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Effect of continuous wound infiltration on patients using intravenous patient-controlled analgesia for pain management after reduced-port laparoscopic colorectal surgery

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Purpose: Continuous wound infiltration (CWI) has been introduced as a component of multimodal analgesia to counteract the adverse effects of the most frequently used opioids. Advantages of reduced-port laparoscopic surgery (RPLS) include cosmetic benefits and decreased postoperative pain. We aimed to investigate the effect of CWI in patients using intravenous (IV) patient-controlled analgesia (PCA) for pain management after RPLS for colorectal cancer.

Methods: This retrospective study included 25 patients who received both CWI (0.5% ropivacaine infused over 72 hours) and IV PCA (fentanyl citrate) and 52 patients who received IV PCA alone. The primary endpoint was pain scores on postoperative days (PODs) 0, 1, and 2. Univariate and multivariate analyses were conducted to determine the factors affecting the pain score on POD 0.

Results: On POD 0, the mean numeric rating scale score was significantly lower in the CWI group than in the control group (3.2±0.8 vs. 3.7±0.9, P=0.042). However, the scores were comparable between the groups during the rest of the period. Within 24 hours of surgery, the CWI group consumed fewer opioids (0.7±0.9 vs. 1.3±1.1, P=0.018) and more nonsteroidal anti-inflammatory drugs (2.0±1.4 vs. 1.3±1.4, P=0.046) than the control group. Time to removal of IV PCA was significantly longer in the CWI group than in the control group (4.4±1.6 days vs. 3.4±1.0 days, P=0.016).

Conclusion: CWI with ropivacaine and IV PCA was more effective than IV PCA alone in controlling postoperative pain within 24 hours of surgery, and opioid use could be reduced further.

Keywords: Pain management; Laparoscopy; Treatment outcome

INTRODUCTION

Acute pain induces a diverse array of pathophysiological responses, which are triggered by the activation of nociceptors following tissue injury, resulting in a local inflammatory response and subsequent behavioral and physiological responses [1, 2]. Controlling acute postoperative pain is essential not only in the immediate postoperative period but also to prevent the development of chronic postsurgical pain, which can occur in up to 10% of the patients [3]. In patient-controlled analgesia (PCA), pa-

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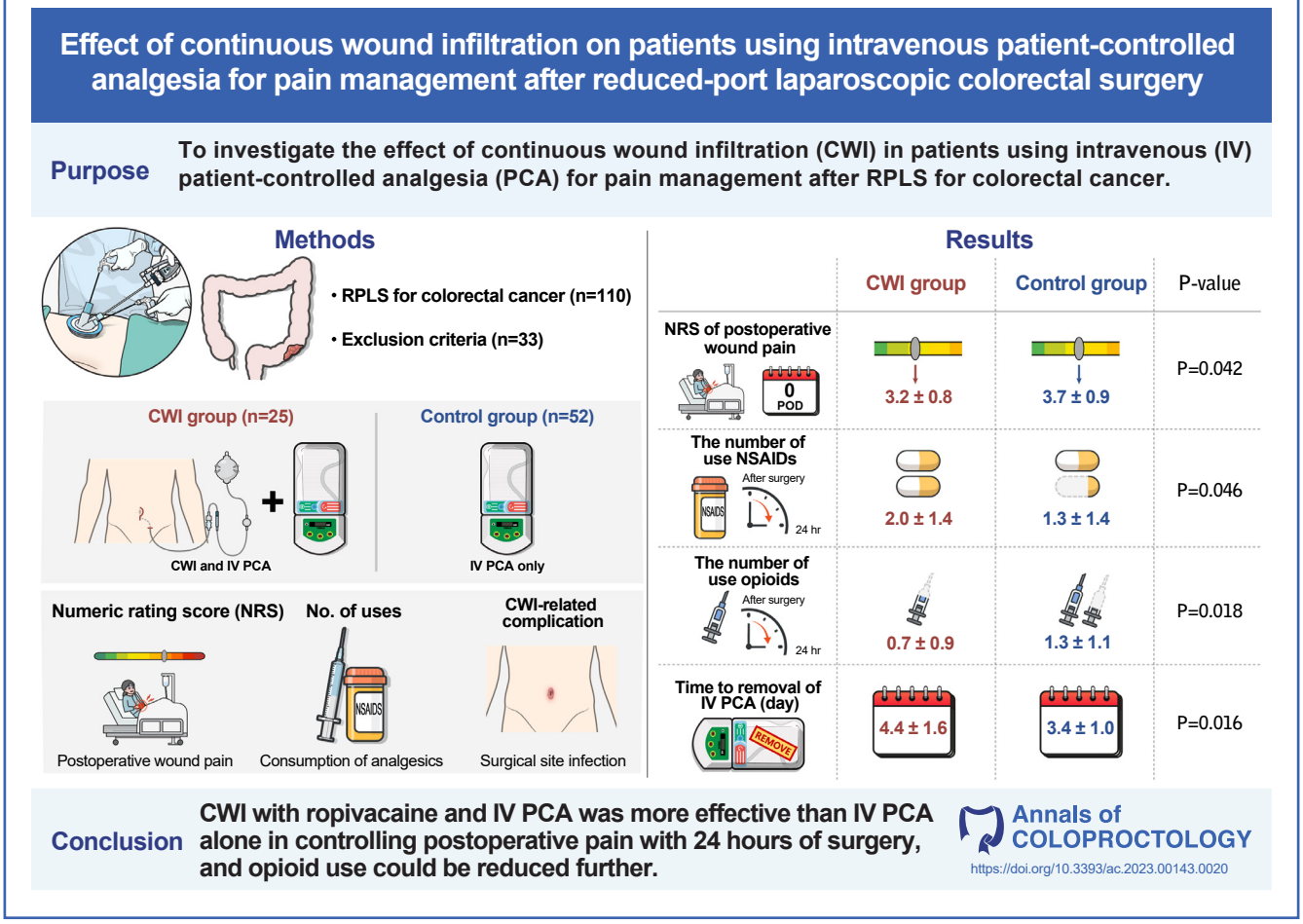
Graphical abstract



tients self-administer predetermined doses of analgesic medication to relieve their pain. Since the late 1960s, opioid-based intravenous (IV) PCA has been widely used for postoperative analgesia due to its efficacy and convenience [4]. However, adverse events such as gastrointestinal side effects (constipation, nausea, and vomiting) and central nervous system side effects (sedation) are responsible for up to 1/5 of the patients discontinuing opioid treatment, frequently resulting in inadequate pain relief and poor quality of life [5].

Minimally invasive surgery is an important factor that can enhance postoperative recovery. Previous studies have demonstrated that laparoscopic surgery for colorectal cancer has advantages over open surgery including reduced blood loss, earlier recovery of intestinal motility, and shorter hospital stay; without affecting the oncologic results [6–8]. Laparoscopic surgeons have a growing interest in single-port or reduced-port colorectal surgery because of efforts to reduce postoperative trauma, surgical stress, and scarring [9]. The reported benefits of these surgical techniques include cosmetic benefits and reduced postoperative pain [10, 11].

Postoperative pain is a crucial component of perioperative management, since it inhibits the healing process. The recent Enhanced Recovery After Surgery (ERAS) guidelines for postoperative analgesia after colorectal surgery recommend avoiding opioids and employing multimodal analgesia. In the era of minimally invasive surgery, techniques such as epidural anesthesia, continuous wound infiltration (CWI), and transversus abdominis plane block have been applied to colorectal cancer surgery to facilitate patient recovery, enhance the quality of life, and reduce the side effects of opioids [12, 13].

Local anesthetic wound infusion provides analgesia by inhibiting the afferent nerves of the abdominal wall, and CWI utilizing local anesthesia has been introduced as a novel method to overcome the limitations of IV PCA [14]. Several studies have been conducted on CWI after laparoscopic colorectal surgery, and the Procedure-Specific Postoperative Pain Management Working Group has recommended wound infiltration with a long-acting local anesthetic at the end of laparoscopic colorectal surgery for pain management [15, 16]. However, few studies have been con-

ducted on the efficacy of CWI in single-port or reduced-port laparoscopic surgery (RPLS) involving only 1 or 2 incisions. We aimed to investigate the effect of CWI in patients using IV PCA for pain management after RPLS for colorectal cancer.

METHODS

Ethics statement

The Institutional Review Board of Keimyung University Dongsan Hospital approved the retrospective study protocol (No. 2022-08-060). Data were collected and analyzed ethically and the patients' right to privacy was respected. The requirement for informed consent was waived due to the retrospective nature of the study.

Patients

Altogether, 110 patients who underwent RPLS for colorectal cancer between August 2014 and August 2020 were included in this study (Fig. 1). The exclusion criteria were stage IV colorectal cancer according to the American Joint Committee on Cancer (AJCC) Staging Manual, 8th edition; patients who did not receive both CWI and IV PCA; and patients who received CWI alone. The CWI group (n = 25) received both CWI (0.5% ropivacaine infused over 72 hours) and IV PCA (fentanyl citrate), while the control group (n = 52) received IV PCA alone.

Data collection and definitions

We searched a prospectively maintained colorectal database and electronic medical record system for information on demographic characteristics, postoperative pain measurement using the numeric rating scale (NRS), and postoperative outcomes. Age, sex, body mass index (BMI; kg/m^2), sidedness, tumor stage, and American Society of Anesthesiologists (ASA) physical status (PS) classification were included in the demographic information of each patient. Perioperative information included the total operation time; surgical procedure; total incision length; time to sips of water, soft diet, and removal of IV PCA; hospital stay duration; and postoperative nausea and vomiting (PONV). Data regarding utilization of analgesics including opioids and nonsteroidal anti-inflammatory drugs (NSAIDs) and pain intensity measured using NRS on postoperative days (PODs) 0, 1, 2, and 3 were extracted from the electronic medical records. In the present study, RPLS was defined as single plus 1 port laparoscopic surgery. The primary outcome measure was NRS score on PODs 0, 1, and 2. Secondary outcomes included opioid use and CWI-related complications such as surgical site infection (SSI) [17].

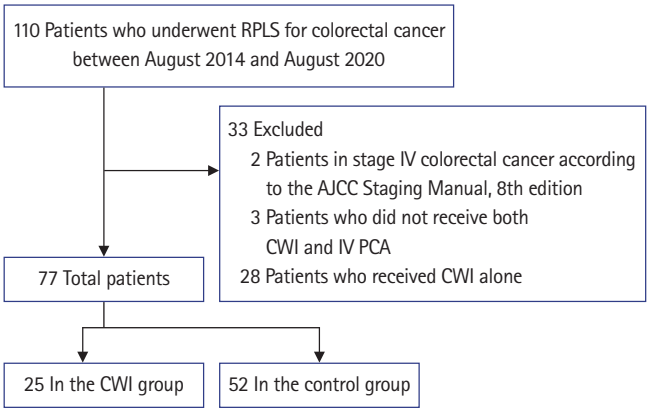


Fig. 1. Flow diagram of the study participants. RPLS, reduced-port laparoscopic surgery; AJCC, American Joint Committee on Cancer; CWI, continuous wound infiltration; IV, intravenous; PCA, patient-controlled analgesia.

Evaluation parameters

On PODs 1 and 2, postoperative wound pain was measured using NRS, with endpoints labeled "no pain" (scale 0) and "worst possible pain" (scale 10). Consumption of analgesics was measured by the number of uses at 24 and 48 hours after the surgery. Vomiting and nausea after surgery were evaluated until discharge. SSI was defined as the presence of clinical signs and symptoms of infection as described by the Centers for Disease Control and Prevention (CDC). Tumor stages were classified using the AJCC Staging Manual, 8th edition.

Surgical procedure

The standard operative procedures including tumor-specific mesorectal excision and complete mesocolic excision with D3 lymphadenectomy were similar in both the groups. A single 30-mm vertical incision was made through the umbilical skin for single-port insertion, and an additional 5- to 12-mm incision was made for an additional port in the right or left lower quadrant, in accordance with the previously reported RPLS technique [18]. The extraction site was created by extending the periumbilical or transumbilical incision for camera insertion.

Anesthetic technique

All patients included in this study were administered IV PCA for postoperative pain control. When major procedures were completed and wound closure began, the IV PCA device (AutoMed 3200, Acemedical) was attached to the patient. The IV PCA solution contained 700 μg fentanyl in 100 mL normal saline. The IV PCA protocol included a 1-mL bolus injection of the IV PCA solution and a 5-minute lockout period without continuous infusion. In both the groups, fentanyl citrate was administered intravenously until the drug was depleted, except when adverse effects

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were observed. Adverse effects included pruritus, PONV, and dyspnea.

The CWI group received ropivacaine infusions using an ON-Q PainBuster device (I-Flow Corp) for 72 hours. Three equal volumes of ropivacaine (0.75%, 20 mL) and normal saline (60 mL) were combined in a 1:1 ratio, diluted, and injected into the CWI device. Through the incision for the additional port, a 17-gauge T-peel introducer and sheath were inserted into the preperitoneal space of the main wound after peritoneal closure. Following removal of the introducer, the catheter was positioned and secured with a 3-0 nylon suture.

Strategy of postoperative pain management

When the patients complained of wound site pain, IV PCA was administered for pain control. If pain persisted, NSAIDs were administered initially, followed by opioid injections. When the patients were pain-free or when the drug was completely administered, IV PCA was discontinued. When the CWI device was exhausted, it was removed.

Statistical analysis

Descriptive statistics were expressed as mean ± standard deviation or number (%). Continuous variables were analyzed using Student t-test, and categorical variables were analyzed using the chi-squared test while comparing the 2 groups. Univariate and multivariate analyses were conducted to determine the factors affecting the pain score on POD 0. Multivariate linear regression analysis was performed for variables with P-values < 0.1 in the univariate analysis. Statistical analysis was conducted using IBM SPSS ver. 26.0 (IBM Corp). Statistical significance was set at $P < 0.05$.

RESULTS

Patient characteristics

The CWI group had a significantly higher mean age (70.6 ± 0.8 years vs. 61.5 ± 8.7 years, $P < 0.001$) and higher proportion of women (68.0% vs. 40.4%, $P = 0.023$) than the control group (Table 1). Left-sided colorectal cancer was significantly more prevalent in the CWI group than in the control group (32.0% vs. 15.4%, $P < 0.001$), and the proportion of patients with ASA PS classes II and III was significantly higher in the CWI group than in the control group ($P = 0.009$). BMI and AJCC stage did not differ significantly between the groups.

Perioperative outcomes

There were no significant differences between the groups in terms of incision length, total operation time, time to sips and soft diet, hospital stay, PONV, or morbidity within 30 days of surgery (Table

Table 1. Patient characteristics

Characteristic	CWI group (n = 25)	Control group (n = 52)	P-value
Age (yr)	70.6 ± 10.8	61.5 ± 8.7	< 0.001
Sex			0.023
Male	8 (32.0)	31 (59.6)	
Female	17 (68.0)	21 (40.4)	
Body mass index (kg/m^2)	24.8 ± 3.2	23.7 ± 3.6	0.788
Sidedness			< 0.001
Right	17 (68.0)	44 (84.6)	
Left	8 (32.0)	8 (15.4)	
Surgical procedure			< 0.001
Right hemicolectomy	17 (68.0)	7 (13.5)	
Anterior resection	5 (20.0)	37 (71.2)	
Low anterior resection	3 (12.0)	6 (11.5)	
Cecectomy	0 (0)	1 (1.9)	
Wedge resection	0 (0)	1 (1.9)	
Tumor stage (AJCC Staging Manual, 8th edition)			0.679
I	10 (40.0)	22 (42.3)	
II	10 (40.0)	16 (30.8)	
III	5 (20.0)	14 (26.9)	
ASA PS classification			0.009
I	3 (12.0)	21 (40.4)	
II	16 (64.0)	28 (53.8)	
III	6 (24.0)	3 (5.8)	

Values are presented as mean ± standard deviation or number (%).
CWI, continuous wound infiltration; AJCC, American Joint Committee on Cancer; ASA, American Society of Anesthesiologists; PS, physical status.

Table 2. Perioperative outcomes

Variable	CWI group (n = 25)	Control group (n = 52)	P-value
Length of incision (cm)	6.5 ± 4.8	5.5 ± 3.0	0.301
Operation time (min)	259.3 ± 58.9	230.2 ± 90.2	0.146
Duration of postoperative hospital stay (day)	10.0 ± 4.5	11.0 ± 10.4	0.323
Time to sips of water (day)	3.5 ± 2.2	4.3 ± 3.1	0.276
Time to soft diet (day)	6.0 ± 2.5	6.8 ± 4.4	0.358
Time to removal of IV PCA (day)	4.4 ± 1.6	3.4 ± 1.0	0.016
Postoperative nausea and vomiting			0.634
No	23 (92.0)	46 (88.5)	
Yes	2 (8.0)	6 (11.5)	
Clavien-Dindo classification			0.442
≥ IIIa	2 (8.0)	2 (3.8)	
< IIIa	23 (92.0)	50 (96.2)	
Presence of morbidity within POD 30			0.334
No	14 (56.0)	35 (67.3)	
Yes	11 (44.0)	17 (32.7)	
Morbidities within POD 30			0.670
Ileus	2 (18.2)	2 (11.8)	
Pseudomembranous colitis	1 (9.1)	1 (5.9)	
Anastomosis leakage	2 (18.2)	1 (5.9)	
Intra-abdominal abscess	0 (0)	1 (5.9)	
Surgical site infection	2 (18.2)	5 (29.4)	
Chyle leakage	0 (0)	3 (17.6)	
Bleeding	2 (18.2)	3 (17.6)	
Voiding difficulty	1 (9.1)	1 (5.9)	
Pneumonia	1 (9.1)	0 (0)	

Values are presented as mean ± standard deviation or number (%).
CWI, continuous wound infiltration; IV, intravenous; PCA, patient-controlled analgesia; POD, postoperative day.

2). Time to removal of IV PCA was significantly longer in the CWI group than in the control group (4.4 ± 1.6 days vs. 3.4 ± 1.0 days, P = 0.016).

Pain intensity assessed using NRS and use of analgesics

The mean NRS score in the CWI group was significantly lower than that in the control group on POD 0 (3.2 ± 0.8 vs. 3.7 ± 0.9, P = 0.042) (Table 3). The NRS scores on PODs 1, 2, and 3 did not differ significantly between the groups (Fig. 2). During the first 24 hours after surgery, there was no significant difference in the total number of analgesics between the groups. However, the CWI group consumed fewer opioids (0.7 ± 0.9 vs. 1.3 ± 1.1, P = 0.018) and more NSAIDs (2.0 ± 1.4 vs. 1.3 ± 1.4, P = 0.046) than the control group (Fig. 3). There was no significant difference in the total number of analgesics, opioids, and NSAIDs between the groups from 24 to 48 hours after the surgery.

Linear regression analysis of NRS score on the operation day

The outcomes of univariate and multivariate linear regression analyses for NRS score on POD 0 are presented in Table 4. The

Table 3. Pain intensity assessed using the numeric rating scale and use of analgesics

Variable	CWI group (n = 25)	Control group (n = 52)	P-value
NRS score			
On POD 0	3.2 ± 0.8	3.7 ± 0.9	0.042
On POD 1	2.8 ± 0.9	2.5 ± 0.8	0.188
On POD 2	2.4 ± 0.6	2.5 ± 0.8	0.750
On POD 3	2.4 ± 0.6	2.4 ± 1.1	0.834
Total analgesics			
< 24 hr	2.6 ± 1.1	2.6 ± 1.3	0.935
24–48 hr	1.0 ± 1.3	1.0 ± 1.1	> 0.999
Usage of opioids			
< 24 hr	0.7 ± 0.9	1.3 ± 1.1	0.018
24–48 hr	0.3 ± 0.7	0.2 ± 0.6	0.334
Usage of NSAIDs			
< 24 hr	2.0 ± 1.4	1.3 ± 1.4	0.046
24–48 hr	0.7 ± 0.9	0.8 ± 1.0	0.548

Values are presented as mean ± standard deviation.
CWI, continuous wound infiltration; NRS, numeric rating scale; POD, postoperative day; NSAID, nonsteroidal anti-inflammatory drug.

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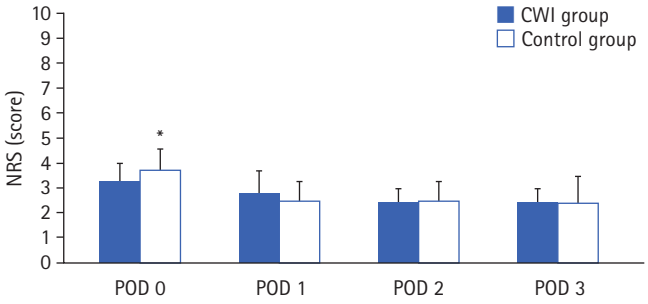

Fig. 2. Mean changes in the numeric rating scale (NRS) scores (range, 0–10) for pain intensity among the continuous wound infiltration (CWI) group and the control group. Values are presented as mean ± standard deviation. POD, postoperative day. *P < 0.05.

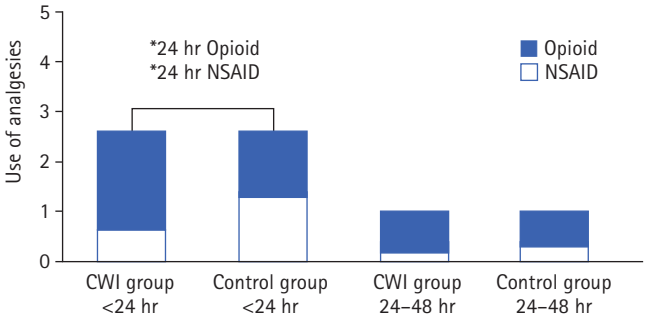

Fig. 3. Analgesic consumption among the continuous wound infiltration (CWI) group and the control group. Values are presented as mean ± standard deviation. NSAID, nonsteroidal anti-inflammatory drug. *P < 0.05.

Table 4. Univariate and multivariate analysis for mean numeric rating scale score on postoperative day 0

Variable	Univariate		Multivariate	
	β (95% CI)	P-value	β (95% CI)	P-value
Anesthetic technique				
IV PCA	1 (Reference)	-	-	-
CWI + IV PCA	−0.483 (−0.947 to −0.019)	0.042	−0.626 (−1.082 to −0.170)	0.008
Age (yr)	−0.012 (−0.035 to 0.010)	0.271	-	-
Sex			-	-
Male	1 (Reference)	-		
Female	−0.185 (−0.637 to 0.267)	0.416		
Body mass index (kg/m^2)	0.070 (−0.001 to 0.141)	0.053	0.092 (0.023 to 0.162)	0.010
Sidedness			-	-
Right	1 (Reference)	-		
Left	0.152 (−0.327 to 0.631)	0.528		
Tumor stage (AJCC Staging Manual, 8th edition)	−0.119 (−0.406 to 0.168)	0.411	-	-
ASA physical status	−0.059 (−0.431 to 0.312)	0.750	-	-
Operation time (min)	0.000 (−0.003 to 0.004)	0.790	-	-
Length of incision (cm)	−0.022 (−0.103 to 0.058)	0.582	-	-

CI, confidence interval; IV, intravenous; PCA, patient-controlled analgesia; CWI, continuous wound infiltration; AJCC, American Joint Committee on Cancer; ASA, American Society of Anesthesiologists.

NRS score on POD 0 showed no correlation with age, sex, surgical procedure, tumor stage, ASA PS classification, operation time, and incision length. Use of CWI (coefficient β, −0.483; 95% confidence interval [CI], −0.947 to −0.019; P = 0.042) was significantly associated with the NRS score on POD 0. BMI (coefficient β, 0.070; 95% CI, −0.001 to 0.141; P = 0.053) showed a tendency to be correlated with the NRS score on POD 0.

DISCUSSION

To the best of our knowledge, this is the first study discussing the effect of CWI on analgesia and clinical outcomes in RPLS using only 2 ports, a single-port insertion and an additional port. We compared the analgesic efficacy of CWI and IV PCA with IV PCA alone in patients who underwent RPLS for colorectal cancer. Within 24 hours, the CWI group (CWI and IV PCA) required significantly fewer opioids and had a significantly lower mean NRS score than the control group (IV PCA alone). Since the time to IV PCA withdrawal was longer in the CWI group, the cumulative IV PCA usage was estimated to be lower. Moreover, method of pain control was a significant independent risk factor for NRS score on POD 0 in the univariate and multivariate analyses. These findings indicate that CWI is an effective component of multimodal strategy for pain control following RPLS in colorectal cancer.

Previous studies have demonstrated the analgesic effect of CWI in colorectal surgery, and local anesthetic infusion was associated with a significant reduction in postoperative pain [19, 20]. In par-

ticular, we believe that the effect of CWI could be amplified during procedures involving a single incision such as caesarean section or single-port surgery. In the present study, all patients underwent single-port laparoscopic surgery with an additional port (RPLS), and the CWI group had significantly lower mean NRS score on POD 0 than the control group. Ropivacaine was continuously infiltrated into the 3 to 5 cm transumbilical incision that caused the most pain during the immediate postoperative period. Hence, we believe that CWI contributed to an effective analgesic effect when combined with IV PCA.

Recent guidelines for enhanced recovery following colorectal surgery recommend multimodal analgesia including regional analgesia or local anesthetic techniques to avoid or minimize the use of opioids and their side effects [21]. CWI is one of the multimodal forms of analgesia, and its role in laparoscopic colorectal surgery is still being studied. However, evidence regarding its role is still insufficient [22–24]. Previous research has demonstrated that CWI decreases opioid consumption and improves postoperative recovery in patients with colorectal disease [20, 25]. In the present study, the CWI group required significantly fewer opioids than the control group within 24 hours after surgery. In addition, time to removal of IV PCA was significantly longer in the CWI group than in the control group. This difference can be attributed to patients pressing the IV PCA button less frequently. Although the exact amount of IV PCA administered is unknown, these facts may suggest that less IV PCA was administered to patients in the CWI group. Even in institutions with no strict implementation of the ERAS protocol for pain management following surgery for colorectal cancer, we believe that CWI would be a significant component of multimodal analgesia.

As CWI requires catheter insertion and travels around the inferior epigastric vessels, surgeons may be concerned about exacerbation of postoperative complications such as SSI or hematoma. Additionally, most of the elective colorectal surgeries are cleancontaminated. Nevertheless, prior research on the association between CWI and SSI has shown that the wound catheter used in CWI does not increase the risk of SSI [15, 26]. In the present study, there was no significant difference in the incidence of SSI between the groups, and none of the significant wound complications were associated with a hematoma. We believe that CWI does not substantially increase SSI, and it is a safe and feasible procedure.

PONV is a common and distressing complication of surgery, and prolonged postoperative ileus significantly contributes to patient discomfort, delayed discharge, and increased costs. Routine use of opioid analgesics for perioperative pain management is a major contributor to PONV. The ERAS Society recommends the use of multimodal analgesia techniques to limit the administration of opioids [21, 27]. Researchers would expect CWI to decrease the incidence of PONV and postoperative ileus if it reduces pain and opioid consumption. Kong et al. [28] reported that CWI is associated with fewer adverse effects than IV PCA, particularly with respect to PONV. On the other hand, Lee at al. [23] demonstrated that the use of CWI had no significant effect on the reduction of PONV. In the present study, there was no significant difference between the groups in terms of PONV and postoperative ileus. We believe that the effect of CWI on PONV and postoperative ileus was insignificant due to the routine use of IV PCA in this study, despite the fact that CWI reduced opioid consumption at 24 hours after the operation.

Postoperative pain following laparoscopic surgery for colorectal cancer is influenced by incision length, port placement, psychosocial factors, preoperative pain, and age [29]. Generally, postoperative pain is most intense on the day of surgery and the 1st day following surgery [30]. In the present study, postoperative anesthetic technique and BMI were significantly associated with the NRS score on POD 0 in the multivariate linear regression analysis. Generally, obese patients have a thick and short mesentery, require a larger incision and traction, and experience more intense pain. We believe that more efforts should be made to alleviate pain in obese patients using various types of multimodal anesthesia including CWI.

This study has several limitations. It was a retrospective study with small sample size. There were significant differences in patient characteristics between the groups, and the possibility of selection bias could not be excluded. Particularly, a higher proportion of left-sided tumors in the CWI group might have had an effect on the outcome, since it was a predictor of increased opioid use in the multivariate analysis. We used the NRS scores from the electronic medical records, which is a patient-reported subjective measure to evaluate the degree of pain. Additionally, there were no records regarding the amount of IV PCA used in this retrospective study. Further prospective and extensive research comparing CWI and IV PCA would help generalize the effect of CWI on pain control after RPLS.

In conclusion, CWI with ropivacaine and IV PCA was more effective than IV PCA alone in controlling postoperative pain within 24 hours of surgery, and opioid use could be reduced further.

ARTICLE INFORMATION

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Author contributions
Conceptualization: all authors; Data curation: HDC; Formal analysis: HDC; Investigation: all authors; Methodology: all authors; Project administration: HDC; Visualization: all authors; Writing–original draft: all authors; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Additional information
This study was presented at the International Colorectal Research Summit (iCRS) on September 3, 2022 in Seoul, Korea.

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