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Research Article

Clinical Study on the Efficacy and Safety of Paracetamol Combined with TAPB Nerve Block in Elderly Patients Undergoing Gastrointest

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Abstract

Objective This study explored the efficacy of paracetamol mannitol injection combined with TAPB for postoperative pain relief in elderly patients after laparoscopic radical gastrectomy, as this combined regimen also reduces postoperative complications including delirium, nausea, vomiting and impaired wound healing, offering a novel strategy for postoperative pain management in such patients. Methods This prospective study included 150 elderly patients (≥65 years) undergoing laparoscopic radical gastrectomy, who were randomly assigned to three groups: sufentanil alone (S), sufentanil plus TAPB (ST), and sufentanil combined with TAPB and paracetamol mannitol (STA). All patients received routine vital sign and BIS monitoring with standardized vascular access establishment before anesthesia. Each group received corresponding preoperative interventions, and multiple perioperative indicators were compared, including opioid consumption, hemodynamic parameters, surgical and anesthetic variables, postoperative pain scores, adverse events, recovery outcomes and patient satisfaction. Results No significant intergroup differences were found in baseline demographics, perioperative indicators, intraoperative vital signs, vasoactive agent use, postoperative adverse reactions, gastrointestinal recovery indicators and bile acid levels among the three groups (all $P>0.05$). Compared with Group S and ST, the STA group presented decreased intraoperative consumption of sufentanil, remifentanil and propofol, reduced postoperative morphine requirement, prolonged time to the first moderate-severe pain, lower postoperative visual analogue scale (VAS) pain scores, higher early postoperative Confusion Assessment Method (CAM) scores without postoperative delirium, superior patient satisfaction, milder shoulder pain, earlier out-of-bed activity and shorter hospital stay; additionally, the ST group consumed fewer intraoperative anesthetics and exhibited better analgesic effects than the S group, while the slight difference in morphine consumption between the STA and ST groups was not statistically significant. Conclusions Combined application of TAPB and paracetamol mannitol can effectively alleviate early postoperative pain, cut down opioid consumption, relieve pain-induced restrictions on out-of-bed activity and improve satisfaction in elderly patients undergoing laparoscopic radical gastrectomy, which greatly optimizes postoperative pain management; meanwhile, paracetamol mannitol brings no extra risks to gastrointestinal function recovery or gastrointestinal bleeding, ensuring its safe application for postoperative analgesia in this elderly patient population.

Keywords

Paracetamol Mannitol, Transversus Abdominis Plane Block (TAPB), Gastric Carcinoma, Multimodal Pain Management, Postoperative Delirium (POD)

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1. Introduction

Gastric cancer is a common malignant digestive tumor, with 1.09 million new cases and 770,000 deaths worldwide in 2020 [1]. Laparoscopic radical gastrectomy causes severe postoperative pain due to extensive surgical trauma and physiological structural changes. Insufficient pain control contributes to multiple complications including cognitive dysfunction, cardiovascular events and delayed wound healing, and may further develop into chronic pain [2, 3]. With population aging, the number of elderly patients undergoing abdominal surgery continues to rise, accompanied by higher risks of postoperative complications and mortality [1, 4]. Postoperative resting pain is an independent risk factor for postoperative delirium (POD), and persistent pain greatly increases delirium risk, severely hindering the recovery of elderly patients [5].

Conventional postoperative analgesia mainly relies on opioids, which frequently induce opioid-related adverse events (ORAE) such as nausea and respiratory depression, prolong hospital stay and increase medical costs [6, 7], while impairing immunity and promoting tumor progression. Multimodal analgesia exerts synergistic effects via multiple targets to reduce drug dosage and adverse reactions [8]. Ultrasound-guided transversus abdominis plane block (TAPB) is widely applied in abdominal surgery, yet it cannot effectively relieve resting pain and shoulder pain, resulting in excessive opioid consumption [9].

As a first-line agent for acute pain in the elderly, paracetamol presents favorable safety without gastrointestinal damage or respiratory depression, and its analgesic mechanism is mediated by endogenous cannabinoid pathways [10, 11]. The domestic paracetamol mannitol injection can additionally alleviate pneumoperitoneum-related injury and incision edema, and it is recommended for elderly opioid-sparing analgesia in clinical consensus. This prospective randomized controlled trial aimed to explore the clinical efficacy of TAPB combined with paracetamol mannitol injection in elderly patients undergoing laparoscopic gastrectomy, and to analyze its effects on postoperative pain, opioid consumption and POD incidence, so as to provide evidence for optimized perioperative analgesia and enhanced recovery.

2. Materials and Methods

2.1. Study Design

This study was a prospective randomized controlled trial. Elderly patients scheduled for elective laparoscopic multi-port radical gastrectomy were enrolled and randomly divided into three groups at a 1: 1: 1 ratio to compare the efficacy of different analgesic regimens. A total of 150 eligible elderly patients received interventions based on group allocation, with 48-hour postoperative morphine rescue consumption recorded as a core indicator. Postoperative delirium incidence was assessed at 2 h, 6 h, day 1, day 2 and day 3 after surgery. Intraoperative anesthetic dosage, extubation time and vital signs were continuously monitored. Postoperative VAS pain scores were measured at multiple time points. Perioperative dynamic changes in bile acids, gastrointestinal function recovery indicators and 48-hour postoperative complications were also documented.

2.2. Grouping and Interventions

From Dec 2023 to Jun 2024, 150 elderly patients awaiting laparoscopic gastrectomy were screened. After signing anesthesia informed consent, 150 qualified participants were assigned serial numbers and randomly divided via a random number table into three groups (50 cases per group): sufentanil group (Group S), sufentanil combined with TAPB group (Group ST), and sufentanil + TAPB + paracetamol mannitol group (Group STA). Thirty minutes before anesthesia induction, Group STA received ultrasound-guided subcostal TAPB combined with intravenous 1 g (100 mL) paracetamol mannitol injection. Group ST underwent identical TAPB and received 100 mL of 0.9% normal saline intravenously. Group S was administered only 100 mL of 0.9% normal saline without nerve block.

2.3. Blinding Design

All patients were informed of alternative postoperative analgesia protocols with specific group allocation concealed. Uniform ultrasound operation procedures were applied in Groups ST and STA to ensure patients were unaware of additional drug administration. Sham abdominal disinfection was performed in Group S to maintain blinding. Postoperative VAS scoring, CAM delirium evaluation and statistical analysis were completed by independent researchers blinded to group assignments.

2.4. Anesthesia Management

2.4.1. Preoperative Preparation

Anesthesia machines, monitors and infusion pumps were fully inspected for normal operation, with breathing circuits and connecting parts strictly checked for air leakage. Soda lime absorbers were examined to prevent carbon dioxide reabsorption. Essential supplies, including laryngoscopes, tracheal tubes and arterial puncture kits, were prepared in advance. All patients fasted for over 8 hours and abstained from drinking for 2 hours preoperatively. Routine monitoring covered SpO_2, NIBP, lead II ECG, respiratory rate and BIS. After a positive Allen test, left radial artery puncture and catheterization were performed under local anesthesia for continuous invasive arterial blood pressure monitoring. Pressure transducers were zeroed at the standard position before formal monitoring. The preoperative interventions for the three groups were implemented uniformly 30 minutes prior to anesthesia induction.

2.4.2. TAPB Procedure

All ultrasound-guided TAPB procedures were performed by experienced anesthesiologists under sterile conditions via a subcostal approach in the supine position. A linear ultrasound probe was placed to visualize the rectus abdominis, oblique abdominal muscles and transversus abdominis layer. Real-time scanning clearly displayed the hierarchical structure of the abdominal wall. An in-plane needle insertion technique was adopted. Normal saline (1–2 mL) was injected for hydrodissection to confirm the correct fascial plane between internal oblique and transversus abdominis muscles. A total of 30 mL of 0.33% ropivacaine was injected gradually under real-time ultrasound guidance to achieve adequate drug diffusion in the target fascia. Contralateral TAPB was completed with the same method. Successful block was confirmed by decreased pinprick sensation in the surgical area.

2.4.3. Anesthesia Induction

Anesthetics were administered sequentially via peripheral venous access: midazolam 0.03 mg/kg, etomidate 0.3 mg/kg, sufentanil 0.3 μg/kg and rocuronium 1.2 mg/kg. After loss of consciousness and spontaneous breathing cessation, jaw-thrust maneuver and pressure-controlled ventilation (15 cmH_2O) were applied. Endotracheal intubation was performed with a video laryngoscope when the jaw was fully relaxed and the BIS value ranged from 40 to 60. Under direct visualization, the glottis was exposed gently to avoid dental injury. A well-lubricated endotracheal tube with appropriate size was inserted into the glottis. After removing the stylet and adjusting the insertion depth, the cuff was inflated properly. Correct tube position was confirmed by breath sounds and end-tidal carbon dioxide, followed by secure fixation. Mechanical ventilation parameters were set as tidal volume 6–10 mL/kg, oxygen flow 2 L/min, FiO_2 60%, respiratory rate 12–20 breaths/min, and inspiratory-expiratory ratio 1: 2.

2.4.4. Intraoperative Anesthesia Maintenance

Combined intravenous-inhalational anesthesia was adopted. Target-controlled infusion (TCI) of propofol (plasma concentration: 2.0–4 μg/mL) and remifentanil (2–4 ng/mL) was administered, together with 0.5%–2.0% sevoflurane inhalation. Anesthetic dosage was titrated to maintain BIS at 40–60 and mean arterial pressure fluctuation within 20%. A quarter of the induction dose of rocuronium was supplemented hourly to sustain muscle relaxation. Before abdominal closure, additional sufentanil 0.1 μg/kg was given and sevoflurane was discontinued. All maintenance anesthetics were ceased 5 minutes before operation completion, with intravenous tropisetron 2 mg administered for postoperative nausea and vomiting prophylaxis.

2.4.5. Anesthesia Recovery

After skin suture, patients were transferred to the post-anesthesia care unit (PACU) for extubation once discharge criteria were met. When the VAS score ≥ 4 (recorded as Tv), patient-controlled intravenous analgesia (PCIA) was initiated with a loading dose of 2 mL. The pump contained 50 μg sufentanil in 100 mL solution, with a background infusion of 1 mL/h, a 2 mL bolus dose and a 15-minute lockout interval. Morphine 2 mg was intravenously administrated as rescue analgesia for persistent moderate-severe pain, and the first morphine administration time (Tm) was recorded. Patients with a Steward score ≥ 4 were transferred back to the ward, and PACU stay time (Tp) was documented.

2.5. Ward Management

Continuous electrocardiographic monitoring was performed for 48 hours postoperatively. Blinded medical staff conducted regular follow-ups to record vital signs at multiple time points: baseline (T0), PACU admission (T1), PACU discharge (T2), and 2, 4, 8, 12, 24, 48 hours after surgery (T3–T8). Postoperative VAS scores from T3 to T8 were assessed, while scores were omitted for sleeping patients. Tropisetron 2 mg was given for nausea and vomiting, with repeated doses if symptoms persisted. The CAM scale was assessed routinely at baseline and 2 h, 6 h, day 1 to day 3 after surgery, with additional evaluation and intervention conducted once POD-related symptoms occurred.

2.6. Observation Indicators

2.6.1. Primary Outcome

Cumulative morphine rescue consumption within 48 hours after surgery.

2.6.2. Secondary Outcomes

Time to first morphine rescue, time to the first VAS score ≥ 4, VAS scores from T3 to T8, incidence of postoperative delirium at 2 h, 6 h, day 1, day 2 and day 3 after surgery, and overall patient satisfaction.

2.6.3. Other Outcomes

Baseline characteristics including age, gender, height, weight and Body Mass Index (BMI); preoperative laboratory parameters such as hemoglobin, total bile acid, total bilirubin, albumin and estimated glomerular filtration rate. Perioperative vital signs including heart rate, blood pressure and SpO_2 at designated time points. Intraoperative data contained operation duration, anesthetic dosage, fluid balance and vasoactive drug administration. Postoperative indicators involved extubation time, PACU stay length, incidences of shoulder pain and postoperative nausea and vomiting, tropisetron consumption, first ambulation time, anal exhaust time and hospital stay.

2.7. Data Analysis

2.7.1. Sample Size Calculation

Based on preliminary trial results, the 48-hour postoperative morphine consumption was 8.75±2.43 mg in Group S, 4.81±2.14 mg in Group ST, and 3.56±1.05 mg in Group STA. With a statistical power (1−β) of 0.8, a significance level (α) of 0.05 and a Cohen's f effect size of 0.35, G*Power 3.1 was applied for one-way ANOVA calculation. A minimum of 55 participants per group (total 165 cases) was required. Allowing for a 10% dropout rate, a total of 186 patients were finally enrolled.

2.7.2. Statistical Methods

All data were analyzed using Excel 2016, SPSS 26.0 and GraphPad Prism 9.5.1. Normally distributed continuous variables were compared by one-way ANOVA with Bonferroni post-hoc correction. Non-normally distributed data were analyzed via the Kruskal-Wallis test. Repeated-measures ANOVA was adopted for time-series data such as VAS scores and vital signs, and interactive effects between time and grouping were analyzed when applicable. Pearson correlation analysis was used to assess the correlation between morphine rescue time and pain scores. A two-tailed P < 0.05 was defined as statistically significant.

3. Results

3.1. Comparison of Baseline Characteristics

There were no statistically significant differences in baseline characteristics among the three groups (P>0.05), including age, gender, BMI, ASA physical status classification, preoperative mini-mental state score, preoperative hemoglobin (Hb), total bilirubin (TBIL), total bile acid (TBA), albumin (ALB), and estimated glomerular filtration rate (eGFR) (Table 1). Similarly, no significant intergroup differences were observed in operation duration, intraoperative blood loss, intraoperative fluid volume, anesthesia duration, or PACU stay time (P>0.05) (Table 2).

Table 1. *General Data Statistics of Patients in Each Group ($\bar{x}$±s).*

n	Group S 50	Group ST 50	Group STA 50	F value	P value
Sex (m/f)	31/31	31/31	29/26	0.981	*0.754*
age	71.35±4.17	71.16±3.86	70.45±4.42	0.331	*0.718*
BMI	23.59±2.34	23.94±2.41	23.38±1.98	1.049	*0.352*
ASA	2.52±0.50	2.63±0.49	2.65±0.50	0.883	*0.601*
IQ	109.93±6.86	108.5±7.39	109.45±6.93	0.899	*0.762*
Hb (g/L)	121.73±10.32	132.25±21.56	129.25±15.39	0.902	*0.867*
TBA (umol/L)	5.51±1.04	5.93±2.01	5.13±2.92	1.219	*0.910*
TBIL (umol/L)	12.33±4.10	13.21±3.95	13.63±4.12	0.945	*0.758*
ALB (g/L)	45.54±7.70	42.32±9.39	47.36±6.26	1.819	*0.110*
eGFR (ml/min)	105.56±10.66	103.23±11.29	112.15±8.74	0.841	*0.473*

Table 2. *The results of operation, anesthesia, PACU time andIntra - operative fluid intake and output in three groups.*

	Group S	Group ST	Group STA	F alue	P value
Operation Duration (min)	242.7±19.08	244.0±22.34	245.2±19.60	0.991	*0.868*
Anesthesia Duration (min)	285.7±9.63	285.2±8.46	284.6±9.33	1.090	*0.584*
PACU Stay Time (min)	68.28±11.72	72.32±9.786	66.82±10.99	0.805	*0.542*
Blood Loss (ml)	305.8±113.8	305.6±102.5	295.8±117.8	0.769	*0.656*
Fluid Infusion (ml)	2300±413.8	2480±400.4	2675±325.5	0.753	*0.654*

	Group S	Group ST	Group STA	F alue	P value
Urine Output (ml)	455±161.2	439±138.8	748±174.4	26.27	*<0.001*

Note: In Table 2, all pairwise comparisons among the three groups showed P > 0.05. Only the P and F values between the STA and ST groups are presented. However, the comparison of urine output revealed a significant difference across groups (P < 0.05).

3.2. Intraoperative Anesthetic Consumption Among the Three Groups

Compared with Group S and Group ST, the STA group presented significantly lower intraoperative dosages of remifentanil, sufentanil and propofol (P < 0.0001), while no significant difference was found in sevoflurane consumption (P = 0.3410). Further analysis showed that remifentanil usage was markedly reduced in Group ST relative to Group S (P < 0.0001), whereas no statistical differences were observed in sufentanil and propofol doses between Group ST and Group S (P > 0.05). Detailed data are shown in Table 3.

Table 3. *Intraoperative consumption of sufentanil, remifentanil, propofol and sevoflurane in three groups (x±s).*

	Group S	Group ST	Group STA	F value	P value
Sufentanil (μg)	45.81±6.32	41.58±4.23	34.07±3.16[*#]	89.521	*<0.001*
Remifentanil (μg)	1244.34±135.34	996.64±180.25[a]	689.63±112.35[*#]	20.822	*<0.001*
Propofol (mg)	1411.38±206.04	1389.56±134.22	1044.77±75.98[*#]	90.181	*<0.001*
Sevoflurane (mL)	65.22±5.23	61.32±4.27	60.72±7.41	1.080	*0.341*

Notes: *$P < 0.05$ vs. Group S; #$P < 0.05$ vs. Group ST; a$P < 0.05$ vs. Group S.

3.3. Comparison of Primary and Secondary Outcomes Among the Three Groups

3.3.1. Morphine Rescue Consumption, First Rescue Time and Time to First VAS ≥ 4

Compared with Group S, both Group ST and Group STA exhibited significantly lower 48-hour postoperative morphine rescue requirements (P < 0.05). The STA group showed slightly less morphine consumption than the ST group, without statistical significance. Although the initial pain intensity was comparable, notable differences were observed in the time to first VAS score ≥ 4. This interval was markedly prolonged in the STA group when compared with the ST and S groups (P < 0.05), and was also significantly longer in the ST group than in the S group (P < 0.05). In addition, the time to first morphine rescue was positively correlated with the time to first VAS ≥ 4 across all three groups. Relevant data are presented in Table 4.

Table 4. *Results of morphine salvage dose within 48 hours and first VAS ≥4 in three groups ($\bar{x} \pm s$).*

	Group S	Group ST	Group STA	F value	P value
48-hour rescue (mg)	8.75±2.43	4.806±2.14[a]	3.56±1.05[*]	70.092	*<0.001*
First VAS ≥ 4	125.71±9.63	205.2±8.46[a]	284.26±9.33[*#]	275.031	*<0.001*
First rescue	385.52±59.73	441.01±47.17	537.24±38.84[*#]	163.220	*<0.001*
score at first VAS ≥ 4	4.65±0.58	4.42±0.34	4.25±0.23	1.571	*0.653*

Notes: *$P < 0.001$ versus Group S; #$P < 0.001$ versus Group ST; a$P < 0.001$ versus Group S. The units of time to first VAS ≥ 4 and first rescue are minutes (min).

3.3.2. Postoperative VAS Scores, CAM Scores and Patient Satisfaction

From T3 to T8, the STA group presented marginally lower VAS scores than the ST group and significantly lower scores than the S group, with statistically significant intergroup differences ($P < 0.05$) (Table 5). At 2 and 6 hours postoperatively, CAM scores in the STA group were significantly higher than those in the ST and S groups ($P < 0.05$). The ST group had slightly higher CAM scores than the S group, but the difference was not statistically significant ($P > 0.05$).

During postoperative days 1 to 3, the mean CAM scores remained above 22 in all three groups. Occasional CAM scores below 19 were noted in the ST and S groups, whereas no such cases occurred in the STA group, with no significant overall intergroup difference. Patient satisfaction was markedly higher in the STA group than in the ST and S groups ($P < 0.05$), while no significant difference was found between the ST and S groups. Detailed data are shown in Table 6.

Table 5. *Results of VAS scores for T3~T8 in three groups of patients ($\bar{x}$±s).*

	Group S	Group ST	Group STA	F value	P value
T3 VAS	5.03±1.40	4.43±0.45	3.14±0.84*#	45.719	<0.001
T4 VAS	5.53±1.94	4.25±1.27	3.06±0.86*#	61.933	<0.001
T5 VAS	5.22±1.76	4.33±1.04	3.03±0.77*#	55.646	<0.001
T6 VAS	4.56±1.39	3.79±0.97	3.12±0.80*#	46.125	<0.001
T7 VAS	4.03±1.52	3.93±0.95	3.15±0.77*#	48.331	<0.001
T8 VAS	3.52±1.07	2.44±1.11	2.17±0.82*#	42.726	<0.001

Notes: In Table 5, *$P < 0.001$ vs. Group S; #$P < 0.001$ vs. Group ST.

Table 6. *Postoperative delirium scores and satisfaction scores at discharge for the three groups of patients ($\bar{x}$±s).*

after surgery	Group S	Group ST	Group STA	F value	P value
2h CAM	17.53±1.12	19.27±2.18	21.82±2.08*#	74.827	<0.001
6h CAM	18.35±1.11	21.36±1.87	26.14±4.10*#	45.534	<0.001
1d CAM	28.19±4.17	28.93±3.84	29.13±3.83	1.526	0.216
2d CAM	28.25±1.39	29.91±0.97	28.94±4.80	1.738	0.487
3d CAM	30.14±4.58	30.95±6.03	31.12±5.27	2.093	0.119
Satisfaction score	6.33±1.00	6.54±1.11	8.44±0.88*#	78.216	<0.001

Notes: *P < 0.0001 versus Group S; #P < 0.001 versus Group ST.

3.4. Adverse Reactions and Postoperative Recovery Outcomes

No significant differences were observed among the three groups in the incidence of postoperative nausea and vomiting, tropisetron consumption, time to first anal exhaust, or perioperative changes in total bile acid ($P > 0.05$), as summarized in Table 7. Compared with the ST and S groups, the STA group achieved earlier first ambulation, milder shoulder pain, and shorter hospital stay, with statistically significant differences ($P < 0.05$). No obvious differences were found between the ST group and the S group ($P > 0.05$) (Table 8).

Table 7. The results of postoperative nausea and vomiting, the use of ondansetron and the time of flatus in three groups of patients ($\bar{x}$±s).

	Group S	Group ST	Group STA	F value	P value
Nausea and vomiting (cases)	55 (11)	62 (12)	62 (12)	12.323	*0.735*
Tropisetron dosage (mg)	2.75±1.57	2.48±1.24	2.72±1.51	0.761	*0.469*
Time to first flatus (h)	27.41±2.90	26.95±3.28	26.89±3.14	0.515	*0.588*

Notes: There were no significant differences in postoperative nausea and vomiting incidence, antiemetic consumption and time to first flatus among the three groups (P > 0.05).

Table 8. The results of the three groups of patients with the time of getting out of bed, the incidence of shoulder pain and the length of hospital.

	Group S	Group ST	Group STA	F value	P value
First ambulation (h)	37.70±3.51	37.02±3.65	32.20±2.50*#	47.478	*<0.001*
shoulder pain (cases)	Mild (23) Moderate (10) Severe (1)	Mild (21) Moderate (8)	Mild (10) Moderate (1)	31.425	*<0.001*
TBA variability	2.34±0.33	2.14±0.69	2.59±0.652	0.067	*0.934*
Hospitalization (days)	9.13±1.30	9.02±1.52	7.02±1.63*#	4.159	0.016

Notes: *$P < 0.05$ vs. Group S; #$P < 0.05$ vs. Group ST.

4. Discussion

With population aging accelerating, balancing postoperative pain control and enhanced recovery has become a critical clinical concern for elderly patients [12]. Due to progressive organ dysfunction, reduced drug metabolism, and multiple comorbidities, analgesic strategies in older adults must balance efficacy and safety. This prospective randomized controlled trial evaluated the multimodal analgesic efficacy of transversus abdominis plane block (TAPB) combined with intravenous paracetamol mannitol in elderly patients undergoing laparoscopic radical gastrectomy. Compared with opioid monotherapy (Group S) and TAPB combined with opioids (Group ST), the multimodal regimen in Group STA markedly reduced postoperative opioid consumption, prolonged analgesic duration, and improved early postoperative CAM scores for delirium assessment. These findings confirm the synergistic advantages of multimodal analgesia and provide evidence-based guidance for optimizing perioperative pain management and implementing enhanced recovery after surgery (ERAS) protocols in elderly surgical populations.

As an effective regional anesthetic technique, ultrasound-guided TAPB blocks anterior abdominal wall neural innervation by depositing local anesthetics within the fascial plane between the internal oblique and transversus abdominis muscles, alleviating somatic incision pain and preserving perioperative immune function [13]. Nevertheless, pain following laparoscopic gastrectomy is multifactorial, with visceral discomfort and inflammatory pain accounting for most postoperative distress induced by surgical traction and carbon dioxide pneumoperitoneum-related peritoneal inflammation [14]. Conventional TAPB alone cannot sufficiently control visceral and persistent inflammatory pain, which explains the sustained opioid requirement observed in Group ST.

The combined administration of paracetamol mannitol exerts complementary analgesic and anti-inflammatory effects. Paracetamol centrally inhibits cyclooxygenase-2 activity and modulates endogenous cannabinoid pathways to mitigate spinal neuronal sensitization and persistent nociceptive signaling [10]. It also attenuates local surgical inflammation by suppressing prostaglandin E2 production and NF-κB pathway activation, thereby augmenting the local anti-inflammatory effects of TAPB. Furthermore, paracetamol metabolites selectively modulate visceral pain transmission, which is particularly beneficial for laparoscopic abdominal surgery. In the present study, the STA group demonstrated substantially lower 48-hour morphine rescue dosage and a prolonged interval to the first VAS score ≥ 4, accompanied by consistently reduced resting VAS scores across early postoperative time points. These outcomes are consistent with previous research investigating multimodal analgesia for laparoscopic gastrointestinal surgery, while intravenous paracetamol offers superior bioavailability and rapid onset compared with oral formulations [7]. Reduced intraoperative sufentanil consumption in the STA group also supports the preemptive analgesic effect of preoperative paracetamol, which blunts central nociceptive sensitization and decreases perioperative opioid demand [16].

Postoperative delirium (POD) is a prevalent and prognostically unfavorable neurological complication among elderly surgical patients, closely linked to severe pain, excessive inflammatory responses, and high opioid exposure [17]. Higher early postoperative CAM scores in the STA group indicated a lower early POD risk, primarily attributable to comprehensive pain relief and decreased intraoperative opioid administration. Uncontrolled surgical pain triggers neuroinflammation by elevating proinflammatory cytokines, disrupting blood-brain barrier integrity, and impairing neuronal function, all of which contribute to delirium development [9, 14]. Excessive opioid use further exacerbates neurocognitive disturbance through glial activation, immune suppression, and cholinergic dysfunction [15]. Although TAPB partially reduces opioid consumption, continuous infusion of short-acting remifentanil in the ST group may still heighten neurological excitability, consistent with earlier clinical observations [18]. In addition, the combined use of paracetamol and long-acting ropivacaine yields a favorable metabolic profile suited to age-related physiological changes. The mannitol component in the formulated paracetamol solution also alleviates cerebral edema caused by carbon dioxide retention during laparoscopy, as reflected by increased urine output in the STA group. After the early postoperative period, CAM scores became comparable across groups, indicating a critical early therapeutic window for POD prevention.

Concerns regarding paracetamol-associated hepatotoxicity remain widespread; however, this study verified the safety of therapeutic-dose intravenous paracetamol in elderly participants. No significant perioperative changes in total bile acid levels were detected in the STA group, supporting stable hepatic function [19]. Intravenous administration avoids first-pass hepatic metabolism, limiting the production of toxic metabolites and lowering liver injury risk at standard clinical doses [20]. Moreover, paracetamol did not delay gastrointestinal recovery or increase adverse abdominal events, conferring advantages over nonsteroidal anti-inflammatory drugs that carry elevated anastomotic leakage risks [10, 11]. Hemodynamic stability was maintained throughout surgery in all groups, confirming the cardiovascular safety of this multimodal strategy. The fixed 1 g preoperative dose adopted in this trial complies with current domestic expert consensus on low-opioid multimodal analgesia for elderly patients, though individualized dosage adjustment is recommended for those with advanced liver disease or malnutrition [21].

Several limitations of this study should be acknowledged. The single-center design may limit generalizability, and subtle variations in surgical techniques and perioperative management were not fully controlled. Routine liver function monitoring was restricted to conventional biochemical indicators, without advanced metabolic or mitochondrial injury biomarkers for detailed hepatotoxicity evaluation [22]. Additionally, only a single fixed preoperative dose of paracetamol was applied, and optimal infusion regimens and drug concentration ratios require further exploration [23]. This study focused exclusively on short-term postoperative outcomes; long-term cognitive changes, chronic pain incidence, and oncological prognosis remain to be clarified through extended follow-up.

5. Conclusion

This multimodal analgesic protocol combining TAPB and preoperative paracetamol effectively optimizes perioperative pain management, reduces opioid reliance, accelerates early postoperative rehabilitation, and improves patient satisfaction. It also lowers the early risk of postoperative delirium via anti-inflammatory, central analgesic, and opioid-sparing mechanisms, with a favorable safety profile in elderly patients with declined hepatic and renal function. This low-opioid, ERAS-compatible regimen is feasible for widespread clinical application, especially in primary hospitals. Further high-quality multicenter trials and personalized protocol optimization will help refine standardized perioperative analgesic strategies for elderly abdominal surgery patients.

Abbreviations

BMI	Body Mass Index
TAPB	Transversus Abdominis Plane Block
ERAS	Enhanced Recovery After Surgery
CAM	Confusion Assessment Method
POD	Postoperative Delirium
VAS	Visual Analogue Scale
ORAE	Opioid-Related Adverse Events

Author Contributions

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Conflicts of Interest

The authors declare no conflicts of interest.

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