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The impact of hydromorphone combined with ropivacaine in serratus anterior plane block on postoperative pain in patients undergoing video-assisted thoracoscopic pulmonary lobectomy: a randomized, double-blind clinical trial

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Abstract

Background This study aimed to assess the effects of hydromorphone as an adjuvant to ropivacaine serratus anterior plane block (SAPB) on postoperative analgesia and inflammatory responses in patients undergoing video-assisted thoracoscopic surgery (VATS).

Methods This was a prospective, randomized, double-blind clinical trial. A total of 120 lung cancer patients, aged 20–75 years, with an American Society of Anesthesiologists classification of I or II and a body mass index of 18–28 kg/m^2, were randomly assigned to three groups: ropivacaine combined with hydromorphone SAPB (HR group), ropivacaine SAPB (R group), and control (C group). Ultrasound-guided deep SAPB was used to inject medications. The main observed indicators were postoperative visual analog scale (VAS) pain scores, serum inflammatory markers (C-reactive protein (CRP), IL-6, TNF-α), intraoperative medication dosage, postoperative complication rates, and analgesic effects.

Results Postoperative VAS pain scores were significantly reduced in the HR and R groups compared to the C group, especially at 6 h postoperatively. The median VAS score in the HR group was 2.00 (inter-quartile ratio (IQR): 2.00, 2.00), which was significantly lower than that of the C group's score of 3.00 (IQR: 3.00, 3.00; $P < 0.001$). The CRP levels at 24 and 48 h postoperatively in the HR group were 23.80 mg/L and 21.65 mg/L, respectively, significantly lower than the C group's levels of 56.65 mg/L and 82.75 mg/L, $P < 0.001$. The levels of IL-6 and TNF-α were also significantly lower in the HR group than in the C group. Intraoperative propofol and remifentanil dosages in the HR group were reduced to 5.22 mg/kg/h and 7.59 μg/kg/h, respectively, lower than the C group's dosages of 5.93 mg/kg/h and 5.74 μg/kg/h,

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$P < 0.001$. The incidence of postoperative nausea and vomiting in the HR group was 12.5%, which was lower than that in Group C (35.7%, $P = 0.032$).

Conclusion Ropivacaine adjuvant with hydromorphone in SAPB reducing postoperative pain and inflammatory in patients undergoing VATS, which contributed to rapid recovery. However, future studies should explore the long-term benefits and concenntration of hydromorphone of SAPB before it taken into clinical use.

Trial registration Chinese Clinical Trial Register on August 19, 2021, NCT number ChiCTR2100053893.

Keywords Lung cancer, Video-assisted thoracoscopic surgery, Serratus anterior plane block, Hydromorphone, Postoperative analgesia, Inflammatory response

Background

Lung cancer is the most prevalent malignant tumor globally, accounting for 11.4% [1] of malignant tumors in 2020, highlighting the critical need for timely diagnosis and effective treatments to enhance patient outcomes [2]. Despite a variety of therapeutic approaches, surgical intervention remains the cornerstone of lung cancer treatment [3]. Video-assisted thoracoscopic surgery (VATS) has become the primary surgical modality because of its minimally invasive and precise nature [4]; however, postoperative pain management remains a challenge, with an incidence rate of 30–50% [4], affecting the recovery process and potentially leading to serious complications such as ventilatory impairment and hypoxemia [5].

The etiology of postoperative pain is multifactorial, impacting not only respiratory and cough functions but also triggering the production of pro-inflammatory cytokines like IL-6 and TNF-α [6]. These cytokines activate the central and peripheral nervous systems, creating a vicious cycle that exacerbates pain. To address these challenges, the enhanced recovery after surgery (ERAS) protocol and its recommendation for multimodal analgesia have emerged [7]. It seeks to reduce surgical trauma and inflammatory responses during the perioperative period, enhancing patient comfort and accelerating recovery [8]. Traditional analgesic methods such as thoracic epidural analgesia and paravertebral block have limitations owing to the risks and complications associated with puncture [9].

Serratus anterior plane block (SAPB) guided by ultrasound is a safe postoperative analgesic technique with a low risk of complications [10]. It is appreciated for its simplicity and extensive analgesic range in clinical practice [11]. However, it is associated with issues such as a short duration of pain relief and suboptimal long-term effects. The integration of hydromorphone as an adjunct to ropivacaine in ultrasound-guided SAPB may offer an innovative therapeutic approach for postoperative analgesia following VATS. Although this combined medication regimen is not frequently encountered in current literature, studies have shown promising results for its effectiveness in managing postoperative pain [12, 13].

This study aimed to optimize postoperative pain management through a prospective clinical trial assessing the combination of hydromorphone and ropivacaine. Aligned with the ERAS philosophy, this multimodal strategy aims to enhance pain relief, minimize analgesic use, and extend the effectiveness of pain control.

Methods

Eligibility criteria for participant recruitment

This study included lung cancer patients who met the following criteria for elective uniportal video-assisted thoracoscopic lobectomy: (1) aged 20–75 years; (2) American Society of Anesthesiologists classification I or II; (3) body mass index (BMI) 18–28 kg/m^2; (4) voluntary participation in this study, with informed consent signed by the patient or a designated representative; (5) absence of language and mental disorders, and the ability to cooperate well with examinations and postoperative follow-up. The exclusion criteria were as follows: (1) refusal to undergo postoperative analgesia; (2) allergy to the test drugs, history of acute or chronic pain, long-term use of analgesic drugs or alcohol abuse, and recent use of opioid drugs; (3) coagulation dysfunction, recent use of anticoagulants, and infection at the puncture site; and (4) presence of active peptic ulcers or bleeding.

The withdrawal and exclusion criteria were as follows: (1) not meeting the inclusion criteria; (2) severe allergic reactions or bleeding exceeding 300 mL during surgery; (3) patients requiring a second surgery; and (4) participants withdrawing midway or with missing data.

Study design

This was a randomized, double-blind, prospective study. Randomization was performed using Excel-generated integers, categorizing participants into the Hydromorphone-Ropivacaine SAPB (HR group), Ropivacaine SAPB (R group), and control group (C group). Allocation concealment was ensured through the use of sequentially numbered, opaque envelopes secured by an individual unrelated to the study's execution and opened post-recruitment. The SAPB was conducted by a proficient attending physician who was not involved in subsequent study phases. Data collection, assessment, and follow-up

were performed by team members who were blinded to the group assignments.

Double-blind integrity was maintained with documentation, evaluation, participant engagement, and data analysis conducted without knowledge of the intervention specifics. Researchers involved in randomization and envelope custody were excluded from the study. This stringent design minimized bias and augmented the reliability and validity of the study.

Sample size

The sample size estimation was based on the difference in the change in VAS score between groups at 6 h after surgery by using the use of G*Power 3.0.10 (University Kiel, Germany). The VAS score was 3.4 cm, 2.9 cm, and 2.4 cm, respectively for the patients in the three groups at 6 h postoparatively according to the pilot study. The required sample size for each group was 111, with the use of a two-sided test with a significance level of 0.05 (alpha) and a power of 0.85 (1-β), assuming a 1:1:1 ratio between the three groups. Considering a 15% withdrawal and loss for follow-up rate, 129 patients were included in this study.

Experimental methods

In this study, eligible patients underwent a comprehensive physical examination and assessment the day before surgery. The study objectives, anesthetic procedures, and potential risks were thoroughly explained to the patients and their families to obtain informed consent. Additionally, patients were instructed on the use of a visual analog scale (VAS) scoring system and patient-controlled intravenous analgesia (PCIA) pumps. All participants were required to fast for 8 h and abstain from drinking for 4 h before surgery. Upon arrival in the operating room, patients were monitored for vital signs. An experienced anesthesiologist performed an ultrasound-guided deep SAPB and administered distinct pharmaceutical agents to each of the three groups, who received an injection of 0.375% ropivacaine combined with 1 mg hydromorphone in a total volume of 30 mL. The ropivacaine group was injected with 30 mL of 0.375% ropivacaine, and the control group received a 30 mL injection of normal saline. The efficacy of the block was assessed by an evaluator blinded to the group assignment at 20 min post-injection, and success was determined by a comparative sensory block of the skin dermatomes (Fig. 1).

This study employed a streamlined protocol for intravenous and tracheal intubation using midazolam, propofol, sufentanil, and cisatracurium besylate to ensure swift and effective anesthesia induction. Anesthesia maintenance was guided by Bispectral Index values and hemodynamics, targeting BIS scores between 40 and 60 for optimal depth and analgesia. Intraoperative monitoring included vigilant tracking of blood pressure and heart rate, with adjustments made via pharmacological intervention, as necessary. Postoperatively, the patients were promptly extubated following cessation of anesthesia and transferred to the Post-Anesthesia Care Unit. Extubation time was recorded from the completion of skin closure. Upon awakening, patients were administered analgesia via a PCIA pump with meticulous parameter settings to maintain VAS scores below 3, and additional analgesic support was provided where required. Inflammatory

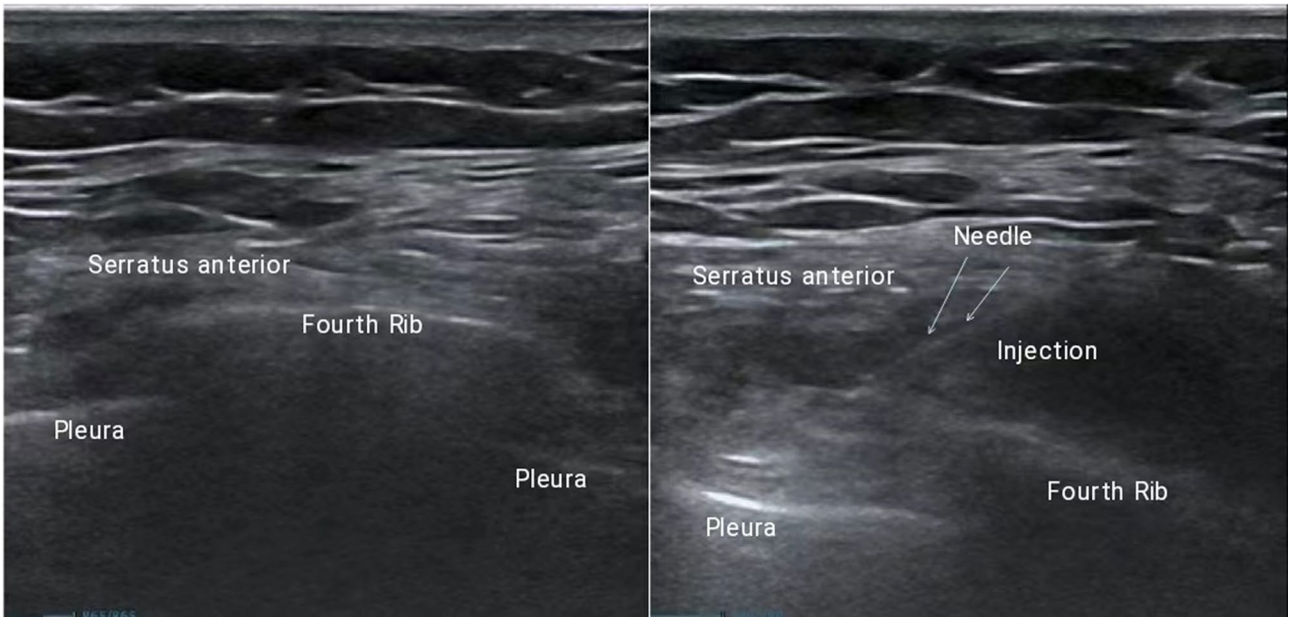

Fig. 1 Anterior serratus plane block. **A**, Before injection of local anesthetic ropivacaine; **B**, After ropivacaine injection of the local anesthetic ropivacaine

biomarkers, CRP, IL-6, and TNF-α, were quantified from venous blood samples collected preoperatively and at 24 and 48 h post-surgery. The Immulite 1000 and ELISA methods were employed for these assays, ensuring precision with an inter-assay variability below 10%. This rigorous approach guaranteed the scientific integrity and reproducibility of the biomarker data.

Outcome measures

A comprehensive set of indicators was delineated to evaluate the patients' preoperative status, intraoperative conditions, and postoperative recovery. The assessment included documentation of demographic and surgical characteristics including sex, age, BMI, operative duration, intraoperative blood loss, analgesic dosage, extubation time, and postoperative hospital stay.

The primary outcome of postoperative pain was evaluated using the VAS at 2, 6, 12, 24, and 48 h after surgery. Additionally, the effectiveness of analgesia was monitored by recording the number of effective PCIA pump activations, total opioid consumption, instances of rescue analgesia, and the timing of the first rescue analgesic administration within the first 48 h postoperatively. The primary endpoint was assessment of VAS at 6 h after surgery based on which, the sample was estimated.

In accordance with the surgical diagnosis and treatment protocols, all patients are required to return for an outpatient follow-up one month after surgery. Personnel who are blinded to the study protocol will review the outpatient medical records and document the VAS scores.

The secondary outcome measures were inflammatory biomarkers, which were assessed by measuring serum levels of CRP, IL-6, and TNF-α pre-anesthetic induction (T1), 24 h postoperatively (T2), and 48 h postoperatively (T3). Hemodynamic parameters were closely monitored at critical junctures from preoperative to postoperative periods, including 10 min before serratus anterior plane block (T0), at anesthetic induction (T1), immediately before intubation (T2), immediately after intubation (T3), at the onset of incision (T4), 10 min after the start of surgery (T5), 30 min after the start of surgery (T6), at the commencement of skin closure (T7), and at extubation (T8), with recording of mean arterial pressure (MAP) and heart rate at these intervals. Finally, postoperative adverse effects, including nausea and vomiting, urinary retention, constipation, puncture site ecchymosis and infection, and local anesthetic toxicity, were meticulously documented. These integrated indicators were used for an in-depth analysis and evaluation of patients' postoperative recovery and therapeutic outcomes.

Statistical analysis

For statistical data analysis, the research team employed two statistical software packages: IBM SPSS 21 and R.4.1.1. The Shapiro-Wilk test was used to determine whether the data conformed to a normal distribution; for normally distributed quantitative data, it was expressed in the form of mean ± standard deviation, and inter-group differences were tested using one-way analysis of variance, with Tukey's test for pairwise comparisons if necessary. Data that did not conform to a normal distribution were represented as the median and interquartile range (M(25th, 75th)), with inter-group differences assessed using the Kruskal-Wallis test and Dunn's test for pairwise comparisons. For non-normally distributed two-factor repeated-measures data, a linear mixed-effects model was used to test inter-group differences, with Tukey's adjustments performed using the 'emmeans' package in R for multiple comparisons. Categorical data are represented by absolute numbers or relative frequencies (rates) and analyzed using the chi-square test. The significance level (α) for all statistical tests was set at 0.05.

Ethics approval

The study was approved by the Ethical Review Committee in the Medical Ethics Committee of Shangyu People's Hospital, Shaoxing City, Zhejiang Province (approval number: SRY-20210809-0005). Written informed consent was obtained from all participants.

Results

Study population

This study initially identified 129 eligible patients, of whom 120 were ultimately included in the analysis and distributed into three groups: 42 in Group C, 38 in Group R, and 40 in Group HR (Fig. 2). A comparative analysis of the three groups revealed no statistically significant differences in demographic and surgical characteristics, including age, sex, BMI, duration of surgery, intraoperative blood loss, time to endotracheal extubation, and duration of postoperative hospitalization (Table 1).

Primary outcome

Table 2 outlines the respective VAS scores at 2, 6, 12, 24, and 48 h postoperatively in the three groups. Initially, Group C had median VAS scores of 3.00 (IQR: 2.25-3.00) at 2 h and 3.00 (IQR: 3.00–3.00) at 6 h. Group R scores were 2.00 (IQR: 2.00–3.00) at 2 h and 3.00 (IQR: 2.00–3.00) at 6 h, whereas Group HR scores were uniformly lower at 2.00 (IQR: 2.00–2.00) for both time points, with significant differences from Group C ($P < 0.001$ at 2 h, $P = 0.001$ for Group R, $P < 0.001$ for Group HR at 6 h).

At 12 h, Group C's score was 3.00 (IQR: 2.00–3.00), contrasting with Group R's reduced score of 2.00 (IQR: 2.00–2.00), where both Group R and HR showed statistical significance compared to Group C ($P < 0.001$). A consistent decline in VAS scores was noted at 24 and 48 h, with Group HR demonstrating significantly lower scores

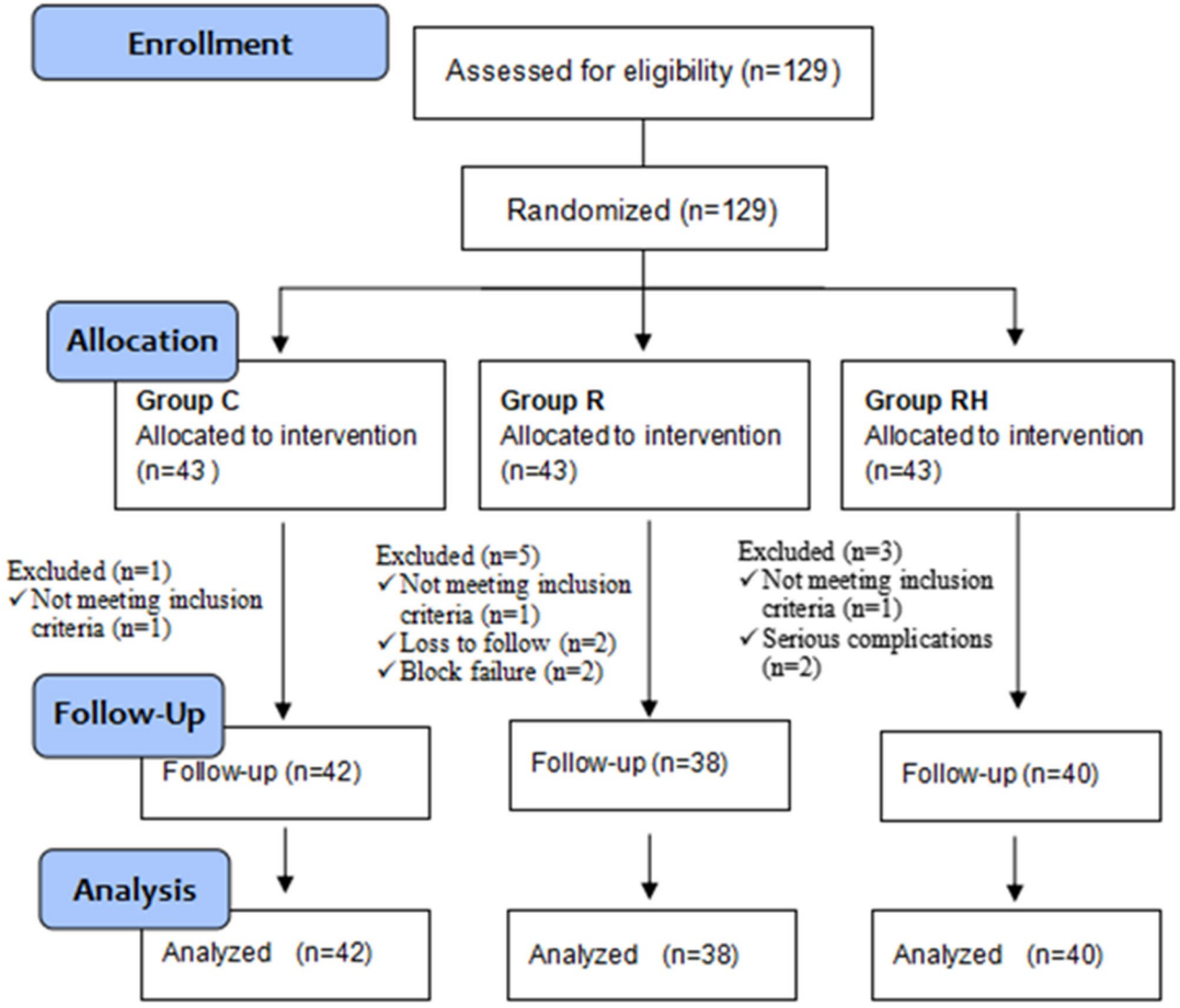

Fig. 2 CONSORT flowchart

Table 1 General demographic information of patients in three groups

Characteristics	Total	Group C	Group *R*	Group HR	*P* value
	***n*(120)**	**(*n* = 42)**	**(*n* = 38)**	**(*n* = 40)**	
Age, yrs	62.50 (55.00, 69.00)	62.00 (54.50, 67.00)	65.00 (58.00, 69.00)	59.00 (52.75, 69.00)	0.208
Gender, male/female	51/69	22/20	17/21	12/28	0.116
BMI, kg/m^2	22.86 (21.28, 25.40)	23.18 (21.99, 25.84)	23.18 (20.59, 25.40)	22.60 (20.60, 25.08)	0.334
Surgery time, min	105.00 (71.50, 146.25)	129.50 (80.25, 157.50)	95.00 (70.50, 141.25)	87.50 (68.75, 127.50)	0.089
Intraoperative blood loss, mL/kg	0.19 (0.11, 0.31)	0.22 (0.15, 0.35)	0.20 (0.10, 0.30)	0.16 (0.09, 0.30)	0.216
Tracheal tube extubation time, min	13.00 (11.00, 18.25)	15.00 (11.00, 32.50)	13.50 (10.25, 37.50)	13.00 (11.00, 15.25)	0.763
Postoperative hospital stay, days	4.00 (4.00, 6.00)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	4.00 (3.00, 5.00)	0.112

than Group C ($P = 0.005$ and $P = 0.019$, respectively), highlighting its enhanced postoperative analgesic effect. One month later, Group C had a score of 1.00 (with an interquartile range of 1.00 to 2.00). In contrast, Group R's score decreased to 1.00 (with an interquartile range of 0.00 to 1.00). Both Group R and Group HR showed statistically significant differences compared to Group C ($P < 0.05$).

A lower VAS score indicates enhanced postoperative pain management. The data consistently showed that Group HR had reduced VAS scores relative to Groups C and R throughout the early and late postoperative

Table 2 Comparison of postoperative VAS pain scores in three groups

Characteristics	Group C	Group *R*	Group HR
	(*n* = 42)	(*n* = 38)	(*n* = 40)
Average	3.00 (2.00, 3.00)	2.00 (2.00, 3.00)^{cc}	2.00 (2.00, 2.00)^{cc}
Postoperative 2 h	3.00 (2.25, 3.00)	2.00 (2.00, 3.00)^{cc}	2.00 (2.00, 2.00)^{cc}
Postoperative 6 h	3.00 (3.00, 3.00)	3.00 (2.00, 3.00)^{c}	2.00 (2.00, 2.00)^{cc}
Postoperative 12 h	3.00 (2.00, 3.00)	2.00 (2.00, 2.00)^{cc}	2.00 (2.00, 2.00)^{cc}
Postoperative 24 h	2.00 (2.00, 3.00)	2.00 (2.00, 2.00)	2.00 (2.00, 2.00)^{c}
Postoperative 48 h	2.00 (2.00, 2.00)	2.00 (1.00, 2.00)	2.00 (1.00, 2.00)^{c}
Postoperative 1 month	1.00 (1.00, 2.00)	1.00 (0.00, 1.00)^{c}	1.00 (0.00, 1.00)^{cc}

Note: Compared with group C, $^{c}P < 0.05$, $^{cc}P < 0.001$

intervals. Particularly at the 6-hour postoperative assessment, Group HR demonstrated significantly superior pain control compared to Group R ($P < 0.001$). These outcomes suggest that Groups R and HR were more effective at mitigating postoperative pain than Group C, with Group HR exhibiting significant pain relief at each evaluated time point.

Intraoperative medication administration

Regarding intraoperative medication administration (Table 3), the Shapiro-Wilk test revealed significant variances in anesthetic drug consumption across the three groups (P-values < 0.001 for all). A marked reduction in propofol dosage was observed in Groups R and HR as compared to Group C (with median values of 5.93 mg/kg/h for Group C, and 5.99 mg/kg/h and 5.22 mg/kg/h for Groups R and HR, respectively, $P < 0.001$), alongside a significant decrease in remifentanil dosage (median values of 8.74 μg/kg/h for Group C, and 8.56 μg/kg/h and 7.59 μg/kg/h for Groups R and HR, respectively, $P < 0.001$). Additionally, Group HR showed a further decrease in both propofol and remifentanil dosages compared to Group R, indicating significant inter-group differences ($P < 0.001$ for both comparisons). No significant differences were noted in the intraoperative sufentanil dosages when the three groups were compared pairwise.

Postoperative inflammatory response

As shown in Table 4, the postoperative inflammatory response was characterized by a significant elevation in serum CRP, IL-6, and TNF-α levels across all study groups, indicative of a systemic inflammatory reaction to surgery ($P < 0.001$). Notably, Group C showed the highest levels of CRP (82.75 mg/L and IL-6 (42.27 pg/mL) 48 h post-surgery. Groups R and HR, which received specific interventions, had lower levels, with Group HR recording the lowest CRP (21.65 mg/L) and IL-6 (19.36 pg/mL) levels at 48 h. TNF-α levels also peaked in Group C (7.90 pg/mL at 48 h), while Groups R and HR showed comparatively lower, albeit non-significantly different, levels.

Table 3 Intraoperative anesthetics of patients in three groups

Characteristics	Total	Group C	Group *R*	Group HR	*P* value
	N (120)	(*n* = 42)	(*n* = 38)	(*n* = 40)	
Intraoperative propofol dosage, mg/kg/h	5.69 (5.18, 6.28)	5.93 (5.58, 6.67)	5.99 (5.15, 7.11)	5.22 (4.79, 5.61)^{ccrr}	< 0.001
Intraoperative remifentanil dosage, μg/kg/h	8.21 (7.24, 9.68)	8.74 (7.26, 10.33)	8.56 (7.92, 10.50)	7.59 (6.89, 8.36)^{crr}	< 0.001
Intraoperative sufentanil dosage, μg/kg/h	0.44 (0.36, 0.58)	0.40 (0.35, 0.52)	0.45 (0.39, 0.60)	0.47 (0.37, 0.56)	0.111

Note: Compared with Group C, $^{c}P < 0.05$, $^{cc}P < 0.001$; compared with Group R, $^{r}P < 0.05$, $^{rr}P < 0.001$

Table 4 Postoperative inflammatory indicator levels in three groups

Characteristics		Group C (*n* = 42)	Group R (*n* = 38)	Group HR (*n* = 40)
CRP	Average	48.80 (1.92, 80.57)	31.90 (2.10, 43.50)	12.90 (1.67, 25.95)
	Preoperative baseline, mg/L	0.95 (0.50, 1.85)	0.80 (0.40, 2.05)	0.80 (0.30, 1.90)
	Postoperative 24 h, mg/L	56.65 (43.47, 74.00)	35.75 (31.35, 43.58)^{cc}	23.80 (10.72, 31.12)^{ccr}
	Postoperative 48 h, mg/L	82.75 (62.13, 105.18)	43.25 (32.80, 62.45)^{cc}	21.65 (13.50, 34.50)^{ccrr}
IL-6	Average	32.20 (1.72, 63.85)	18.26 (1.90, 31.13)	11.07 (1.81, 25.05)
	Preoperative baseline, pg/mL	1.51 (1.19, 1.71)	1.65 (1.32, 1.88)	1.52 (1.26, 1.82)
	Postoperative 24 h, pg/mL	62.34 (40.29, 95.49)	29.18 (21.10, 38.17)^{cc}	21.36 (11.37, 28.66)^{cc}
	Postoperative 48 h, pg/mL	42.27 (26.29, 91.31)	25.99 (16.79, 34.65)^{cc}	19.36 (10.98, 33.66)^{cc}
TNF-α	Average	5.53 (1.96, 9.55)	6.50 (2.52, 11.25)	5.27 (2.23, 8.92)
	Preoperative baseline, pg/ml	1.95 (1.03, 4.14)	3.62 (1.82, 6.68)	2.98 (1.36, 6.28)
	Postoperative 24 h, pg/ml	8.52 (5.28, 11.70)	7.64 (5.38, 13.93)	5.79 (4.08, 7.65)
	Postoperative 48 h, pg/ml	7.90 (4.53, 11.43)	7.56 (4.99, 11.56)	6.87 (3.39, 10.00)

Note: Compared to group C, $^{c}P < 0.05$, $^{cc}P < 0.001$; compared to group R, $^{r}P < 0.05$, $^{rr}P < 0.001$

Table 5 Comparison of MAP and heart rate in three groups

Characteristics		Group C (*n* = 42)	Group R (*n* = 38)	Group HR (*n* = 40)
MAP	Average	88.83 (79.67, 99.33)	90.17 (81.33, 100.25)	89.00 (78.58, 98.67)
	T0, mmHg	100.33 (93.42, 107.25)	103.17 (95.08, 111.75)	105.67 (94.58, 112.17)
	T1, mmHg	99.67 (91.42, 105.33)	99.83 (92.67, 111.50)	97.00 (92.00, 103.58)
	T2, mmHg	86.50 (79.33, 96.17)^{aa}	89.50 (78.75, 99.67)^{aa}	89.50 (78.67, 97.92)^{aa}
	T3, mmHg	86.67 (79.17, 97.25)^{aa}	85.00 (76.92, 97.25)^{aa}	83.83 (76.08, 89.92)^{aa}
	T4, mmHg	83.33 (77.83, 87.17)^{aa}	85.00 (75.00, 93.00)^{aa}	82.17 (73.33, 88.75)^{aa}
	T5, mmHg	89.00 (81.67, 100.58)^{a}	88.83 (82.08, 97.92)^{aa}	91.50 (82.75, 100.17)^{aa}
	T6, mmHg	81.50 (71.08, 87.33)^{aa}	83.17 (77.08, 88.17)^{aa}	79.33 (73.58, 90.25)^{aa}
	T7, mmHg	81.33 (76.08, 90.67)^{aa}	86.00 (82.75, 96.50)^{aa}	82.50 (74.92, 89.25)^{aa}
	T8, mmHg	96.83 (90.42, 104.33)	91.33 (83.33, 99.42)^{aa}	96.00 (84.33, 102.50)^{a}
Heart Rate	Average	72.00 (65.00, 81.00)	74.00 (66.00, 80.00)	74.00 (65.00, 83.00)
	T0, bpm	74.50 (68.25, 82.00)	78.00 (72.25, 84.75)	79.00 (72.75, 88.25)
	T1, bpm	75.00 (67.25, 82.25)	78.50 (71.25, 83.50)	77.00 (69.00, 87.25)
	T2, bpm	74.50 (64.50, 84.00)	71.00 (64.25, 79.75)	77.50 (64.75, 87.25)
	T3, bpm	73.50 (68.00, 79.75)	78.50 (63.25, 82.75)	75.50 (66.75, 83.50)
	T4, bpm	67.00 (61.25, 74.25)^{aa}	71.00 (61.00, 77.50)^{aa}	65.50 (59.00, 77.00)^{aa}
	T5, bpm	69.50 (64.00, 79.00)	73.50 (66.25, 79.00)^{a}	76.00 (69.00, 79.75)
	T6, bpm	70.50 (64.00, 80.75)	71.50 (64.00, 80.00)^{a}	74.00 (65.75, 81.00)
	T7, bpm	70.00 (62.00, 74.75)	71.00 (64.00, 76.75)^{aa}	66.00 (60.75, 75.75)^{aa}
	T8, bpm	75.00 (69.25, 81.75)	75.00 (70.25, 79.75)	74.50 (67.25, 82.00)

Note: The superscript "a" indicates a significant difference compared to the T0 time point with $P < 0.05$, and "aa" indicates $P < 0.001$

Table 6 Postoperative complications and analgesic effects in three groups

Characteristics		Group C	Group R	Group HR
		(*n* = 42)	(*n* = 38)	(*n* = 40)
Postoperative Complications	Infection	0	0	0
	Subcutaneous Hematoma	0	0	0
	Local Anesthetic Toxicity	0	0	0
	Urinary Retention	0	0	0
	Constipation	0	0	0
	Nausea and Vomiting	15 (35.7)	7 (18.4)	5 (12.5)^{c}
Analgesic Effect Related Indicators	Total PCIA Presses*	27 (12.9)	4 (2.1)^{cc}	3 (1.5)^{cc}
	Rescue Analgesic Instances*	11 (5.2)	7 (3.7)	3 (1.5)

Note: Compared to group C, $^{c}P < 0.05$, $^{cc}P < 0.001$; *accumulated within 48 h, n (%)

The findings indicate that the interventions in Groups R and HR, especially HR, effectively reduced the postoperative inflammatory response compared to the control Group C. This suggests a potential therapeutic advantage of modulating the inflammatory process following surgery, with implications for pain management and recovery.

Hemodynamic parameters and postoperative complications

Hemodynamic parameters, specifically MAP and heart rate, were assessed at multiple time points (T0–T8) (Table 5). Group C experienced a significant decline in MAP from T2 to T7, except at T5, where $P = 0.002$ and $P < 0.001$ for all other comparisons. Groups R and HR displayed statistically significant MAP reductions at T2–T8. In terms of heart rate, a significant decrease was observed in Group C at T4 ($P < 0.001$), and similar significant reductions were noted in Groups R and HR at both T4 and T7 ($P < 0.001$).

Table 6 shows the incidence of postoperative complications and efficacy of analgesia in the three groups. No major postoperative complications, including infection, subcutaneous hematoma, local anesthetic toxicity, urinary retention, or constipation, were observed in any group. However, nausea and vomiting were observed with significantly higher frequency in Group C (35.7%, $P = 0.032$) compared to the lowest rate in Group HR (12.5%). In terms of analgesic outcomes, Groups R and HR exhibited a markedly reduced cumulative count of PCIA activations within 48 h, with four and three instances, respectively (both $P < 0.001$), which were significantly fewer than the 27 instances in Group C, indicating enhanced analgesic efficacy in Groups R and HR. Within 48 h postoperatively, no patient exhibited symptoms of nerve injury attributable to the SAPB procedure, such as localized numbness, tingling, burning sensations, decreased sensation, or motor dysfunction. Additionally,

no patient developed local allergic reactions potentially caused by hydromorphone, such as rashes or itching.

Discussion

In this double-blind, randomized controlled trial, we assessed the efficacy of 1 mg hydromorphone as an adjunct to ropivacaine in SAPB for postoperative analgesia in patients undergoing VATS. The hydromorphone-ropivacaine combination significantly enhanced pain control compared to ropivacaine alone. At the 6-hour postoperative assessment, the median VAS score in the combination group was 2.00 (IQR: 2.00), significantly lower than the control group's 3.00 (IQR: 3.00), $P < 0.001$. The combination also significantly reduced PCIA activation to three within 48 h compared to 27 in the control group ($P < 0.001$). Furthermore, the incidence of rescue analgesia requirement was reduced by half, with 12.5% in the combination group and 35.7% in the control group ($P = 0.032$). These results underscore the superior pain control provided by the addition of hydromorphone to ropivacaine in SAPB in patients undergoing VATS.

Moderate-to-severe postoperative pain is prevalent after thoracic surgery [14], necessitating effective analgesic strategies to mitigate opioid reliance and side effects [15]. SAPB, introduced in 2013 [16], has become the standard for postoperative analgesia following thoracic wall surgery [17, 18]. Our research affirms that SAPB significantly reduces the intraoperative use of anesthetics [19, 20] like propofol and analgesics such as remifentanil, with the hydromorphone-ropivacaine group demonstrating a marked decrease to 5.22 mg/kg/h and 7.59 μg/kg/h, respectively, versus the control group's 5.93 mg/kg/h and 8.74 μg/kg/h ($P < 0.001$). The findings of this study highlight the safety of SAPB, with no severe complications observed, which is attributed to the precision of the ultrasound-guided injections and the expertise of the operators. However, despite these benefits, we did not observe a reduction in muscle relaxant dosage or a significant impact on intraoperative hemodynamics, likely due to the minimally invasive single-port thoracoscopic approach and the anesthesiologists' proactive medication adjustments in response to surgical demands. Further research is essential to refine SAPB techniques, including optimal dosing and respiratory impact assessment, with future studies aimed at enhancing the efficacy of this established method.

Surgical trauma triggers a localized inflammatory response leading to the release of both pro- and anti-inflammatory cytokines [21]. This reaction not only affects postoperative recovery but can also precipitate complications. Thus, optimal anesthetic techniques should not only alleviate pain but also suppress the inflammatory response. Effective management can reduce neutrophil accumulation, curb the release of inflammatory mediators, and boost antioxidant protein levels, thereby reducing post-lobectomy lung injury [22]. Serum levels of IL-6, TNF-α, and CRP are pivotal biomarkers of inflammation [23]. Postoperatively, patients who underwent VATS lobectomy for lung cancer exhibited increased CRP levels, which were significantly attenuated by SAPB. The analgesic regimen combining hydromorphone and ropivacaine not only provided potent pain relief but also exerted a synergistic effect on CRP levels, significantly dampening the expression of IL-6 and TNF-α. Specifically, at 24 and 48 h post-surgery, the hydromorphone-ropivacaine group showed CRP levels of 23.80 mg/L and 21.65 mg/L, respectively, which were substantially lower than the control group's levels of 56.65 mg/L and 82.75 mg/L ($P < 0.001$). These findings indicate that SAPB, when combined with hydromorphone and ropivacaine, offers significant postoperative analgesia and inflammation reduction, potentially contributing to improved patient recovery.

In this study, no patient experienced postoperative neurologic injury or local complications attributable to hydromorphone within 48 h after surgery. The failure to observe long-term complications is a limitation of this study. Previous studies have shown that the use of hydromorphone in brachial plexus block [12] or sacral plexus block [24] in children did not result in long-term complications.

Ropivacaine is favored for its longevity and low systemic toxicity under local anesthesia and is a mainstay in regional analgesic procedures [25, 26]. In our study, along with established research and safety guidelines [27], we administered a preoperative 30 mL injection of 0.375% ropivacaine combined with 1 mg hydromorphone via the SAPB. Hydromorphone's potent analgesic profile and lipid solubility complement ropivacaine, potentially modulating peripheral and central μ-opioid receptors for enhanced pain relief [28]. Our findings support evidence that hydromorphone-ropivacaine SAPB outperforms fentanyl in post-mastectomy pain management [29]. The synergy of hydromorphone with ropivacaine has also been noted to boost analgesia in diverse nerve blocks, such as epidural, brachial plexus, and iliac crest blocks [12, 30, 31]. In our study, hydromorphone significantly enhanced the efficacy of ropivacaine in SAPB, as evidenced by decreased pain scores at the six-hour postoperative peak, delayed need for rescue analgesia, and extended analgesic duration of ropivacaine. These results highlight the advantages of this combination for optimizing postoperative pain control using SAPB.

Although this study provides valuable insights, it has certain limitations. Its status as a single-center study may restrict the broader applicability of the results. Additionally, the absence of long-term follow-up data indicates that the long-term implications of

hydromorphone-ropivacaine SAPB on patient recovery and prognosis remain unclear. Future studies should use a multicenter approach to enlarge the cohort and perform extended follow-up assessments. Such endeavors will not only substantiate the discoveries of this research, but also elucidate the efficacy of the method across various surgical procedures and patient demographics. Finally, our study did not compare SAPB with thoracic epidural analgesia or paravertebral blocks, these need further randomized controlled trials to investigate.

Conclusion

Ropivacaine adjuvant with hydromorphone in SAPB is a promising strategy for postoperative pain management with attenuating the inflammatory response and adverse events in patients undergoing VATS. Future studies should explore the long-term benefits and concenntration of hydromorphone of SAPB in thoracic surgery.

Abbreviations

CRP	C-reactive protein
ERAS	Enhanced recovery after surgery
IQU	Inter-quartile ratio
MAP	Mean arterial pressure
PCIA	Patient-controlled intravenous analgesia
SAPB	Serratus anterior plane block
VAS	Visual analog pain scores
VATS	Video-assisted thoracoscopic surgery

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Author contributions

XC and WZ designed the study, extracted the data and constructed the database. XC and LW analyzed the data. XC drafted the manuscript—original draft. WW and YL conducted critical revisions of the manuscript—review and editing. All authors read and approved the final manuscript.

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Data availability

The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethical Review Committee in the Medical Ethics Committee of Shangyu People's Hospital, Shaoxing City, Zhejiang Province (approval number: SRY-20210809-0005). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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