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Randomised Controlled Trial

Comparison of pharmacologic therapies alone versus operative techniques in combination with pharmacologic therapies for postoperative analgesia in patients undergoing laparoscopic cholecystectomy: A randomized controlled trial

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ABSTRACT

Background: Laparoscopic cholecystectomy (LC) causes moderate pain. Various operative analgesic techniques and pharmacologic treatments can reduce postoperative pain. This single-center, single-surgeon randomized controlled study aimed to assess the efficacy of combined operative analgesic techniques and pharmacologic analgesia in decreasing pain in patients undergoing LC.

Materials and methods: Fifty-nine patients scheduled for LC were assigned into two groups. In the pharmacologic analgesia (P) group (n = 29), patients were treated with pharmacologic intervention, including preoperative celecoxib (200 mg), intraoperative acetaminophen (1 g), and dexamethasone (8 mg). In the operative analgesic treatments with pharmacologic analgesia (OP) group (n = 30), patients were treated with both operative analgesic techniques and pharmacologic analgesia, including low-pressure pneumoperitoneum, intraperitoneal normal saline irrigation, and aspiration of intraperitoneal carbon dioxide. The area under the curve (AUC) of pain score for postoperative 24 h was assessed at 0, 2, 6, and 24 h post-operation. The analgesic requirements and sleep quality at postoperative day 1 were assessed.

Results: The AUC/24 h of pain scores at rest and on cough were lower in the OP group ($p < 0.001$ and $p = 0.001$, respectively). The pain scores at rest were lower in the OP group at postoperative 2, 6, and 24 h ($p = 0.001$, $p = 0.001$, and $p = 0.048$, respectively). The pain scores on cough were lower in the OP group at postoperative 2 and 6 h ($p = 0.004$ and $p = 0.008$, respectively). Analgesic requirements were comparable. The sleep quality score at postoperative day 1 was higher in the OP group (56 ± 18 vs. 67 ± 15, absolute difference, 10; 95% confidence interval, 2 to 19; $p = 0.017$).

Conclusions: Combined operative analgesic therapies and pharmacologic analgesia compared to pharmacologic analgesia alone decreased pain scores and increased sleep quality in patients undergoing LC.

1. Introduction

Laparoscopic cholecystectomy (LC) is a minimally invasive procedure, which shows less infection and pneumonia compared to open cholecystectomy [1]. Although LC is a less invasive procedure, LC causes moderate-intensity postoperative pain immediately after the surgery [2,3], which can present challenges for postoperative management. The intense pain at the immediate postoperative period can decrease the quality of life and prevent early discharge. Postoperative pain after LC may also result in sleep disorder [4].

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Many analgesic modalities have been investigated to decrease postoperative pain after LC [5–8]. Pharmacologic modalities using pregabalin and celecoxib have been investigated [9]. A combination of pharmacologic analgesic treatments decreases postoperative pain in patients following LC [10]. Moreover, operative analgesic techniques have been investigated for postoperative analgesia in patients following LC [6]. Among these techniques, low-pressure pneumoperitoneum and active gas suction are recommended to decrease postoperative pain and analgesic requirements in patients undergoing LC. Combining operative analgesic modalities with pharmacologic treatments may be beneficial for reducing pain in patients following LC when compared with patients who are treated with pharmacologic therapies only.

We hypothesized that adding operative analgesic treatments to pharmacologic analgesia may reduce patients' postoperative pain following LC compared with the multiple treatments of pharmacologic analgesia alone.

2. Materials and Methods

This single-center, single-surgeon randomized controlled study was performed in accordance with the tenets of the Declaration of Helsinki. The work has been reported in line with the Consolidated Standards of Reporting Trials (CONSORT) Guidelines. This study was registered with ClinicalTrials.gov (NCT04788654, https://clinicaltrials.gov/ct2/show/NCT04788654).

Written informed consent was acquired before patient enrollment. Patients with the American Society of Anesthesiologists physical status I-III, aged ≥19 years, and scheduled for LC were enrolled from March 2021 to July 2021. Patients with recent gastric ulcer disease; severe hepatic impairment (Child-Pugh score>9); chronic renal disease (estimate glomerular filtration rate<60 ml/min/1.73 m^2); contraindication to non-steroidal anti-inflammatory drugs, acetaminophen, and dexamethasone; morbid obesity (body mass index >35 kg/m^2), chronic pain with opioid treatment; sleep disorder requiring medical treatments; and psychiatric disease were excluded from this study.

Patients were randomly assigned to the pharmacologic analgesia (P) group or the operative analgesic treatments with pharmacologic analgesia (OP) group using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria) and the closed envelope technique. Patients were blinded to their group allocation. The physician and nurse who managed the patients postoperatively were blinded to group allocation and the study's protocol. The surgeon was not blinded to group allocation and did not participate in data collection and postoperative pain management.

2.1. General anesthesia

Upon arrival at the operating room, each patient was monitored using non-invasive blood pressure measurement, electrocardiography, and pulse oximetry. Anesthetic depth was evaluated using a patient state index measured by Sedline® (Masimo, Irvine, CA, USA), and neuromuscular blockade quantification was monitored using acceleromyography (TOF-watch SX; MSD BV, Oss, the Netherlands). Anesthetic induction was performed using intravenous propofol (2 mg/kg), remifentanil (1 μg/kg), and rocuronium (0.8 mg/kg). After the full neuromuscular blockade, tracheal intubation was performed. Sevoflurane, remifentanil, and rocuronium were used to maintain anesthesia. A mean blood pressure of ±20% of the baseline value and a patient state index <50 were maintained. The infusion rate of intraoperative remifentanil was set using a surgical plethysmographic index measured by an S/5 monitor (GE Healthcare, Helsinki, Finland). Perioperative hypotension during anesthesia was treated with ephedrine (4–8 mg) or phenylephrine (50–100 μg).

2.2. Surgical procedures

After general anesthesia induction, the entire abdomen was cleaned with povidone-iodine solution and draped with sterile towels and disposable drapes. An 18-mm skin incision was made in the supraumbilical area. A 12-mm camera port was inserted after the fascia was opened using a monopolar electrosurgery handle. Pneumoperitoneum was created. Three 5-mm working ports were inserted after a 10-mm infra xiphoid incision, and two right upper quadrant incisions were made. For visualization of Calot's triangle, the gallbladder fundus was pushed toward the right upper direction using a laparoscopic grasper on the lateral right upper quadrant port. The cystic duct and cystic artery were skeletonized by a laparoscopic dissector and clipped with Hemo-O-lock clips. After the cystic duct and artery were transected by laparoscopic scissors, the gallbladder was detached from the liver in a retrograde manner using a laparoscopic monopolar electrosurgery hook. After confirming that there was no bleeding, the gallbladder was removed using an endopouch from the abdominal cavity through a camera port site. After specimen removal, the surgical site was irrigated for bleeding and debris clearance. Additional irrigation, using 2 L of saline, was done to decrease the irritation of the diaphragm and peritoneum by carbon dioxide and carbonic acid. A Jackson-Pratt (JP) drain was inserted at the liver dome using the lateral right upper quadrant port site for full aspiration of carbon dioxide. Supraumbilical site fascia and skin incisions, except for at the JP drain insertion site, were closed. The carbon dioxide was aspirated through the JP drain using negative pressure, and the drain was then removed. The lateral right upper quadrant skin incision was then closed. All laparoscopic procedures were recorded for assessment.

In the P group, only pharmacologic analgesic treatments were applied. Pharmacologic analgesia included medical agents, which are known to reduce postoperative pain in patients following LC. Pharmacologic analgesic therapies were as follows: celecoxib 200 mg, administration orally 1 h before the anesthetic induction and acetaminophen 1 g and dexamethasone 8 mg infusion after the anesthetic induction. Lidocaine was injected at the skin incision site. In the P group, pneumoperitoneum pressure was maintained at 12 mmHg. In the OP group, the pharmacologic analgesic treatments that were used in the P group were also applied. Wound infiltration with lidocaine was also performed. Additionally, operative techniques for analgesia were performed. Operative techniques for analgesia included various surgical maneuvers, which are known to decrease postoperative pain in patients following LC. Pneumoperitoneum pressure was maintained below 10 mmHg during the laparoscopic procedure. After specimen removal, the right diaphragm was irrigated with 2 L of normal saline. After supraumbilical site fascia and skin incision were approximated, carbon dioxide was fully aspirated.

2.3. Postoperative pain management

Tramadol of 50 mg was administered 3 times a day as a routine analgesic protocol. Rescue analgesia was performed when a patient's pain score was ≥4 using intravenous fentanyl (0.5–1 μg/kg) at the postanesthesia care unit and intravenous tramadol (50 mg) at the ward. Tramadol (50 mg), ketorolac (30 mg), or pethidine (2 mg) was administered when a patient's pain score did not decrease, or the patient requested analgesia after rescue analgesic treatment.

2.4. Assessment of operation and patient pain

After the surgical procedure was completed, another surgeon, who was blind to the group, reviewed unedited surgical videos except for the operative analgesia techniques that were added to the OP group and assessed the view of the surgical field (0, worst view; 100, best view) and the satisfaction of the surgical condition (0, most dissatisfied; 100, most satisfied) using a visual analog scale. Postoperative pain scores at rest

and on cough were evaluated at postoperative 0, 2, 6, and 24 h using a visual analog scale (0, no pain; 100, most imaginable pain). The incidence of shoulder discomfort was assessed at postoperative 0, 2, 6, and 24 h. The incidence of back pain, nausea, and vomiting were evaluated for postoperative 24 h. Metoclopramide (10 mg) was administered when severe nausea and vomiting were reported or when patients requested antiemetic treatment. The sleep quality at postoperative day 1 was evaluated using the Richards-Campbell Sleep Questionnaire [11]. The requirements of rescue analgesics were assessed at postoperative 24 h.

The primary endpoint was the area under the curve (AUC) of postoperative pain score at postoperative 24 h. The secondary endpoints were postoperative pain scores at postoperative 0, 2, 6, and 24 h; the incidence of shoulder discomfort, back pain, nausea, vomiting, analgesic requirements, antiemetic requirements, and sleep quality. The time to discharge and side effects of celecoxib, acetaminophen, and dexamethasone were recorded using electrical medical recording in a retrospective manner. The time to discharge was defined as the interval from the end of surgery to discharge. Serious side effects of celecoxib, acetaminophen, and dexamethasone were recorded and were defined as side effects requiring medical treatment, which delayed the discharge.

2.5. Statistical analysis

A previous investigation showed that the AUC of postoperative pain score at postoperative 24 h was 34 ± 18 [12]. Combined application of pharmacologic and surgical analgesia was presumed to decrease the AUC of postoperative pain score at postoperative 24 h to 50%, which was regarded as clinically significant. Nineteen patients per group were necessary to attain 5% alpha and 80% power in a two-sided comparison. Thirty patients in each group were necessary to compensate for a compliance rate of 80% and a possible dropout rate of 20%.

Continuous variables, including pain score, the dose of rescue analgesics, score of surgical view and satisfaction, sleep quality score, and the time to discharge, were evaluated for normal distribution using the Kolmogorov–Smirnov test. The Student's t-test or Mann–Whitney *U* test was applied according to the data distribution. Categorical outcomes, including the incidence of nausea, vomiting, and rescue antiemetics use, were analyzed using a chi-square test or Fisher's exact test when necessary. Bonferroni correction was performed for the analysis of variables using multiple comparisons, including pain scores. All analyses were performed using R version 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria), MedCalc version 20 (MedCalc, Ostend, Belgium), and Statistical Package for the Social Sciences version 25 (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

3. Results

Seventy-five patients were screened from March 2021 to July 2021, of whom 15 were excluded because they met the exclusion criteria (n = 6) or refused to participate (n = 9). One patient in group P withdrew consent, leaving 59 patients for the analysis (Fig. 1). The baseline characteristics of the patients were similar between the groups except for the duration of surgery (Table 1). The duration of surgery was longer in the OP group (p = 0.005) than in the P group. The scores of surgical view and surgical condition satisfaction were comparable between the groups.

The AUC/24 h of pain scores at rest was lower in the OP group (35 ± 14 vs 22 ± 8, difference, 13; 95% confidence interval [CI], 7–19; p < 0.001, Table 2) than in the P group. The AUC/24 h of pain scores on cough was lower in the OP group (41 ± 16 vs 28 ± 10; difference, 13; 95% CI, 5–20; p = 0.001) than in the P group. The pain scores at rest were lower in the OP group at postoperative 2, 6, and 24 h (p = 0.001, p = 0.001, and p = 0.048, respectively) than in the P group. The pain scores on cough were lower in the OP group at postoperative 2 and 6 h (p = 0.004 and p = 0.008, respectively) than in the P group. Analgesic

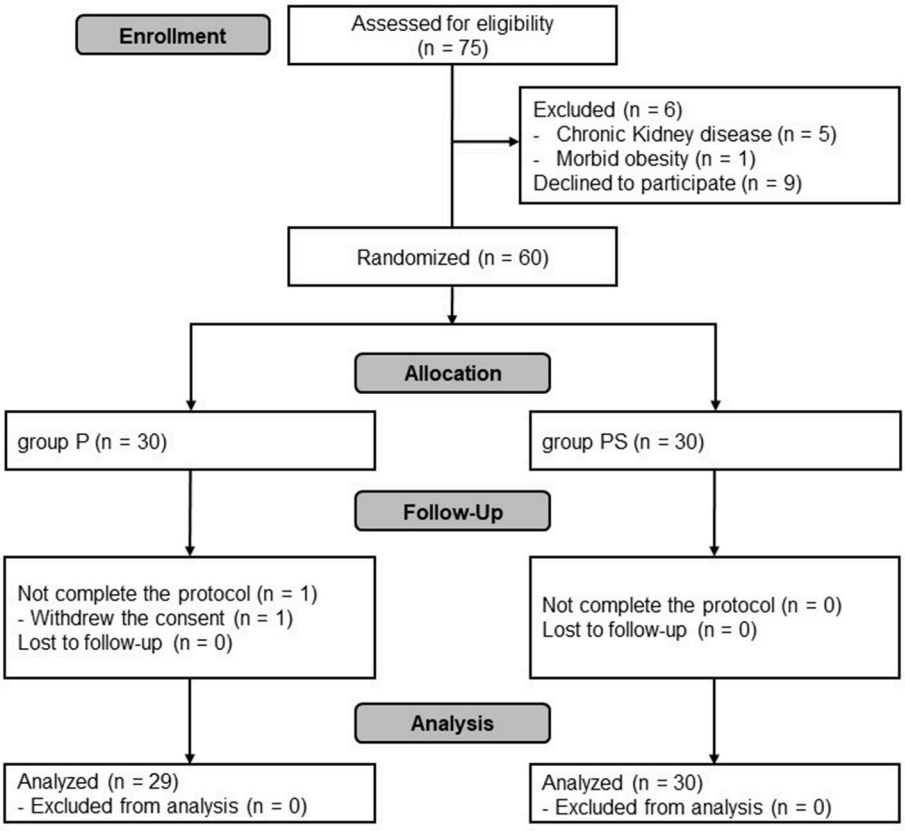

Fig. 1. CONSORT diagram.

Table 1
Patient characteristics and operation details.

	Group P (n = 29)	Group OP (n = 30)	P
Women	14 (48)	16 (53)	0.698
Age (y)	56 ± 15	60 ± 17	0.348
Height (cm)	164 ± 9	164 ± 8	0.903
Weight (kg)	68 ± 13	69 ± 11	0.802
BMI (kg/m^2)	25.1 ± 3.5	25.5 ± 3.5	0.730
ASA physical status (I/II/III)	12 (41)/5 (17)/ 12 (41)	9 (30)/10 (33)/ 11 (37)	0.346
Intraoperative dose of remifentanil (μg/kg/hr)	4.1 ± 2.3	3.8 ± 1.4	0.499
Intraoperative crystalloid intake (ml/kg/hr)	5.0 ± 2.0	4.2 ± 1.5	0.093
Operation time (min)	25 (23)	36.5 (15)	0.005
Anesthesia time (min)	63 ± 22	67 ± 16	0.523
Time to discharge (hr)	31 ± 22	32 ± 17	0.839
Surgical view score[a]	43 ± 8	45 ± 8	0.279
Surgical condition satisfaction score†	43 ± 8	45 ± 8	0.457

Values are presented as mean ± standard deviation, median (interquartile range), or number of patients (%). ASA, American Society of Anesthesiologists; BMI, body mass index.

[a] After the surgical procedure was completed, another surgeon who was blind to the group reviewed unedited surgical videos except for the operative analgesia techniques added to the OP group and assess the view of the surgical field (0, worst view; 100, best view) and the satisfaction of the surgical condition (0, most dissatisfied; 100, most satisfied) using the visual analog scale.

requirements were comparable between the groups. The incidences of shoulder discomfort at postoperative 0, 2, 6, and 24 h were similar between the groups (p = 0.992, p = 1.000, p = 1.000, and p = 1.000, respectively). The incidence of back pain was comparable between the two groups [6 (21%) vs 6 (21%); 95% CI, -22–23%; p = 0.948].

Total score of sleep quality using Richards-Campbell Sleep Questionnaire at postoperative day 1 was higher in the group OP (56 ± 18 vs 67 ± 15; absolute difference, 10; 95% CI, 2–19; p = 0.017, Table 3) than in the P group. The scores of sleep depth, sleep latency, and sleep quality were higher in the OP group (p = 0.024, p = 0.032, and p = 0.005, respectively) than in the P group. There were no significant differences in the incidences of nausea [14 (48%) vs 13 (43%); 95% CI, -22–31%; p = 0.703] or vomiting between the two groups [2 (7%) vs 0 (0%); 95% CI, -8–24%; p = 0.237]. The incidence of rescue antiemetics use was similar between the groups [5 (17%) vs 6 (20%); 95% CI, -20–25%; p = 1.000]. Serious complications, including infection and bleeding, were not reported. Serious side effects of celecoxib, acetaminophen, and dexamethasone were not reported.

4. Discussion

This investigation demonstrated that combined analgesic operative techniques and pharmacologic treatments decreased postoperative pain scores 24 h after surgery when compared to the administration of pharmacologic treatments alone at the expense of longer surgical procedure duration in relatively healthy patients undergoing LC. Surgical techniques combined with pharmacologic treatments for analgesia also increased the quality of sleep after surgery in our small cohort of patients. The combination of analgesic operative techniques and pharmacologic treatments did not decrease the supplemental analgesic requirements or the incidence of nausea and vomiting.

Various pharmacologic treatments or surgical techniques for analgesia were shown to reduce pain in patients following LC [2,3,6,7,9,12]. In our investigation, operative techniques for analgesia combined with pharmacologic treatments reduced AUC/24 h pain scores more than pharmacologic analgesia alone. The lower pain scores at postoperative 2 and 6 h may reduce AUC/24 h of pain scores for postoperative 24 h. The mechanism of pharmacologic analgesia is different from that of surgical

Table 2
Postoperative pain outcomes.

	Group P (n = 29)	Group OP (n = 30)	Difference (95% CI)	P	Adjusted P[a]
VAS pain scores at rest					
0 h after surgery	61 ± 25	50 ± 25	11 (-2–24)	0.107	0.428
2 h after surgery	54 ± 17	36 ± 17	18 (9–27)	<0.001	0.001
6 h after surgery	37 ± 17	22 ± 11	15 (7–23)	<0.001	0.001
24 h after surgery	23 ± 16	14 ± 09	9 (2–16)	0.012	0.048
AUC/24 h	35 ± 14	22 ± 8	13 (7–19)	<0.001	
VAS pain scores on cough					
0 h after surgery	68 ± 25	53 ± 25	15 (1–23)	0.030	0.120
2 h after surgery	61 ± 20	42 ± 19	19 (9–29)	0.001	0.004
6 h after surgery	43 ± 19	28 ± 14	14 (6–23)	0.002	0.008
24 h after surgery	29 ± 20	21 ± 13	8 (0–17)	0.061	0.244
AUC/24 h	41 ± 16	28 ± 10	13 (5–20)	0.001	
Incidence of shoulder tip pain					
0 h after surgery	0 (0%)	3 (10%)	–	0.248	0.992
2 h after surgery	4 (14%)	5 (17%)	–	1.000	1.000
6 h after surgery	5 (17%)	4 (13%)	–	0.956	1.000
24 h after surgery	4 (14%)	3 (10%)	–	0.962	1.000
Amount of analgesics administered during 24 h after surgery					
Fentanyl (μg)	40 ± 31	35 ± 27	5 (-10–20)	0.540	
Pethidine (mg)	0 (0)	0 (0)	0 (0–0)	0.258	
Tramadol (mg)	167 ± 71	153 ± 45	14 (-17–45)	0.377	
Ketorolac (mg)	0 (30)	0 (0)	0 (0–0)	0.270	
Opioid consumption (mg) †	48 ± 32	39 ± 18	10 (-4–23)	0.161	

Values are presented as mean ± standard deviation, number of patients (%) or median (interquartile range). Group P received pharmacologic analgesia treatment only; Group OP received operative analgesic treatments with pharmacologic analgesia. AUC, area under the curve of postoperative pain score; CI, confidence interval; VAS, visual analog scale (0: no pain, 100: most imaginable pain).

[a] P value was corrected using the Bonferroni method for multiple comparisons. †Opioid consumption was converted to mg of oral morphine equivalents.

Table 3
Sleep quality assessed using the Richards-Campbell Sleep Questionnaire on postoperative day 1.

	Group P (n = 29)	Group OP (n = 30)	Difference (95% CI)	P
Average RCSQ score	56 ± 18	67 ± 15	10 (2–19)	0.017
Sleep depth	54 ± 22	67 ± 20	13 (2–24)	0.024
Sleep latency	63 ± 31	78 ± 17	15 (1–28)	0.032
Awakenings	43 ± 20	51 ± 24	7 (-4–19)	0.213
Returning to sleep	66 ± 20	68 ± 23	2 (-9–13)	0.709
Overall sleep Quality	54 ± 23	70 ± 18	16 (5–26)	0.005
Noise	63 ± 26	57 ± 27	−7 (-21–7)	0.329

Values are presented as mean ± standard deviation. Group P received pharmacologic analgesia treatment only; Group OP received operative analgesic treatments with pharmacologic analgesia. CI, confidence interval; RCSQ, Richards-Campbell Sleep Questionnaire.

maneuver analgesia. Celecoxib is a COX-2-selective nonsteroidal anti-inflammatory agent [9]. Acetaminophen affects both peripheral and central antinociception [13]. Dexamethasone is well known for its analgesic effect although the mechanism of dexamethasone is not well described [14]. Low-pressure pneumoperitoneum, aspiration of carbon dioxide gas, and saline irrigation may decrease irritation of the peritoneum by carbon dioxide and carbonic acid [6]. Considering that the cause of postoperative pain is multifactorial [6], combinations of these various mechanisms through operative analgesic techniques and pharmacologic treatments may reduce postoperative pain in patients following LC.

AUC/24 h of pain score on cough was 41 ± 16 in patients using pharmacologic analgesic treatments and was relatively higher than that in the previous investigation using transversus abdominis plane block [12]. Pain after LC arises from the incision sites, the pneumoperitoneum, and the cholecystectomy [15]. Local anesthetic infusion at the surgical wound, which was applied in both groups in our investigation, may not be as effective as transversus abdominis plane block for reducing pain in postoperative incision sites. Transversus abdominis plane block, however, does not decrease postoperative pain at rest in patients undergoing LC [12]. In our small cohort of patients, surgical analgesic maneuver decreased postoperative pain at rest in patients following LC.

Pneumoperitoneum results in diaphragmatic expansion, peritoneum irritation by carbon dioxide, sympathetic nervous system activation by hypercarbia and local tissue inflammation, and splanchnic perfusion decrease, which may increase postoperative pain after LC [16,17]. Surgical analgesic maneuvers, such as low-pressure pneumoperitoneum, intraperitoneal saline irrigation, and aspiration of infused intraperitoneal carbon dioxide, may decrease deteriorating factors by pneumoperitoneum while transversus abdominis plane block may affect only somatic pain at incision sites. Combined surgical analgesic techniques and pharmacologic treatments decreased somatic and visceral pain in patients undergoing LC in our small cohort of patients.

Perioperative sleeping disorder can cause a negative impact on outcomes such as pain, mental disorder, delirium, cognitive disorder, and recovery [18]. Postoperative sleep disorder is also related to cardiovascular events [19] and a longer hospital stay [20]. Operative analgesic techniques added by pharmacologic treatments increased sleep quality in this investigation. Perioperative sleeping disorder is influenced by many factors, including age, gender, pain, surgery and anesthesia, mental disorder, and environment [18]. Postoperative pain in patients undergoing minimally invasive surgery is a risk factor for sleep disturbance [21]. Decreased pain scores by combined operative analgesic techniques and pharmacologic treatments may result in a better quality of sleep postoperatively.

The surgical procedure time was longer in the OP group. The procedure time of LC is related to higher costs and risks of complications [22]. Low-pressure pneumoperitoneum may affect surgical view and condition, which is related to the difficulty and time of the procedure. However, the surgical view and condition satisfaction scores were similar between groups in this investigation. Additional maneuvers, such as saline irrigation and aspiration of gas, may prolong the surgical procedure time. In our investigation, however, the surgical analgesia maneuver did not increase the total time of anesthesia. Although surgical analgesia increased the procedure time, surgical analgesia decreased postoperative pain scores and improved sleep quality, which are associated with better outcomes and quality of life.

Several limitations of the current investigation should be considered. First, additional opioid requirements and incidence of opioid-related side effects, such as nausea and vomiting, were not different between the groups. The sample size in this investigation was not calculated to assess these differences. Second, the surgeon who performed the main procedure of LC was not blinded to the group assignment, which may have increased bias. However, the surgeon who performed the main procedure of LC did not participate in patient management regarding analgesia to address and presumably decrease this bias. Third, our investigation evaluated the benefit of combined operative analgesic techniques and pharmacologic analgesia in patients undergoing LC only at the immediate postoperative period. In our study, the postoperative outcomes, such as the amount of oral pain control after discharge and the time taken to return to work, were not evaluated. Time taken to return to work may affect the economy regarding the number of work hours lost and should not be underestimated. Future investigations are necessary to assess the long-term benefits of combined operative analgesic techniques and pharmacologic analgesia in patients undergoing LC. Fourth, although we included geriatric patients and patients with comorbidities (ASA class III), our study was conducted in a small group of people who had undergone elective laparoscopic cholecystectomy performed by a single surgeon in a single center. The design of our investigation inhibits the external validity of the trial. Therefore, it is difficult to generalize our study results by comorbidities, age, and diagnosis, such as acute cholecystitis and/or gallbladder empyema. It is necessary to conduct a large-scale study through a prospective multicenter study.

In conclusion, combined pharmacologic and surgical maneuver analgesia decreased pain and increased sleep quality in patients following LC when compared with treatments of pharmacologic analgesia alone. This study provides proof-of-concept for combined pharmacologic and surgical maneuver analgesia, which needs to be tested in a larger, multi-center, randomized cohort. This combined surgical and pharmacologic analgesia may be recommended in patients undergoing LC.

Ethical approval

The study protocol was approved by the Institutional Review Board and Hospital Research Ethics Committee of Gangnam Severance Hospital (#3-2020-0494) in January 2021.

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Hyperlink to your specific registration (must be publicly accessible and will be checked): https://clinicaltrials.gov/ct2/show/NCT04788654

Guarantor

Hyun-Chang Kim, Jin Hong Lim, and Do Hyeong Kim are guarantors.

Conflict of interest

No competing interests are to be declared.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

The data of this investigation is shared in Mendeley Data.

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CRediT authorship contribution statement

Hyun-Chang Kim: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Young Song:** Conceptualization, Writing – review & editing. **Jong Seok Lee:** Conceptualization, Writing – review & editing. **Myeong Eun Jeong:** Conceptualization, Methodology, Writing – review & editing. **Yongmin Lee:** Conceptualization, Methodology, Writing – review & editing. **Jin Hong Lim:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Do-Hyeong Kim:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

No competing interests are to be declared.

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