의학박사 학위논문

수술 후 통증 조절을 위한 선행진통효과: 부위마취 시점의 역할

Preemptive Analgesic effect for Postoperative Pain : Implication for Timing of Regional Blocks

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이 논문을 의학박사 학위 논문으로 제출함

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이 외에도 미처 언급하지 못한 많은 분들의 이름을 모두 되새기지 못해 죄송하며 고마운 마음을 전하며 글을 마칩니다. 처음 연구를 시작할 때 가졌던 흥미와 열정을 잊지않고 박사라는 학위를 가진 것이 부끄럽지 않은 사람이 될 수 있도록 앞으로 더욱 노력해 나가겠습니다. 감사합니다.

2020년 1월 이종혁

ABSTRACT

Introduction

Preemptive analgesia is an antinociceptive treatment that prevents the establishment of central sensitization caused by incisional and inflammatory injuries, which amplifies postoperative pain. There are many drugs in use for preemptive analgesia, but clinical research related to regional blocks is lacking. The purpose of this study is to confirm the preemptive analgesic effect of regional block.

Methods

In the all Pre group, ultrasound guided allocated regional block were performed after anesthesia induction and before skin incision. In the all Post group, allocated regional block were performed after skin closure and before emergence from anesthesia.

Chapter I: Adult patients scheduled for elective laparoscopic cholecystectomy (LC) were randomly assigned to one of four groups. Pre-rectus sheath block (RSB) group or Post-RSB group with 0.25% ropivacaine and pre-RSB group or Post-RSB group with 0.375% ropivacaine (Pre-0.25, Post-0.25, Pre-0.375, Post-0.375 group, respectively). Rescue analgesic consumption during 24 hours after surgery was a primary outcome. Postoperative numerical rating scale (NRS), intraoperative data and side effect of regional block were recorded.

Chapter II: Adult patients scheduled for elective LC were randomly assigned to one of two groups. (Pre-paravertebral block (PVB) and Post-PVB group). Pre-incisional RSB was performed to all patients in study. Also according to the allocation, pre incisional PVB or Post incisional PVB were performed to patients. Rescue analgesic consumption during 24 hours after surgery was a primary outcome. Postoperative NRS, intraoperative data and side effect of regional block were recorded.

Results

Chapter I: Total rescue analgesic consumption during 24 hours after surgery (μg) was significantly lower in the all pre groups than in the all post group (Pre-0.25: 240.4 ± 109.3 μg vs. Post-0.25: 304.9 ± 126.5 μg, P = 0.018, Pre-0.375: 209.0 ± 97.2 μg vs Post-0.375: 260.2 ± 112.6 μg, P = 0.028). There was no significant difference in the total rescue analgesic consumption between all groups when the timing of the regional block was compared divided by the concentrations of ropivacaine (0.25% vs 0.375%) during the first 24 hours after surgery Chapter II: The total rescue analgesic consumption during the 24 hours after surgery (μg) was significantly lower in the pre-PVB group than in the post-PVB group (140.0 (100.0; 255.0) μg vs. 250.0 (165.0; 307.5) μg, P = 0.003). The NRS was significantly lower in the pre-PVB group than in the post-PVB group at 0.5, 1, 2, and 6 hours after surgery (4.4 ± 1.5 μg vs. 3.2 ± 1.6 μg, P = 0.002; 02.8 ± 1.2 μg vs. 1.8 ± 1.1 μg, 0.001; 5.2 ± 1.7 μg vs. 3.5 ± 1.9 μg, < 0.001; and 4.3 ± 1.8 μg vs. 3.2 ± 1.5 μg, P = 0.014, respectively)

Conclusion

These results demonstrate that the timing of regional block is clinically significant for postoperative pain relief.

Key words: Numerical Rating Scale; Paravertebral Block; Preemptive Analgesic Effect; Pre-incisional Block; Rectus Sheath Block; Ropivacaine.

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BACKGROUND AND GENERAL INTRODUCTION

Preemptive analgesic effect is an antinociceptive treatment to reduce the incidence of postoperative hyperalgesia and allodynia by preventing the establishment of peripheral and central sensitization caused by incisional and inflammatory injuries [1, 2]. Although many studies have been conducted in the past, it is still controversial [1-4]. But there is still a widespread belief of the efficient analgesia among clinicians. In the past, NSAIDs, local anesthetics infiltration, NMDA receptor antagonists, and opioids were considered not significant for preemptive analgesia [3, 4]. Recently, however, COX-2 inhibitor, gabapentin and regional block are effective for preemptive analgesia due to drug development and improvement of block technique such as ultrasound guidance [5].

An important point of preemptive analgesia is on the pathophysiologic phenomenon that it should prevent: altered sensory processing. Therefore, the word “preemptive” may not simply mean “before incision.” An insufficient afferent blockade cannot be preemptive, even if it is administered before the incision. And effective analgesia should not only be well established prior to the surgical incision but should be continued well into the postoperative period. The timing to stop delivery of the local anesthetic agent should be judged against the healing of the wound and degree of anticipated tenderness. Discontinuation of regional blockade when significant afferent input is still likely to be present would merely delay the onset of surgical pain until after the pharmacologic effects of the local anesthetic subside. For these reasons, epidural analgesia may be the most effective analgesic method. Thus, continuous epidural analgesia has a preemptive effect and is still considered to be effective in many studies [4, 6-8].

The pain pathway consists of transduction, transmission, modulation, and perception. Continuous epidural analgesia blocks the transmission in to dorsal horns [9]. Regional blocks, like epidural blocks, also can block transmission in pain pathway and avoid the adverse effects

associated with neuraxial blockade (eg, hypotension, urinary retention, and motor paresis leading to delayed ambulation). The introduction of ultrasound technology has improved the success rate of block placement and possibly associated complications. However, single-injection regional blocks are limited by the relative short duration of action of the local anesthetic and abrupt termination of analgesia, it is controversial for preemptive analgesic effects. Thus, author believed that the preemptive analgesic effect can be identified using regional blocks if the time of operation is short and the pain is localized. Therefore, Preemptive analgesic effects of regional block were investigated in patients undergoing laparoscopic cholecystectomy (LC). In addition, both somatic and visceral pain can be observed in patients undergoing LC, LC is suitable for identifying the preemptive analgesic effects of somatic and visceral blocks.

To determine possible efficacy of preemptive analgesic effect for postoperative acute pain management, three outcome variables can be considered: postoperative pain scores, total analgesic consumption, and time to first rescue analgesic [(4)].

1. Pain intensity in the form of the various pain scores, NRS scores during the first 24 postoperative hours.
2. Supplemental postoperative analgesic requirements.
3. Time to first rescue analgesic.

The study divided the following two chapters to identify the preemptive analgesic effect of regional block on somatic and visceral pain after LC respectively.

In Chapter I, to determine whether the regional block had a preemptive analgesic effect on somatic pain, author checked “total analgesic consumption” and “postoperative pain scores”. Pre and post incisional rectus sheath block (RSB) & intercostal nerve block (ICNB) with varying concentrations of local anesthetics were performed in patients undergoing LC.

In Chapter II, to determine whether the regional block had a preemptive analgesic effect on visceral pain, author checked “total analgesic consumption” and “postoperative pain scores”. Pre and post incisional paravertebral block (PVB) was performed in patients with minimized somatic pain by pre-incisional RSB.

CHAPTER I

The differential effect of somatic blocks before and after incision on postoperative pain in patients who underwent laparoscopic cholecystectomy

INTRODUCTION

Cholecystectomy is one of the most commonly performed elective surgical procedures, and laparoscopic cholecystectomy (LC) has become the method of choice for most benign conditions [10, 11]. Compared with open cholecystectomy, LC is considered a minimally invasive surgery with less postoperative pain [12]. However, in the immediate postoperative period, LC causes moderate to severe postoperative pain [13, 14], which is usually not sufficiently managed, resulting in patient discomfort and delayed recovery [14-16].

Pain after LC is multifactorial, as incisional pain, visceral pain, and referred shoulder pain are all implicated. The overall pain is most intense on the day of LC, with the incisional pain predominating over the visceral pain [14, 17, 18]. To provide procedure-specific pain management, various multimodal analgesic strategies for patients undergoing LC have been attempted [15, 19-22] and the administration of NSAIDs, COX-2 inhibitors, dexamethasone, and port site local anesthetic infiltration is recommended (20-22). Abdominal truncal blocks have been recommended as a part of multimodal analgesia in laparoscopic abdominal surgery [17, 18]. However, the analgesic effect of transversus abdominis plane (TAP) block is debatable in LC [22, 23]. Although few studies are available on RSB in LC, considering the analgesic effects of RSB in laparoscopic surgery and umbilical surgery [24-26], RSB may be effective for pain relief after LC.

Preemptive analgesia is an antinociceptive treatment that prevents the establishment of central sensitization caused by incisional and inflammatory injuries, which amplify postoperative pain. Sufficient blockade of perioperative nociceptive input may reduce pathologic hypersensitivity, thereby improving the pain experienced after surgery [27, 28]. Preemptive analgesia has been studied in diverse surgical settings; however, the results of experimental studies on its effects are still controversial [27-30]. In addition, some studies have shown that the higher the concentration of local anesthetic used for truncal blocks is, the better

the outcome of the block will be [31, 32].

In the present study, we hypothesized that pre incisional RSB (pre-RSB) may lessen the deleterious impact of intraoperative and early postoperative noxious input, better preventing the induction of central sensitization and pathologic pain than post incisional RSB (post-RSB), and that higher concentrations of local anesthetics will produce greater preemptive effects. We aimed to investigate the preemptive effect of pre incisional RSB on the pain experienced by the patient after LC according to the drug concentration administered.

MATERIALS AND METHODS

1. Patients

This single-center, prospective, randomized, single-blind study was conducted at Asan Medical Center in Seoul, Republic of Korea. The study protocol was approved by the Institutional Review Board of Asan Medical Center (2017-0301), and written informed consent was received from all participants in the study. This study was registered at ClinicalTrials.gov (NCT03413280). Adult patients scheduled for elective LC were considered eligible for the study. Patients were enrolled if they were aged 20–80 years with American Society of Anesthesiologists physical status class ≤ 2. We excluded patients who 1) declined to participate; 2) had used an anticoagulant; 3) were suspected to have severe adhesions; 4) were allergic to local anesthetics; 5) had serious neurological or psychiatric disorders; 6) were pregnant or breastfeeding; and 7) were scheduled to undergo a single-port LC.

2. Randomization

Using a computer-generated randomization sheet, the enrolled patients were randomly assigned to one of four groups: pre-RSB group or post-RSB group with 0.25% ropivacaine and pre-RSB group or post-RSB group with 0.375% ropivacaine (pre-0.25, post-0.25, pre-0.375, post-0.375 groups, respectively). For random allocation of the participants, a web-based randomization software (Random Allocation Software version 1.0, Isfahan University of Medical Sciences, Isfahan, Iran) was used with random block sizes of 8 and an allocation ratio of 1:1:1:1. The allocation sequence was concealed from the first investigator, who was responsible for enrolling and assessing the participants, in opaque, sealed, and sequentially numbered envelopes. The envelopes were given to the intervention staff, who conducted anesthesia, ultrasound-guided RSB, and intercostal nerve block (ICNB). A second investigator,

who was blinded to treatment allocation, administered analgesics at the post-anesthesia care unit (PACU) and general ward during the 24-hour period after surgery and assessed the postoperative outcomes. Although the treatment allocation was un-blinded to the intervention staff, it was kept blinded to the second investigators and participants.

3. Surgical technique

The same team of experienced laparoscopic surgeons (each surgeon have experience with more than 300 LCs) performed all operations. All patients underwent standard procedures for LC. Three trocars were inserted below the xiphoid process (5 mm), right costal arch (5 mm), and umbilicus (10 mm). Through an infraumbilical incision, a camera port was inserted and the gallbladder was retracted. Pneumoperitoneum was created and maintained using carbon dioxide insufflation with intraperitoneal pressure of 12 mmHg. LC was conducted in the supine position with a 30° reverse Trendelenburg position.

4. Anesthesia and analgesia

In the operating room, all patients were routinely monitored using electrocardiography, non-invasive blood pressure measurement, and pulse oximetry. Anesthesia was induced with a continuous infusion of propofol (2 mg/kg), rocuronium (0.6 mg/kg), and remifentanil using a target-controlled infusion pump (Orchestra®, Fresenius Vial, France). After tracheal intubation, anesthesia was maintained with desflurane (5–6%) in 50% oxygen/air and a continuous infusion of remifentanil (2–5 ng/ml of effect-site concentration) was administered to maintain the systolic blood pressure (SBP) within 20% of baseline values. When skin closure was started, the effect-site concentration of remifentanil was reduced and maintained at 1.5 ng/dl until extubation. After emergence from general anesthesia, the patients were transferred to

the PACU. The need for rescue analgesia was evaluated from 0 to 24 hours after surgery. In the PACU, intravenous fentanyl (0.4 μg/kg) was administered when NRS was ≥ 4 or when the patient was in need of pain relief. Administration of fentanyl was repeated until NRS < 4 or when the patient did not request further pain relief. In the general ward, 30 mg of ketorolac was administered first when NRS was ≥ 4 or when the patient was in need of pain relief. When the effect of ketorolac was insufficient, 50 mg of tramadol or 25 mg of meperidine was administered within 24 hours after surgery. The total doses of rescue analgesics during 24 hours after surgery were recorded and converted to equianalgesic doses of intravenous fentanyl based on the previously published conversion factors (intravenous fentanyl 100 μg = ketorolac 30 mg = tramadol 100 mg) [33, 34]. The total or cumulated rescue analgesic consumption (CRA) was expressed in intravenous fentanyl equivalents (μg).

5. Ultrasound-guided RSB and ICNB

In the pre-RSB group, RSB and ICNB were performed after anesthesia induction and before skin incision. In the post-RSB group, RSB and ICNB were performed after skin closure and before emergence from anesthesia. RSB and ICNB were performed using the NextGen LOGIQ e ultrasound console (GE Healthcare, Madison, WI, USA) with a 12 MHz high-frequency linear array transducer.

For the RSB, the ultrasound probe was positioned transversely on the rectus abdominis muscle, below the umbilicus. Guided by real-time ultrasound, a 23-gauge Quincke needle (TaeChang Industrial Co., Gongju, Korea) was inserted in-plane with caution to avoid injury to nearby vessels from the medial to lateral direction, until the tip was positioned in the plane between the lateral side of the rectus abdominis muscle and the posterior rectus sheath. After negative pressure aspiration, 17 mL of 0.25% or 0.375% ropivacaine was administered and the block was repeated on the opposite side (Figure 1-1).

For the ICNB, the ultrasound probe was positioned in the parasagittal axis to obtain a complete view of the pleura and three layers of intercostal muscles (external, internal, and innermost) between two adjacent ribs at the target level. The targets were the right sixth, seventh, and eighth intercostal nerves, determined based on the subxiphoid and subcostal port sites. The needle was inserted in-plane from the caudal to cephalad direction until the tip was positioned between the internal intercostal muscle and the innermost intercostal muscle. After aspiration, 2 mL of 0.25% ropivacaine was injected for each intercostal nerve (Figure 1-2). The total doses of ropivacaine for RSB and ICNB were the same for all patients in both groups: 40 mL of 0.25% or 0.375% ropivacaine.

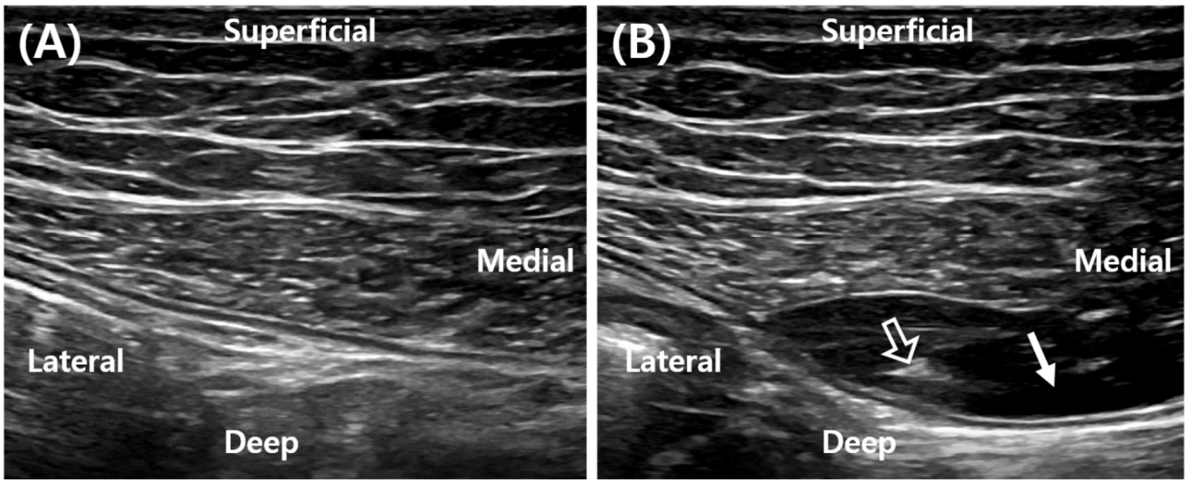

Figure 1-1. Ultrasound guided rectus sheath block. (A) Ultrasound guided rectus muscle image using axial view. (B) The echogenic needle (black arrow) is approaching to the posterior rectus sheath with in-plane technique. The local anesthetic hydro-dissects the potential space (white arrow) between the rectus muscle and posterior rectus sheath.

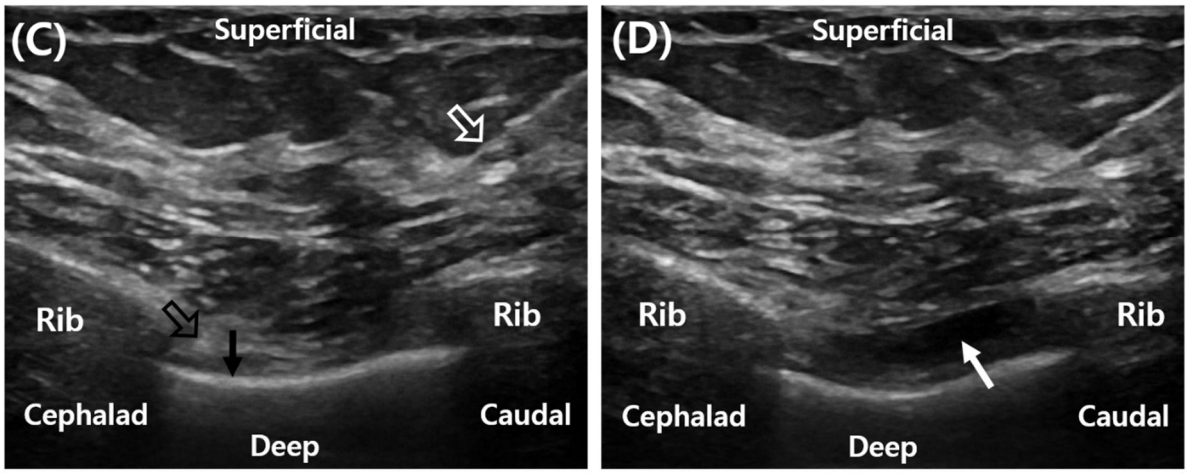

Figure 1-2. Ultrasound guided intercostal nerve block. (A) Ultrasound guided intercostal nerve block (ICNB) using the sagittal view. The echogenic needle (white empty arrow) tip (black empty arrow) is approaching to the innermost intercostal muscle layer with the in-plane technique. (B) The local anesthetic hydro-dissects the potential space (white arrow) between the innermost intercostal muscle and the intermediate intercostal muscle layer.

6. Outcome measures and data collection

The primary outcome was the total rescue analgesic consumption during the 24-hour period after surgery. Secondary outcomes were cumulated rescue analgesic consumption and postoperative pain scores at 0, 1, 2, 6, 9, 18, and 24 hours after surgery. The other outcomes were intraoperative remifentanil consumption, changes in vital signs related to skin incision, the adverse effects of analgesics, and complications associated with RSB and ICNB.

Intraoperative evaluation was performed by the intervention staff and postoperative evaluation was performed by the second investigator who was blinded to treatment allocation. The first postoperative evaluation of the RSB and ICNB was performed in the PACU. An algometer (Baseline algometer, Baseline®, India) was used to induce experimental pressure pain on each of the three trocar sites (below the xiphoid process, right costal arch, and umbilicus). Pressure was applied for 5 seconds on each trocar site to exclude patients with insufficient RSB, which was determined based on a pressure pain threshold lower than 2 kg/cm2 pressure [35, 36]. Cumulated rescue analgesic consumption and postoperative pain scores were measured at 0, 1, 2, 6, 9, 18, and 24 hours after surgery. Postoperative pain scores were assessed using the 11-point NRS, with 0 = no pain and 10 = worst pain imaginable. The side effects of analgesics, such as dizziness, sedation, respiratory depression, nausea, and vomiting were all evaluated. In addition, the complications associated with RSB and ICNB were evaluated, including pneumothorax and hematoma.

7. Statistical Analysis

Sample size was calculated based on the results of our previous study, in which the means ± standard deviations of opioid requirements during the 24-hour period post-surgery in the pre-RSB and post-RSB groups were 220 ± 65 μg and 265 ± 80 μg, respectively. To detect

this difference with an alpha of 0.05 (two-sided) and a power of 0.8, 85 patients per group were needed. Allowing for a 15% dropout rate during the study period, 50 patients were recruited for each group.

Continuous parameters were summarized as the mean (± standard deviation) or median (interquartile range), and categorical parameters as frequency (percentage), as appropriate. To compare the values between the groups, the Kruskal-Wallis test or ANOVA for continuous data and Pearson's Chi-squared test or Fisher's Exact Test for categorical data were performed after a normality test, as appropriate. Repeated measurements of cumulative fentanyl consumption were performed using a linear mixed-effect model to evaluate the interaction of time and treatment between the groups. Statistical significance was set at $P < 0.05$. Data manipulation and analyses were performed using R software, version 3.3.1 (CRAN, R Foundation, Vienna, Austria).

RESULTS

Of the 221 patients screened from March 2017 to January 2018, 21 patients were excluded from the study (Figure 1-3). Two hundred patients were randomized into four groups (Pre-0.25 (n = 50), post-0.25 (n = 50), pre-0.375 (n = 50), and post-0.375 (n = 50)). All 100 people in the pre-group were treated with RSB, but 10 patients in the pre-0.25 group and 8 patients in the pre-0.375 group were excluded due to paraumbilical port insertion, bile leakage, bleeding, and additional port insertion. In addition, 12 patients in the post-0.25 group and 8 patients in the post-0.375 group who had paraumbilical port insertion, bile leakage, bleeding, and additional port insertion, respectively, during surgery were also excluded. Consequently, 162 patients were included in the final analysis.

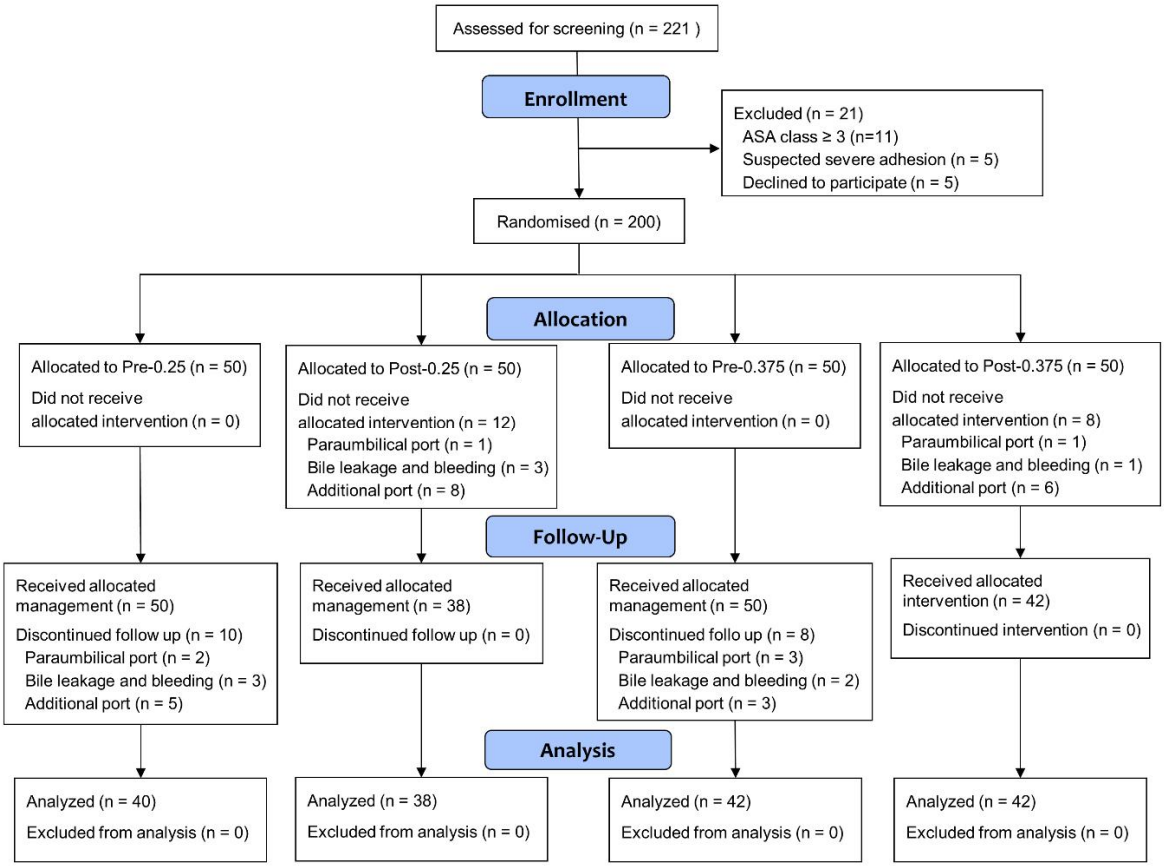

Figure 1-3. Flowchart of the study population. Abbreviations: ASA, American Society of Anesthesiologists

There were no significant differences in the baseline characteristics between the four groups (Table 1-1).

Table 1-1. Baseline characteristics of the study participants.

	Pre-0.25 (N=40)	Post-0.25 (N=38)	Pre-0.375 (N=42)	Post-0.375 (N=42)	P-value
Age	59.5 (54.5;65.5)	55.0 (43.0;65.0)	51.5 (43.0;60.0)	54.5 (41.0;63.0)	0.018
Sex (Male)	18 (45.0%)	12 (31.6%)	21 (50.0%)	23 (54.8%)	0.190
BMI (kg/m2)	25.0 (23.2;27.0)	24.1 (21.5;26.2)	24.2 (22.6;26.0)	24.4 (22.8;26.3)	0.450
ASA PS					0.574
1	13 (32.5%)	13 (34.2%)	19 (45.2%)	14 (33.3%)	
2	27 (67.5%)	25 (65.8%)	23 (54.8%)	28 (66.7%)	
Hypertension	10 (25.0%)	12 (31.6%)	10 (23.8%)	10 (23.8%)	0.838
Diabetes	2 (5.0%)	5 (13.2%)	5 (11.9%)	6 (14.3%)	0.535
Diagnosis					0.585
Acute chole.	27 (67.5%)	30 (78.9%)	36 (85.7%)	30 (71.4%)	
Chronic chole.	8 (20.0%)	5 (13.2%)	3 (7.1%)	7 (16.7%)	
GB polyp	5 (12.5%)	3 (7.9%)	3 (7.1%)	5 (11.9%)	
Pre-op drain					0.142
None	32 (80.0%)	34 (89.5%)	37 (88.1%)	36 (85.7%)	
ENBD	6 (15.0%)	0 (0.0%)	3 (7.1%)	5 (11.9%)	
PTBD	2 (5.0%)	4 (10.5%)	2 (4.8%)	1 (2.4%)	
Pre-op pain					0.151
No	39 (97.5%)	37 (97.4%)	38 (90.5%)	36 (85.7%)	
Yes (NRS 1)	1 (2.5%)	1 (2.6%)	4 (9.5%)	6 (14.3%)	

Data are expressed as median (interquartile range) or numbers (%), as appropriate. Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine; ASA PS, American Society of Anesthesiologists Physical Status; chole., cholecystitis; ENBD, endoscopic nasobiliary drainage; PTBD, percutaneous transhepatic biliary drainage; NRS, numerical rating scale.

The duration of surgery and anesthesia were not significantly different between the four groups. The pre-0.25 group had significantly lower intraoperative remifentanil consumption (μg/kg/min) than the post-0.25 group (0.09 ± 0.03 vs. 0.11 ± 0.04, P = 0.008), but there was no significantly different between the pre-0.375 group and the post-0.375 group. All post-RSB groups showed statistically significant changes in vital signs (SBP, diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR)) related to the skin incision compared to the changes in the pre-RSB group. The differences in the changes in the vital signs were greater between the 0.25 groups than between the 0.375 groups (Table 1-2).

Table 1-2. Intraoperative data.

	Pre (N=40)	0.25 % post (N=38)	P-value	Pre (N=42)	0.375 % post (N=42)	P-value
Duration of surgery (min)	40.0 (30.0;50.0)	40.0 (30.0;40.0)	0.651	35.0 (25.0;45.0)	40.0 (30.0;50.0)	0.068
Duration of anesthesia (min)	75.0 (65.0;82.5)	70.0 (65.0;85.0)	0.375	65.0 (60.0;75.0)	75.0 (65.0;85.0)	0.014
SBP change (%)	0.0 (-2.8; 2.3)	13.4 (7.0;18.7)	< 0.001	0.0 (-5.0; 1.8)	8.1 (3.3;13.0)	< 0.001
DBP change (%)	0.0 (-3.5; 6.0)	11.9 (7.3;18.5)	< 0.001	0.7 (-1.9; 3.3)	8.6 (3.5;19.7)	< 0.001
MBP change (%)	0.0 (-2.9; 3.5)	13.8 (8.5;20.5)	< 0.001	0.0 (-2.8; 1.7)	8.6 (3.7;15.6)	< 0.001
HR change (%)	0.0 (-2.3; 1.8)	6.2 (1.9;12.1)	< 0.001	-0.7 (-2.0; 1.4)	4.9 (1.2;13.8)	< 0.001
Bile leakage			0.828			0.755
0	33 (82.5%)	33 (86.8%)		37 (88.1%)	35 (83.3%)	
1	7 (17.5%)	5 (13.2%)		5 (11.9%)	7 (16.7%)	
GB bed injury			0.676			1.000
1	36 (90.0%)	36 (94.7%)		38 (90.5%)	37 (88.1%)	
2	4 (10.0%)	2 (5.3%)		4 (9.5%)	5(11.9%)	
Intraoperative Remifentanil						
(μg)	452.2 ± 128.8	482.4 ± 127.6	0.302	456.6 ± 177.4	553.0 ± 203.4	0.023
(μg/kg/min)	0.09 ± 0.03	0.11 ± 0.04	0.008	0.10 ± 0.03	0.11 ± 0.02	0.230

Values are expressed as median (interquartile range) or mead (standard deviation). Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate; GB, gallbladder.

Total rescue analgesic consumption during 24 hours after surgery (μg) was significantly lower in the pre groups than in the post groups (pre-0.25: 240.4 ± 109.3 vs. post-0.25: 304.9 ± 126.5, P = 0.018, pre-0.375: 209.0 ± 97.2 vs post-0.375: 260.2 ± 112.6, P = 0.028) (Table 1-3). There was a 21% opioid reduction in the 0.25% groups and 20% reduction in the 0.375% groups during the first 24 hours after surgery. Within the postoperative 24 hours, the cumulated rescue analgesic consumption (μg) was significantly lower in the pre-0.25 group than in the post-0.25 group at 9, 18, and 24 hours after surgery (Figure 1-4) and lower in the pre-0.375 group than in the post-0.375 group at 1, 6, 9 ,18, and 24 hours after surgery (Figure 1-5).

Table 1-3. Cumulated rescue analgesic consumption based on concentration of ropivacaine during 24 hours after surgery.

	0.25 %			0.375 %		
	Pre (N=40)	post (N=38)	P-value	Pre (N=42)	post (N=42)	P-value
CRA 0h	21.2 ± 14.4	21.1 ± 12.8	0.949	17.0 ± 14.3	19.6 ± 15.5	0.422
CRA 0.5h	61.0 ± 30.6	60.1 ± 28.5	0.897	56.3 ± 26.0	66.4 ± 32.4	0.118
CRA 1h	71.0 ± 37.1	80.7 ± 31.8	0.222	63.9 ± 30.6	81.4 ± 40.5	0.028
CRA 2h	155.1 ± 53.0	154.7 ± 50.3	0.974	145.8 ± 55.7	164.2 ± 51.3	0.120
CRA 6h	171.0 ± 49.2	181.7 ± 46.8	0.328	157.7 ± 63.6	188.6 ± 62.7	0.028
CRA 9h	192.9 ± 48.6	219.6 ± 53.1	0.023	175.4 ± 73.4	209.0 ± 76.8	0.043
CRA 18h	220.4 ± 66.0	263.0 ± 67.3	0.006	198.6 ± 85.4	246.0 ± 88.1	0.014
CRA 24h	240.4 ± 109.3	304.9 ± 126.5	0.018	209.0 ± 97.2	260.2 ± 112.6	0.028

Data are expressed as median (interquartile range) or mean (standard deviation). Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine; CRA, cumulated rescue analgesic consumption used up to each hour.

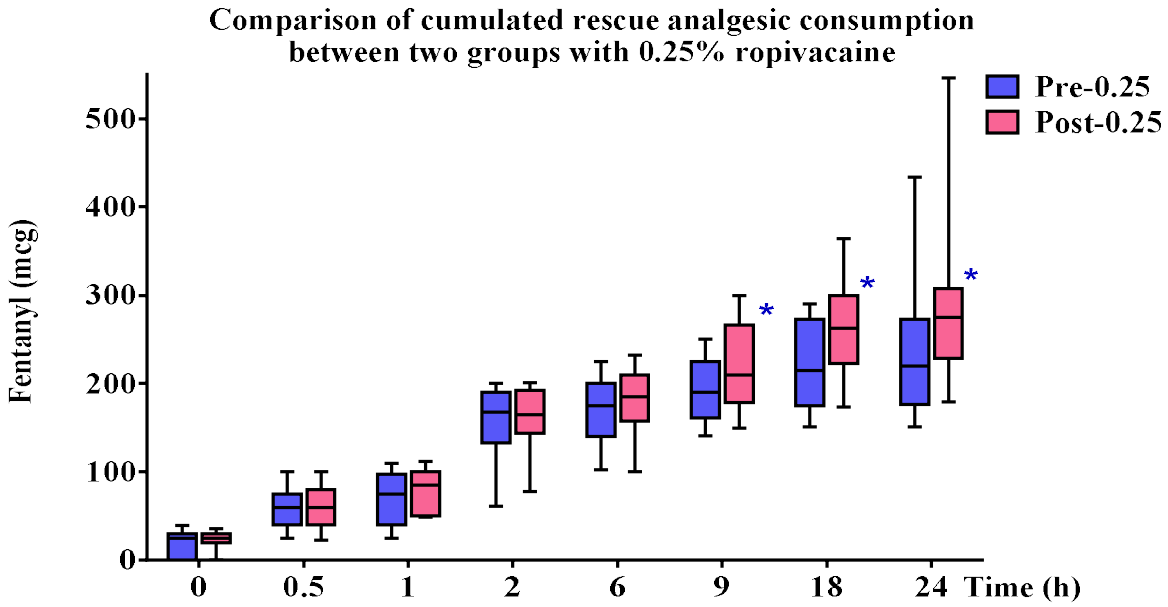

Figure 1-4. Cumulated rescue analgesic consumption during 24 hours after surgery between pre-0.25 and post-0.25 group. Data are expressed as mean (standard deviation). Horizontal lines, boxes, and error bars represent the mean, standard deviation and 10th and 90th percentile, respectively. *P < 0.05. Abbreviations: Pre-0.25, pre-incisional rectus sheath block with 0.25% ropivacaine; Post-0.25, post-incisional rectus sheath block with 0.25% ropivacaine.

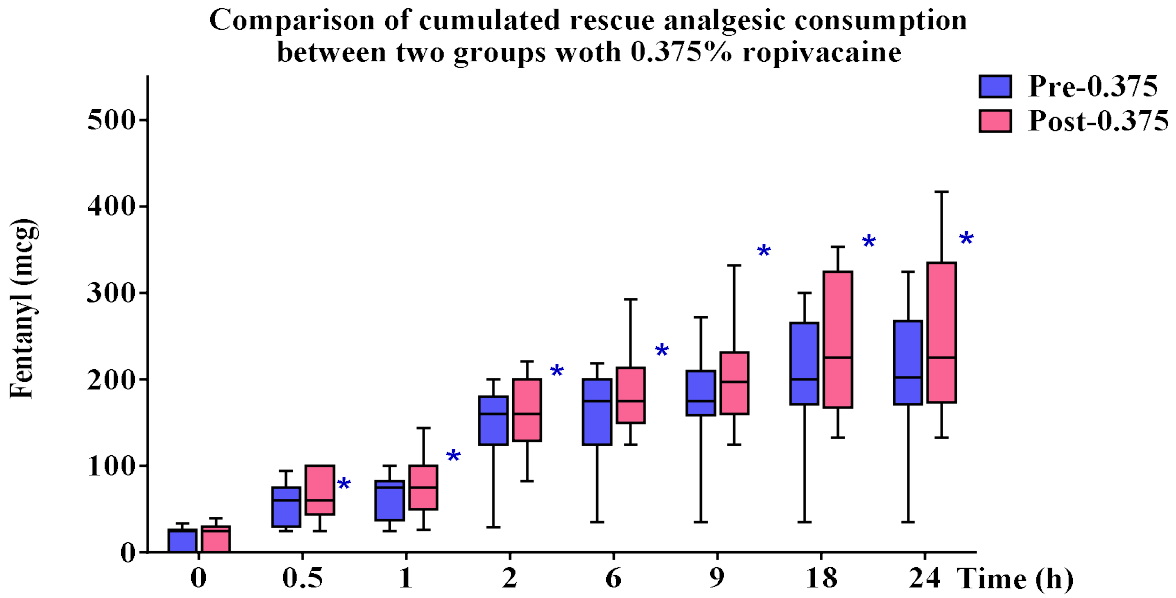

Figure 1-5. Cumulated rescue analgesic consumption during 24 hours after surgery between pre-0.375 and post-0.375 group. Data are expressed as mean (standard deviation). Horizontal lines, boxes, and error bars represent the mean, standard deviation and 10th and 90th percentile, respectively. *P < 0.05. Abbreviations: Pre-0.375, pre-incisional rectus sheath block with 0.375% ropivacaine; Post-0.375, post-incisional rectus sheath block with 0.375% ropivacaine.

However, there was no significant difference in the total rescue analgesic consumption between all groups when the timing of the regional block was compared divided by the concentrations of ropivacaine (0.25% vs 0.375%) during the first 24 hours after surgery (Table 1-4). Additionally, there was no difference in the cumulative rescue analgesic consumption (μg) over a set period of time for each group within the 24-hour period.

Table 1-4. Cumulated rescue analgesic consumption based on timing of rectus sheath block during 24 hours after surgery.

	Pre			Post		
	0.25 (N=40)	0.375 (N=42)	P-value	0.25 (N=38)	0.375 (N=42)	P-value
CRA 0h	21.2 ± 14.4	17.0 ± 14.3	0.186	21.1 ± 12.8	19.6 ± 15.5	0.660
CRA 0.5h	61.0 ± 30.6	56.3 ± 26.0	0.455	60.1 ± 28.5	66.4 ± 32.4	0.361
CRA 1h	71.0 ± 37.1	63.9 ± 30.6	0.349	80.7 ± 31.8	81.4 ± 40.5	0.925
CRA 2h	155.1 ± 53.0	145.8 ± 55.7	0.442	154.7 ± 50.3	164.2 ± 51.3	0.410
CRA 6h	171.0 ± 49.2	157.7 ± 63.6	0.296	181.7 ± 46.8	188.6 ± 62.7	0.584
CRA 9h	192.9 ± 48.6	175.4 ± 73.4	0.205	219.6 ± 53.1	209.0 ± 76.8	0.473
CRA 18h	220.4 ± 66.0	198.6 ± 85.4	0.201	263.0 ± 67.3	246.0 ± 88.1	0.337
CRA 24h	240.4 ± 109.3	209.0 ± 97.2	0.174	304.9 ± 126.5	260.2 ± 112.6	0.099

Data are expressed as mean (standard deviation). Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine; CRA, cumulated rescue analgesic consumption used up to each hour.

Difference of cumulated analgesic consumption between pre-0.25 and post-0.25 were small in PACU, but continues to grow from 2 hours to 24 hours after surgery. However, the difference in CRA between pre-0.375 and post-0.375 were increased continuously for 24 hours after the end of anesthesia (Figure 1-6).

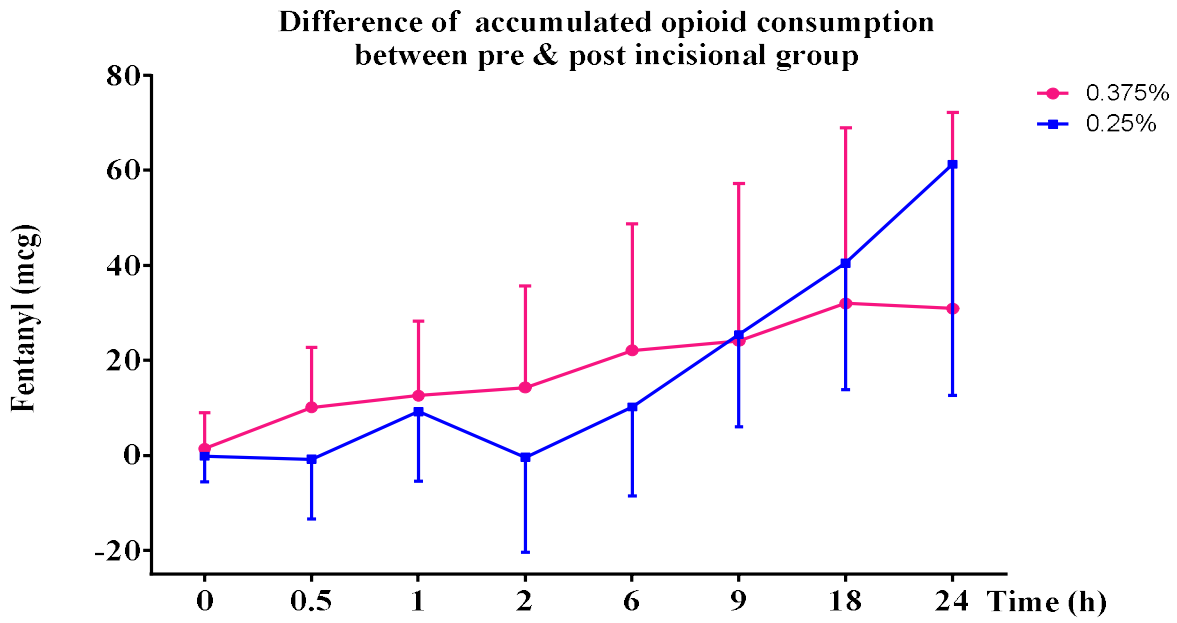

Figure 1-6. Difference of cumulated rescue analgesic consumption between pre & post incisional group during 24 hours after surgery. Data are expressed as mean and 95% confidence interval.

NRS was significantly lower in the pre-0.25 group than in the post-0.25 group at 0 hours after surgery (5.0 (3.0–6.0) vs. 6.0 (5.0; 6.0), P = 0.030) (Table 1-5). Except at 0 hour, the NRS was not significantly different between the four groups throughout the 24-hour period after surgery (Figure 1-7). Between the pre-0.375 group and post-0.375 group, there was no difference in NRS for the first 24 hours after surgery (Figure 1-8).

No patient complained of significant side effects related to the analgesics or complications associated with RSB or ICNB.

Table 1-5. Postoperative NRS.

	0.25 %			0.375 %		
	Pre (N=40)	post (N=38)	P-value	Pre (N=42)	post (N=42)	P-value
NRS 0h	5.0 (3.0; 6.0)	6.0 (5.0; 6.0)	0.030	5.0 (3.0; 6.0)	5.0 (3.0; 6.0)	0.895
NRS 0.5h	5.0 (4.0; 6.0)	6.0 (4.0; 7.0)	0.096	5.0 (3.0; 6.0)	5.0 (4.0; 6.0)	0.113
NRS 1h	3.0 (3.0; 3.0)	3.0 (3.0; 3.0)	0.500	3.0 (2.0; 3.0)	3.0 (3.0; 3.0)	0.323
NRS 2h	3.0 (2.0; 3.5)	3.0 (3.0; 4.0)	0.612	3.0 (3.0; 5.0)	3.0 (3.0; 3.0)	0.351
NRS 6h	3.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.496	3.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.741
NRS 9h	2.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.243	3.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.919
NRS 18h	3.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.540	2.0 (2.0; 3.0)	3.0 (2.0; 3.0)	0.935
NRS 24h	2.0 (2.0; 3.0)	2.0 (2.0; 3.0)	0.444	2.0 (2.0; 3.0)	2.0 (2.0; 3.0)	0.934

Data are expressed as median (interquartile range). Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine; NRS, numerical rating scale.

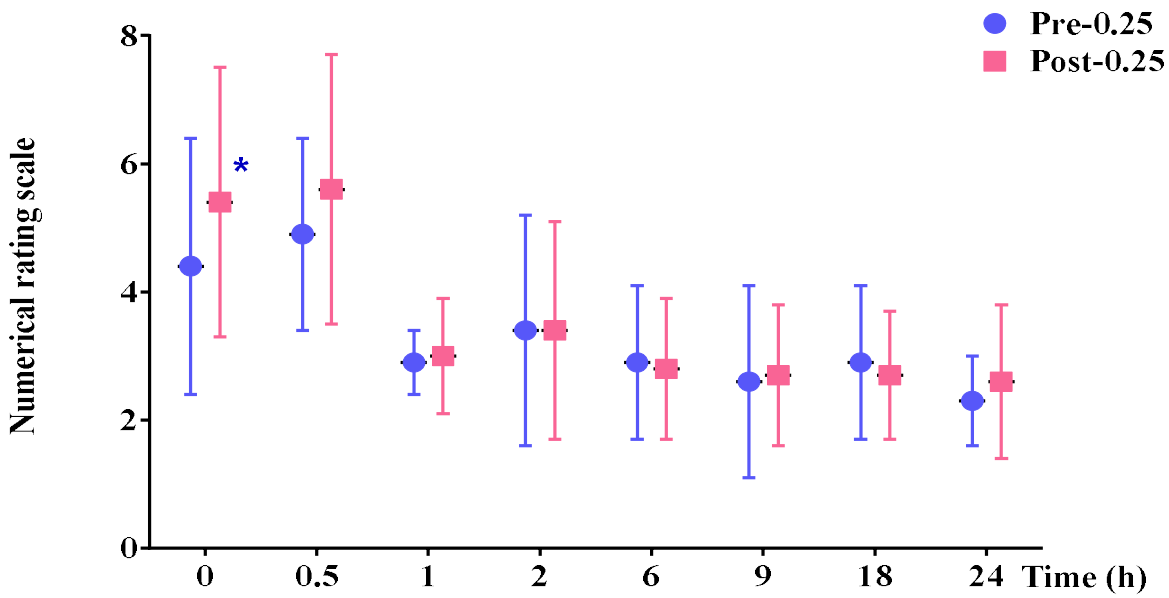

Figure 1-7. Postoperative pain scores (numerical rating scale 0 to 10) of pre-0.25 and post-0.25 group during 24 hours after surgery. Data are expressed as mean (standard deviation). *P < 0.05. Abbreviations: Pre-0.25, pre-incisional rectus sheath block with 0.25% ropivacaine; Post-0.25, post-incisional rectus sheath block with 0.25% ropivacaine.

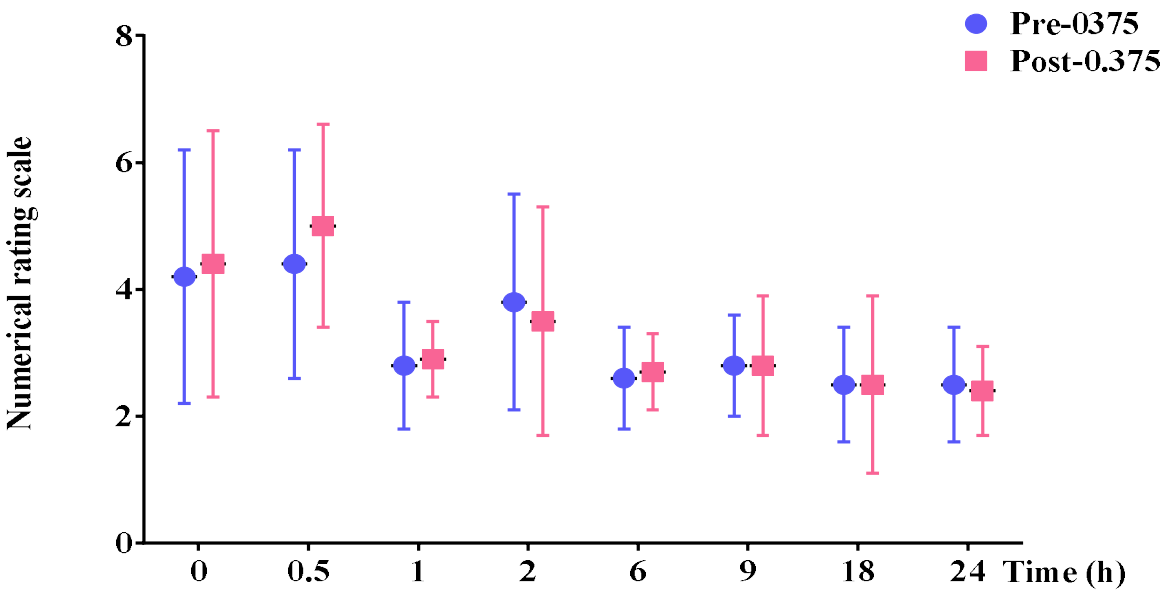

Figure 1-8. Postoperative pain scores (numerical rating scale 0 to 10) of pre-0.375 and post-0.375 group during 24 hours after surgery. Data are expressed as mean (standard deviation). *P < 0.05. Abbreviations: Pre-0.375, pre-incisional rectus sheath block with 0.375% ropivacaine; Post-0.375, post-incisional rectus sheath block with 0.375% ropivacaine.

The most painful locations recorded in the PACU are shown in Table 1-6 and Figure 1-9, with no statistically significant differences among the four groups.

Table 1-6. The painful area measured at PACU.

Group	Pre-0.25 (N=40)	Post-0.25 (N=38)	Pre-0.375 (N=42)	Post-0.375 (N=42)	Total (N=162)	P-value
Pain location						0.319
Xyphoid area	30 (75.0%)	32 (84.2%)	28 (66.7%)	30 (71.4%)	120 (74.1%)	
Subcostal area	8 (20.0%)	3 (7.9%)	8 (19.0%)	10 (23.8%)	29 (17.9%)	
Umbilical area	2 (5.0%)	3 (7.9%)	6 (14.3%)	2 (4.8%)	13 (7.0%)	

Values are expressed as numbers (%). Abbreviations: Pre-0.25, pre-incisional block with 0.25% ropivacaine; Post-0.25, post-incisional block with 0.25% ropivacaine; Pre-0.375, pre-incisional block with 0.375% ropivacaine; Post-0.375, post-incisional block with 0.375% ropivacaine.

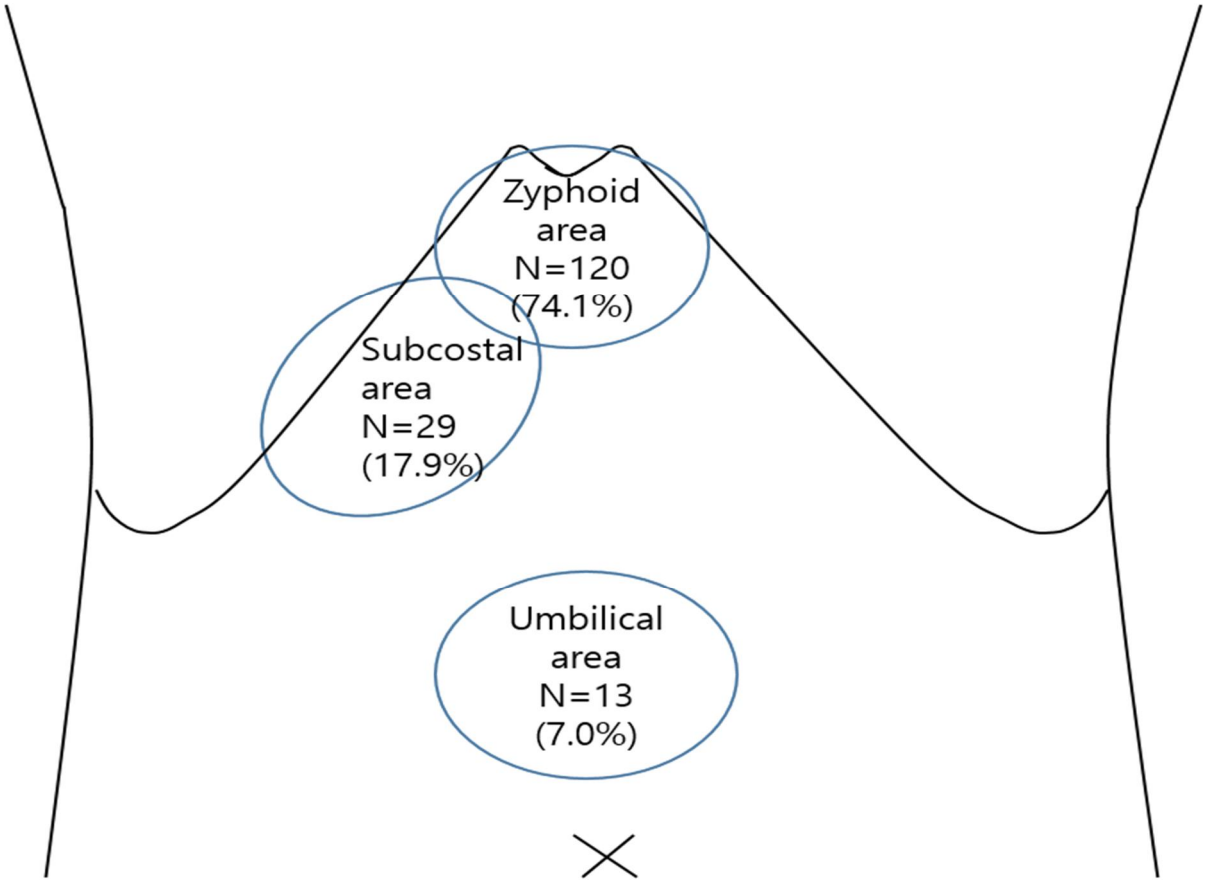

Figure 1-9. The most painful area measured at PACU. Values are expressed as numbers (%).

DISCUSSION

This study demonstrated that in patients undergoing LC, pre-incisional RSB resulted in significantly lower intraoperative remifentanil consumption and postoperative 24-hour total analgesic consumption compared with post-incisional RSB. However, the concentration of local anesthetic agent did not affect. There was no significant difference in the postoperative NRS between the four groups except in the 0.25 group at 0 hour after surgery (Table 5).

Pain relief after LC is an issue of great practical importance. Pain after LC remains the primary reason for delayed hospital stay and prolonged convalesce after surgery [14, 16]. In the first 24 hours after surgery, classic LC causes moderate to severe postoperative pain [14], with the incisional pain dominating over the visceral pain, and the port-site wounds are the most painful regions [14, 17, 18]. The complexity (incisional, visceral, and referred shoulder pain) and severity of the pain after LC suggests that multimodal analgesic management may be necessary in patients undergoing LC [15, 19-22].

Multimodal analgesic regimens for patients undergoing LC have been studied. The administration of NSAIDs, COX-2 inhibitors, preoperative single-dose dexamethasone, and port site infiltration of local anesthetics is recommended. The efficacy of gabapentinoids, intraperitoneal instillation of local anesthetics, and TAP block is debatable and the use of opioids is reserved for rescue analgesia [15, 19-22]. Notably, the infiltration of local anesthetics in trocar incisions has been recommended as a routine analgesic regimen for LC [21]. Compared with local anesthetic infiltration in LC, the analgesic effect of RSB in classic LC is not well proven. However, RSB may provide superior analgesia for the infraumbilical port site, which is the main source of pain in the immediate postoperative period, compared with local anesthetic infiltration [24]. In addition, RSB has been proven to improve the pain after laparoscopic gynecologic surgery and LC, compared with intraincisional or intraperitoneal infiltration of local anesthesia [37, 38]. Although TAP block has been evaluated for pain relief

after classic LC, its analgesic effect over placebo or local anesthetic infiltration has not been confirmed [23, 39, 40]. Compared with TAP, RSB may provide a more satisfactory block for midline incisions. In addition, RSB may provide prolonged blockade of noxious input from the incision site due to a slower absorption kinetics profile than TAP [41]. Therefore, we performed bilateral RSB instead of local anesthetic infiltration or TAP block to relieve the somatic pain from the main trocar site (infraumbilical site).

Several randomized double-blinded studies have demonstrated the preemptive analgesic effect of peripheral nerve blocks [42-44]. When the degree of afferent blockade is sufficient and the blockade extends into the initial postoperative period, the analgesic effect of peripheral nerve block lasts beyond the duration of the nerve block, resulting in a lower pain intensity and/or analgesic consumption for more than 24 hours after surgery. To our knowledge, this is the first study to evaluate the preemptive effect of RSB in patients undergoing classic LC. In this study, pre-RSB resulted in a significantly lower analgesic requirement during the first 24 hours post-surgery, compared with post-RSB. Considering the median duration of LC was 35-40 min in the pre-RSB group, the effect of pre-incisional RSB may have well extended into the initial postoperative period. Therefore, both pre-RSB and post-RSB may have reduced pain hypersensitivity owing to the postoperative inflammatory input compared with either pre-RSB or post-RSB. However, pre-RSB resulted in lower postoperative analgesic requirements than post-RSB because of its additional blockade of the intraoperative noxious input, minimizing the development of central sensitization [45].

Studies on the preemptive effect of RSB in patients undergoing laparoscopic surgery are limited and some results conflict with ours. First, Kim et al. reported that bilateral RSB decreased the intensity of superficial pain only during the first hour after robotic cholecystectomy, compared with a placebo group [46]. Second, Jin et al. reported that there was no significant difference in the pain, analgesic requirements, or time to first rescue

analgesic after transabdominal gynecological surgery between the pre-RSB and post-RSB groups [47]. However, in both studies, only female patients were included, and the ports or incisional sites were limited in the lower abdomen, which usually involves less postoperative pain than port placement in the upper abdomen. Unlike in our study, RSB was performed in the lower abdomen below the arcuate line, and the efficacy of the blockade was not confirmed in either study. In the first study of robotic cholecystectomy, only the main port site (one 12 mm) was blocked, not the smaller port sites (two 7 mm). In the second study on transabdominal gynecological surgery, bilateral single-shot RSB may have been insufficient to cover intraoperative and initial postoperative afferent input from the median 9 cm incision site. Furthermore, drug leakage, which is always detected in the pre-RSB group following the surgeon's incision, may have attenuated the effect of preoperative block. Therefore, our results may not be directly comparable with the above studies.

Preincisional blocks have the effect of reducing intra operative surgical stimulation, which can be seen in the results of this study. Since only patients with complete RSB were included in the study, somatic pain at the largest troca site during LC surgery would be completely blocked. As a result, all post-RSB groups showed significantly increased SBP, DBP, MBP, and HR related to the skin incision on the umbilicus compared to the pre-RSB groups (Table 2).

In several studies, the duration and density of truncal blocks were reported to increase with higher drug concentrations [37, 38]. Consequently, the authors expected less rescue analgesic consumption in the 0.375% ropivacaine groups than in the 0.25% ropivacaine groups, but that was not the case in this study. Even the pre-0.25 groups showed lower cumulated rescue analgesic consumption than the post-0.375 groups during the first 24 hours after surgery (Table 4). The authors suspect that the differences in concentration were statistically masked, because only the somatic pain was blocked by the RSB, not the visceral

pain, and the sample size of this study was determined based on rescue analgesic doses. Similarly, the average or median values of rescue analgesic consumption in high-concentration groups were lower. It is thought that further studies using blocks that can affect visceral pain are needed.

This study has a limitation. Including a placebo group (neither pre-RSB nor post-RSB) may have been a more reasonable approach to demonstrate the preemptive effect of RSB in patients undergoing LC [45]. With such a group, the efficacy of pre-RSB or post-RSB on postoperative pain scores over the placebo group may have been detected. The relative efficacy of post-RSB on postoperative analgesic requirements over the placebo group may have also been detected.

In conclusion, pre-incisional RSB and ICNB lowered the analgesic requirements during the intra-operative and post-operative 24-hour period for patients undergoing LC, compared with postoperative RSB. Additionally, the administration of 0.25% and 0.375% of ropivacaine resulted in no statistically significant differences in the postoperative analgesic requirements. The timing of RSB is clinically significant for postoperative pain following LC.

CHAPTER II

The differential effect of visceral blocks before and after incision on postoperative pain in patients who underwent laparoscopic cholecystectomy

INTRODUCTION

Preemptive analgesic effect is an antinociceptive treatment that reduces the incidence of postoperative hyperalgesia and allodynia by preventing the establishment of peripheral and central sensitization caused by incisional and inflammatory injuries [1, 2]. Decreasing sensitization is thought to reduce the magnitude and duration of postoperative pain. Although several studies have been conducted, this effect remains controversial [1-4]. Nevertheless, there is still a widespread belief in analgesic efficiency among clinicians.

In comparison with open cholecystectomy, LC is considered to be minimally invasive with less postoperative pain [12]. However, in the immediate postoperative period, LC causes moderate to severe postoperative pain [48, 49]. Pain after LC is multifactorial, as incisional pain, visceral pain, and referred shoulder pain are all implicated. The overall pain is most intense on the day of LC with incisional pain predominating over visceral pain [48, 50].

In recent years, with the development of ultrasound technology and the activation of truncal blocks, somatic pains of operations such as laparoscopic surgery can be easily controlled, and multimodal analgesia is recommended [51, 52]. However, it is difficult to prevent and control visceral and referred pains. The target of most thoracic and abdominal truncal blocks, except paravertebral block (PVB), is the somatic nerve branch of the ventral ramus of the spinal nerve. As a result, few studies have been conducted to investigate the preemptive effect on visceral pain using regional blocks.

The criteria for evaluating preemptive analgesic effect can be divided into three parts: decreased postoperative pain, reduced total analgesic consumption, and prolonged time to first rescue analgesic [4]. Various studies have confirmed these effects; however, with the exception of continuous epidural analgesia, these effects remain controversial [4]. The result of chapter I identified the preemptive analgesic effect of somatic regional block in patients undergoing LC and found that the visceral pain of LC is localized mainly in the xiphoid area

and the right subcostal area. The purpose of this study was to evaluate the effects of visceral preemptive analgesic effect on “postoperative pain scores “and “total analgesic consumption” in patients undergoing LC with pre-incisional and post-incisional PVB with minimal somatic pain using pre-incisional RSB.

MATERIALS AND METHODS

1. Patients

This single-center, prospective, randomized, single-blind study was conducted at Asan Medical Center in Seoul, Republic of Korea. The study protocol was approved by the Institutional Review Board of Asan Medical Center (2019-0334), and written informed consent was obtained from all participants in the study. This study was registered at the Clinical Research Information Service (KCT0003810). Adult patients scheduled for elective LC were considered eligible for the study. Patients were enrolled if they were aged 20–80 years with American Society of Anesthesiologists physical status class ≤ 2. Exclusion criteria were as follows: contraindications for regional anesthesia, such as history of local anesthetic allergy; use of anticoagulants; pregnancy or breastfeeding; history of previous abdominal surgery; pre-existing vertebral or chest wall abnormality; and refusal to participate. The study also excluded patients with severe intraperitoneal inflammation or adhesions resulting from cholecystitis (Parkland grade > 3), those with a single port insertion, those with intraoperative bile duct injury, and those who maintained percutaneous drainage before and after surgery.

2. Randomization

By using a computer-generated randomization sheet, the enrolled patients were randomly assigned to either the pre-PVB or post-PVB group. For the random allocation of participants, a web-based randomization software (Random Allocation Software version 1.0; Isfahan University of Medical Sciences, Isfahan, Iran) was used with random block sizes of 4 and an allocation ratio of 1:1.

The researchers are divided into the intervention staff, anesthesia staff, investigator staff, and research coordinator with specific roles are as follows. After induction, pre-incisional RSB

and PVB or pre-incisional RSB were performed according to the allocation by the intervention staff. Then, the anesthesia staff, who was blinded to treatment allocation, maintained anesthesia and recorded data during surgery. After the surgery, the intervention staff performed post-incisional PVB or dose not performed additional procedure according to allocation, and the patient was transferred to the recovery room. The investigator staff, who was blinded to treatment allocation, administered analgesics in the post-anesthesia care unit (PACU) and general ward during the 24 hours after surgery and assessed postoperative outcomes. Although treatment allocation was un-blinded to the intervention staff, it was kept blinded to the investigators or research coordinator and participants.

3. Surgical technique

The same team of experienced laparoscopic surgeons (carried out more than 300 LCs) performed all operations. Standard procedures for LC were followed for all patients. Three trocars were inserted below the xiphoid process (5 mm), right costal arch (5 mm), and umbilicus (10 mm). A camera port was inserted via the infraumbilical incision, and the gallbladder was retracted. A pneumoperitoneum was created and maintained by carbon dioxide insufflation with an intraperitoneal pressure of 12 mmHg. LC was conducted in the supine position with a 30–40° reverse Trendelenburg position.

4. Anesthesia and analgesia

In the operating room, all patients were routinely monitored by electrocardiography, non-invasive blood pressure measurement, and pulse oximetry. Anesthesia was induced by propofol (2 mg/kg), rocuronium (0.6 mg/kg), and remifentanil (continuous infusion) using a target-controlled infusion pump (Orchestra®; Fresenius Vial, Brezins, France). After tracheal

intubation, anesthesia was maintained with desflurane (5–6%) in 50% oxygen/air and continuous infusion of remifentanil (1.5–5 ng/mL of effect-site concentration) to maintain the systolic blood pressure within 20% of baseline values. When skin closure was started, the effect-site concentration of remifentanil was reduced and maintained at 1.5 ng/dL until extubation. After emergence from general anesthesia, the patient was transferred to the PACU. The need for rescue analgesia was evaluated from 0 to 24 hours after surgery. In the PACU, intravenous fentanyl (0.4 μg/kg) was administered when NRS was ≥ 4 or when the patient was in need of pain relief. The administration of fentanyl was repeated until a NRS of < 4 or the patient did not request further pain relief. In the general ward, 30 mg of ketorolac was administered first when the NRS was ≥ 4 or when the patient was in need of pain relief. When the effect of ketorolac was insufficient, 25 mg of meperidine was administered during the 24 hours after surgery. The total doses of rescue analgesics during the 24 hours after surgery were recorded and converted to equianalgesic doses of intravenous fentanyl based on previously published conversion factors (intravenous fentanyl 100 μg = pethidine 100 mg = ketorolac 30 mg) [33, 34]. The total or CRA consumption can be expressed in intravenous fentanyl equivalents (μg).

5. Ultrasound-guided RSB and PVB

In the pre-PVB group, RSB and PVB were performed after anesthesia induction and before skin incision. In the post-PVB group, RSB was performed after anesthesia induction and before skin incision, and PVB was performed after skin closure and before emergence from anesthesia. RSB and PVB were performed using the NextGen LOGIQ e ultrasound console (GE Healthcare, Madison, WI, USA) with a 12 MHz high-frequency linear array transducer.

For RSB, the ultrasound probe was positioned transversely on the rectus abdominis

muscle below the umbilicus. Guided by real-time ultrasound, a 23-gauge Quincke needle (TaeChang Industrial Co., Gongju, Korea) was inserted in-plane with caution to avoid injury to nearby vessels from the medial to lateral direction until its tip was positioned in the plane between the lateral 1/3 of the rectus abdominis muscle and the posterior rectus sheath. After negative pressure aspiration, 15 mL of 0.25% ropivacaine was administered, and the block was repeated on the opposite side.

PVB was performed in the transverse view with an in-plane technique. The ultrasound probe was positioned parallel to the rib to obtain the overall view of the pleura and intercostal muscles (external, internal, and innermost). In the previous study, we found that the visceral pain of LC is localized mainly in the xiphoid area and the right subcostal area. Therefore, PVB was applied to the right 6th and 8th paravertebral space to control the visceral pain of LC. Under the left lateral decubitus position of the patient, the right 12th rib was visualized and counted to the 6th and 8th rib to confirm the location of the 6th and 8th paravertebral space. After identifying the paravertebral space, a 23-gauge Quincke needle (TaeChang Industrial Co., Gongju, Korea) was inserted under aseptic conditions in the lateral to medial direction using an in-plane technique until the needle tip was positioned between the parietal pleura and transverse process. The location of the needle tip was confirmed by a visible linear spread of local anesthetics that pushed the pleura downward on ultrasonographic imaging. At one level, 14 mL of 0.25% ropivacaine was injected (a total of 28 mL of 0.25% ropivacaine was injected) (Figure 2-1).

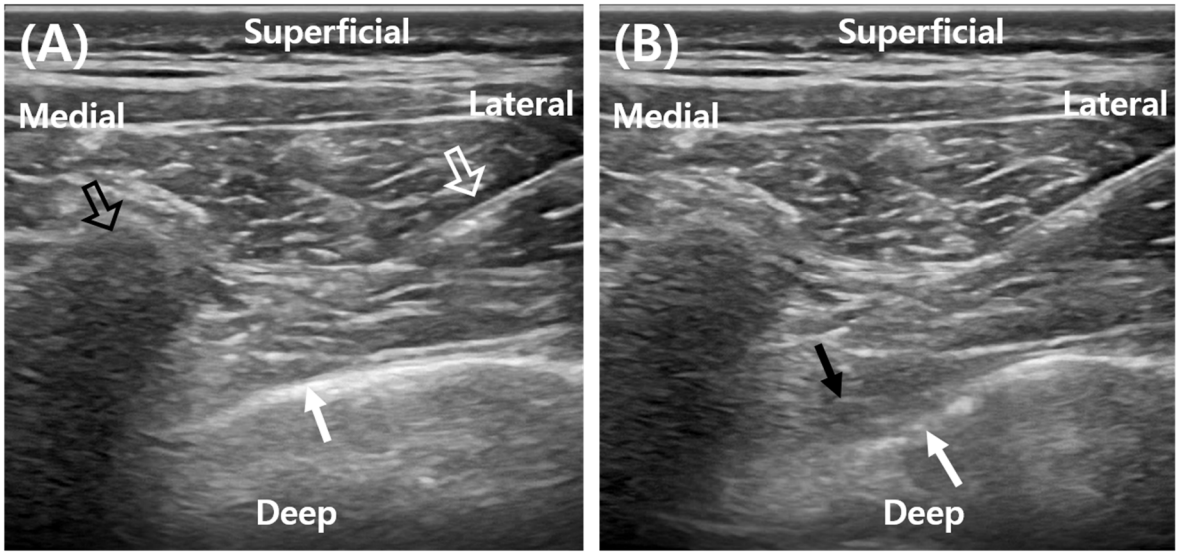

Figure 2-1. Ultrasound-guided paravertebral block. (A) Ultrasound-guided intercostal space image in the axial view. The echogenic needle (white empty arrow) is approaching to the paravertebral space between the intercostal muscles and pleura (white arrow) using an in-plane technique. The black empty arrow indicates the transverse process of the thoracic spine. (B) Local anesthetics hydro-dissect the potential space (black arrow) between the intercostal muscles and pleura, which is downshifted (white arrow).

6. Outcome measures and data collection

The primary outcome was the total rescue analgesic consumption during the 24 hours after surgery. The secondary outcomes were the CRA consumption and postoperative pain scores at 0, 1, 2, 6, 9, 18, and 24 hours after surgery.

Intraoperative and postoperative evaluation was performed by the investigator staff, who was blinded to treatment allocation. Additional factors associated with visceral pain, such as the severity of adhesion and cholecystitis inflammation status, were graded according to the Parkland scale (range 0–5) [53] by the operating surgeon upon visual inspection. Surgical procedure characteristics related to visceral pain, such as the duration of surgery, peak abdominal gas pressure, severity of gallbladder bed injury during surgery, or rate of intraoperative bile leakage, were also compared between the groups. The severity of gallbladder bed injury was reported by the surgeon as follows: 1 - insignificant injury to the liver; 2 - mild injury to the liver; 3 - moderate injury to the liver. Vital signs such as the mean blood pressure (mm Hg) and heart rate (beats per minute) measured before incision and the maximum value after incision and before the induction of pneumoperitoneum were recorded. Furthermore, other outcomes including intraoperative remifentanil consumption, adverse effects of analgesics (such as nausea and vomiting), and complications associated with RSB or PVB (such as hematoma or pneumothorax), if any, were also recorded.

In the PACU, the first postoperative evaluation of the RSB and PVB was performed. Initially, an algometer (Baseline algometer, Baseline®, India) was used to induce experimental pressure pain on the umbilicus. The pressure was applied for 5 seconds to exclude patients with insufficient RSB, which was determined by a threshold of pressure pain lower than 2 kg/cm^2 pressure [35, 36]. Subsequently, the same pressure was applied to the other two port sites (below the xiphoid process and the right costal arch) to examine the degree of somatic block resulting from the PVB (complete, partial, or no block).

CRA consumption and postoperative pain scores were measured at 0, 1, 2, 6, 9, 18, and 24 hours after surgery. Postoperative pain scores were assessed using an 11-point NRS, where 0 = no pain and 10 = worst pain imaginable. The side effects of analgesics, such as dizziness, sedation, respiratory depression, nausea, and vomiting, were all evaluated. In addition, complications associated with RSB and PVB were evaluated, which included pneumothorax and hematoma.

7. Statistical analysis

The sample size was calculated based on the results of our previous data, in which the means ± standard deviations of opioid requirements during the 24 hours post-surgery in the pre-PVB and post-PVB groups were 140 ± 69 μg and 170 ± 69 μg, respectively. To detect this difference with an alpha of 0.05 (two-sided) and a power of 0.8, 30 patients per group were required. Allowing for a 15% dropout during the study period, 35 patients were recruited for each group.

Continuous parameters were summarized as the mean (± standard deviation) or median (interquartile range), and categorical parameters were presented as the frequency (percentage) as appropriate. Between-group comparisons were evaluated with Student's t-test or Mann-Whitney U-test for continuous variables and Chi-square or Fisher's exact test for categorical variables as appropriate. The repeated measurements of cumulative fentanyl consumptions were performed using a linear mixed-effect model to evaluate the interaction of time and treatment between the two groups. Statistical significance was set at $P < 0.05$. Data manipulation and analyses were performed using R software, version 3.3.1 (CRAN, R Foundation, Vienna, Austria).

RESULTS

Of the 73 patients screened from March 2019 to October 2019, 3 patients were excluded from the study (Figure 2-2). The remaining 70 patients were randomized into two groups (pre-PVB (N = 35); post-PVB (N = 35)). All 33 patients in the pre-PVB group were treated with RSB; however, 2 patients were excluded due to left side gallbladder and incomplete RSB. In addition, 4 patients in the post-PVB group who had percutaneous drainage after surgery, Parkland grade 4, and poorly controlled infection were also excluded. Consequently, 64 patients were included in the final analysis. There were no significant differences in the baseline characteristics between the two groups (Table 2-1).

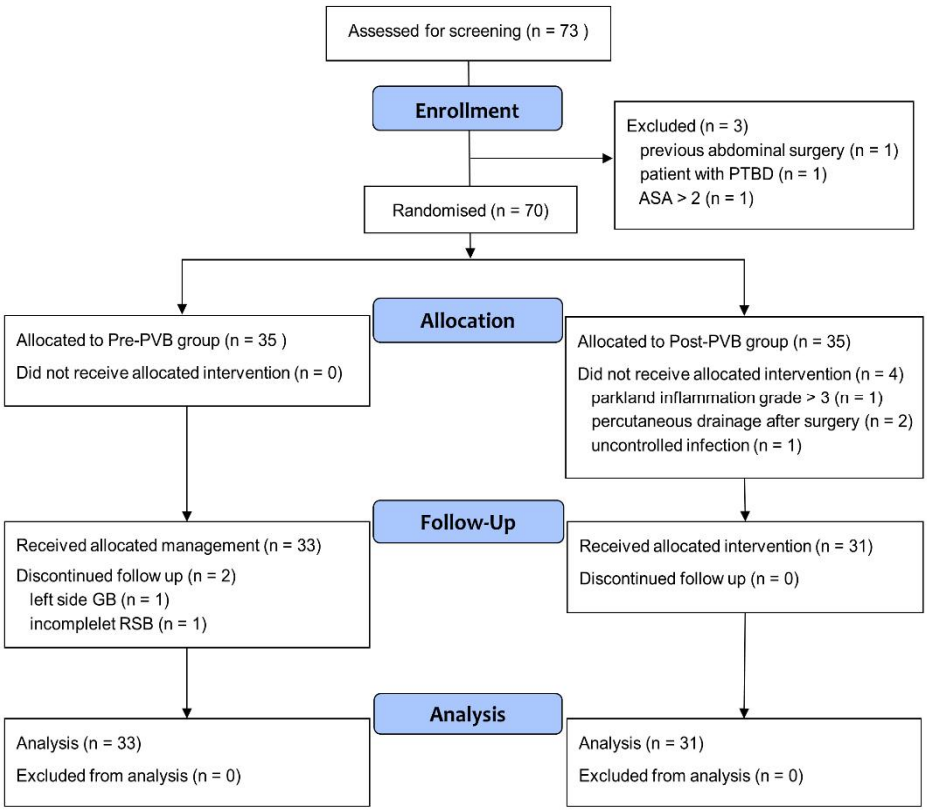

Figure 2-2. Flowchart of the study population. Abbreviations: PTBD, percutaneous transhepatic biliary drainage; ASA, American Society of Anesthesiologists Physical Status; GB, gallbladder; RSB, rectus sheath block.

Table 2-1. Baseline characteristics of the study participants.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
Age	50.5 ± 11.2	48.1 ± 11.2	0.399
Sex (Male)	17 (51.5%)	10 (32.3%)	0.192
BMI	24.2 ± 2.9	24.6 ± 3.3	0.635
ASA PS			0.543
1	20 (60.6%)	22 (71.0%)	
2	13 (39.4%)	9 (29.0%)	
Hypertension	8 (24.2%)	5 (16.1%)	0.620
Diabetes	4 (12.1%)	5 (16.1%)	0.729
Others	7 (21.2%)	2 (6.5%)	0.150
Diagnosis			0.236
Acute cholecystitis	6 (18.2%)	10 (32.3%)	
Chronic cholecystitis	18 (54.5%)	17 (54.8%)	
Gallbladder polyp	9 (27.3%)	4 (12.9%)	
Pre-op drain			1.000
None	31 (93.9%)	29 (93.5%)	
ENBD	2 (6.1%)	2 (6.5%)	
Pre-op pain			0.050
No	33 (100.0%)	27 (87.1%)	
Yes	0 (0.0%)	4 (12.9%)	

Data are expressed as mean (standard deviation) or numbers (%), as appropriate. Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine; ASA PS, American Society of Anesthesiologists Physical Status; ENBD, endoscopic nasobiliary drainage; NRS, numerical rating scale.

There were no significant differences in the duration of surgery and anesthesia, changes in vital signs (SBP, DBP, MBP, and HR) related to skin incision, Parkland grade, intraoperative bile leakage, grade of gallbladder bed injury, and intraoperative remifentanil requirement between the two groups (Table 2-2).

Table 2-2. Intraoperative data.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
Duration of surgery (min)	30.0 (25.0;38.0)	33.0 (25.0;40.0)	0.404
Duration of anesthesia (min)	65.0 (58.0;80.0)	65.0 (60.0;74.0)	0.877
Interval between PVB to Skin incision (min)	12.0 (9.0;13.0)	-	
Interval between PVB to wake up (min)	-	7.0 (6.0; 8.5)	
SBP change (%)	0.0 (-1.0; 2.0)	0.0 (-2.0; 2.5)	0.813
DBP change (%)	2.0 (-2.0; 4.0)	0.0 (-4.0; 3.5)	0.268
MBP change (%)	0.0 (0.0; 4.0)	0.0 (-1.5; 2.5)	0.259
HR change (%)	0.0 (-2.0; 2.0)	-2.0 (-3.5; 0.0)	0.088
Parkland Grade			0.582
1	23 (69.7%)	22 (71.0%)	
2	7 (21.2%)	4 (12.9%)	
3	3 (9.1%)	5 (16.1%)	
Bile leakage			1.000
0	32 (97.0%)	30 (96.8%)	
1	1 (3.0%)	1 (3.2%)	
GB bed injury			0.849
1	29 (87.9%)	27 (87.1%)	
2	3 (9.1%)	4 (12.9%)	
3	1 (3.0%)	0 (0.0%)	
remifentanil requirement (μg)	292.0 (244.0;355.0)	304.0 (254.5;336.0)	0.638
remifentanil requirement (μg/min/kg)	0.068 (0.060;0.079)	0.067 (0.060;0.074)	0.393

Values are the expressed as the median (interquartile range) or numbers (%). Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; HR, heart rate; GB, gallbladder.

The rescue analgesics used for each hour (μg) was significantly lower in the pre-PVB group than in the post-PVB group at 0.5, 1, and 2 hours after surgery (20.0 (0.0; 30.0) vs. 25.0 (25.0; 35.0), P = 0.050; 0.0 (0.0; 25.0) vs. 25.0 (0.0; 30.0), P = 0.018; and 100.0 (0.0; 100.0) vs.100.0 (100.0; 100.0), P = 0.001, respectively) (Table 2-3). The total rescue analgesic consumption during the 24 hours after surgery (μg) was significantly lower in the pre-PVB group than in the post-PVB group (140.0 (100.0; 255.0) vs. 250.0 (165.0; 307.5), P = 0.003) (Table 2-4). In addition, the CRA consumption (μg) was significantly lower in the pre-PVB group than in the post-PVB group at 0.5, 1, 2, 6, 9, 18, and 24 hours after surgery (Figure 2-3).

Table 2-3. Rescue analgesic does for each hour during 24 hours after surgery.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
RA_0h	0.0 (0.0; 0.0)	0.0 (0.0;25.0)	0.245
RA_0.5h	20.0 (0.0;30.0)	25.0 (25.0;35.0)	0.050
RA_1h	0.0 (0.0;25.0)	25.0 (0.0;30.0)	0.018
RA_2h	100.0 (0.0;100.0)	100.0 (100.0;100.0)	0.001
RA_6h	0.0 (0.0;25.0)	25.0 (0.0;25.0)	0.223
RA_9h	25.0 (0.0;100.0)	25.0 (0.0;100.0)	0.479
RA_18h	0.0 (0.0; 0.0)	0.0 (0.0;25.0)	0.247
RA_24h	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)	0.603

Data are expressed as the median (interquartile range). Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine; RA, rescue analgesic consumption for each hour.

Table 2-4. Cumulated rescue analgesic consumption during 24 hours after surgery.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
CRA 0h	0.0 (0.0; 0.0)	0.0 (0.0;25.0)	0.245
CRA 0.5h	25.0 (0.0;30.0)	30.0 (25.0;60.0)	0.037
CRA 1h	30.0 (0.0;50.0)	60.0 (35.0;85.0)	0.006
CRA 2h	100.0 (25.0;140.0)	150.0 (127.5;177.5)	0.001
CRA 6h	125.0 (35.0;155.0)	175.0 (135.0;200.0)	< 0.001
CRA 9h	140.0 (100.0;245.0)	225.0 (162.5;300.0)	0.003
CRA 18h	140.0 (100.0;255.0)	250.0 (165.0;307.5)	0.003
CRA 24h	140.0 (100.0;255.0)	250.0 (165.0;307.5)	0.003

Data are expressed as the median (interquartile range). Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine; CRA, cumulated rescue analgesic consumption up to each hour.

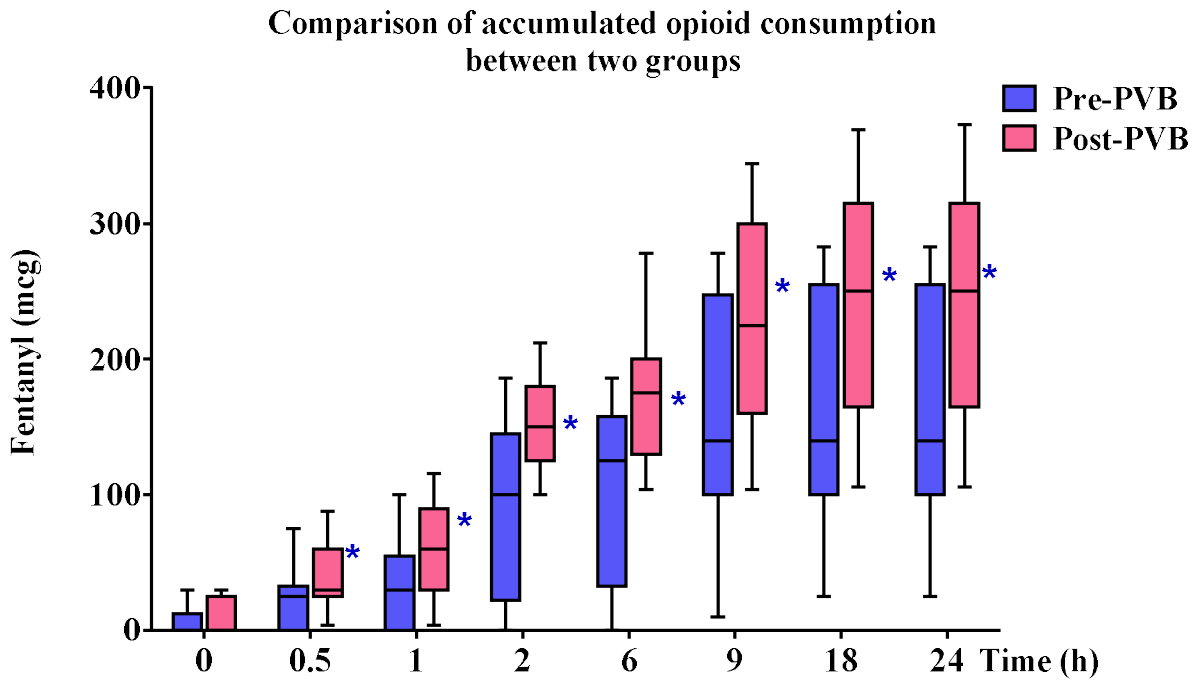

Figure 2-3. Cumulated rescue analgesic (CRA) consumption during the 24 hours after surgery. Data are expressed as the median (interquartile range). Horizontal lines, boxes, and error bars represent the median, interquartile range, and 10th and 90th percentile, respectively. *P < 0.05. Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine.

Differences in the cumulative analgesic consumption between the two groups were increased up to 24 hours after surgery; however, the degree of increase was decreased from 6 hours after surgery (Figure 2-4).

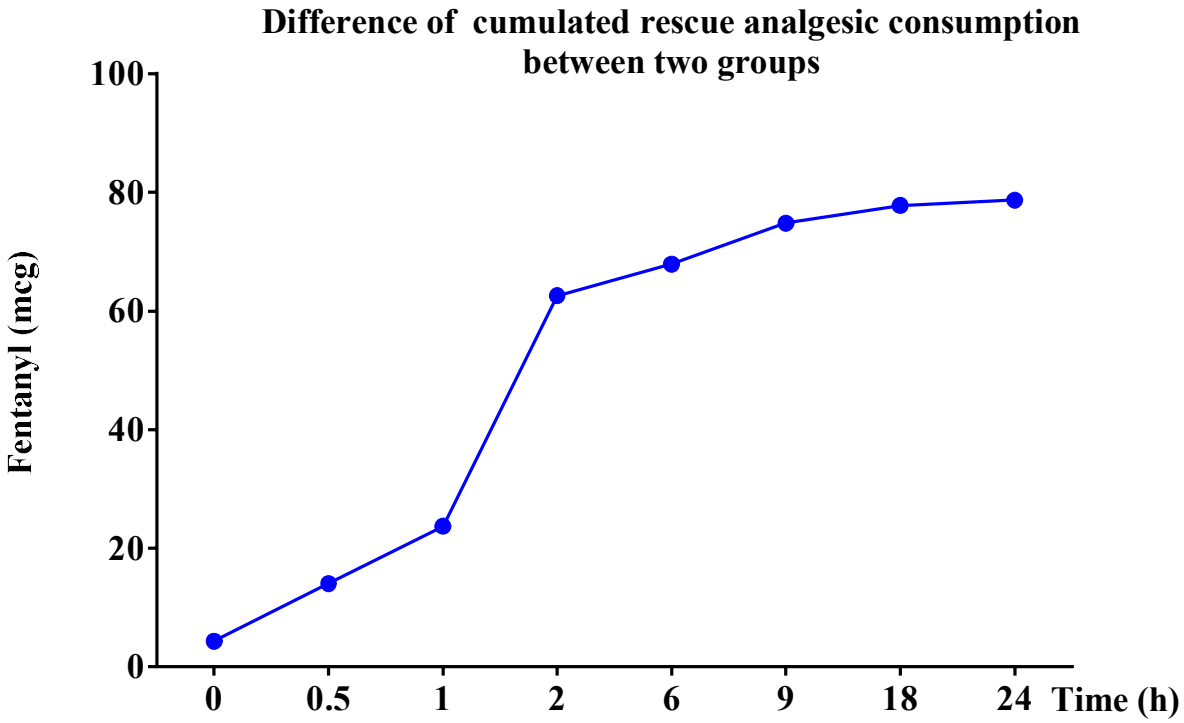

Figure 2-4. Difference of cumulated rescue analgesic (CRA) consumption during the 24 hours after surgery. Data are expressed as the mean.

The NRS was significantly lower in the pre-PVB group than in the post-PVB group at 0.5, 1, 2, and 6 hours after surgery (4.4 ± 1.5 vs. 3.2 ± 1.6, P = 0.002; 2.8 ± 1.2 vs. 1.8 ± 1.1, P = 0.001; 5.2 ± 1.7 vs. 3.5 ± 1.9, P < 0.001; and 4.3 ± 1.8 vs. 3.2 ± 1.5, P = 0.014, respectively) (Table 2-5. Figure 2-5).

Table 2-5. Postoperative NRS.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
NRS_0h	2.0 (1.0; 3.0)	3.0 (2.0; 4.0)	0.147
NRS_0.5h	4.0 (2.0; 4.0)	4.0 (4.0; 5.0)	0.008
NRS_1h	2.0 (1.0; 2.0)	2.0 (2.0; 3.5)	0.001
NRS_2h	3.0 (2.0; 5.0)	5.0 (4.0; 6.0)	< 0.001
NRS_6h	3.0 (2.0; 4.0)	4.0 (3.0; 5.0)	0.021
NRS_9h	4.0 (2.0; 5.0)	4.0 (3.0; 5.0)	0.555
NRS_18h	2.0 (2.0; 3.0)	3.0 (2.0; 5.0)	0.116
NRS_24h	2.0 (2.0; 3.0)	2.0 (2.0; 3.0)	0.065

Data are expressed as the median (interquartile range). Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine; NRS, numerical rating scale.

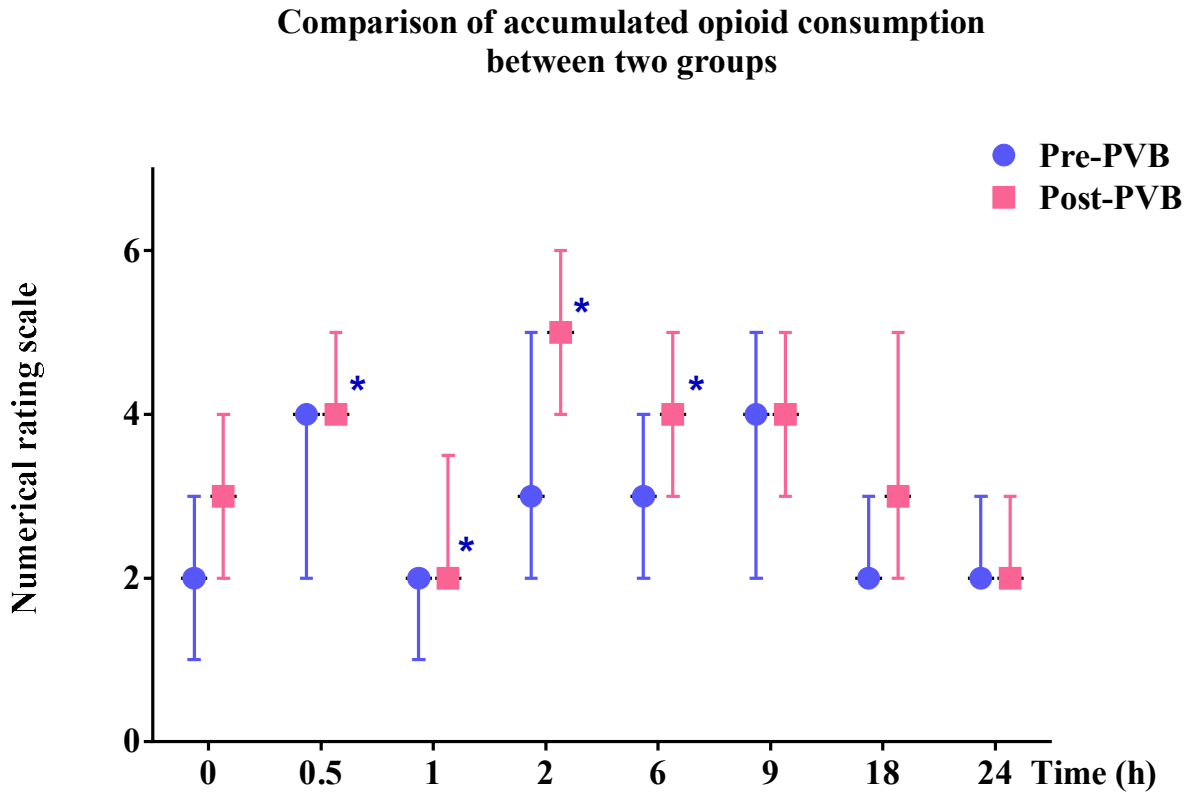

Figure 2-5. Postoperative pain scores (numerical rating scale: 0 to 10) during the 24 hours after surgery. Data are expressed as the mean (standard deviation). *P < 0.05. Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine.

The most painful locations measured in the PACU are shown in Table 2-6 and Figure 2-6 with no statistically significant differences between the two groups.

Table 2-6. The painful area measured at PACU.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	P-value
Pain location			0.345
Xyphoid area	18 (54%)	22 (71%)	
Subcostal area	8 (24.2%)	6 (19.4%)	
Umbilical area	6 (18.2%)	3 (9.7%)	
No pain	1 (3.0%)	0 (0.0%)	
Pain depth			1.000
Deep area	32 (97.0%)	31 (100.0%)	
No Pain	1 (3.0%)	0 (0.0%)	

Values are expressed as numbers (%). Abbreviations: Pre-PVB, pre-incisional paravertebral block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block with 0.25% ropivacaine.

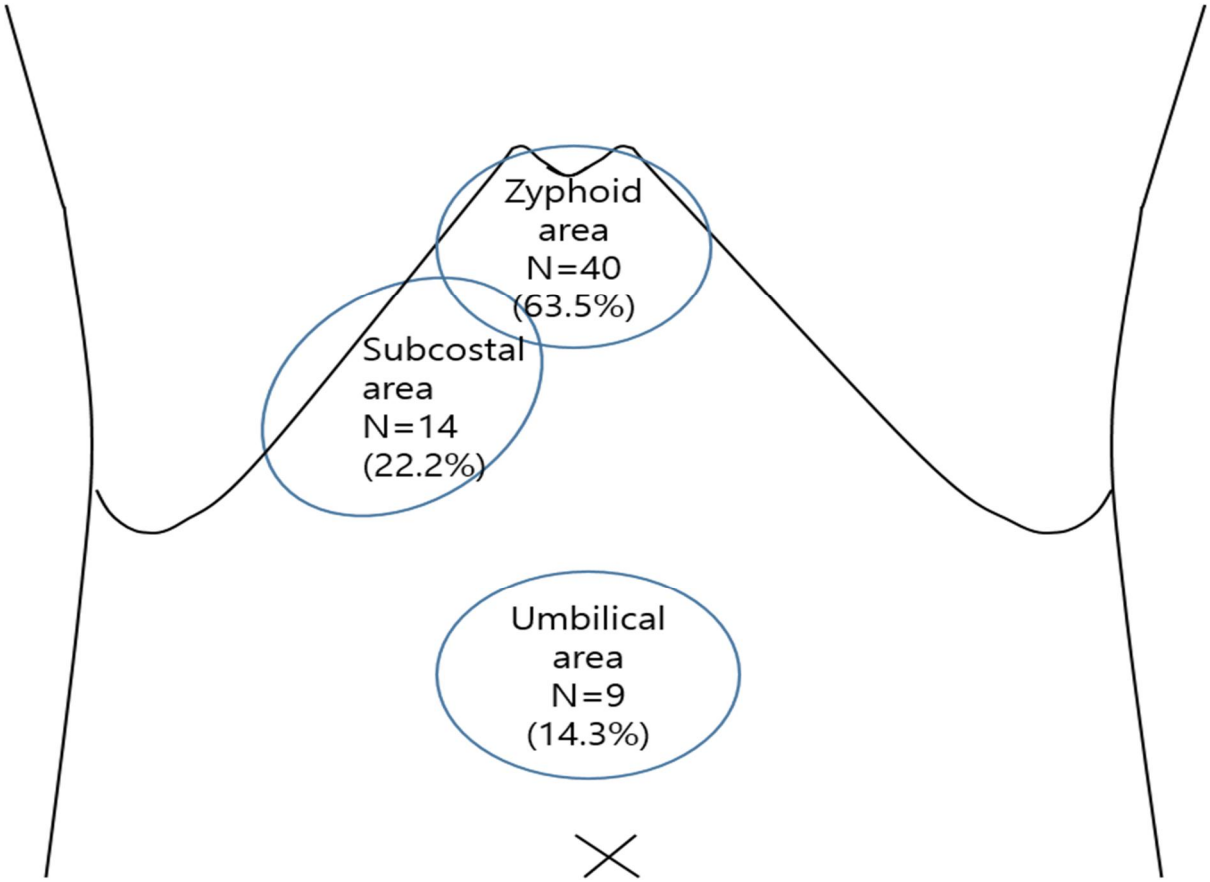

Figure 2-6. The most painful areas measured in the PACU. Values are expressed as numbers (%).

DISCUSSION

This study demonstrated that the postoperative 24-hour total analgesic consumption was reduced among patients undergoing LC with pre-incisional PVB compared with post-incisional PVB (Table 2-3). Because PVB can block visceral pain, pre-incisional visceral block may be clinically effective in reducing postoperative pain.

The importance of preemptive analgesia is the preemptive analgesic effect is on the pathophysiologic phenomenon that it should prevent altered sensory processing. Therefore, preemptive may not simply mean “before incision.” An insufficient afferent block cannot be preemptive, even if it is administered before the incision. There are tools that can indirectly measure the patient's pain during anesthesia; however, they remain controversial [54, 55]. Clinically, it is possible to assume that there will be surgical stimulation if the patient's blood pressure, pulse rate, or systemic vascular resistance increases; however, this is not clear. Furthermore, some surgical procedures may stimulate the neural plexus (vagus nerve, celiac plexus, or hypogastric plexus), which may result in a change in vital signs; conversely, the change in vital signs may be masked by anesthetic agents.

Therefore, we believe that when using pre-incisional single oral or IV drugs for preemptive analgesic effects, it is difficult to objectively evaluate the effects of the drugs during surgery, and it is difficult to sufficiently prevent altered sensory processing with commonly used pain control doses. This is consistent with the findings of previous studies [4, 5]. It is thought that central sensitization is not only due to surgical stimulation caused by skin incision but also tissue damage during surgery, perioperative inflammatory reaction, and stress hormones [1-3]. Therefore, to maximize the preemptive analgesic effect, perioperative multimodal analgesia based on regional blocks that can completely block pain afferent pathways are important. However, single bolus regional blocks have a short duration. Additional single bolus injections may be given if necessary; however, invasive procedures are not preferred for patients who

are awake after surgery. Recently, the potential of local anesthetics with long durations has been investigated [56]. It is expected that the various limitations of truncal blocks can be overcome if they are commercially available.

The most important assumption of this study is that the RSB could control somatic pains. If not, the postoperative CRA may be mixed with rescue analgesics due to somatic pains, thereby resulting in unreliable PVB for visceral pain control. In our hospital, three ports were used in LC. The largest one is the 10 mm port just below the umbilicus. This is where the gallbladder is taken out; thus, it is the most stimulated (retraction of the abdominal wall) area during surgery and the most painful site after surgery. The effectiveness of the RSB was verified with two methods: one involves the identification of the change in vital signs due to the skin incision, and the other involves the use of an algometer in the PACU. In a previous study comparing pre-incisional vs. post-incisional RSB, there was a significant increase in vital signs in the post-RSB group due to the umbilical port site incision, which led to a difference in postoperative CRA consumption (Table 1-3, Figure 1-4 & 1-5 in chapter I). However, in this study, there was no significant difference in vital signs related to skin incision (Table 2-2), indicating that pre-incisional RSB was well performed. Furthermore, the RSB at the umbilical port site was confirmed using an algometer in the PACU and was well controlled in all patients in the study, except for one patient who was excluded based on a threshold of pressure pain lower than 2 kg/cm2 pressure. Therefore, the effect of visceral block by via the PVB is considered to be well reflected in the study results.

The duration of ropivacaine varies slightly depending on the dose used and the type of block used. However, there are limited studies on the duration of paravertebral single bolus injection with ropivacaine. El Nasr et al. [56] reported that visual analog scale (VAS) pain scores were lower among patients in the PVB group than among patients in the general anesthesia group for the first 6 postoperative hours. Other studies revealed that the NRS or VAS tended

to increase around 6 hours after injection [38, 57, 58]. The RSB also varies slightly from study to study; however, blocks typically last for 3-4 hours with more than 0.25% ropivacaine (15–20 mL) [59]. In this study, CRA consumption differed for up to 2 hours except at 0 hours, and the NRS differed only for 6 hours except at 0 hours. As shown in Figure 2-3, the difference in CRA consumption between the two groups was smaller 6 hours after surgery compared with 2 hours after surgery. Based on the results of this study, the PVB did not last longer than 6 hours. Nevertheless, after 6 hours, there was a significant difference in CRA consumption between the two groups, and the difference in CRA consumption was gradually increased (Figure 2-4), which may suggest visceral preemptive analgesia. However, in surgery where visceral pain persists for a long time, continuous infusion via a catheter may be necessary for preemptive analgesic effect.

The inclusion and exclusion criteria used for patients in the pre-0.25 group in the previous study were also used for those in this study, and the same concentration of local anesthetics was used. Therefore, the effects of pre-incisional PVB can be indirectly confirmed by statistical analysis of patients in the pre-0.25 group and in chapter II (Supplementary table 1). The intraoperative remifentanil requirement and total rescue analgesic consumption during the 24 hours after surgery (μg) was significantly lower in the pre-PVB group than in the pre-0.25 group (0.07 (0.06; 0.07) vs. 0.10 (0.08; 0.11), $P < 0.001$; and 140.0 (100.0; 255.0) vs. 220.0 (177.5; 270.0), $P < 0.001$, respectively). Intraoperative remifentanil consumption was decreased by 23%, and postoperative opioid consumption was decreased by 32%. However, in comparison between the pre-0.25 group and the post-PVB group, opioid consumption was significantly lower in the post-PVB group until 2 hours after the operation, and there was no difference between the two groups from 6 hours after the operation.

The results once again highlight the preemptive analgesic effect of pre-incisional PVB. The visceral pain signal was not blocked during surgery in both the pre-0.25 and post-PVB

groups, resulting in a lower pain threshold. However, patients in the post-PVB group experienced less pain compared with patients who received only RSB, while the post-incisional PVB effect was maintained. However, after the effect of the PVB was worn off, opioid consumption was increased due to the sudden onset of pain rather than the pre-0.25 group from 6 hours to 24 hours after surgery (100 μg in the post-PVB group vs. 53.5 μg in the pre-0.25 group). In contrast, compared with the pre-0.25 group, the pre-PVB group, in which the visceral pain signal was sufficiently blocked with pre-incisional PVB, showed lower opioid consumption at all times. Based on this observation, even a single regional block may provide preemptive analgesic effect.

In conclusion, compared with post-incisional PVB, pre-incisional PVB reduced analgesic requirements during the postoperative 24 hours of patients who underwent LC. In addition, the NRS was low in the pre-incisional PVB group for up to 6 hours after surgery. Therefore, the visceral preemptive analgesic effect of the PVB may be maintained after 6 hours of surgery.

Supplementary table 1. Postoperative opioid consumption during 24 hours after surgery.

Group	Pre-PVB (N=33)	Post-PVB (N=31)	Pre-RSB (N=40)	p
CRA_0	0.0 (0.0;0.0)	0.0 (0.0;25.0)	25.0 (0.0;30.0)	< 0.001
CRA_0.5	25.0 (0.0;30.0)	30.0 (25.0;60.0)	60.0 (40.0;75.0)	< 0.001
CRA_1	30.0 (0.0;50.0)	60.0 (35.0;85.0)	75.0 (40.0;95.0)	< 0.001
CRA_2	100.0 (25.0;140.0)	150.0 (127.5;177.5)	167.5 (135.0;190.0)	< 0.001
CRA_6	125.0 (35.0;155.0)	175.0 (135.0;200.0)	175.0 (140.0;200.0)	< 0.001
CRA_12	140.0 (100.0;245.0)	225.0 (162.5;300.0)	190.0 (162.5;225.0)	0.012
CRA_18	140.0 (100.0;255.0)	250.0 (165.0;307.5)	215.0 (175.0;270.0)	0.007
CRA_24	140.0 (100.0;255.0)	250.0 (165.0;307.5)	220.0 (177.5;270.0)	0.007

Data are expressed as the median (interquartile range). Abbreviations: Pre-PVB, pre-incisional paravertebral block and pre-incisional rectus sheath block with 0.25% ropivacaine; Post-PVB, post-incisional paravertebral block and pre-incisional rectus sheath block with 0.25% ropivacaine; Pre-RSB, only pre-incisional rectus sheath block with 0.25% ropivacaine; CRA, cumulated rescue analgesic consumption up to each hour.

CONCLUSION

The present study was performed to confirm the preemptive analgesic effect of regional block, further to check the effect on the timing of the block, the dose of local anesthetics and postoperative somatic & visceral pain.

The preemptive analgesic effect for postoperative pain relief were examined on next criteria.

1. Less total analgesic consumption

Pre-incisional block lowered the analgesic requirements during the intra-operative and post-operative 24-hour period in patients undergoing LC, compared with postoperative RSB (Chapter I, II). And difference of local anesthetics concentration does not affect the postoperative analgesic requirements (Chapter I).

2. Decrease in postoperative pain

If both somatic & visceral pains are adjusted by applying a regional block to the patients undergoing LC, the pre-incisional blocks showed significant difference in postoperative NRS compared to the post-incisional blocks during the period of the effect of block maintained (Chapter II). However, in patients who were performed PSNB, there were no significant differences between NRS and patient satisfaction.

As a result, pre-incisional regional block statistically significantly reduce post-operative rescue analgesic dose and pain intensity. Although not statistically significant, the use of high doses of local anesthetics tends to reduce opioid consumption after surgery.

These results demonstrate that the timing of regional block is clinically significant for postoperative pain relief.

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국문요약

서론

선행 진통 효과는 절개 및 염증성 부상에 의한 중추성 감작을 막아 수술 후 통증을 줄여주는 효과이다. 여러가지 약물들이 사용되고 있지만 부위마취와 관련된 임상적인 연구는 부족하다. 이 연구의 목적은 수술 후 통증과 연관된 부위 마취의 선행 진통 효과를 확인하는 것이다.

연구방법

모든 Pre 그룹에서는 전신마취 후 피부 절개 전에, 그리고 모든 Post 그룹에서는 수술 종료 후 환자 각성 전에 각 그룹에 해당되는 부위 마취가 초음파 유도하에 시행되었다.

Chapter I: 정규로 복강경 담낭절제술을 수술 받기로 계획된 성인 환자들은 4군으로 나뉘었다. 0.25% 로피바케인으로 RSB을 시술 받는 Pre-RSB 그룹과 Post-RSB 그룹. 그리고 0.375% 로피바케인으로 RSB을 시술 받는 pre-RSB 그룹과 Post-RSB 그룹. Primary outcome은 수술 후 24시간 동안의 추가 진통제 사용량이며, 수술 중 활력징후의 변화, 수술 후의 숫자 통증 등급, 그리고 부위마취와 관련된 부작용들이 모두 기록되었다.

Chapter II: 정규로 복강경 담낭절제술을 수술 받기로 계획된 성인 환자들은 2군으로 나뉘었다(Pre-PVB and Post-PVB 그룹). 연구에 참여하는 모든 환자에게 피부절개 전 복직 근초 차단술 이 시행되었으며, 각 그룹에 맞게 피부절개 전 방척추 차단술과 수술 종료 후 방척추 차단술이 시행되었다. Primary outcome은 수술 후 24시간 동안의 추가 진통제 사용량이며, 수술 중 활력징후의 변화, 수술 후의 숫자 통증 등급, 그리고

부위마취와 관련된 부작용들이 모두 기록되었다.

연구결과

Chapter I: 수술 후 24시간 동안의 추가 진통제 사용량은 (μg) 모든 Pre 그룹에서 Post 그룹에 비해 유의하게 낮았다. (Pre-0.25: 240.4 ± 109.3 vs. Post-0.25: 304.9 ± 126.5, P = 0.018, Pre-0.375: 209.0 ± 97.2 vs Post-0.375: 260.2 ± 112.6, P = 0.028). 그리고 0.25%와 0.375% 로피바케인을 비교해 보면 의미 있는 차이를 보이지 않았다.

Chapter II: 수술 후 24시간 동안의 추가 진통제 사용량은 (μg) 모든 Pre-PVB 그룹에서 Post-PVB 그룹에 비해 유의하게 낮았다 (140.0 (100.0–255.0) vs. 250.0 (165.0–307.5), P = 0.003). 그리고 수술 후 숫자통증등급도 pre-PVB 그룹에서 유의하게 낮았다.

결론

피부 절개 전 시행한 부위 마취는 피부 봉합 후 시행하는 부위마취에 비해 수술 후 통증에 도움이 된다고 생각된다. 부위 마취의 시점은 수술 후 통증 조절에 임상적으로 중요하다.

중심단어: 로피바케인; 방척추 차단술; 복직 근초 차단술; 선행진통효과; 수술 후 숫자 통증 등급; 피부절개전 블록.