



Review Article

Research Progress of Multimodal Analgesia in Postoperative Analgesia of Elderly Patients After Laparoscopic Gastric Cancer Surgery

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Abstract

Postoperative pain is a major clinical challenge for surgical patients, often leading to adverse physiological and psychological events such as hypertension, myocardial ischemia, gastrointestinal dysfunction, delirium, and sleep disorders. Effective postoperative analgesia is crucial as it mitigates excessive stress responses, thereby playing a key role in ensuring safety and promoting recovery. Traditional analgesic methods often rely heavily on single-drug regimens, particularly opioids, which are associated with a high incidence of severe adverse effects such as depression, nausea, vomiting, and constipation. In response, multimodal analgesia has emerged as a superior paradigm. This strategy integrates drugs and regional techniques with different mechanisms of action—for example, combining nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetics, and adjuvant drugs—to achieve synergistic analgesic effects while minimizing dosage and side effects of individual components. With the rapid development of Enhanced Recovery After Surgery (ERAS) concepts, the advantages of multimodal analgesia have become increasingly prominent. Technological advancements, such as ultrasound-guided nerve blocks and advanced patient-controlled analgesia pumps, have made these regimens more refined and individualized. As a cornerstone of ERAS pathways, multimodal analgesia effectively controls pain, significantly reduces opioid-related complications, promotes early mobilization and functional recovery, and shortens length of stay, thereby utilizing medical resources more efficiently. This study reviews various strategies for postoperative pain management in patients undergoing laparoscopic radical gastrectomy for gastric cancer.

Keywords

Elderly Patients, Postoperative Analgesia, Multimodal Analgesia, Laparoscopic Radical Gastrectomy for Gastric Cancer

1. Introduction

As China's aging population continues to grow, the proportion of elderly patients undergoing surgical procedures has markedly increased [1]. These patients frequently experience organ function degeneration, diminished physical capabilities, and reduced reserve capacity in vital organs, which heightens

their surgical risks. In the realm of gastric cancer treatment, laparoscopic gastric cancer resection has emerged as a widely adopted surgical technique, primarily due to its minimally invasive benefits [2]. Nevertheless, this procedure still inflicts considerable trauma to the abdominal cavity and necessitates

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digestive tract reconstruction, leading to significant incision pain, visceral pain, and inflammatory pain postoperatively, which can severely impede patient recovery. Consequently, the establishment of an effective postoperative analgesia protocol with minimal adverse effects is crucial for facilitating the early recovery of these patients. This article seeks to review the commonly employed analgesic methods for elderly patients following laparoscopic radical gastrectomy for gastric cancer.

2. Common Drugs for Multimodal Analgesia

2.1. Opioid Analgesics

Opioid analgesics remain the standard intravenous treatment for acute pain; however, their receptor-mediated side effects, including nausea, vomiting, respiratory depression, urinary retention, and pruritus, are challenging to entirely mitigate, particularly in elderly patients with declining organ function [3]. Consequently, multimodal analgesic approaches are frequently employed in clinical settings to minimize opioid dosages while preserving analgesic efficacy. Sufentanil, a highly selective and long-acting μ opioid receptor agonist, exhibits a strong affinity for μ receptors and is noted for its rapid onset, potent analgesic effect, relatively low incidence of side effects, and hemodynamic stability [3, 4]. In the patient-controlled intravenous analgesia (PCIA) protocol for multimodal analgesia during laparoscopic radical gastrectomy for gastric cancer, sufentanil is frequently employed as the primary agent and is often combined with other medications to enhance synergistic effects. Research has substantiated the benefits of this composite approach. Chi Yan et al. [5] demonstrated that the PCIA regimen incorporating dexmedetomidine with sufentanil outperforms sufentanil monotherapy in reducing postoperative pain, enhancing sedation, and improving safety for patients undergoing laparoscopic gastric cancer resection. Furthermore, the PCIA regimen combining nalbuphine with sufentanil has been shown to provide superior analgesic efficacy and safety, as well as to alleviate visceral pain through the modulation of pain-related factors [6]. Additionally, the PCIA regimen of sufentanil combined with dezocine offers effective sedation and analgesia, mitigates pain-related stress, and protects immune function, evidenced by its relatively minor effects on interleukin-2 and interleukin-6 levels, while also reducing the incidence of micrometastases in the bloodstream [7].

2.2. Opioid Receptor Agonist-Antagonist

Opioid receptor agonists - antagonists are a class of drugs that have both agonistic and antagonistic activities against opioid receptors, mainly including pentazocine, butorphanol, nalbuphine, buprenorphine and dezocine, etc. Compared with

simple μ receptor agonists such as morphine and fentanyl, these drugs have the advantages of definite analgesic effect, lower addiction, and fewer side effects such as coughing, itching and respiratory depression. Its pharmacological properties stem from the excitatory effects on κ -opioid receptors and δ -opioid receptors as well as varying degrees of antagonistic effects on μ -opioid receptors. This unique mechanism of action gives it an advantage in suppressing visceral pain, while significantly reducing typical opioid adverse reactions such as nausea and vomiting, respiratory depression and intestinal paralysis [8].

Based on the above advantages, opioid receptor agonists - antagonists play a particularly prominent role in surgical analgesia involving abdominal internal organs. A randomized controlled trial on elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer demonstrated that the patient-controlled intravenous analgesia regimen of dezocine combined with butorphanol not only effectively alleviated postoperative pain but also regulated immune function and reduced the incidence of postoperative complications [9]. This is consistent with the conclusions of multiple clinical studies on the use of drugs such as nalbuphine and dezocine for postoperative analgesia, all of which confirm that these drugs have better safety while achieving effective analgesia [10, 11]. Therefore, opioid receptor agonists - antagonists are an important component of multimodal analgesia, especially in perioperative analgesia protocols for abdominal surgery.

2.3. Non-opioid Analgesics

2.3.1. Nonsteroidal Antiinflammatory Drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs (NSAIDs) comprise a class of anti-inflammatory medications devoid of steroidal structures, including aspirin, flurbiprofen axetil, ketorolac, diclofenac, ibuprofen, piroxicam, and celecoxib. These drugs are extensively utilized in perioperative pain management. They serve not only to alleviate mild to moderate pain but also as adjunctive treatment for moderate to severe pain. The analgesic and anti-inflammatory effects of NSAIDs arise from their inhibition of cyclooxygenase, which subsequently reduces the synthesis of prostaglandins [12]. As a crucial element of multimodal analgesia, NSAIDs effectively decrease the need for opioid medications post-surgery, thereby minimizing adverse reactions such as nausea, vomiting, and respiratory depression, while also producing a synergistic analgesic effect.

The increasing clinical application of NSAIDs has raised significant concerns regarding their safety. A retrospective analysis involving 2,150 patients who underwent laparoscopic gastric cancer resection indicated that postoperative NSAID use may be linked to a higher incidence of complications, including anastomotic leakage, duodenal stump leakage, intra-abdominal hemorrhage, and intra-abdominal inflammation

[13]. Regarding cardiovascular safety, findings from the PRECISION trial, a prospective randomized study conducted from 2006 to 2014 with 24,222 participants, suggest that NSAIDs should be avoided in patients at elevated risk for cardiovascular disease. If NSAIDs are deemed necessary, the lowest effective dose should be utilized, and the duration of treatment should be minimized. Notably, animal studies have not demonstrated any impact of NSAIDs on the healing strength of anastomoses [14], implying that the clinical risks may be influenced by species differences, timing of administration, or individual patient factors.

Given the aforementioned potential complications, the use of NSAIDs must be meticulously assessed when developing postoperative analgesia protocols for elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer. Clinical decisions should be grounded in a thorough evaluation of each patient's individual circumstances, including cardiovascular status, renal function, and gastrointestinal history. Adhering to the principle of "the shortest course of treatment and the lowest effective dose" is essential. Priority should be given to medications such as selective COX-2 inhibitors, which exert a reduced impact on gastrointestinal and platelet functions. This approach aims to achieve effective analgesia while maximizing patient safety.

2.3.2. Paracetamol

Acetaminophen, also known as paracetamol, is one of the most popular and widely used drugs for treating pain and fever, holding a unique position among painkillers. It is not an NSAIDs drug. Unlike NSAIDs, acetaminophen has low anti-inflammatory activity and does not cause gastrointestinal damage or adverse effects on the heart and kidneys [15]. A number of prospective trials on acetaminophen versus placebo have shown that acetaminophen can improve pain relief, have the effect of saving opioids, increase patient satisfaction, and reduce the need for emergency drugs for burst pain. Especially its intravenous preparations, which do not go through the first stage of elimination, have a high bioavailability. However, its analgesic effect is relatively weak. It is often combined with other analgesic regimens to enhance the analgesic effect and reduce adverse reactions [16].

2.3.3. Others

Tramadol, glucocorticoids, and non-steroidal anti-inflammatory drugs are essential components of multimodal analgesia. A prospective study by Mikami et al. evaluated the analgesic effects of an oral regimen combining tramadol and acetaminophen with celecoxib, in comparison to epidural analgesia following laparoscopic radical gastrectomy for gastric cancer. The findings demonstrated that the oral analgesic regimen is a feasible and safe method for pain management, characterized by a low incidence of adverse events and a non-invasive approach. This study indicates that the combination of tramadol and acetaminophen with celecoxib may serve as an effective option for postoperative analgesia after laparoscopic

radical gastrectomy for gastric cancer [17].

The application of glucocorticoids in perioperative analgesia can achieve ideal results, which is helpful to improve the clinical treatment effect and reduce related adverse reactions. However, for elderly patients, the use of glucocorticoids requires special caution as it may induce or aggravate common comorbidities in the elderly such as hypertension and diabetes, and increase the risk of infection, osteoporosis and peptic ulcers, etc. [18] Therefore, when applied in elderly patients, the benefits and risks must be strictly evaluated, and monitoring during the medication period should be strengthened.

3. Commonly Used Nerve Block Techniques in Multimodal Analgesia

3.1. Patient Controlled Epidural Analgesia (PCEA)

Epidural analgesia, achieved by placing a catheter in the epidural space and administering analgesic agents to target nerve roots directly, offers effective postoperative pain relief and diminishes the risks of pneumonia, cardiovascular, and cerebrovascular events. Historically, it was considered a fundamental analgesic strategy within the enhanced recovery after surgery framework for abdominal procedures [19]. Clinical investigations have demonstrated that patient-controlled epidural analgesia (PCEA) is both safe and effective for patients undergoing radical gastrectomy due to gastric cancer. In comparison to patient-controlled intravenous analgesia, PCEA significantly reduces postoperative pain scores, mitigates the body's stress response, enhances intestinal function recovery, and consequently expedites the rehabilitation process post-surgery [20]. Nonetheless, epidural analgesia presents certain limitations in clinical practice. The failure rate for epidural catheter placement can reach 30%, while the incidence of intraoperative and postoperative hypotension may be as high as 40%. Additionally, urinary retention occurs in 21.5% to 38.1% of cases. Elderly patients face an elevated risk of severe hypotension and complications associated with epidural techniques [21]. Concurrently, the advancement of minimally invasive surgical techniques has led to the widespread adoption of laparoscopic surgery for abdominal procedures, including radical gastrectomy for gastric cancer. Laparoscopic surgery offers distinct advantages over open surgery, including reduced trauma, diminished postoperative pain, less impact on respiratory function, and shorter hospital stays. Therefore, there is controversy in the academic community as to whether it is still necessary to routinely use epidural analgesia after laparoscopic surgery. Relevant retrospective research analyses indicate that for laparoscopic radical gastrectomy for gastric cancer, patient-controlled epidural analgesia may not be indispensable. Studies have

shown that regardless of whether PCIA or PCEA is used after laparoscopic gastric cancer surgery, there is no significant difference in tumor recurrence rate and patient mortality [22]. In terms of pain control effect, postoperative complication rate and hospital stay, PCEA did not show a clear advantage over PCIA [23]. In conclusion, with the increasing popularity and improvement of laparoscopic technology, the traditional core position of epidural analgesia in postoperative analgesia of abdominal surgery is gradually being replaced by ultrasound-guided regional nerve block technology and multimodal analgesia regimens based on intravenous administration.

3.2. Transversus Abdominis Plane Block (TAPB)

The transversus abdominis plane block (TAPB) technique was first described by Rafi in 2001. This approach relies on neuroanatomical localization, involving the injection of local anesthetics into the fascial space between the internal oblique and transverse abdominis muscles, thereby facilitating effective regional analgesia for abdominal surgeries [24]. With the advent of ultrasound visualization technology, the use of TAPB in clinical settings has become increasingly prevalent. Clinicians have gradually recognized and accepted its analgesic mechanism, operational methods, injection sites, drug selection, and dosage protocols [25]. The indications for TAPB have continuously expanded, now encompassing nearly all types of abdominal surgeries. In laparoscopic procedures, ultrasound-guided subcostal TAPB and Petit triangle block are among the most commonly employed and effective techniques [26]. Notably, subcostal TAPB is particularly advantageous for upper abdominal surgeries, as it effectively blocks the sensory distribution of the T7 to T12 spinal nerves, aligning closely with the incision pain range (T6-T12) experienced during laparoscopic radical gastrectomy for gastric cancer. Clinical studies have demonstrated that ultrasound-guided subcostal TAPB provides effective analgesia following laparoscopic gastric cancer surgery and significantly reduces opioid consumption [27].

To further optimize the analgesic effect and reduce the adverse reactions related to opioids, some studies have adopted a multimodal analgesic regimen combining bilateral double transversus abdominis plane block with patient-controlled intravenous analgesia. This protocol has been proven to significantly reduce the incidence of postoperative nausea and vomiting, improve the postoperative experience of patients, and is particularly suitable for elderly patients undergoing laparoscopic radical gastrectomy for gastric cancer [28].

Ropivacaine, a long-acting amide local anesthetic, is often selected for TAPB. To prevent systemic toxicity of local anesthetics and prolong the block time, Yao Xiaorong et al. [29] combined ropivacaine with dexmedetomidine for TAPB. Research has found that this composite protocol can improve the postoperative recovery quality of elderly patients undergoing

laparoscopic radical gastrectomy for gastric cancer, enhance the analgesic effect, prolong the duration of analgesia, reduce the dosage of postoperative intravenous analgesic drugs, and has good safety. Other clinical studies have further confirmed the efficacy and safety of dexmedetomidine as an adjuvant in TAPB.

3.3. Erector Spine Plane Block (ESPB)

The erector spinae plane block, an emerging regional analgesic technique, has demonstrated promising applications in providing analgesia for abdominal surgery due to its notable analgesic efficacy, extensive block coverage, relatively straightforward execution, and high safety profile [30]. The mechanism of action involves the injection of local anesthetics into the fascial plane situated between the deep surface of the erector spinae muscle and the transverse process. This allows the anesthetic agents to diffuse into the paravertebral space, effectively blocking both the ventral and dorsal branches of the spinal nerves. In the context of laparoscopic radical gastrectomy for gastric cancer, this technique theoretically encompasses the pain-controlled regions (T6-T12) associated with surgical incisions and visceral interventions, thereby fulfilling the requirements for surgical analgesia while mitigating the risks of circulatory fluctuations and respiratory depression that may arise from excessive segmental block.

Clinical studies have confirmed that ultrasound-guided ESPB can effectively alleviate postoperative pain after laparoscopic gastric cancer surgery, reduce the dosage of opioids during the perioperative period, and help alleviate the inflammatory response caused by surgical trauma [31]. Compared with traditional epidural analgesia, ESPB operation is more convenient, and the risk of serious complications (such as epidural hematoma and abnormally extensive block) is significantly reduced. However, the application of this technology in abdominal surgeries, especially radical gastrectomy for gastric cancer, is still in the stage of exploration and optimization. The current research focuses on the optimal concentration and volume of ropivacaine, the influence of injection speed on the onset time and effect of block [32], and its impact on the hemodynamic stability of elderly patients. In addition, the duration of a single block is limited. To provide continuous analgesia, continuous catheter placement (ESPB) has become an important direction for prolonging analgesia time. However, the optimal catheter placement position, administration mode, and long-term safety in abdominal surgery still require more high-quality clinical studies to be clarified [30].

In conclusion, ESPB provides an effective multimodal analgesic component for laparoscopic radical gastrectomy for gastric cancer. However, the standardization and optimization of its clinical application plan, especially for elderly patients and those seeking long-acting analgesia, are key issues that need to be addressed in future research.

3.4. Quadratus Lumborum Block (QLB)

The quadratus lumborum block is a trunk nerve block technique initially described by Blanco. This technique involves the injection of local anesthetics into the fascial space surrounding the quadratus lumborum, thereby providing simultaneous analgesic effects that encompass both the body surface and internal organs during abdominal and hip surgeries. Theoretically, the blocked dermatomes can extend from T6 to L1 [33]. Research indicates that this technique effectively reduces resting visual analogue scale scores in elderly patients at various time points following laparoscopic radical gastrectomy for gastric cancer. Furthermore, it may enhance postoperative cognitive function and improve patient prognosis by alleviating pain and stress [34].

The clinical application of the quadratus lumborum block encounters several challenges. Notably, there are substantial individual variations in the block plane and its efficacy. Depending on the insertion paths and injection sites, this technique can be categorized into various methods, including the lateral, posterior, and anterior approaches [35]. While this technological diversity offers flexibility, it also results in issues such as low operational standardization and inconsistent predictability of outcomes. Consequently, it is challenging to rely solely on this technique to provide comprehensive analgesia in the surgical area for all patients undergoing gastric cancer surgery. Therefore, in clinical practice, the quadratus lumborum block is frequently employed as a critical component of multimodal analgesia regimens rather than as the exclusive analgesic approach.

3.5. Paravertebral Thoracic Nerve Block (PVNB)

Paravertebral nerve block (PVNB) achieves a segmental blockade of the motor, sensory, and sympathetic nerves on the ipsilateral side by administering local anesthetics at the nerve root outlet of the thoracic paravertebral space. This technique is crucial for regional anesthesia and postoperative analgesia in thoracic and abdominal surgeries [36]. Regarding postoperative analgesia, research indicates that the analgesic efficacy of PVNB can be comparable to that of epidural analgesia, effectively reducing the incidence of adverse reactions such as nausea, vomiting, urinary retention, and hypotension. Consequently, it has gained widespread application in thoracic surgeries [37]. In contrast, the use of PVNB in abdominal surgery is relatively limited. Nevertheless, existing studies suggest that, without primarily considering its potential effects on hemodynamics [38], ultrasound-guided bilateral paravertebral nerve block for patients undergoing radical gastrectomy for gastric cancer can yield significant clinical benefits and effective postoperative analgesia [39]. A prospective randomized controlled trial involving elderly patients with gastric cancer further demonstrated that preoperative bilateral PVNB can significantly decrease the dosage of general anesthetics,

shorten patient recovery time, and may positively influence postoperative cognitive function. These findings imply that PVNB, as a vital component of multimodal analgesia, holds considerable promise for optimizing perioperative management in major abdominal surgeries, particularly radical gastrectomy for gastric cancer.

4. Common Traditional Chinese Medicine Analgesic Methods in Multimodal Analgesia

Transcutaneous electrical acupoint stimulation (TEAS) is a non-invasive physical therapy technique that has evolved from traditional Chinese acupuncture. This approach integrates the benefits of acupoint stimulation with transcutaneous nerve electrical stimulation, characterized by its ease of use, safety, and non-invasive nature. TEAS has found extensive application in peripheral operative management in China [40]. Research indicates that TEAS can serve multiple functions during the perioperative period by modulating the nervous, endocrine, and immune systems. Its benefits include facilitating pain management, reducing postoperative nausea and vomiting, enhancing immune function, promoting gastrointestinal recovery, and decreasing the incidence of postoperative complications [41].

In elderly patients undergoing laparoscopic gastric cancer surgery, the combined use of transcutaneous electrical acupoint stimulation (TEAS) and transversus abdominis plane block has been shown to produce a synergistic effect. Clinical randomized controlled trials have demonstrated that this combination significantly alleviates postoperative pain, shortens the time to first flatulence, reduces the incidence of postoperative nausea and vomiting, and partially restores the balance of T lymphocyte subsets, thereby enhancing immune function [41]. Collectively, these effects contribute to improved quality of early postoperative recovery for patients. Furthermore, additional studies indicate that the perioperative application of TEAS can decrease the incidence of postoperative fatigue syndrome in elderly patients. This mechanism may be associated with increased release of endogenous β -endorphins, inhibition of inflammatory responses, and alleviation of oxidative stress [42]. Consequently, TEAS combined with regional nerve block can serve as a vital non-pharmaceutical intervention to optimize perioperative management and promote rapid recovery in elderly patients undergoing laparoscopic gastric cancer surgery.

5. Others

Individualized analgesia regimens and optimized early postoperative fluid and food intake can effectively facilitate recovery in patients undergoing laparoscopic gastric cancer resection without increasing the risk of complications, such as anastomotic fistula [43]. In this patient population, the implementation of an acute pain service model, which involves

nurse execution and joint supervision by anesthesiologists and specialists, can significantly reduce postoperative pain, promote the recovery of physiological functions, and improve patient satisfaction with analgesic management [44]. Additionally, research has demonstrated that postoperative consumption of green tea is a safe intervention that can diminish pain intensity following laparoscopic gastric cancer resection and aid in the recovery process. Within the enhanced recovery after surgery program, green tea serves as an adjunct to enhance analgesic and anti-inflammatory effects [45].

6. Summary

Adequate postoperative analgesia is a fundamental component of the enhanced recovery after surgery (ERAS) protocol and serves as a critical indicator for assessing surgical effectiveness, rehabilitation outcomes, quality of medical care, and patient satisfaction. With advancements in medical technology, the promotion of patient-centered care, the widespread adoption and refinement of endoscopic techniques, the introduction of novel analgesic agents, and ongoing innovations in analgesic methodologies, the options for multimodal analgesia following laparoscopic gastric cancer resection in elderly patients are becoming increasingly varied. These developments enhance the ability to effectively manage postoperative pain, decrease the incidence of complications, and expedite the recovery of gastrointestinal function, thereby facilitating rapid postoperative recovery and positively influencing long-term prognoses for patients.

Abbreviations

ERAS	Enhanced Recovery After Surgery
TEAS	Transcutaneous Electrical Acupoint Stimulation
QLB	Quadratus Lumborum Block
PNVB	Paravertebral Nerve Block
ESPB	Erector Spine Plane Block
TAPB	Transversus Abdominis Plane Block
PCEA	Patient Controlled Epidural Analgesia
PCIA	Patient Controlled Intravenous Analgesia
NSAIDs	Nonsteroidal Antiinflammatory Drugs

Author Contributions

Li Liu: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Writing – original draft

Dan Zhou: Conceptualization, Project administration, Supervision, Validation, Writing – review & editing

Conflicts of Interest

The authors declare that they have no conflict of interest.

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