Review

Evidence-Based Multimodal Analgesia After Laparoscopic Cholecystectomy: Integrating Pharmacologic and Non-Pharmacologic Strategies for Optimal Recovery

Masoud Sharifian[1], Atefeh Marzban[2*]

[1] Assistant Professor of Surgery, Department of Surgery, School of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran.

[2] Assistant Professor, Department of Anesthesiology, Lorestan University of Medical Sciences, Khorramabad, Iran.

***Corresponding author:** Atefeh Marzban, Assistant Professor, Department of Anesthesiology, Lorestan University of Medical Sciences, Khorramabad, Iran. Email: atefehmarzban92@gmail.com

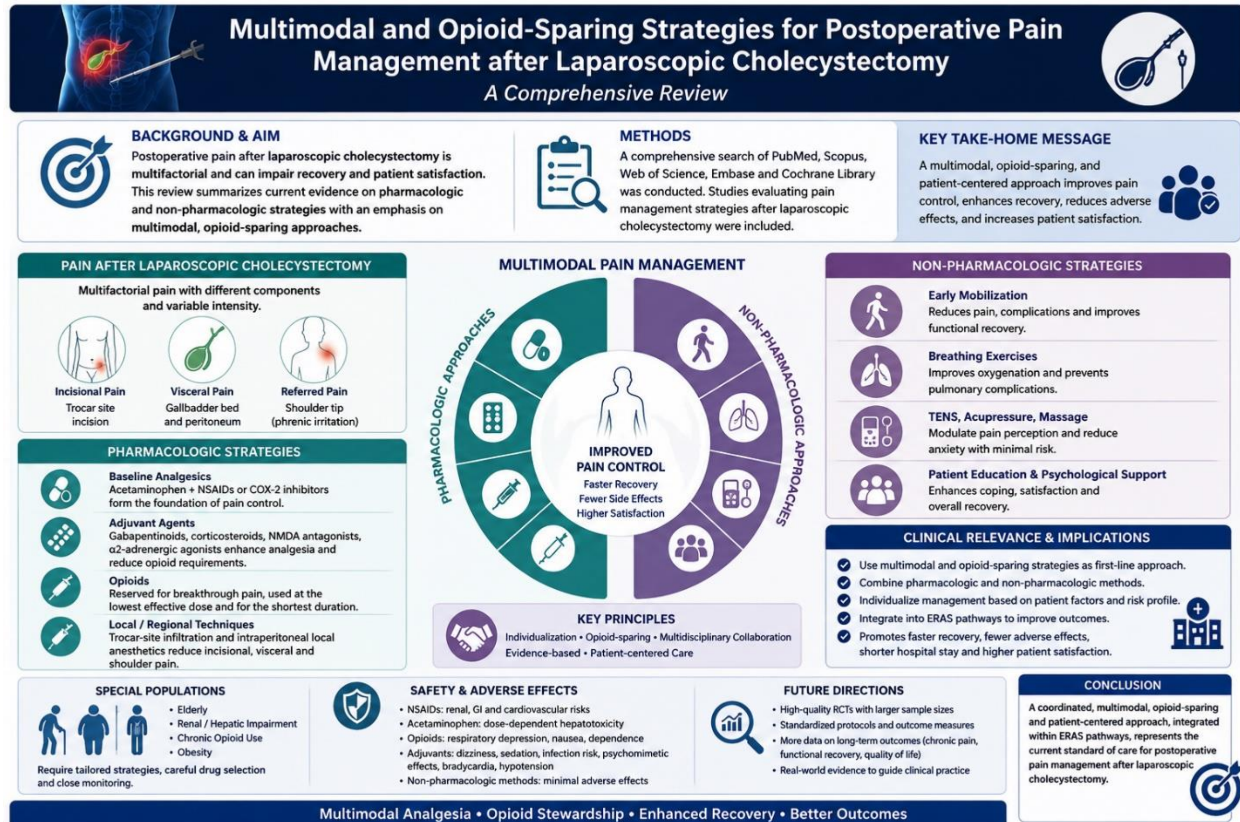
Received: February 20, 2026; **Revised:** April 03, 2026; **Accepted:** April 10, 2026; **Published online:** April 15, 2026.
Nex. Integr. Clin. Sci. J. 2026; 1:002, https://doi.org/10.22034/nics.2026.1.002

© The Author(s) 2026, under exclusive licence to Nexus of Integrated Clinical Science Journal

Abstract

Postoperative pain following laparoscopic cholecystectomy remains a clinically important factor affecting recovery, patient satisfaction, and healthcare utilization. Despite being a minimally invasive procedure, pain is often multifactorial, involving incisional, visceral, and referred components, which makes single-agent analgesia insufficient. This review aimed to provide an updated and integrated overview of pharmacologic and non-pharmacologic strategies for postoperative pain management with an emphasis on multimodal and opioid-sparing approaches. Current evidence supports multimodal analgesia as the most effective strategy for pain control. Pharmacologic management typically includes acetaminophen combined with non-steroidal anti-inflammatory drugs or COX-2 inhibitors, supplemented by selective use of adjuvant agents and local or regional anesthesia techniques. Opioids should be reserved for breakthrough pain and used at the lowest effective dose to reduce the risk of adverse effects, including respiratory depression, nausea, and long-term dependence. Non-pharmacologic interventions such as early mobilization, breathing exercises, transcutaneous electrical nerve stimulation, and structured patient education further enhance recovery by reducing pain perception, anxiety, and functional limitations. Evidence also highlights the importance of individualized pain management based on patient-specific factors such as age, comorbidities, and surgical risk profile. Integration of these strategies within Enhanced Recovery After Surgery (ERAS) pathways improves clinical outcomes, shortens hospital stay, and enhances patient satisfaction. From a clinical perspective, postoperative pain management should shift toward a coordinated, multidisciplinary, and patient-centered approach that prioritizes opioid stewardship and functional recovery. The combination of pharmacologic and non-pharmacologic interventions represents the current standard of care and supports improved perioperative outcomes in laparoscopic cholecystectomy.

Keywords: Postoperative Pain, Cholecystectomy, Multimodal Analgesia, Pharmacologic and Non-Pharmacologic Strategies, Opioid Reduction.



Graphical Abstract: Multimodal Pain Management Strategies Following Laparoscopic Cholecystectomy. This graphical abstract summarizes multimodal pain management strategies following laparoscopic cholecystectomy. It highlights the integration of pharmacologic and non-pharmacologic approaches targeting different pain pathways to optimize postoperative analgesia. The proposed strategy emphasizes opioid-sparing management through the combined use of non-opioid analgesics, adjuvant therapies, and local anesthetic techniques together with early mobilization, respiratory exercises, and patient education. This integrated approach reduces opioid consumption, minimizes adverse effects, and supports enhanced postoperative recovery. Overall, a multimodal and patient-centered approach improves pain control and contributes to better functional recovery and patient outcomes.

Introduction

Laparoscopic cholecystectomy is the standard and most widely performed treatment for symptomatic gallbladder disease. It is a minimally invasive procedure and is associated with faster postoperative recovery compared to open surgery (1). Despite its advantages, postoperative pain remains a significant clinical challenge. It may delay recovery, prolong hospital stay, increase complications, and, if not managed properly, contribute to chronic pain (2). Postoperative pain after laparoscopic cholecystectomy is multifactorial. It includes incisional, visceral, and shoulder pain. These arise from surgical trauma, trocar insertion, and diaphragmatic irritation. As a result, single-agent analgesia is often not sufficient to control all pain components (3). Effective perioperative pain management requires a multimodal approach with an emphasis on opioid-sparing strategies. Although opioids are effective, they are associated with important side effects and the risk of dependence (2). Multimodal analgesia combines pharmacologic and non-pharmacologic methods to target different pain pathways. This approach improves analgesia while reducing adverse effects (4). However, current evidence on pain management after laparoscopic

cholecystectomy is still fragmented. Most studies focus on either pharmacologic or non-pharmacologic strategies separately. This highlights the need for a more integrated and guideline-based approach (3, 5). The aim of this review is to provide an up-to-date overview of pharmacologic and non-pharmacologic strategies for postoperative pain management after laparoscopic cholecystectomy, with a focus on multimodal analgesia. It also aims to identify current evidence gaps and suggest directions for future research (Table 1).

Approach Type	Name of Medication/Method	Advantages	Disadvantages	Research Evidence
Pharmacologic	Opioid Analgesics	Rapid pain relief, effective for severe pain	Risk of dependence, side effects such as nausea	Evidence supports short-term effectiveness
Pharmacologic	NSAIDs	Reduces inflammation and mild to moderate pain	Gastrointestinal side effects, increased bleeding risk	Limited evidence for long-term effects
Non-Pharmacologic	Physical Therapy	Reduces reliance on medications, aids in recovery	Longer onset of action, requires more time for benefit	Evidence is less robust compared to medications
Non-Pharmacologic	Breathing and Relaxation Techniques	Reduces stress and helps control pain and anxiety	May not be as effective as medications	Limited studies on effectiveness

Table 1. Comparison of Pharmacologic and Non-Pharmacologic Approaches to Postoperative Pain Management After Laparoscopic Cholecystectomy. This table provides a comparison of both pharmacologic and non-pharmacologic methods used for managing postoperative pain following laparoscopic cholecystectomy. It highlights the advantages and disadvantages of each approach, as well as the available research evidence supporting their effectiveness. The goal is to provide a clearer understanding of the different pain management strategies and guide clinical decision-making.

Pathophysiology of Postoperative Pain After Laparoscopic Cholecystectomy

Postoperative pain after laparoscopic cholecystectomy is multifactorial. It results from a combination of incisional, visceral, and referred mechanisms, despite the minimally invasive nature of the procedure (6). Incisional pain occurs after trocar insertion and is related to tissue injury and local inflammation. It is usually localized and well defined. The pain is most intense within the first 24 hours after surgery (7). Visceral pain originates from manipulation of the gallbladder and surrounding tissues. Inflammation, ischemia, and traction activate visceral afferent fibers. This type of pain is typically deep, dull, and poorly localized. It may persist longer than incisional pain (8). Shoulder pain after laparoscopic surgery is mainly caused by diaphragmatic irritation due to residual CO_2. This stimulates the phrenic nerve and may last for several hours postoperatively

(9). Pneumoperitoneum also contributes to postoperative pain. It increases intra-abdominal pressure and reduces splanchnic blood flow. This may lead to ischemia, local acidosis, and release of inflammatory mediators. These changes sensitize peripheral nociceptors (10, 11). Surgical trauma triggers a broader inflammatory response. Mediators such as prostaglandins, bradykinin, and cytokines are released. These enhance both peripheral and central sensitization and increase pain intensity (12). Central sensitization develops due to repeated nociceptive input. It can amplify and prolong postoperative pain (13). This highlights the importance of early and adequate analgesia.

Overall, the overlap of incisional, visceral, and referred pain mechanisms makes single-agent analgesia insufficient. This further supports the need for a multimodal analgesic approach after laparoscopic cholecystectomy (14).

Pharmacologic Management

Effective postoperative pain management after laparoscopic cholecystectomy relies on a combination of pharmacologic interventions, ideally integrated within a multimodal analgesic strategy to optimize pain control while minimizing adverse effects (15). NSAIDs inhibit cyclooxygenase enzymes and reduce prostaglandin synthesis, effectively controlling inflammatory pain and sparing opioid use (16). Selective COX-2 inhibitors provide similar analgesia with lower gastrointestinal risk, but their use should be individualized based on patient comorbidities, taking into account cardiovascular and renal status (17, 18). Acetaminophen plays a key role in multimodal analgesia, providing effective pain and fever control. When combined with NSAIDs or opioids, acetaminophen enhances analgesia while reducing opioid consumption, likely through central prostaglandin inhibition and serotonergic modulation (19, 20). Opioids, though effective for moderate to severe postoperative pain via μ-opioid receptor–mediated inhibition of nociceptive signaling, are generally reserved for breakthrough pain due to their side effects and risk of dependence, highlighting the importance of opioid-sparing strategies (2). Adjuvant agents, including gabapentin, low-dose ketamine, corticosteroids, and α2-adrenergic agonists, can further enhance analgesia by modulating central sensitization and inflammation. When used appropriately, these agents help reduce pain scores and opioid requirements (21, 22). Local anesthetic techniques, such as trocar-site infiltration to reduce incisional pain and intraperitoneal administration to attenuate visceral and shoulder pain, further enhance analgesia. Their efficacy depends on timing, dose, and technique, and proper administration is essential to achieve optimal benefit (23, 24). When combined in a multimodal pharmacologic regimen, these agents exert complementary effects that improve overall pain control, minimize reliance on systemic opioids, and enhance postoperative recovery (4). Current evidence supports the routine implementation of multimodal pharmacologic strategies, including NSAIDs or COX-2 inhibitors, acetaminophen, local anesthetics, and selective adjuvant agents, as the preferred approach for managing postoperative pain after laparoscopic cholecystectomy (3, 25). Overall, the presented evidence suggests that herbal therapies are associated with clinically significant drug–herb interactions and adverse outcomes, warranting cautious use alongside conventional pharmacologic regimens (26).

Non-Pharmacologic Management

Non-pharmacologic interventions serve as important complementary strategies for postoperative pain management after laparoscopic cholecystectomy. They aim to reduce pain intensity, improve patient comfort, and decrease reliance on pharmacologic analgesics, particularly opioids (27). Transcutaneous electrical nerve

stimulation (TENS) is a non-invasive method that reduces postoperative pain and analgesic use by stimulating peripheral nerves and activating endogenous inhibitory pathways (28). Acupressure and acupuncture are traditional techniques that are increasingly used in perioperative care. They help reduce postoperative pain and related symptoms such as nausea and vomiting. This effect is mainly mediated through modulation of neurohumoral pathways, including endorphin release and autonomic regulation (29). Massage therapy can reduce pain by promoting muscle relaxation, improving circulation, and reducing stress-related physiological responses. Aromatherapy with essential oils may also help decrease perceived discomfort through central nervous system and psychological effects (30, 31). Physical and behavioral interventions, such as early mobilization, optimized positioning, and guided breathing exercises, support functional recovery and also contribute to pain reduction. Furthermore, patient education, reassurance, and psychological support can reduce anxiety-related pain amplification and improve overall postoperative outcomes (32).

Non-pharmacologic interventions are generally safe and well tolerated. Their effectiveness increases when used as part of a multimodal analgesic strategy alongside pharmacologic treatment, rather than as standalone approaches (33). Multimodal analgesia is the cornerstone of modern postoperative pain management. It involves the combined use of multiple interventions targeting different pain pathways, with the goal of maximizing analgesic efficacy while minimizing side effects of single-agent therapy (34). Pharmacologic multimodal analgesia usually includes acetaminophen combined with NSAIDs or COX-2 inhibitors for baseline pain control. Opioids are reserved for breakthrough pain at the lowest effective dose. Adjuvant agents such as gabapentinoids, corticosteroids, NMDA antagonists, and α2-adrenergic agonists may be used in selected patients to enhance analgesia and reduce opioid requirements (35). Non-pharmacologic strategies complement pharmacologic therapy by reducing pain perception, lowering anxiety, and improving patient comfort. These include TENS, acupuncture, massage therapy, and structured patient education with psychological support (36). Evidence demonstrates that multimodal Evidence shows that multimodal analgesia improves postoperative pain control, reduces opioid consumption and related adverse effects, supports earlier mobilization and faster recovery, and increases patient satisfaction (37).

Successful implementation requires individualized strategies based on patient factors, surgical complexity, and available resources. Interdisciplinary collaboration among surgeons, anesthesiologists, and nursing staff is also essential for optimal outcomes (38). Overall, multimodal analgesia is a safe, effective, and evidence-based approach for postoperative pain management after laparoscopic cholecystectomy. It supports enhanced recovery pathways and improves perioperative care (39) (Table 2).

Opioid-Sparing Strategies

Opioid-sparing strategies have become a central goal in postoperative pain management due to concerns regarding opioid-related adverse effects and the potential for long-term dependence (2). Following laparoscopic cholecystectomy, these strategies primarily rely on multimodal analgesia, which provides effective baseline pain control while minimizing opioid requirements (40).

Routine use of acetaminophen in combination with NSAIDs or COX-2 inhibitors offers substantial analgesia and significantly reduces the need for opioids in the postoperative period (41).

Pharmacologic adjuvants such as gabapentinoids (gabapentin, pregabalin), corticosteroids (e.g., dexamethasone), NMDA receptor antagonists (e.g., low-dose ketamine), and α2-adrenergic

agonists (e.g., dexmedetomidine, clonidine) enhance opioid-sparing effects by modulating central sensitization and inflammatory pathways (21, 42).

Intervention	Mechanism of Action	Pain Control Effectiveness	Additional Benefits	Key Considerations
Transcutaneous Electrical Nerve Stimulation (TENS)	Stimulates peripheral nerves, activates endogenous inhibitory pathways	Reduces postoperative pain and analgesic use	Non-invasive, easy to apply	Requires proper placement and duration for optimal effect
Acupressure and Acupuncture	Modulates neurohumoral pathways (endorphin release, autonomic regulation)	Alleviates pain, nausea, and vomiting	Can reduce anxiety and promote relaxation	Techniques may require trained practitioners
Massage Therapy	Promotes muscle relaxation, enhances circulation, modulates stress-related responses	Reduces muscle tension and improves circulation	Alleviates stress, promotes relaxation	Should be applied with care to avoid excessive pressure
Aromatherapy	Uses essential oils to influence central nervous system and psychological mechanisms	Reduces perceived discomfort and promotes relaxation	Enhances mood and overall comfort	Need for appropriate essential oil selection
Physical and Behavioral Interventions	Early mobilization, optimized positioning, guided breathing exercises	Reduces pain and promotes functional recovery	Improves overall postoperative outcomes	Requires patient participation and guidance
Patient Education and Psychological Support	Reduces anxiety, mitigates pain amplification	Enhances patient comfort and satisfaction	Improves coping mechanisms and emotional well-being	Ongoing support may be required for maximum effect

Table 2. Non-Pharmacologic Approaches to Postoperative Pain Management Following Laparoscopic Cholecystectomy. This table outlines various non-pharmacologic interventions used in postoperative pain management following laparoscopic cholecystectomy. It highlights the mechanisms of action, effectiveness in reducing pain, additional benefits, and key considerations for each approach. These strategies, when integrated into a multimodal analgesic plan, help optimize pain relief, improve patient comfort, and minimize reliance on pharmacologic agents, especially opioids.

These agents reduce pain intensity and allow lower opioid consumption. As a result, they are important components of multimodal analgesia.

Additionally, local anesthetic techniques, including trocar-site infiltration and intraperitoneal administration, provide effective additional analgesia, particularly for incisional, visceral, and shoulder pain, further reducing opioid requirements (43).

Non-pharmacologic interventions such as TENS, acupressure, acupuncture, massage therapy, patient education, and psychological support enhance pain management by modulating pain perception and reducing anxiety. They are generally safe and well tolerated (36). The implementation of opioid-sparing protocols has been associated with reduced opioid-related adverse effects, improved early mobilization, faster functional recovery, and higher patient satisfaction (44).

However, careful patient selection, individualized dosing, and close monitoring are essential to ensure adequate analgesia while avoiding excessive opioid exposure (44, 45). In conclusion, combining pharmacologic and non-pharmacologic strategies within a structured multimodal framework represents an effective, evidence-based approach for achieving opioid-sparing goals after laparoscopic cholecystectomy (2, 46).

Practical Recommendations

Effective postoperative pain management following laparoscopic cholecystectomy should prioritize multimodal analgesia, combining acetaminophen with NSAIDs or COX-2 inhibitors for baseline pain control (3, 47).

Opioids should be reserved for breakthrough pain, used at the lowest effective dose, and carefully titrated, particularly in vulnerable populations such as the elderly or those with respiratory compromise (48, 49).

Non-pharmacologic interventions such as TENS, acupressure, acupuncture, massage therapy, and structured patient education enhance analgesia, reduce anxiety, and improve patient comfort (50, 51). Early mobilization, optimized positioning, and guided breathing exercises support recovery and help reduce complications such as atelectasis and venous thromboembolism (52, 53).

The individualization of analgesic regimens based on patient characteristics, including age, comorbidities, and surgical complexity, is essential. Furthermore, perioperative care should also address long-term outcomes, such as prevention of chronic pain and reduction of long-term opioid use (4, 54).

Interdisciplinary collaboration between surgeons, anesthesiologists, pain specialists, and nursing staff is critical for the successful implementation of multimodal protocols. This collaboration ensures better coordination of pain management, reduced opioid use, and improved overall patient outcomes (55). Integrating multimodal strategies into Enhanced Recovery After Surgery (ERAS) programs has been shown to significantly reduce hospital length of stay and improve patient satisfaction, demonstrating the effectiveness of these protocols in optimizing postoperative recovery (56). In conclusion, a patient-centered multimodal approach to postoperative pain management after laparoscopic cholecystectomy is essential for optimizing analgesic efficacy, minimizing opioid-related risks, facilitating faster functional recovery, and improving overall perioperative care (57).

Special Populations

Certain patient populations require tailored approaches to postoperative pain management following laparoscopic cholecystectomy, as physiologic differences and comorbidities can significantly influence both pain perception and analgesic response (5).

Elderly patients experience age-related changes in pharmacokinetics and pharmacodynamics,

including reduced hepatic and renal clearance, altered body composition, and increased CNS sensitivity (58). These factors increase the risk of adverse drug effects such as oversedation, delirium, respiratory depression, and falls. This necessitates dose adjustments, lower starting doses, longer dosing intervals, and careful monitoring to ensure safety and efficacy (59, 60). Patients with renal or hepatic impairment face additional challenges in pain management (61, 62). NSAIDs should generally be avoided due to nephrotoxicity and fluid retention. Gabapentinoids may also cause excessive sedation or ataxia in this population (63, 64).

Drugs with extensive hepatic metabolism, such as high-dose acetaminophen or opioids, require careful titration or the use of safer alternatives (58, 61, 65). Analgesics with more favorable metabolic profiles should be preferred, and non-pharmacologic strategies should be considered to minimize overall drug exposure (49). Individuals with chronic opioid use, opioid tolerance, or prior opioid-related adverse effects require specialized management strategies (66, 67). Given the variability in analgesic responses across different populations and the reported safety concerns, limited regulatory oversight, and potential for herb–drug interactions associated with herbal compounds, the available evidence suggests a need for further research focusing on their safety profile and their potential role within personalized, multimodal pain management strategies (68). Moreover, opioid tolerance and receptor adaptations may increase postoperative analgesic requirements and contribute to opioid-induced hyperalgesia (69, 70).

Enhanced multimodal analgesia—combining non-opioid pharmacologic agents, regional anesthesia techniques, and non-pharmacologic interventions—is essential for adequate pain control while minimizing opioid use. Adjuvants such as NMDA receptor antagonists or α2-adrenergic agonists may be useful in targeting central sensitization (71, 72). Obese patients also require careful analgesic management due to altered drug distribution, increased adipose tissue, drug sequestration in fat, and changes in hepatic blood flow, all of which affect pharmacokinetics and pharmacodynamics (73). These factors, combined with increased postoperative pain and respiratory risk, require careful dosing and monitoring (74). Accurate dose selection, use of safer agents, and integration of non-pharmacologic approaches are essential to minimize adverse outcomes (36, 49).

Across all special populations, key principles include individualized analgesic planning, careful drug selection and dosing, early incorporation of non-pharmacologic strategies, and interdisciplinary coordination. This approach improves pain control, enhances recovery, and reduces adverse events through a patient-centered and evidence-based perioperative strategy (75, 76) (Table 3).

Safety and Adverse Effects Considerations

Safety is crucial in postoperative pain management, especially with multimodal analgesia (77). While it improves pain control and reduces opioid use, each intervention carries potential risks that must be balanced against its benefits (34). Non-steroidal anti-inflammatory drugs (NSAIDs) effectively reduce inflammatory pain and opioid requirements. However, their mechanism—cyclooxygenase inhibition—can impair renal function and increase the risk of acute kidney injury, particularly in patients with preexisting renal disease or dehydration (78, 79). NSAIDs also increase the risk of gastrointestinal bleeding and peptic ulcers, especially in older adults or patients with a history of gastrointestinal disease (80, 81). In addition, some NSAIDs may increase cardiovascular risk, including myocardial infarction and stroke, which requires careful patient selection and monitoring (82, 83).

COX-2 inhibitors offer reduced gastrointestinal toxicity but still require careful consideration of cardiovascular safety (84, 85).

Patient Population	Challenges	Recommended Strategies	Key Considerations
Elderly Patients	Age-related changes in pharmacokinetics and pharmacodynamics, CNS sensitivity	Lower initial doses, extended intervals, careful monitoring	Risk of oversedation, delirium, respiratory depression, and falls
Renal or Hepatic Impairment	Reduced clearance, risk of nephrotoxicity and fluid retention	Avoid NSAIDs, use drugs with favorable metabolic profiles, cautious with gabapentinoids	Careful titration of acetaminophen and opioids
Chronic Opioid Use / Opioid Tolerance	Receptor adaptations, opioid-induced hyperalgesia	Multimodal analgesia (non-opioid pharmacologics, regional anesthesia, NMDA antagonists, α2-adrenergic agonists)	Increased postoperative analgesic needs, higher risk of opioid dependence
Obese Patients	Altered pharmacokinetics due to adipose tissue, increased drug sequestration	Accurate dose calculation, use of safe agents, non-pharmacologic adjuncts	Increased postoperative pain and respiratory risks

Table 3. Tailored Postoperative Pain Management Strategies for Special Populations Following Laparoscopic Cholecystectomy. This table summarizes the tailored postoperative pain management strategies for special populations following laparoscopic cholecystectomy. It outlines the unique challenges faced by elderly patients, those with renal or hepatic impairment, individuals with chronic opioid use or opioid tolerance, and obese patients. The table also presents recommended strategies for each group, focusing on careful selection and dosing of pharmacologic agents, as well as the importance of multimodal analgesia and non-pharmacologic interventions to optimize pain control and minimize risks.

Acetaminophen is generally safe and effective, but overdose can lead to hepatotoxicity due to accumulation of the toxic metabolite NAPQI, particularly in patients with liver disease, chronic alcohol use, or malnutrition (86). Opioids are effective for moderate to severe pain, but they are associated with adverse effects such as nausea, constipation, and respiratory depression. These risks are higher in patients with sleep apnea or underlying pulmonary disease (87). The risk of tolerance, dependence, and misuse further supports the need for opioid-sparing strategies in perioperative care (88).

Adjuvant agents also carry important safety considerations. Gabapentinoids may cause dizziness and ataxia (89), corticosteroids can impair glucose control and increase infection risk (90), NMDA antagonists such as ketamine may induce psychomimetic effects (91), and α2-adrenergic agonists like dexmedetomidine may cause bradycardia and hypotension (92). These effects require careful monitoring, especially in high-risk patients.

Non-pharmacologic interventions, including TENS, acupressure, massage therapy, and psychological support, are generally well tolerated and have minimal adverse effects. They

are particularly useful in patients at higher risk of drug-related toxicity or those with contraindications to pharmacologic agents (27, 93).

Personalized pain assessment combined with multimodal strategies improves analgesic effectiveness while reducing adverse effects. Clinical guidelines emphasize preoperative risk stratification and careful selection of analgesic modalities (94). Clear communication with patients regarding benefits and risks supports shared decision-making and helps align multimodal analgesia strategies with modern perioperative care standards (95).

Evidence Gaps and Future Directions

Despite extensive research on postoperative pain management after laparoscopic cholecystectomy, important evidence gaps still remain and limit the development of standardized clinical guidelines. Challenges include variability in study design, patient populations, analgesic protocols, and outcome measures, which makes direct comparison difficult. Most studies focus on single pharmacologic or non-pharmacologic interventions rather than integrated multimodal strategies. In addition, the optimal combination, timing, and sequence of analgesics remain unclear, with findings that are often inconsistent across studies. Many trials are limited by small sample sizes, short follow-up periods, and insufficient blinding, which reduce statistical power and increase the risk of bias. Pain assessment tools are also used inconsistently, while long-term outcomes such as chronic pain, functional recovery, and quality of life are often underreported or not systematically assessed.

Evidence for non-pharmacologic interventions such as acupuncture and TENS remains variable, influenced by operator skill, study design, and patient expectations. Future research should focus on large, well-designed randomized trials with standardized protocols, consistent outcome measures, and real-world clinical data to better inform postoperative pain management strategies.

Limitations of the Review

This review has several limitations. The included studies show significant heterogeneity in study design, patient populations, and analgesic protocols, which limits direct comparison and meaningful synthesis of findings. Most available evidence focuses on short-term postoperative pain outcomes, while long-term outcomes such as chronic pain and functional recovery are less consistently evaluated across studies.

The evidence for non-pharmacologic interventions is also variable, affected by small sample sizes, lack of blinding, and inconsistent implementation across studies. Publication bias and differences in outcome measurement tools may further affect the interpretation and generalizability of the findings. Despite these limitations, this review provides a comprehensive synthesis of the current literature, identifies key evidence gaps, and highlights important directions for future research to strengthen evidence-based postoperative pain management after laparoscopic cholecystectomy.

Conclusion

Postoperative pain remains a common and clinically significant challenge following laparoscopic cholecystectomy. Although the procedure is minimally invasive, inadequate pain control can adversely affect recovery, functional outcomes, and patient satisfaction. Pain after laparoscopic cholecystectomy is multifactorial and includes incisional, visceral, and referred components. This complexity requires an approach that targets multiple pain pathways rather than relying on a single analgesic modality. Current evidence strongly supports multimodal analgesia as the most effective strategy for postoperative pain management. This approach combines pharmacologic agents such as acetaminophen, non-steroidal anti-inflammatory drugs, adjuvant analgesics, and carefully titrated

opioids to achieve adequate pain control while reducing opioid-related adverse effects.

Non-pharmacologic interventions, including transcutaneous electrical nerve stimulation, acupressure, massage therapy, and structured patient education, serve as useful adjuncts. They help improve analgesia, enhance patient comfort, and are generally associated with minimal risk. Optimal outcomes depend on an individualized and evidence-based approach that takes into account patient characteristics, comorbidities, surgical complexity, and available institutional resources. Interdisciplinary collaboration among surgeons, anesthesiologists, and nursing staff is also essential for the effective implementation of multimodal pain management protocols.

Overall, the integration of pharmacologic and non-pharmacologic strategies within a multimodal framework represents the current standard of care for postoperative pain management after laparoscopic cholecystectomy. Further research is needed to refine these strategies and optimize patient-centered perioperative outcomes.

Clinical Relevance and Implications for Patient Care

Postoperative pain after laparoscopic cholecystectomy remains an important factor influencing recovery, patient satisfaction, and healthcare utilization. This review highlights the importance of a multimodal, opioid-sparing approach to pain management. It integrates pharmacologic and non-pharmacologic strategies to better address the multifactorial nature of postoperative pain.

From a clinical perspective, the use of baseline non-opioid analgesics such as acetaminophen in combination with NSAIDs or COX-2 inhibitors is recommended. These agents can be combined with adjuvant medications and local or regional anesthesia techniques. This combination provides effective pain control while reducing the need for opioids. As a result, opioid-related adverse effects such as nausea, sedation, respiratory depression, and long-term dependence are minimized. Non-pharmacologic methods also play an important role in recovery. Early mobilization, breathing exercises, transcutaneous electrical nerve stimulation, and structured patient education can enhance postoperative recovery. These interventions help reduce anxiety, improve functional outcomes, and support earlier return to normal daily activities. Pain management should be individualized based on patient-specific factors. Age, comorbidities, and surgical risk profile should all be considered. Elderly patients, as well as those with chronic opioid use or organ dysfunction, often require more cautious and tailored strategies with close clinical monitoring.

Finally, integrating these approaches into Enhanced Recovery After Surgery (ERAS) programs helps standardize perioperative care. It improves recovery outcomes, reduces hospital length of stay, and increases patient satisfaction. Overall, these findings support a coordinated, multidisciplinary, and patient-centered approach to postoperative pain management with careful opioid stewardship.

Funding Statement

This research received no external funding.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

All authors contributed to the conception and design of the study, literature search, data interpretation, drafting of the manuscript, and critical revision of the article. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Data Availability Statement

No new data were generated or analyzed in this study. Data sharing is not applicable to this article, as it is based on previously published literature.

Acknowledgments

The authors would like to thank all researchers whose work contributed to the evidence synthesized in this review.

Reference:

1. Zhang Y, Dai X, Duan R, Wei L. Research progress in the treatment of gallstones with laparoscopic and endoscopic surgery: a narrative review. BMC Surg. 2025;25(1):238.

2. Zhang Z, Wang JJ, Ping ZG, Jin XG, Yang JJ, Wang Y, et al. The Impact of Opioid-Sparing Analgesia on Postoperative Pain and Recovery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Pain Ther. 2025;14(5):1473-97.

3. Bayoumi HM, Abdelaziz DH, El Said NO, Boraii S, Bendas ER. Postoperative pain management following laparoscopic cholecystectomy-non-opioid approaches: a review. Future Journal of Pharmaceutical Sciences. 2024;10(1):125.

4. Joshi GP. Rational Multimodal Analgesia for Perioperative Pain Management. Curr Pain Headache Rep. 2023;27(8):227-37.

5. Bourgeois C, Oyaert L, Van de Velde M, Pogatzki-Zahn E, Freys SM, Sauter AR, et al. Pain management after laparoscopic cholecystectomy: A systematic review and procedure-specific postoperative pain management (PROSPECT) recommendations. Eur J Anaesthesiol. 2024;41(11):841-55.

6. Zhang D, Wang X, Yang X, Xia D. The effect of intraperitoneal instillation of drugs on postoperative analgesia after laparoscopic cholecystectomy: a network meta-analysis. Front Pharmacol. 2025;16:1646917.

7. Shrestha BB, Lakhe G, Ghimire P. Postoperative Pain after Laparoscopic Cholecystectomy in a Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2024;62(276):502-6.

8. Mactier I, Al-Ani T. Visceral pain. Anaesthesia & Intensive Care Medicine. 2025;26(7):420-5.

9. Zhao Y, Xin W, Luo X. Post-laparoscopic Shoulder Pain Management: A Narrative Review. Current Pain and Headache Reports. 2025;29(1):18.

10. Umano GR, Delehaye G, Noviello C, Papparella A. The "Dark Side" of Pneumoperitoneum and Laparoscopy. Minim Invasive Surg. 2021;2021:5564745.

11. Rashdan M, Daradkeh S, Al-Ghazawi M, Abuhmeidan JH, Mahafthah A, Odeh G, et al. Effect of low-pressure pneumoperitoneum on pain and inflammation in laparoscopic cholecystectomy: a randomized controlled clinical trial. BMC Research Notes. 2023;16(1):235.

12. Chang C, Wu X, Liu K, Wang L, Adu M, Lin Q, et al. A comprehensive review on pain: Model, target, therapy, and prospect. International Journal of Molecular Medicine. 2025;57(2):46.

13. Tassou A, Richebe P, Rivat C. Mechanisms of chronic postsurgical pain. Reg Anesth Pain Med. 2025;50(2):77-85.

14. Hafez Elsayyed MSE, Massoud SM, Abdellatif HK, Mohamed AM. Postoperative Analgesia in Laparoscopic Cholecystectomy in Obese Patients. Zagazig University Medical Journal. 2025;31(2).

15. Sharifian M, Marzban A. Advances and Challenges in Postoperative Pain Management: Innovations in Anesthesia Techniques for Acute Care. Interdisciplinary Journal of Acute Care. 2025;6(2):165-7.

16. Ghai B, Jafra A, Bhatia N, Chanana N, Bansal D, Mehta V. Opioid sparing strategies for perioperative pain management other than regional anaesthesia: A narrative review. J Anaesthesiol Clin Pharmacol. 2022;38(1):3-10.

17. Govindaswamy S, Ponnusamy K, S. I, Anil V, Venugopal J, Sundaram DP. A Systematic Review

and Meta-analysis of Selective Cyclooxygenase-2 Inhibitors and Non-selective Non-steroidal Anti-inflammatory Drugs for Acute Gout. Journal of Pharmacology and Pharmacotherapeutics. 2024;15(2):122-32.

18. Moses G. COX-2 selective nonsteroidal anti-inflammatory drugs: what is their place in managing dental pain? Australian Prescriber. 2025;48(4):145.

19. Freo U. Paracetamol for multimodal analgesia. Pain Manag. 2022;12(6):737-50.

20. Tsuchiya H, Mizogami M. Old and New Analgesic Acetaminophen: Pharmacological Mechanisms Compared with Non-Steroidal Anti-Inflammatory Drugs. Future Pharmacology. 2025;5(3):40.

21. Carron M, Tamburini E, Linassi F, Pettenuzzo T, Boscolo A, Navalesi P. Efficacy of nonopioid analgesics and adjuvants in multimodal analgesia for reducing postoperative opioid consumption and complications in obesity: a systematic review and network meta-analysis. British Journal of Anaesthesia. 2024;133(6):1234-49.

22. Kummer I, Lüthi A, Klingler G, Andereggen L, Urman RD, Luedi MM, et al. Adjuvant Analgesics in Acute Pain – Evaluation of Efficacy. Current Pain and Headache Reports. 2024;28(9):843-52.

23. Karczewska M, Szukalska S, Lichwala K, Samborska A, Balajewicz B, Wróblewski K, et al. Local Anaesthetic Infiltration at Trocar Sites for Early Postoperative Pain Control in Laparoscopic Surgery. Cureus. 2026;18(1):e101138.

24. Dubey N, Bellamy F, Bhat S, MacFacter W, Rossaak J. The impact of timing, type, and method of instillation of intraperitoneal local anaesthetic in laparoscopic abdominal surgery: a systematic review and network meta-analysis. British Journal of Anaesthesia. 2024;132(3):562-74.

25. Cao L, Yang T, Hou Y, Yong S, Zhou N. Efficacy and Safety of Different Preemptive Analgesia Measures in Pain Management after Laparoscopic Cholecystectomy: A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. Pain Ther. 2024;13(6):1471-97.

26. Spanakis M, Bakaros E, Papadopoulou SN, Fournaraki A, Symvoulakis EK. Pharmacoepidemiological data on drug–herb interactions: serotonin syndrome, arrhythmias and the emerging role of artificial intelligence. Pharmacoepidemiology. 2025 Oct 9;4(4):22. https://doi.org/10.3390/pharma4040022

27. Lei T, Peng Y, Liu Y, Xie Y, Wang J. Effectiveness of Non-Pharmacological Interventions for Pain Management After Laparoscopic Cholecystectomy: A Systematic Review and Network Meta-Analysis. J Pain Res. 2025;18:6933-46.

28. Viderman D, Nabidollayeva F, Aubakirova M, Sadir N, Tapinova K, Tankacheyev R, et al. The Impact of Transcutaneous Electrical Nerve Stimulation (TENS) on Acute Pain and Other Postoperative Outcomes: A Systematic Review with Meta-Analysis. J Clin Med. 2024;13(2).

29. Shah S, Godhardt L, Spofford C. Acupuncture and Postoperative Pain Reduction. Curr Pain Headache Rep. 2022;26(6):453-8.

30. Liu C, Chen X, Wu S. The effect of massage therapy on pain after surgery: A comprehensive meta-analysis. Complementary Therapies in Medicine. 2022;71:102892.

31. Biachi FB, de Oliveira Faria MF, Oliveira RA, de Brito Poveda V, Rizzo Gnatta J. Effect of Aromatherapy for Postoperative Pain Management in the Postanesthesia Recovery Room: A Systematic Review. J Perianesth Nurs. 2025;40(4):1016-23.e2.

32. Nadinda PG, van Ryckeghem DM, Peters ML. Can perioperative psychological interventions decrease the risk of postsurgical pain and disability? A systematic review and meta-analysis of randomized controlled trials. Pain. 2022;163(7):1254-73.

33. Kichili N, Brown MK, Armer DS, Mashaw SA, Gennuso SA, Ahmadzadeh S, Shekoohi S, Kaye AD. Analyzing the Efficacy and Potential

Risks of Nitrous Oxide for Pain Management During Labor: A Narrative Review. Clinical Pharmacology: Advances and Applications. 2026 Dec 31:577932.

34. Kianian S, Bansal J, Lee C, Zhang K, Bergese SD. Perioperative multimodal analgesia: a review of efficacy and safety of the treatment options. Anesthesiology and Perioperative Science. 2024;2(1):9.

35. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. JAMA surgery. 2017;152(7):691-7.

36. Niyonkuru E, Iqbal MA, Zhang X, Ma P. Complementary approaches to postoperative pain management: a review of non-pharmacological interventions. Pain and therapy. 2025;14(1):121-44.

37. Kehlet H, Dahl JB. Anaesthesia, surgery, and challenges in postoperative recovery. The Lancet. 2003;362(9399):1921-8.

38. Zhang Q, Sun Q, Li J, Fu X, Wu Y, Zhang J, et al. The Impact of ERAS and Multidisciplinary Teams on Perioperative Management in Colorectal Cancer. Pain and Therapy. 2025;14(1):201-15.

39. Shim J-W, Ko J, Bae JH, Park J, Lee HM, Kim Y-S, et al. Pre-emptive multimodal analgesic bundle with transversus abdominis plane block enhances early recovery after laparoscopic cholecystectomy. Asian Journal of Surgery. 2022;45(1):250-6.

40. Toleska M, Dimitrovski A, Shosholcheva M, Kartalov A, Kuzmanovska B, Dimitrovska NT. Pain and Multimodal Analgesia in Laparoscopic Cholecystectomy. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 2022;43(2):41-9.

41. Park JH, Lee DW, Kim EJ, Cho JS. Analgesic Efficacy of Acetaminophen/Ibuprofen as an Adjuvant in Patient-Controlled Analgesia for Postoperative Pain After Oncoplastic Breast Surgery: A Randomized Controlled Trial. Journal of Clinical Medicine. 2025;14(22):7901.

42. Kim M, Huh J, Choi H, Hwang W. Impact of dexmedetomidine-based opioid-sparing anesthesia on opioid use after minimally invasive repair of pectus excavatum: A prospective randomized controlled trial. Journal of Clinical Medicine. 2024;13(23):7264.

43. Elsaeed UA, Algyoushy EAFIH, Hatem DLM. Effect of port-site and intraperitoneal local anesthetic injection versus placebo on postoperative pain and recovery after gynecologic laparoscopic surgery: a randomized controlled trial. Scientific Reports. 2025;15(1):32466.

44. Gazendam A, Ekhtiari S, Horner NS, Simunovic N, Khan M, de Sa DL, et al. Effect of a Postoperative Multimodal Opioid-Sparing Protocol vs Standard Opioid Prescribing on Postoperative Opioid Consumption After Knee or Shoulder Arthroscopy: A Randomized Clinical Trial. Jama. 2022;328(13):1326-35.

45. Cordero-Pérez FJ, Pérez-Baena MJ, Pina-Ruviralta N, Fernández-Testa A, Holgado-Madruga M. Optimizing Opioid Use in Pain Management: A Comprehensive Review of Clinical Benefits, Risks, and Dependence. InHealthcare 2026 Feb 11 (Vol. 14, No. 4, p. 457). MDPI.

46. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment of the evidence. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. 2006.

47. Barazanchi AWH, MacFater WS, Rahiri JL, Tutone S, Hill AG, Joshi GP. Evidence-based management of pain after laparoscopic cholecystectomy: a PROSPECT review update. Br J Anaesth. 2018;121(4):787-803.

48. D'Amore T, Meghpara M, Ramtin S, Fillingham YA, Lonner JH. Evidence-based orthopaedic post-operative opioid prescribing recommendations following hip and knee arthroplasty. SurgiColl. 2023;1(2).

49. Chen X, Chu Q, Peng Y, Chen Y, Kaye AD, Liu H, et al. Clinical practice guidelines for

postoperative pain management in adults (2024 edition). Journal of Anesthesia and Translational Medicine. 2025;4(3):161-85.

50. Kukimoto Y, Ooe N, Ideguchi N. The Effects of Massage Therapy on Pain and Anxiety after Surgery: A Systematic Review and Meta-Analysis. Pain Manag Nurs. 2017;18(6):378-90.

51. Liu X-L, Tan J-Y, Molassiotis A, Suen LKP, Shi Y. Acupuncture-Point Stimulation for Postoperative Pain Control: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Evidence-Based Complementary and Alternative Medicine. 2015;2015(1):657809.

52. Altman AD, Helpman L, McGee J, Samouëlian V, Auclair MH, Brar H, et al. Enhanced recovery after surgery: implementing a new standard of surgical care. Cmaj. 2019;191(17):E469-e75.

53. Talec P, Gaujoux S, Samama CM. Early ambulation and prevention of post-operative thrombo-embolic risk. J Visc Surg. 2016;153(6s):S11-s4.

54. Xu J, Liu X, Zhao J, Zhao J, Li H, Ye H, et al. Comprehensive review on personalized pain assessment and multimodal interventions for postoperative recovery optimization. Journal of pain research. 2025:2791-804.

55. Komasawa N. Revitalizing Postoperative Pain Management in Enhanced Recovery After Surgery via Inter-departmental Collaboration Toward Precision Medicine: A Narrative Review. Cureus. 2024;16(4):e59031.

56. Sauro KM, Smith C, Ibadin S, Thomas A, Ganshorn H, Bakunda L, et al. Enhanced recovery after surgery guidelines and hospital length of stay, readmission, complications, and mortality: a meta-analysis of randomized clinical trials. JAMA Network Open. 2024;7(6):e2417310.

57. Soni AK, Dubey R, Baghel K, Shukla A. Impact of ERAS Protocol on Postoperative Recovery and Complications in Patients Undergoing Laparoscopic Cholecystectomy: A Prospective Comparative Analysis. J Pharm Bioallied Sci. 2025;17(Suppl 3):S2265-s7.

58. Ruiz A, DiCristina S. Absorption to excretion: The aging body's take on drugs–A review of pharmacokinetic changes and their impact on medication management. Current Pharmacology Reports. 2025;11(1):42.

59. Davies E, O'mahony M. Adverse drug reactions in special populations–the elderly. British journal of clinical pharmacology. 2015;80(4):796-807.

60. Zazzara MB, Palmer K, Vetrano DL, Carfì A, Onder G. Adverse drug reactions in older adults: a narrative review of the literature. European geriatric medicine. 2021;12(3):463-73.

61. Ma J, Björnsson ES, Chalasani N. The safe use of analgesics in patients with cirrhosis: a narrative review. The American journal of medicine. 2024;137(2):99-106.

62. Roy PJ, Weltman M, Dember LM, Liebschutz J, Jhamb M. Pain management in patients with chronic kidney disease and end-stage kidney disease. Curr Opin Nephrol Hypertens. 2020;29(6):671-80.

63. Moore N, Pollack C, Butkerait P. Adverse drug reactions and drug-drug interactions with over-the-counter NSAIDs. Ther Clin Risk Manag. 2015;11:1061-75.

64. Athavale A, Murnion B. Gabapentinoids: a therapeutic review. Aust Prescr. 2023;46(4):80-5.

65. Bosilkovska M, Walder B, Besson M, Daali Y, Desmeules J. Analgesics in patients with hepatic impairment: pharmacology and clinical implications. Drugs. 2012;72(12):1645-69.

66. Coluzzi F, Bifulco F, Cuomo A, Dauri M, Leonardi C, Melotti RM, et al. The challenge of perioperative pain management in opioid-tolerant patients. Therapeutics and clinical risk management. 2017:1163-73.

67. Hyland SJ, Brockhaus KK, Vincent WR, Spence NZ, Lucki MM, Howkins MJ, et al., editors. Perioperative pain management and opioid stewardship: a practical guide. Healthcare; 2021: MDPI.

68. Jahromi B, Pirvulescu I, Candido KD, Knezevic NN. Herbal medicine for pain management: efficacy and drug interactions. Pharmaceutics. 2021 Feb 11;13(2):251. doi: 10.3390/pharmaceutics13020251

69. Colvin LA, Bull F, Hales TG. Perioperative opioid analgesia—when is enough too much? A review of opioid-induced tolerance and hyperalgesia. The Lancet. 2019;393(10180):1558-68.

70. Xie W-J, Hong J-S, Feng C-F, Chen H-F, Li W, Li Y-C. Pharmacological interventions for preventing opioid-induced hyperalgesia in adults after opioid-based anesthesia: a systematic review and network meta-analysis. Frontiers in Pharmacology. 2023;Volume 14 - 2023.

71. Phillips JK, Ford MA, Bonnie RJ, editors. Pain management and the opioid epidemic: balancing societal and individual benefits and risks of prescription opioid use.

72. Podder D, Stala O, Hirani R, Karp AM, Etienne M. Comprehensive Approaches to Pain Management in Postoperative Spinal Surgery Patients: Advanced Strategies and Future Directions. Neurology International. 2025;17(6):94.

73. Gouju J, Legeay S. Pharmacokinetics of obese adults: not only an increase in weight. Biomedicine & Pharmacotherapy. 2023;166:115281.

74. Smit C, De Hoogd S, Brüggemann RJM, Knibbe CAJ. Obesity and drug pharmacology: a review of the influence of obesity on pharmacokinetic and pharmacodynamic parameters. Expert Opin Drug Metab Toxicol. 2018;14(3):275-85.

75. El-Boghdadly K, Levy NA, Fawcett WJ, Knaggs RD, Laycock H, Baird E, et al. Peri-operative pain management in adults: a multidisciplinary consensus statement from the Association of Anaesthetists and the British Pain Society. Anaesthesia. 2024;79(11):1220-36.

76. Kim MK, Kang H. Personalized perioperative pain management: a narrative review. Ewha medical journal. 2025;48(4).

77. Fang Y, Yu Y. Comparison of ERAS-based multimodal pain nursing versus conventional analgesic care on postoperative pain and recovery after total hip arthroplasty: A retrospective study. Medicine. 2026 Jan 2;105(1):e46508.

78. Kunitsu Y, Hira D, Nakagawa S, Tsuda M, Morita SY, Yamamoto Y, et al. NSAID-Induced acute kidney injury risk in patients on renin-angiotensin system inhibitors and diuretics: nationwide cohort study. J Pharm Health Care Sci. 2025;11(1):77.

79. Lim JS, Han S, Kim JS, Kim S, Oh B. Effects of NSAIDs on Early CKD Development: A 10-Year Population-Based Study Using the Korean Senior Cohort. Drugs Aging. 2025;42(10):953-61.

80. Tawfik AG, Gomez-Lumbreras A, Del Fiol G, Kawamoto K, Trinkley KE, Reese T, et al. Nonsteroidal Anti-Inflammatory Drugs and Risk of Gastrointestinal Bleeding: A Systematic Review and Meta-Analysis. Clin Pharmacol Ther. 2026;119(1):46-62.

81. Kei M, Uesawa Y. Comprehensive Analysis of Gastrointestinal Injury Induced by Nonsteroidal Anti-Inflammatory Drugs Using Data from FDA Adverse Event Reporting System Database. Pharmaceuticals. 2025;18(8):1204.

82. Martín Arias LH, Martín González A, Sanz Fadrique R, Vazquez ES. Cardiovascular Risk of Nonsteroidal Anti-inflammatory Drugs and Classical and Selective Cyclooxygenase-2 Inhibitors: A Meta-analysis of Observational Studies. J Clin Pharmacol. 2019;59(1):55-73.

83. Ahsan A, Sahu MA. A Literature Review Assessing Whether the Use of Non-steroidal Anti-inflammatory Drugs (NSAIDs) Increases the Risk of Cardiovascular Events. Cureus. 2025;17(9):e92361.

84. Beaudart C, Brabant C, Alokail M, Reginster JY, Bruyère O. Current Evidence on Celecoxib Safety in the Management of Chronic

Musculoskeletal Conditions: An Umbrella Review. Drugs. 2025;85(10):1289-306.
85. Leal-Ramos OJ, Arias-Ruiz LF, Huerta-Velázquez JM, Lamoreaux-Aguayo JP, Butcher D, López-Cuellar AB, et al. Mechanisms Involved in the Adverse Cardiovascular Effects of Selective Cyclooxygenase-2 Inhibitors. Cardiovascular Medicine. 2025;28(1):5.
86. Chidiac AS, Buckley NA, Noghrehchi F, Cairns R. Paracetamol (acetaminophen) overdose and hepatotoxicity: mechanism, treatment, prevention measures, and estimates of burden of disease. Expert Opin Drug Metab Toxicol. 2023;19(5):297-317.
87. Zimmerman A, Laitman A. Safe Management of Adverse Effects Associated with Prescription Opioids in the Palliative Care Population: A Narrative Review. Journal of Clinical Medicine. 2024;13(10):2746.
88. Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. Anesth Analg. 2017;125(5):1733-40.
89. Toth C. Pregabalin: latest safety evidence and clinical implications for the management of neuropathic pain. Ther Adv Drug Saf. 2014;5(1):38-56.
90. Cho JH, Suh S. Glucocorticoid-Induced Hyperglycemia: A Neglected Problem. Endocrinol Metab (Seoul). 2024;39(2):222-38.
91. Soin A, Reddy Y, Ferguson K, Flores R, Tsirulnikov Y, Davis C, et al. Ketamine and its Regulatory Implications: A Review. Journal of Medical Regulation. 2025;111(3):41-8.
92. Ding Y, Wang X, Li X, He J, Teng X, Chen G. Safety and adverse events associated with dexmedetomidine for sedation in adult ICU patients: a systematic review and meta-analysis. Front Med (Lausanne). 2025;12:1677955.
93. Wang Y, Aaron R, Attal N, Colloca L. An update on non-pharmacological interventions for pain relief. Cell Reports Medicine. 2025 Feb 18;6(2).
94. Yang L, Lou W, Jiang Y, Yang L, Wang D, Wang J. The clinical application progress of multimodal analgesia strategy in enhanced recovery after surgery: a narrative review. Frontiers in Pain Research. 2025 Dec 11;6:1680157.
95. Hoque F. Shared decision-making in patient care: advantages, barriers and potential solutions. Journal of Brown Hospital Medicine. 2024 Oct 1;3(4):13. doi: 10.56305/001c.122787