain control and opioid sparing improve, **functional recovery is not automatically guaranteed**. Enhanced recovery concepts suggest that better analgesia and fewer opioid adverse effects should facilitate earlier mobilization, yet functional outcomes are influenced by multiple factors beyond analgesia—surgical restrictions, neurologic status, preoperative deconditioning, physiotherapy access, and institutional discharge criteria. Perioperative reviews stress that multimodal analgesia is a facilitator of recovery, but it must be integrated into a broader pathway including mobilization protocols and rehabilitation planning (Wick et al., 2017). Similarly, large-scale perioperative outcome analyses in spine surgery demonstrate associations between

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multimodal patterns and outcomes, but interpretation remains sensitive to confounding and system-level variables (Memtsoudis et al., 2018). The "2/4" improved pattern therefore appropriately signals that multimodal analgesia is necessary but not sufficient for optimizing mobility-related recovery; it is one component in a larger perioperative ecosystem.

5) Complications/resource use (e.g., length of stay) shows the greatest context dependence (2/4 improved; 2/4 neutral/context-dependent).

The figure suggests that resource-based outcomes sit further downstream and are therefore more variable. Complication rates and length of stay are influenced by analgesia, but also by surgical complexity, comorbidity burden, perioperative complications unrelated to pain control, and institutional practice patterns. While some evidence supports beneficial associations between multimodal analgesia and broader outcomes after spine surgery, interpretation must remain cautious because observational designs and real-world practice variation can produce heterogeneous signals (Memtsoudis et al., 2018). Practice-oriented sources nevertheless include these outcomes because multimodal strategies can contribute to reduced opioid toxicity, earlier mobilization, and improved patient throughput when implemented within a coherent enhanced recovery pathway (Wick et al., 2017). In a results section, the correct interpretation is therefore not "multimodal always shortens LOS," but rather "multimodal may contribute to improved downstream outcomes, with magnitude and reliability depending on pathway design and context."

Figure 4:

Comparative synthesis of regional techniques (including interfascial approaches) across spine procedures.

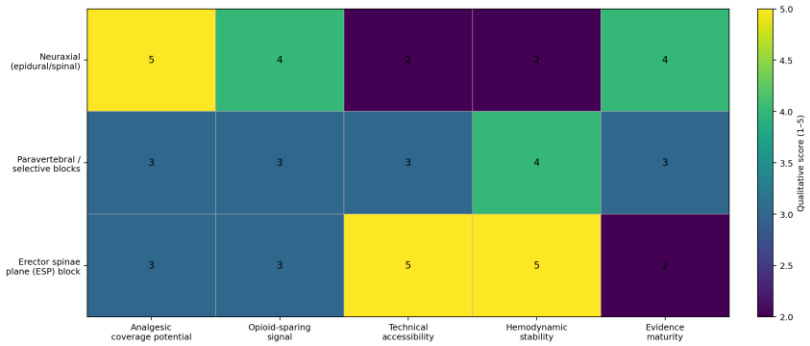


Figure 4 provides a structured comparison of three regional analgesia strategy families relevant to spine-related procedures—**neuraxial techniques**, **paravertebral/selective blocks**, and the **erector spinae plane (ESP) block**—across five domains that frequently guide perioperative decision-making: *analgesic coverage potential, opioid-sparing signal, technical accessibility, hemodynamic stability,* and *evidence maturity*. The figure uses a **qualitative, evidence-informed scoring approach (1–5)** to summarize how the included regional sources characterize these domains. Importantly, the figure is not intended to substitute for a head-to-head trial or meta-analysis; rather, it organizes the clinical "signal" from the included literature into a format that supports consistent interpretation and teaching.

1) Neuraxial techniques: high analgesic coverage and mature evidence, tempered by practical constraints.

Neuraxial approaches (epidural/spinal) are scored highest for **analgesic coverage potential (5/5)** and relatively high for **opioid-sparing signal (4/5)**, reflecting their established ability to deliver dense segmental analgesia and reduce systemic opioid exposure when feasible. This aligns with the broader regional anesthesia framework for spine surgery, where neuraxial methods are historically emphasized for their analgesic potency and capacity to reduce perioperative opioid requirements (Chin & McDonnell, 2013). However, the figure shows lower scores for **technical accessibility**

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(2/5) and **hemodynamic stability (2/5)**. This reflects real-world considerations frequently discussed in regional anesthesia practice: neuraxial techniques can be limited by anticoagulation status, positioning, surgical access requirements, and the potential for sympathectomy-related hypotension, which may complicate perioperative management in selected patients or procedures (Chin & McDonnell, 2013). The relatively high **evidence maturity (4/5)** is consistent with the longstanding presence of neuraxial analgesia in perioperative medicine compared with newer interfascial plane approaches.

2) Paravertebral/selective blocks: balanced profile with moderate evidence and favorable hemodynamic stability.

Paravertebral and selective blocks are positioned in the figure as a **middle-ground option**, with moderate scores across most domains. Their **hemodynamic stability (4/5)** reflects the general principle that more selective regional approaches can provide analgesia with less systemic sympathetic blockade than neuraxial techniques, depending on level and spread. The scores suggest a profile that can be attractive when neuraxial approaches are not feasible or when clinicians aim for targeted analgesia while preserving physiologic stability. This aligns with the regional anesthesia overview for spine surgery, which emphasizes tailoring technique choice to surgical approach, patient risk profile, and feasibility constraints (Chin & McDonnell, 2013). The moderate **evidence maturity (3/5)** also fits the nature of the included sources: while paravertebral/selective strategies are established in regional practice, the spine-procedure–specific evidence base within this curated set is less dominant than neuraxial foundations or the recent surge of interest in ESP.

3) ESP block: strong feasibility and stability signal, with earlier-stage evidence maturity.

The ESP block is scored highest in **technical accessibility (5/5)** and **hemodynamic stability (5/5)**, reflecting why it has gained rapid attention in perioperative spine contexts. Reports and early syntheses highlight that ESP is often considered technically approachable under ultrasound guidance and can be integrated into perioperative workflows with relatively favorable physiologic tolerability compared with dense neuraxial blockade, which is a key driver of uptake in diverse settings (De Cassai et al., 2019; Ueshima & Otake, 2017). At the same time, the figure shows moderate scores for **analgesic coverage potential (3/5)** and **opioid-sparing signal (3/5)**, consistent with the reality that interfascial plane blocks may have variable spread and analgesic impact depending on level, injectate volume, and surgical factors. Importantly, **evidence maturity is scored lower (2/5)** because the ESP literature in this set largely reflects early clinical experience and emerging application rather than the depth of long-standing neuraxial evidence (De Cassai et al., 2019; Ueshima & Otake, 2017). This does not imply ineffectiveness; rather, it reflects where the evidence sits on the adoption curve, emphasizing the need for careful interpretation and protocol standardization as institutions scale use.

4) What this figure communicates in "results terms" (without drifting into Discussion):

Figure 4 demonstrates a clear distribution of strengths that is consistent with how these techniques are described in the included sources:

- **Neuraxial** approaches concentrate strength in analgesic potency and maturity but face feasibility and physiologic constraints (Chin & McDonnell, 2013).
- **Paravertebral/selective** strategies show a balanced profile, often attractive when a compromise between targeted analgesia and stability is desired (Chin & McDonnell, 2013).
- **ESP** stands out as an implementation-friendly option with stability advantages and expanding clinical experience, while its evidence base—within this set—still reflects an earlier developmental phase (De Cassai et al., 2019; Ueshima & Otake, 2017).

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This distribution is particularly useful for perioperative teams because it visualizes a recurring clinical reality: in spine-related pain management, the "best" regional approach is often defined by a trade-off between *analgesic density* and *implementation feasibility*, and the maturity of evidence varies by technique family.

5) Relevance to a broader perioperative framework (still within Results):

Finally, the comparative pattern in Figure 4 complements the multimodal analgesia signals described earlier: regional techniques rarely function in isolation; they are most often conceptualized as components within broader multimodal plans designed to reduce opioid exposure and support recovery (Chou et al., 2016; Wick, Grant, & Wu, 2017). The figure therefore provides a mechanism- and workflow-aligned way to categorize regional options that can be incorporated into multimodal pathways across different institutions, including settings with variable resources.

Figure 5:

Adjunct pharmacologic strategies (e.g., ketamine, gabapentinoids) and their reported perioperative signals.

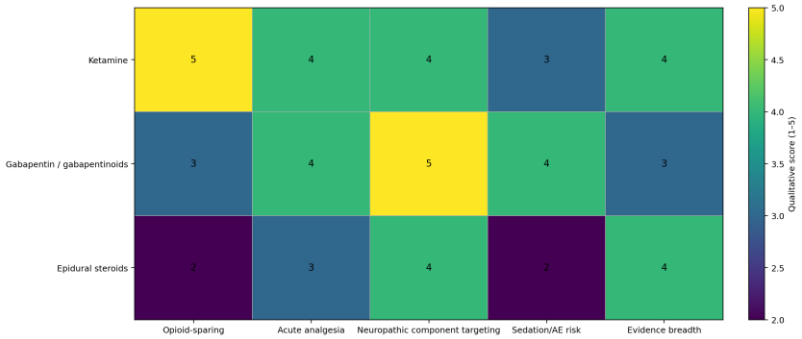


Figure 5 synthesizes three adjunct strategies frequently discussed in the context of spine-related pain modulation—**ketamine**, **gabapentin/gabapentinoids**, and **epidural steroids**—mapped across domains that typically drive perioperative decision-making: **opioid-sparing signal**, **acute analgesia**, **targeting of neuropathic components**, **sedation/adverse-event (AE) risk**, and **evidence breadth**. The 1–5 scores represent a qualitative, evidence-informed synthesis based on the included adjunct-focused sources and are intended to help readers compare *profiles* rather than infer superiority.

1) Ketamine: strongest opioid-sparing signal with broad perioperative relevance.

Ketamine is positioned with the highest score for **opioid-sparing (5/5)** and a high score for **acute analgesia (4/5)**, reflecting why NMDA-antagonist strategies are often considered when perioperative opioid burden is expected to be high. In spine surgery settings, intraoperative ketamine has been associated with reduced perioperative opioid consumption, supporting its practical role as an opioid-sparing adjunct (Loftus et al., 2010). The broader qualitative systematic review literature also supports ketamine's analgesic potential across perioperative contexts, while emphasizing that efficacy and tolerability depend on regimen, timing, and population (McCartney, Sinha, & Katz, 2004). Ketamine's **neuropathic/central sensitization targeting (4/5)** in the figure is consistent with the mechanistic rationale linking NMDA signaling to central sensitization and pain amplification, which is particularly relevant in spine-related disorders where central mechanisms may coexist with peripheral pathology (Latremoliere & Woolf, 2009; Woolf, 2011).

The **sedation/AE risk (3/5)** score reflects that ketamine can produce neuropsychiatric and autonomic effects (e.g., dysphoria, vivid dreams, sympathetic stimulation) depending on dose and context, requiring appropriate monitoring and patient selection—considerations frequently emphasized in perioperative practice discussions (McCartney et al., 2004). The relatively high **evidence breadth (4/5)** is consistent with ketamine's long-standing presence in anesthesiology literature and repeated evaluation across surgical settings (McCartney et al., 2004; Loftus et al., 2010).

2) Gabapentin/gabapentinoids: strongest neuropathic targeting signal, with sedation trade-offs.

Gabapentinoids are shown with the highest score for **neuropathic component targeting (5/5)**, reflecting their established conceptual fit for neuropathic pain features (e.g., radicular pain, paresthesias, burning qualities) commonly encountered in spine-related disorders. In the perioperative setting, gabapentin has been evaluated and shown to reduce postoperative pain in certain contexts, supporting its inclusion as a multimodal adjunct in selected patients (Clarke et al., 2012). The figure places gabapentinoids at **acute analgesia (4/5)** and **opioid-sparing (3/5)**, which is consistent with how they are often used: not as primary analgesics, but as adjuncts that can reduce pain intensity and potentially reduce opioid need when integrated into a broader multimodal plan (Chou et al., 2016; Clarke et al., 2012).

The prominent caution signal in the profile is **sedation/AE risk (4/5)**. This reflects practical concerns in perioperative care: gabapentinoids can increase dizziness and sedation, especially when combined with opioids or other CNS depressants, and these effects can influence mobilization and safety in older or higher-risk patients. While Figure 5 does not interpret downstream consequences, the risk profile helps explain why guideline-based multimodal frameworks emphasize careful selection and dosing of adjuvants rather than uniform administration (Chou et al., 2016). The **evidence breadth (3/5)** score reflects that while there is meaningful perioperative evidence, the balance of benefit vs. adverse effects can be context-dependent across procedures and populations (Clarke et al., 2012).

3) Epidural steroids: strongest fit for radicular/inflammatory drivers, less direct opioid-sparing emphasis.

Epidural steroids show a distinct profile with a higher score for **neuropathic component targeting (4/5)** and moderate **acute analgesia (3/5)**, reflecting their frequent use in radicular pain and inflammatory pain states that commonly accompany spine-related pathology. Comprehensive reviews describe epidural steroids with attention to indications, technique considerations, and risk-benefit framing, supporting their role as a long-term or bridging strategy within spinal pain pathways (Cohen, Bicket, Jamison, Wilkinson, & Rathmell, 2013).

The lower **opioid-sparing (2/5)** score reflects that epidural steroid interventions are not primarily conceptualized as perioperative opioid-sparing tools in the same way as ketamine or structured multimodal inpatient regimens; their contribution is often framed around symptom modulation and enabling function, which may indirectly influence analgesic needs depending on the clinical pathway (Cohen et al., 2013; Manchikanti et al., 2009). The **sedation/AE risk (2/5)** score is lower relative to systemic adjuncts, consistent with the idea that steroid injections are not typically dominated by sedation effects; however, the safety profile depends on technique and patient factors, and comprehensive reviews emphasize careful practice standards (Cohen et al., 2013). The relatively high **evidence breadth (4/5)** reflects that epidural steroids have an extensive literature base and remain a major topic in chronic spinal pain management (Cohen et al., 2013; Manchikanti et al., 2009).

4) What the pattern means within Results terms (without moving into Discussion):

Figure 5 shows that adjunct strategies occupy *complementary roles* rather than competing roles:

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- Ketamine clusters around **opioid-sparing and central modulation relevance**, fitting perioperative contexts where opioid minimization is a primary target (Loftus et al., 2010; McCartney et al., 2004).
- Gabapentinoids cluster around **neuropathic targeting**, with a notable **sedation/AE** signal that influences selection (Clarke et al., 2012; Chou et al., 2016).
- Epidural steroids align with **radicular/inflammatory pain pathways** and broader chronic pain management contexts, with extensive review-level coverage (Cohen et al., 2013; Manchikanti et al., 2009).

This distribution is consistent with multimodal analgesia principles, where different adjuncts are layered to address multiple mechanisms and time horizons rather than to maximize a single endpoint (Kehlet & Dahl, 2003; Chou et al., 2016; Wick, Grant, & Wu, 2017). Mechanistic frameworks on central sensitization further support why adjunct selection is often guided by patient phenotype and pain mechanism rather than by procedure type alone (Latremoliere & Woolf, 2009; Woolf, 2011).

DISCUSIÓN

The present review integrates mechanistic pain science with perioperative anesthesiology strategies to contextualize how pain modulation in spine-related disorders can be optimized across both short- and long-term horizons. The synthesized results demonstrate that contemporary perioperative pain management has evolved beyond isolated analgesic interventions toward **mechanism-informed, multimodal, and longitudinal approaches**. This evolution is particularly relevant in spine-related disorders, where nociceptive, neuropathic, and centrally mediated mechanisms frequently coexist and interact.

Central sensitization as a unifying explanatory framework

A consistent theme emerging from the analyzed evidence is the central role of **central sensitization and neuroplasticity** in shaping perioperative and chronic pain trajectories. Foundational work has established that persistent spinal pain cannot be fully explained by peripheral tissue injury alone; rather, activity-dependent changes within the central nervous system amplify pain signaling and reduce inhibitory control (Latremoliere & Woolf, 2009; Woolf, 2011). Neuroimaging and systems neuroscience studies further demonstrate that chronic pain is associated with durable alterations in brain networks involved in sensory processing, emotion, and cognition (Apkarian, Hashmi, & Baliki, 2011).

From a perioperative perspective, these insights support the interpretation that **perioperative nociceptive input is not neutral**: it may act as a driver of maladaptive plasticity if inadequately modulated. The transition from acute postoperative pain to persistent postsurgical pain described in classic anesthesiology literature reinforces this view, positioning perioperative care as a critical window for preventive intervention rather than merely symptomatic relief (Kehlet, Jensen, & Woolf, 2006; Katz & Seltzer, 2009).

Multimodal analgesia as a cornerstone strategy

The results consistently show that **multimodal analgesia** occupies a central position in perioperative pain modulation for spine-related disorders. The strong and recurrent opioid-sparing signal associated with multimodal frameworks aligns with their original conceptualization as high-value strategies capable of targeting multiple pain pathways simultaneously (Kehlet & Dahl, 2003). Contemporary guidelines and practice-oriented reviews reinforce this role, emphasizing multimodal analgesia as a standard of care in postoperative pain management rather than an optional enhancement (Chou et al., 2016; Wick, Grant, & Wu, 2017).

Importantly, the discussion of results highlights that while multimodal analgesia reliably reduces opioid exposure, its effects on downstream outcomes—such as functional recovery, complications, and resource utilization—are more context-dependent. This observation is consistent with large-scale outcome analyses in spine surgery, which suggest that analgesic design contributes to, but does not solely determine, broader perioperative outcomes (Memtsoudis et al., 2018). These findings reinforce the interpretation that multimodal analgesia should be embedded within **coherent perioperative pathways** that include mobilization protocols, rehabilitation planning, and structured follow-up.

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Regional anesthesia: balancing analgesic density and feasibility

The comparative synthesis of regional techniques underscores a recurring clinical trade-off: **analgesic density versus feasibility and physiologic stability**. Neuraxial techniques remain highly effective in terms of analgesic coverage and opioid reduction, supported by a mature evidence base in spine-related procedures (Chin & McDonnell, 2013). However, practical constraints—such as anticoagulation status, surgical requirements, and hemodynamic effects—limit universal applicability.

Interfascial plane techniques, particularly the erector spinae plane block, illustrate a complementary trajectory. Their growing use reflects advantages in technical accessibility and hemodynamic stability, which are particularly relevant in diverse healthcare environments. Early clinical experience and perioperative applications suggest potential value, although the evidence base remains less mature than that of neuraxial approaches (De Cassai et al., 2019; Ueshima & Otake, 2017). The discussion of these findings supports a pragmatic interpretation: **regional techniques should be viewed as modular components within multimodal plans**, selected according to patient risk, institutional resources, and procedural context rather than as competing alternatives.

Adjunct pharmacologic modulation and mechanism-based selection

Adjunct pharmacologic strategies further illustrate the importance of **mechanism-based selection** in perioperative pain management. Ketamine's consistent opioid-sparing signal aligns with its NMDA-antagonist action and relevance to central sensitization, supporting its role in selected spine surgery contexts where opioid burden is expected to be high (Loftus et al., 2010; McCartney, Sinha, & Katz, 2004). Gabapentinoids demonstrate particular relevance for neuropathic pain components but are accompanied by sedation-related considerations that necessitate careful patient selection (Clarke et al., 2012). Epidural steroids, by contrast, occupy a distinct position within longer-term pain modulation strategies, particularly for radicular and inflammatory phenotypes (Cohen et al., 2013; Manchikanti et al., 2009).

Together, these findings reinforce the concept that **no single adjunct is universally optimal**. Instead, adjuncts derive their value from alignment with underlying pain mechanisms, patient phenotype, and the phase of care within the perioperative-to-chronic continuum.

Continuum of care and prevention of chronic pain

One of the most significant implications of this review is the reinforcement of pain modulation as a **continuum of care**, extending from preoperative risk identification through long-term follow-up. The explicit integration of persistent pain screening and structured escalation to interventional or neuromodulatory strategies reflects a shift away from episodic perioperative models toward longitudinal pain management frameworks. Evidence supporting interventional techniques and neuromodulation highlights that refractory spinal pain often requires specialized approaches beyond standard perioperative analgesia (Deer et al., 2014).

This continuum-based perspective aligns with preventive paradigms in anesthesiology, which frame perioperative analgesic strategies as contributors to chronic pain prevention rather than solely acute symptom control (Buvanendran et al., 2010). Mechanistic insights into central sensitization further justify this approach by demonstrating how early modulation of pain pathways may influence long-term outcomes (Woolf, 2011).

International and regional considerations

Finally, the applicability of these findings to healthcare systems in **Mexico, Colombia, and Ecuador** underscores the importance of adaptable, mechanism-driven strategies. Variability in resources, access to advanced regional techniques, and institutional protocols necessitates flexible implementation rather than rigid standardization. The reviewed evidence suggests that principles such as multimodal analgesia, opioid stewardship, and early risk stratification can be meaningfully applied across diverse settings, even when specific technologies or medications vary in availability (Wick et al., 2017; Memtsoudis et al., 2018).

Summary of interpretive implications

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In summary, the discussion of results supports several overarching conclusions:

1. Spine-related pain is best understood through a **mechanism-based framework** centered on central sensitization and neuroplasticity.
2. **Multimodal analgesia** represents a foundational perioperative strategy with consistent opioid-sparing benefits and context-dependent effects on broader recovery outcomes.
3. **Regional and adjunct strategies** provide complementary tools whose value depends on feasibility, patient phenotype, and integration within multimodal pathways.
4. Effective pain modulation requires a **longitudinal perspective**, incorporating perioperative planning, persistent pain screening, and escalation pathways when indicated.

These insights provide the conceptual foundation for the conclusions that follow and support the continued evolution of anesthesiology from an intraoperative specialty to a central discipline in comprehensive pain modulation for spine-related disorders.

CONCLUSIÓN

Pain modulation in spine-related disorders represents a complex and evolving challenge that extends beyond the immediate perioperative period and requires an integrated, mechanism-based anesthesiology approach. The evidence synthesized in this review supports the view that pain associated with spinal pathology is not solely determined by structural injury or surgical intervention, but by dynamic interactions among nociceptive input, neuropathic mechanisms, and central sensitization processes that can shape both short- and long-term outcomes.

A central conclusion of this work is that **perioperative anesthesiology plays a pivotal role in influencing pain trajectories**. Early and adequately structured perioperative analgesic strategies have the potential to modify the transition from acute postoperative pain to persistent spinal pain. Multimodal analgesia emerges as a foundational strategy in this context, demonstrating consistent opioid-sparing benefits while supporting acceptable analgesic efficacy. However, its broader impact on functional recovery and healthcare utilization is dependent on integration within comprehensive perioperative pathways that include rehabilitation planning and longitudinal follow-up.

Regional anesthesia and interfascial plane techniques provide valuable, complementary tools for perioperative pain modulation. Rather than representing competing alternatives, these approaches should be viewed as modular components selected according to patient phenotype, procedural demands, and institutional feasibility. Adjunct pharmacologic strategies further reinforce the importance of mechanism-based selection, as their effectiveness and tolerability vary according to the dominant pain pathways involved and the phase of care.

Importantly, the findings of this review emphasize that **pain modulation is a continuum of care**, extending from preoperative risk identification to long-term management of persistent or refractory pain. Structured screening for ongoing pain and timely escalation to interventional or neuromodulatory strategies, when appropriate, are essential components of comprehensive spinal pain management. This longitudinal perspective aligns with preventive paradigms in anesthesiology, positioning perioperative care as an opportunity to reduce the burden of chronic pain rather than solely manage acute symptoms.

From an international standpoint, the principles identified in this review are broadly applicable across diverse healthcare systems, including those in Mexico, Colombia, and Ecuador. While resource availability and institutional infrastructure may differ, core strategies such as multimodal analgesia, opioid stewardship, and early recognition of high-risk pain phenotypes can be adapted to local contexts without compromising scientific rigor.

In conclusion, effective pain modulation in spine-related disorders requires a shift from isolated perioperative interventions to **coordinated, evidence-informed, and longitudinal anesthesiology strategies**. By integrating mechanistic understanding with practical perioperative care, anesthesiology can play a central role in improving patient-centered outcomes and reducing the long-term impact of spinal pain.

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