REVIEW ARTICLES

Ketamine and Spine Surgery – Review

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ABSTRACT

INTRODUCTION:

Various multimodal analgesic approaches have been proposed for spine surgery. This article aims to review the evidence regarding the effect of perioperative ketamine on postoperative opioid consumption, pain scores, and side effects.

MATERIALS AND METHODS:

We included clinical trials in the adult population. Our primary outcome was pain management. Randomized controlled trials published in the English language from January 1995 to September 2025 assessing postoperative pain after spine surgery were identified from the MEDLINE database.

RESULTS:

A total of 16 clinical trials were selected for inclusion in the Review.

CONCLUSION:

Perioperative low doses of ketamine demonstrated analgesic and opioid-sparing effects with no increased adverse events after spine surgery. Further studies of qualitative randomized controlled trials are required to assess the optimal protocol of ketamine administration for postoperative pain relief.

Keywords: ketamine; spine surgery; opioids; pain management

Introduction

Spine surgeries are among the most commonly performed surgical procedures. (1) Worldwide, there is a significant increase in the overall number of spinal decompression and spinal fusion surgical procedures performed for degenerative lumbar spine disease. (2) Many of these patients suffer from chronic postoperative pain, and nearly 20% of those undergoing spine surgery will require secondary surgery for persistent pain or surgery-related complications during subsequent years. (2) Severe pain often accompanies major spine surgery. (3) In a study comparing pain scores in 179 surgical procedures, 3 of the 6 surgeries with a median pain score of 7 on postoperative day 1 (rated on a scale of 0 to 10) were major spinal procedures. (4) Patients undergoing spinal fusion surgery are at high risk for moderate-to-severe postoperative pain and associated complications. (5) Risk factors for severe postoperative pain include preexisting neuropathic pain, preoperative opioid use, perioperative anxiety/mood disorders, level of invasiveness of the surgery, spine segments involved, and degree of difficulty in exposing the surgical field. (1,5) Inadequate analgesia results in poor surgical outcomes, delayed mobilization and rehabilitation, higher rates of readmission, and poor patient satisfaction. (6)

Opioid medications, have historically served as the mainstay for acute postoperative pain management, particularly in procedures associated with severe pain intensity such as spinal surgery. While opioids are effective for managing moderate-to-severe pain, their use carries significant risks, including the development of tolerance, respiratory depression, physical dependence, pruritus, hallucination, nightmare, sedation, urinary retention, gastrointestinal dysfunction such as ileus, which can result in prolonged hospital length of stay and subsequent delayed rehabilitation. (6–8) There is also a clear association between prolonged preoperative opioid use and adverse postoperative outcomes, including delayed wound healing, higher readmission rates, and increased mortality. (7) Additionally, opioids do not always fully relieve pain, and patients often develop a tolerance. (9) In addition to these acute adverse events, another complication of opioid use is opioid induced hyperalgesia (OIH), a condition where opioid exposure leads to an increased sensitivity to painful stimuli, higher postoperative analgesic requirements and an elevated risk of chronic postsurgical pain (CPSP). (9,10) Although the precise mechanism of OIH is not yet fully understood, proposed mechanisms include an enhanced nociceptive response from sensitized spinal neurons and decreased reuptake of neurotransmitters from primary afferent nociceptive fibers. (9) OIH is believed to be responsible for the decreased effectiveness of opioid medications in certain patients, particularly those without a known underlying pathology or disease progression. (9) Additionally, perioperative opioid use is a significant risk factor for persistent postoperative opioid use (PPOU), defined as continued opioid consumption beyond 90–365 days after surgery. (10)

In recent years, clinicians have employed multimodal analgesic regimens which employ agents with varying mechanisms of action to reduce reliance on opioids and their adverse effects. (5–7) Agents that are antagonists of the NMDA receptor may provide particular analgesic benefit in this patient population via an inhibition of sensitization of nociceptive pathways, prevention of opioid-related activation of pro-nociceptive systems, and attenuation of opioid tolerance and hyperalgesia. (6) NMDA antagonists can provide specific treatment of central hypersensitivity, given the involvement of the NMDA receptor in the generation of neuronal hyperexcitability (11). One such non-opioid agent is ketamine, which has been noted to prevent opioid-induced hyperalgesia. (12,13)

Ketamine is a non-competitive, NMDA receptor antagonist that prevents the induction of synaptic potentiation. (11) While all of the exact mechanisms have not been entirely agreed upon, the primary effect of the drug is related to its NMDA receptor antagonism. (14) This interaction decreases the activation of NMDA receptors, leading to a reduction in neuronal excitability, which plays a crucial role in its ability to alleviate pain. (15) The analgesic effects of ketamine do not end with NMDA receptors. Ketamine enhances opioid-induced analgesia through its binding to spinal μ receptors, which increases the effectiveness of opioid signaling and supports an opioid-sparing effect. (15) At high ketamine concentrations, sigma opioid receptors and muscarinic receptors are also affected. (16)

While it was initially developed as a unique anesthetic drug in the 1950s, clinicians later realized its potential for treating various forms of pain with sub-anesthetic doses, including post-operative pain, chronic pain, complex regional pain syndrome, phantom limb pain, and other analgesia-requiring neuropathic conditions. (4) Ketamine may be administered as a single-dose, continuous intravenous (IV) infusion, IV patient-controlled analgesia (IV-PCA), or epidural infusion. (13) It may be administered preoperatively, intraoperatively, and/or postoperatively. (13) Esketamine is a dextrose isolated from ketamine, with a greater potency and stronger analgesic effect, about twice as much as conventional ketamine. (17) Esketamine mildly depresses respiration and has mild excitatory effects on the circulatory system, mildly increasing blood pressure and heart rate. (17)

Although supplemental ketamine has been studied broadly in a variety of procedures and operations, there is no consensus regarding the effectiveness of adjunctive ketamine analgesic use specifically in spine surgery. (13) This review has been designed to present evidence from clinical trials about the efficacy and safety of the application of perioperative ketamine for the prevention and management of pain after spine procedures.

Materials and Methods

Search strategy: This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement recommendations. Publications listed in PUBMED were considered to identify clinical trials suitable for inclusion in this systematic review. The following keywords were used: spine surgery AND ketamine AND adults.

Study selection and inclusion criteria: Inclusion criteria were: clinical trials in adult population (older than 18 years old); about analgesia in spine procedures (i.e. including studies regardless of the anatomical sites and number of levels of the spine, accomplished after both open and percutaneous procedures, microdiscectomy, spine fusion and laminectomy); ketamine was administered; the article described a clinical trial; postoperative analgesia and pain scores were reported; general anesthesia was administered. (1,13,18) Only full papers in the English language that included human data were considered for eligibility. Articles that met any of the following exclusion criteria were excluded from the analysis: the article described a non-human study; non-spine surgery was conducted; the article did not describe a clinical trial; postoperative analgesia and pain scores were not reported; general anesthesia was not administered; abstracts and meeting/symposium proceedings. (1,13,18)

Results

A total of 58 full-text articles were assessed. Eventually, a total of 16 studies were eligible for inclusion in the review. Specific totals from database, and reasons for exclusion, can be found in the diagram (Figure 1).

In a clinical trial, a combination of ketamine and methadone led to reduced use of hydromorphone during the first 24 postoperative hours, and the time until first hydromorphone rescue in the PACU was longer in the methadone/ketamine group compared to the methadone group. (5) Pain scores at rest, with coughing, and with movement were lower in the methadone/ketamine group. Patient-reported satisfaction scores were high in both study groups. (5) After induction of the anesthesia, in methadone group patients were applicated 0.2 mg/kg methadone or 0.2 mg/kg methadone intraoperatively and a ketamine infusion (0.3 mg/kg/h infusion, without bolus, intraoperatively and then 0.1 mg/kg/h for next 48 h (both medications dosed at ideal body weight) in the methadone/ketamine group. (5)

In another study, perioperative ketamine–methadone combination significantly decreased opioid consumption by PCA (the patients who received combined methadone and ketamine (MK) required around 70% less opioid and had similar analgesia degree as the patients treated with methadone alone (M)). (19) Differences in side effects between the study groups were not found. However, the intraoperative administration of ketamine did not improve immediate post-operative analgesia. In the MK group, a ketamine bolus (0.5 mg/kg) was given after tracheal intubation, followed by an infusion of 0.15 mg/kg/h, or a saline bolus plus infusion in the M group. Postoperative analgesia – during 48 h – was provided by patient-controlled analgesia (PCA), delivering a bolus containing the following: ME 0.25 mg plus ketamine 0.5 mg in the MK group or ME 0.5 mg in the M group. (19)

In one investigation, ketamine improved postoperative pain, reduced side effects, and fentanyl use after cervical spine surgery, but could not do so after lumbar surgery. (20) The patients were divided into three groups: the ket-1 group (bolus ketamine 1 mg/kg before incision followed by continuous ketamine 0.042 mg/kg/h for 24 h), the ket-2 group (bolus ketamine 1 mg/kg followed by continuous ketamine 0.083 mg/kg/h for 24 h), control group (isotonic saline was administered). The PCA was programmed to deliver 0.5 μg/kg/h of fentanyl on basal infusion and 0.5 μg/kg on demand with 6 minute lockout for 48 h. Ketamine 2 protocol enhanced the analgesic effects of PCA fentanyl, reduced side effects, and increased patient satisfaction in cervical spine surgery. (20)

Zhang et al published the trial in which they investigated the combination of esketamine–dexmedetomidine combination to supplement analgesia for patients after scoliosis correction surgery. (21) The incidence of moderate-to-severe pain during the first 72 h was significantly lower in the supplement group than the control group (65.7% vs. 86.0%). Subjects who received the supplement experienced less pain at some time points and improved sleep quality without increasing adverse events, including sedation and psychiatric symptoms. (21) In this randomised controlled trial, patients were randomised to patient-controlled sufentanil analgesia (4 μg/kg in normal saline) with either a combined supplement (esketamine 0.25 mg/ml and dexmedetomidine 1 μg/ml) or placebo. (21)

Similar results were provided by Garg et al in who studied ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery. (22) Both ketamine (ketamine bolus 0.25 mg/kg followed by infusion of 0.25 mg/kg/h with midazolam bolus 10 μg/kg and infusion of 10 μg/kg/h mixed in the same infusion pump) and dexmedetomidine (dexmedetomidine bolus 0.5 μg/kg followed by 0.3 μg/kg/h infusion) in small infusions, provide good and safe analgesia, decreasing morphine requirement and increasing the pain-free period during the postoperative period. (22)

In one clinical trial, they investigated different dosages of esketamine and its effect on pain management. (17) Low-dose esketamine relieves patients' early postoperative pain, reduces the perioperative dose of sufentanil, improves intraoperative circulatory stability of elderly patients, reduces the risk of postoperative respiratory depression, without increasing the risk of adverse events, such as psychiatric symptoms, in the first 5 days after surgery. (17) The doses of 0.2 mg/kg at induction and 0.25 mg/kg/h infusion maintenance during operation were more effective. (17)

In contrast to previous studies, Brinck et al. showed that neither a 0.12 nor a 0.6 mg/kg/h infusion of intraoperative IV S-ketamine was superior to the placebo in reducing oxycodone consumption at 48 hours after lumbar fusion surgery in an opioid-naïve adult study population. (3) Differences in the occurrence of adverse events between study groups were nonsignificant. (3)

In one randomized, double-blind, placebo-controlled study, they evaluated the effect of adding incremental doses of S-ketamine to oxycodone PCA in patients who underwent major lumbar spinal fusion surgery. (23) Patients who received oxycodone: S-ketamine ratio 1:0.75 (a bolus containing oxycodone 1 mg + S-ketamine 0.75 mg per ml) for postoperative analgesia consumed significantly less oxycodone postoperatively compared with participants who received lower S-ketamine doses or oxycodone alone. (23) There was a significant opioid sparing effect long after the S-ketamine was removed from PCA at 24 h postoperatively among patients who received an oxycodone: S-ketamine ratio of 1:0.75 compared with participants in other groups. (23) The occurrence of adverse events was similar among the groups. (23)

One study examined the role of oral ketamine in improving recovery after major spine surgery. (4) Ketamine was given orally ketamine (30 mg) or a matching placebo for three days (nine doses total) or until hospital discharge. (4) Patients in the ketamine group spent significantly fewer days on oral opioids and tended to be discharged from the hospital earlier. (4) The incidence of psychotomimetic side effects in the ketamine group was not significantly different compared to the control group. (4)

Czarnetzki and coauthors investigated ketamine in patients with neuropathic lower back pain. (2) In this patient population undergoing major lower back surgery, a perioperative intravenous low-dose ketamine infusion did not affect the prevalence and intensity of neuropathic lower back pain at 6 or 12 months postoperatively. (2) They used intravenous ketamine 0.25 mg/kg after induction, followed by 0.25 mg/kg/hr intraoperatively, and 0.1 mg/kg/hr from 1 hr before the end of surgery until the end of recovery room stay. (2)

In one trial, Nielsen et al. found that opioid-dependent patients who received esketamine during spine surgery reported reduced opioid consumption, pain, and improved labour market attachment one year after ery as compared to patients who received a placebo. (24) The protocol for esketamine was a perioperative esketamine bolus of 0.5 mg/kg followed by esketamine 0.25 mg/kg/h infusion. (24)

Nitta and associates investigated the combination of intravenous ketamine and oral clonidine. Although either ketamine (bolus of ketamine (10 mg) during the induction of anesthesia and 2 mg/kg/hour thereafter during the operation) or clonidine (preoperative 4 μg/kg orally) alone had not reduced the postoperative PCA morphine in patients undergoing spine surgery, the combination of oral clonidine premedication and intra- and postoperative subanesthetic ketamine administration reduced the IV-PCA morphine requirements. (25) In the postoperative period, patients were arranged to use IV-PCA mode for administration of drugs, which was programmed to deliver a bolus dose of 2 mg morphine (control and clonidine group), or boluses of 2 mg morphine and 2 mg ketamine (groups ketamine and ketamine/clonidine). (25)

In a prospective, double-blind, randomized controlled study, a subanaesthetic dose of ketamine mixed with fentanyl-based IV-PCA (patients received either ketamine 0.3 mg/kg i.v. or normal saline after anaesthetic induction with fentanyl-based IV-PCA either with or without a ketamine mixture (3 mg/kg in 180 ml) reduced the postoperative 48 h cumulative fentanyl consumption in high-risk patients for PONV undergoing lumbar spinal surgery on PONV but did not reduce the incidence of PONV. (26) Moreover, ketamine administration was associated with an increase in the severity of nausea, incidence of dizziness, and the occurrence of psychomimetic side-effects. (26)

Loftus et al had demonstrated that intraoperative ketamine reduces opioid consumption in the acute postoperative period by 37% in opioid-dependent patients with chronic pain who are undergoing back surgery. (27) Ketamine also reduced pain intensity postoperatively in the PACU and at 6 weeks and reduced consumption of morphine at the first postoperative visit. (27) This benefit is without an increase in side effects. Ketamine was administered 0.5 mg/kg intravenously on induction of anesthesia, and a continuous infusion at 0.6 mg/kg/h was begun on induction and terminated at wound closure. (27)

In the study by Aveline et al, the study documented that, in lumbar disk surgery, a combined bolus of morphine (0.1 mg/kg) and ketamine (0.15 mg/kg) after anaesthetic induction improved postoperative analgesia, and resulted in a significant reduction in titrated morphine dose in the PACU, and in the PCA morphine 24 h consumption compared to a bolus of each single agent. (28) The incidence of postoperative nausea and vomiting was decreased in the combined treatment group compared to the morphine group. (28)

Subramanian reported that the addition of continuous very low-dose ketamine IV infusion (patients in the treatment group received IV bolus ketamine 0.15 mg/kg at induction and continued on 0.12 mg/kg/h IV ketamine infusion intraoperatively and postoperatively for 24 hours) did not improve postoperative analgesia in patients taking opioids preoperatively. Side effects were not increased with low-dose ketamine. (12)

Various multimodal analgesic approaches have been proposed for spine surgery. One of them was a combination of single preoperative oral doses of acetaminophen 1,000 mg and gabapentin 600 mg, an infusion of ketamine 0.3 mg/kg/h throughout surgery, and an infusion of lidocaine 1.5 mg/kg/h intraoperatively and during the initial hour of recovery. The multimodal analgesic pathway did not improve day 3 Quality of Recovery or reduce pain scores or 48-h opioid consumption in patients who had multilevel spine surgery. (29)

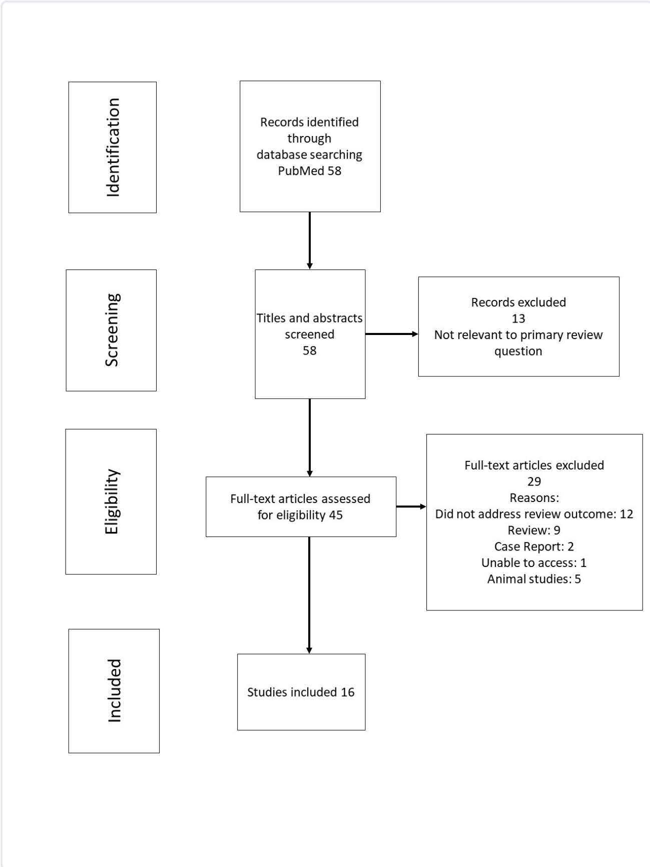

Figure 1. Flowchart depicting the literature review, search strategy, and selection process.

Discussion

Spinal procedures constitute perhaps some of the most painful surgical interventions, as they often encompass extensive muscle dissection, tissue retraction, and surgical implants, as well as prolonged operative duration. (11) Postoperative analgesic management remains a major challenge in spine fusion surgery, given the severity of associated pain. (4) Pain management in this population is further complicated by the number of patients with chronic pain, as well as the paucity of patients who have never received treatment with an opioid. (11) Inadequate postoperative analgesia or excessive pharmacotherapy may lead to diminished functional capacity and prolonged hospitalization. (11)

In this study, we investigated perioperative use of ketamine for pain management in spine surgery. Ketamine was historically used primarily as an anesthetic agent during surgery and is now used for analgesia in the postoperative period in intensive care, postoperative care units, and emergency departments. (15) The evidence supports the beneficial influence of ketamine in controlling postoperative pain, increasing time to first analgesic request, and decreasing overall opioids consumption. Applied as an intravenous continuous infusion during surgery and resumption during postoperative period (as continuous infusion or in combination with opioids in the PCA pump) for the first 48-72 postoperative hours, ketamine appears to be the most effective modality for postoperative pain control. Our finding was consistent with the results of a previous meta-analysis who reported that to obtain the analgesic effect and morphine-sparing effect, only ketamine administrated in postoperative period or through the perioperative period could prolong the analgesic time up to 48 h postoperatively. (15) In contrast to other hypnotics, such as propofol, ketamine has strong analgesic and sedative effects, but absence of significant cardiovascular and respiratory depression effects. It can be used for analgesia and sedation, alone or in combinations with other hypnotic, not only in the operation room but also in the intensive care and postoperative care units, in the emergency department, in the ambulance during transportation, and even in battlefields. (15)

The available literature in our research does not provide enough evidence to determine the most effective dose of ketamine due to the broad variation in dosing, differences in timing, or mode of ketamine application among trials and inconsistent efficacy outcomes. In several studies ketamine dosage was reduced in the postoperative period compared with the intraoperative dose, or the ketamine infusion was canceled. Furthermore, in several trials, continuous IV infusions during the intraoperative period were replaced by IV-PCA postoperatively, introducing variables such as patient decision-making and differences in lockout intervals. (13)

The other conclusion that can be drawn from the aforementioned studies is that although ketamine was effective in many of the trials, other trials showed that it provided no benefit when compared to a placebo. While ketamine holds a place in the prevention and treatment of postoperative pain, more large, high-quality controlled studies are necessary in order to determine which procedures it is best suited for and at what dosages and frequencies it should be administered. Future research could focus on determining the optimal ketamine dose and treatment duration, as well as its long-term effects, to improve perioperative outcomes and pain management efficiency. (15) More research needs to be performed to look at what doses, amounts (single bolus vs. multiple boluses), and what diferences exist between different patient populations (opioid naive vs. opioid dependent and patients with chronic pain). (9)

The lack of consistent findings concerning efficacy of the ketamine potentially resulting from the different types of surgical procedures. The types of spine surgery varied (lumbar or cervical) as well as the magnitude of incision (large or small), which were likely to affect the postoperative pain. (25) The more complex and painful spine procedures were the ones most likely to be associated with ketamine administration as a continuous infusion. (30)

The side effects most commonly associated with higher doses of ketamine, including vomiting, nausea, hallucinations, vivid dreams, and dissociation, are a significant concern and often limit its use. In contrast, when low doses of ketamine are used for the treatment of acute pain, studies show that there is no significant difference in the incidence of side effects compared with morphine, suggesting that lower doses may offer an effective alternative with a similar safety profile. (15)

Postoperative pain management in opioid users remains challenging. In this study, opioid-naive patients were largely enrolled, who consumed small amounts of opioid medications and were reasonably comfortable in the postoperative period, making it difficult to assess the impact on the reduction in analgesic consumption and on the opioid-related side effects, (27) what would it mean that ketamine may be most efficacious in patients who consume higher amounts of preoperative opioid medications. (27) It is well known, that preoperative opioid use is an important risk factor for severe acute postoperative pain and the development of chronic postsurgical pain. (31) Underlying mechanisms for increased pain and opioid consumption include those related to opioid-related tolerance and hyperalgesia. Hyperalgesia is associated with an up-regulation of NMDA receptors induced by activation of opioid receptors. Due to NMDA receptor involvement in opioid-related modulation responsible for hyperalgesia, ketamine as NMDA receptor blocker is suggested to be a reasonable adjuvant in the multimodal analgesia regime, especially for long term opioid tolerant patients. (31) The systematic review showed that in patients with preoperative opioid intake perioperative ketamine has no or only slight effects on pain intensity during movement or at rest 24 h after surgery. (31) However, perioperative ketamine reduced cumulative mean opioid consumption associated with a reduced risk for postoperative sedation and without increased harm. (31) In literature we can see that perioperative there are different dosage of opioid analgetic with emphasis that this often includes diverse opioids (fentanyl, remifentanil, morphine, hydromorphone, methadone). (5) Quantification of opioid requirements would have been simplified if a single opioid had been given. Furthermore, intraoperative dosing of opioids is at the discretion of the anesthesia care provider. (5)

In conclusion, this review presents that intraoperative and postoperative administration of low doses of ketamine reduces opioid consumption during the perioperative time in patients who have undergone spine surgery. There are no differences regarding the assessed side effects. Furthermore, there was significant heterogeneity associated with the trials that were included in this study. The optimal ketamine administration regimen remains to be determined, as well as patient population characteristics that will benefit the most from perioperative ketamine.

REFERENCES

1. Waelkens P, Alsabbagh E, Sauter A, Joshi GP, Beloeil H; PROSPECT Working group of the European Society of Regional Anaesthesia and Pain therapy (ESRA). Pain management after complex spine surgery: A systematic review and procedure-specific postoperative pain management recommendations. Eur J Anaesthesiol. 2021;38(9):985-94. DOI: 10.1097/EJA.0000000000001448.
2. Czarnetzki C, Desmeules J, Tessitore E, Faundez A, Chabert J, Daali Y, et al. Perioperative intravenous low-dose ketamine for neuropathic pain after major lower back surgery: A randomized, placebo-controlled study. Eur J Pain. 2020;24(3):555-67. DOI: 10.1002/ejp.1507.
3. Brinck ECV, Maisniemi K, Kankare J, Tielinen L, Tarkkila P, Kontinen VK. Analgesic Effect of Intraoperative Intravenous S-Ketamine in Opioid-Naïve Patients After Major Lumbar Fusion Surgery Is Temporary and Not Dose-Dependent: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. Anesth Analg. 2021;132(1):69-79. DOI: 10.1213/ANE.0000000000004729.
4. Dinsmore M, Nijs K, Plitman E, Al Azazi E, Venkatraghavan L, Ladha K, et al. Oral ketamine for acute postoperative analgesia (OKAPA) trial: A randomized controlled, single center pilot study. J Clin Anesth. 2025;100:111690. DOI: 10.1016/j.jclinane.2024.111690.
5. Murphy GS, Avram MJ, Greenberg SB, Benson J, Bilimoria S, Maher CE, et al. Perioperative Methadone and Ketamine for Postoperative Pain Control in Spinal Surgical Patients: A Randomized, Double-blind, Placebo-controlled Trial. Anesthesiology. 2021;134(5):697-708. DOI: 10.1097/ALN.0000000000003743.
6. Rajan S, Devarajan J, Krishnaney A, George A, Rasouli JJ, Avitsian R. Opioid Alternatives in Spine Surgery: A Narrative Review. J Neurosurg Anesthesiol. 2022;34(1):3-13. DOI: 10.1097/ANA.0000000000000708.
7. 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. Neurol Int. 2025;17(6):94. DOI: 10.3390/neurolint17060094.
8. Zhou L, Yang H, Hai Y, Cheng Y. Perioperative Low-Dose Ketamine for Postoperative Pain Management in Spine Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Pain Res Manag. 2022;2022:1507097. DOI: 10.1155/2022/1507097.
9. Edinoff AN, Askins D, Bobo E, White KL, Eswani Z, Jackson ED, et al. The Emerging Role of Ketamine in Acute Postoperative Pain Management. Curr Pain Headache Rep. 2023;27(9):387-397. DOI: 10.1007/s11916-023-01134-1.
10. Zhang Q, Ma Y, Liu J, Liu H. Opioid-Sparing and Opioid-Free Anaesthesia: A Review of Clinical Evidence and Implementation Considerations. Br J Hosp Med (Lond). 2026;87(5):54057. DOI: 10.31083/BJHM54057.
11. Rivkin A, Rivkin MA. Perioperative nonopioid agents for pain control in spinal surgery. Am J Health Syst Pharm. 2014;71(21):1845-57. DOI: 10.2146/ajhp130688.
12. Subramaniam K, Akhouri V, Glazer PA, Rachlin J, Kunze L, Cronin M, et al. Intra- and postoperative very low dose intravenous ketamine infusion does not increase pain relief after major spine surgery in patients with preoperative narcotic analgesic intake. Pain Med. 2011;12(8):1276-83. DOI: 10.1111/j.1526-4637.2011.01144.x.
13. Pendi A, Field R, Farhan SD, Eichler M, Bederman SS. Perioperative Ketamine for Analgesia in Spine Surgery: A Meta-analysis of Randomized Controlled Trials. Spine. 2018;43(5):E299-E307. DOI: 10.1097/BRS.0000000000002318.
14. Radvansky BM, Shah K, Parikh A, Sifonios AN, Le V, Eloy JD. Role of ketamine in acute postoperative pain management: a narrative review. Biomed Res Int. 2015;2015:749837. DOI: 10.1155/2015/749837.
15. Viderman D, Mukazhan D, Kapessova K, Tungushpayev M, Badenes R. The Impact of Ketamine on Outcomes in Acute Pain Management: An Umbrella Review. J Clin Med. 2024;13(24):7699. DOI: 10.3390/jcm13247699.
16. Gropper MA, Eriksson LI, Fleisher LA, Cohen NH, Leslie K, Johnson-Akeju O, editors. Miller's Anesthesia, 2-Volume Set. 10th ed. Elsevier; 2023.
17. Hou NN, Zhang MY, Zhang YW, Wu HJ, Luo H, Yang H. Safety and efficacy of low-dose esketamine weakly opioidized anesthesia in elderly patients with lumbar spinal stenosis undergoing surgery: a prospective, double-blind randomized controlled trial. BMC Anesthesiol. 2025;25(1):57. DOI: 10.1186/s12871-025-02908-3.
18. Licina A, Silvers A, Laughlin H, Russell J, Wan C. Pathway for enhanced recovery after spinal surgery-a systematic review of evidence for use of individual components. BMC Anesthesiol. 2021;21(1):74. DOI: 10.1186/s12871-021-01281-1.
19. Pacreu S, Fernández Candil J, Moltó L, Carazo J, Fernández Galinski S. The perioperative combination of methadone and ketamine reduces post-operative opioid usage compared with methadone alone. Acta Anaesthesiol Scand. 2012;56(10):1250-6. DOI: 10.1111/j.1399-6576.2012.02743.x.
20. Yamauchi M, Asano M, Watanabe M, Iwasaki S, Furuse S, Namiki A. Continuous low-dose ketamine improves the analgesic effects of fentanyl patient-controlled analgesia after cervical spine surgery. Anesth Analg. 2008;107(3):1041-4. DOI: 10.1213/ane.0b013e31817f1e4a.
21. Zhang Y, Cui F, Ma JH, Wang DX. Mini-dose esketamine-dexmedetomidine combination to supplement analgesia for patients after scoliosis correction surgery: a double-blind randomised trial. Br J Anaesth. 2023;131(2):385-96. DOI: 10.1016/j.bja.2023.05.001.

22. Garg N, Panda NB, Gandhi KA, Bhagat H, Batra YK, Grover VK, et al. Comparison of Small Dose Ketamine and Dexmedetomidine Infusion for Postoperative Analgesia in Spine Surgery—A Prospective Randomized Double-blind Placebo Controlled Study. J Neurosurg Anesthesiol. 2016;28(1):27-31. DOI: 10.1097/ANA.0000000000000193.
23. Brinck ECV, Virtanen T, Mäkelä S, Soini V, Hynninen VV, Mulo J, et al. S-ketamine in patient-controlled analgesia reduces opioid consumption in a dose-dependent manner after major lumbar fusion surgery: A randomized, double-blind, placebo-controlled clinical trial. PLoS One. 2021;16(6):e0252626. DOI: 10.1371/journal.pone.0252626.
24. Nielsen RV, Fomsgaard JS, Nikolajsen L, Dahl JB, Mathiesen O. Intraoperative S-ketamine for the reduction of opioid consumption and pain one year after spine surgery: A randomized clinical trial of opioid-dependent patients. Eur J Pain. 2019;23(3):455-60. DOI: 10.1002/ejp.1317.
25. Nitta R, Goyagi T, Nishikawa T. Combination of oral clonidine and intravenous low-dose ketamine reduces the consumption of postoperative patient-controlled analgesia morphine after spine surgery. Acta Anaesthesiol Taiwan. 2013;51(1):14-27. DOI: 10.1016/j.aat.2013.03.003.
26. Song JW, Shim JK, Song Y, Yang SY, Park SJ, Kwak YL. Effect of ketamine as an adjunct to intravenous patient-controlled analgesia, in patients at high risk of postoperative nausea and vomiting undergoing lumbar spinal surgery. Br J Anaesth. 2013;111(4):630-5. DOI: 10.1093/bja/aet192.
27. Loftus RW, Yeager MP, Clark JA, Brown JR, Abdu WA, Sengupta DK, et al. Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery. Anesthesiology. 2010;113(3):639-46. DOI: 10.1097/ALN.0b013e3181e90914.
28. Aveline C, Hetet HL, Vautier P, Gautier JF, Bonnet F. Peroperative ketamine and morphine for postoperative pain control after lumbar disk surgery. Eur J Pain. 2006;10(7):653-8. DOI: 10.1016/j.ejpain.2005.10.005.
29. Maheshwari K, Avitsian R, Sessler DI, Makarova N, Tanios M, Raza S, et al. Multimodal Analgesic Regimen for Spine Surgery: A Randomized Placebo-controlled Trial. Anesthesiology. 2020;132(5):992-1002. DOI: 10.1097/ALN.0000000000003143.
30. Schwenk ES, Goldberg SF, Patel RD, Zhou J, Adams DR, Baratta JL, et al. Adverse Drug Effects and Preoperative Medication Factors Related to Perioperative Low-Dose Ketamine Infusions. Reg Anesth Pain Med. 2016;41(4):482-7. DOI: 10.1097/AAP.0000000000000416.
31. Meyer-Frießem CH, Lipke E, Weibel S, Kranke P, Reichl S, Pogatzki-Zahn EM, et al. Perioperative ketamine for postoperative pain management in patients with preoperative opioid intake: A systematic review and meta-analysis. J Clin Anesth. 2022;78:110652. DOI: 10.1016/j.jclinane.2022.110652.

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