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석사학위 논문

Analgesic effect of continuous wound infusion combined with intravenous patient-controlled analgesia for thoracic surgery - A retrospective study

조선대학교 대학원

의 학 과

장 보 현

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이 논문을 의학석사학위 신청 논문으로 제출함

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장 보 현

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ABSTRACT

흉부 수술에서 정맥 자가조절 진통법과 지속적 상처 주입 병합 요법의 수술 후 진통효과 – 후향적 연구

장 보 현
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배경 및 목적: 다공 카테터를 사용하여 국소마취제를 지속적으로 상처 부위에 주입하는 진통법(지속적 상처 주입 진통, continuous wound infusion analgesia; CWA)은 다중 통증 조절을 위한 방법 중 하나이다. CWA는 다양한 수술 후 통증 조절을 위해 안전하고 효과적인 방법으로 사용되고 있다. 흉부 수술을 받은 환자에서 통증 조절을 위해 CWA의 단독 또는 다른 진통법들과 병합 요법의 효과를 비교한 여러 연구들이 있지만, CWA의 진통 효과는 여전히 명확하지 않다. 본 연구의 목적은 전자의무기록의 검토를 통해 개흉술과 개방 정복술 및 내고정술(open reduction and internal fixation; ORIF)을 받은 환자의 수술 후 통증 조절에서 정맥 자가조절 진통법(patient-controlled analgesia; PCA)단독보다 CWA와의 병합 요법이 더 효과적인지와 수술 후 3, 6개월 후에 수술 후 통증 증후군(postsurgical pain syndrome; PSPS)의 발생에 대한 영향을 분석하기 위한 것이었다.

대상 및 방법: 본 연구는 2010년 1월 1일부터 2020년 11월 30일까지 흉부 수술 후 정맥 PCA 단독(PCA 그룹) 또는 정맥 PCA 및 CWA의 병합 요법(PCA-CWA 그룹)을 받은 1658명의 환자를 등록했다. 본 연구는 20세에서 75세 사이의 개흉술과 ORIF수술을 받은 환자들을 포함했다. 펜타닐을 사용하지 않은 정맥 PCA, 미국마취과학회 신체분류등급 IV과 V, 10건 미만의 수술은 연구의 분석에서 제외하였다. 연구 대상자 등록에 충족하는 총 481명의 환자를 등록하여 PCA 그룹과 PCA-CWA 그룹 간의 수술 후 통증 조절 효과를 비교하였다. 연령, 성별, 체질량 지수, 수술명, 마취 기간, 정맥 PCA에 사용한

펜타닐 선량, 보조 진통제 종류 및 수술 후 0일 통증 숫자 척도 (numeric rating score; NRS)와 관련하여 성향 점수 매칭(propensity score matching; PSM)을 사용하여 1:1 비율과 0.1 일치 허용 오차로 각 그룹 당 83명의 환자를 최종 선정했다. 일차 평가 변수는 수술 후 0, 1, 2, 3, 4, 5일의 NRS이며, 이차 평가 변수는 수술 후 3개월과 6개월 동안 통증 지속 여부에 대한 것이었다.

결과: PSM 이후, NRS는 수술 후 0일을 제외한 전체 기간 동안 PCA-CWA 그룹에서 PCA 그룹보다 낮았다($p < 0.001$). 수술 후 진정의 발생률은 PCA-CWA 그룹(1.2%)이 PCA 그룹(9.6%)보다 낮았으며($p = 0.034$), 다른 합병증은 유의한 차이가 없었다. 수술 후 3개월 및 6개월 후 지속적인 통증인 PSPS는 유의한 차이가 없었다($p = 1.000$).

결론: 흉부 수술 후 통증 조절을 위해 정맥 PCA를 받는 환자에서 CWA의 추가 병합 요법은 합병증 증가가 없는 효과적인 진통방법이다.

Ⅰ. INTRODUCTION

Patients after thoracic surgeries frequently complain of postoperative pain, which induces a poor respiratory effort and impaired pulmonary function, resulting in atelectasis, airway obstruction, shunting, and hypoxemia [1]. These postoperative complications are related to a longer hospital stay due to an increased cost of expensive treatment. Furthermore., adequate postoperative analgesia is crucial for the prevention of chronic post-surgical pain syndrome (PSPS), because the incidence of PSPS is as high as 80% at 3 months, 75% at 6 months [1]. Therefore, controlling pain effectively with an ideal analgesic technique is paramount to prevent postoperative complications and early mobilization.

Various modalities for postoperative analgesia after thoracic surgeries have been used, but there is no internationally accepted policy on the best strategy. The easiest and most common method is intravenous patient-controlled analgesia (PCA) using opioids [1]. However, it is difficult to achieve a balance between effective analgesia and undesirable effects such as respiratory depression, nausea, vomiting, ileus, and urinary retention [1, 2]. So, thoracic epidural analgesia has been considered as the gold standard analgesic modality with superior analgesia, less opioid requirement, and highest patient satisfaction [1, 3]. However, it is associated with many risks such as dural puncture, spinal cord damage, epidural hematoma, infection and abscess, hypotension, and urinary retention [1, 3]. In other ways, inter-pleural and extra-pleural analgesia (paravertebral, intercostal block) have been reported as valid alternatives to epidural analgesia [1, 3]. However, there is a high risk of systemic toxicity of local anesthetics, even though these modalities are easier and have no risk of opioid-related complications compared with systemic opioid and epidural analgesia [4].

The continuous wound infusion of local anesthetics (continuous wound infusion

analgesia, CWA) through a multi-perforated catheter is one of the loco-regional anesthetic modality for multimodal analgesia management. The CWA has been used to control postoperative pain as a safe and effective alternative modalit in various surgeries with less pain and rescue opioid requirement [5-11]. However, the analgesic effect of CWA is still unclear in patients who underwent thoracic surgeries, even though several studies are the postoperative analgesic effects of CWA alone or in combination with other postoperative analgesic modalities [2, 12-15].

This study hypothesized that the combined modality of Intravenous PCA and CWA would show more effective postoperative analgesia and fewer postoperative complications than PCA alone in patients undergoing thoracic surgeries. The aim of this study was to analyze whether the combination modality of intravenous PCA and CWA was more effective to control postoperative pain than PCA alone in patients who underwent thoracotomy and open reduction/internal fixation (ORIF) and to prevent PSPS after postoperative 3 and 6 months through a review of electronic medical records.

Ⅱ. MATERIALS and METHODS

1. Study Design and Ethical Statement

The Institutional Review Board (IRB) of Chosun University Hospital approved this retrospective study based on an electronic medical record review (CHOSUN 2020-12-048) on December 17, 2020. The IRB also waived the need to obtain written informed consent from patients because the patients' identifying information was anonymized before the analysis, and this study did not pose more than minimal risk to subjects. This study was conducted according to the Declaration of Helsinki of 1964 and all its subsequent revisions.

2. Selection of Study Population

This study enrolled 1658 patients who received postoperative intravenous patient-controlled analgesia (PCA) alone (PCA group) or combined modality of intravenous PCA and CWA (PCA-CWA group) after thoracic surgery and from January 1, 2010, to November 30, 2020 (Fig. 1). This study included patients, between 20 and 75 years of age, with thoracotomy and ORIF, because continous wound infusion analgesia was only applied for postoperative analgesia in patients who underwent these operations. This study excluded patients who underwent operations with less than 10 incidences, receiving intravenous PCA without fentanyl, and with the American Society of Anesthesiologists physical status (ASA-PS) classification of IV and V.

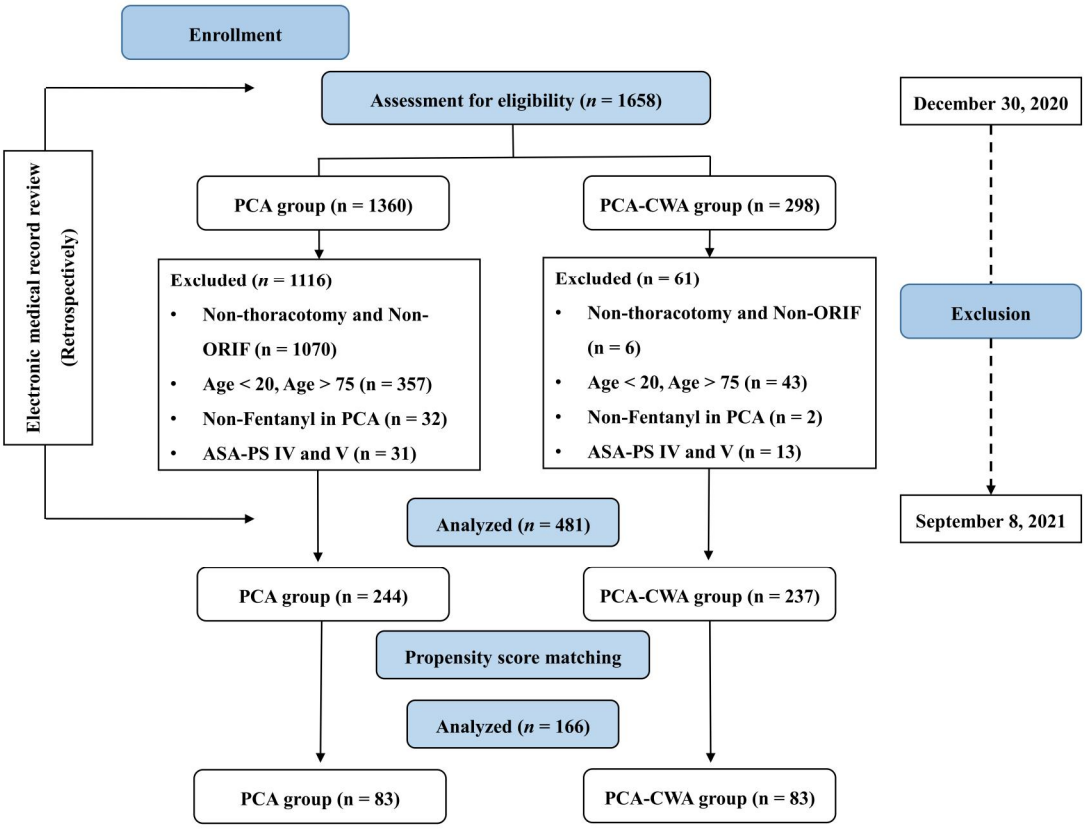

Fig. 1. Flowchart of this study. ASA-PS, American Society of Anesthesiologists - Physical Status; ORIF, open reduction and internal fixation; PCA, intravenous patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia.

3. Interventions

3.1. PCA

Every application of PCA was performed in accordance with the hospital protocol for postoperative pain management. On the day before surgery, anesthesiologists explained the usage of the PCA devices to all patients, who

agreed to use intravenous PCA for postoperative analgesia. For PCA devices with bolus dosing, the patients were instructed to push the “demand” button of each device whenever they experienced pain of >4 points on the numeric rating scale (NRS: 0 = no pain, 10 = worst pain).

The attending anesthesiologists operated each PCA device at the end of the surgery. A total PCA volume of 100 mL, consisting of normal saline, fentanyl, adjuvant analgesics (nefopam, or ketorolac), and adjuvant antiemetic (ramosetron), was used. PCA devices were set with a background infusion rate of 2 mL/h, bolus volume of 2 mL, and lockout interval of 30 min. The attending anesthesiologist determined the drug dosage and devices for PCA according to their judgment, considering the patient’s safety.

In patients receiving PCA, rescue analgesics and antiemetics were administrated only on demand and not routinely. When patients experienced pain with NRS score > 4, the patient pushed the “demand” button for administration of a preset bolus volume. When patients required additional rescue analgesics within the lockout interval, physicians or nurses injected opioids, nonsteroidal anti-inflammatory drugs, or other analgesics. Postoperative nausea and vomiting (PONV) with NRS > 4 was controlled by intravenous injection of 10 mg metoclopramide or 0.3 mg ramosetron.

The nurses, who were trained in the hospital to assess patients using the NRS, recorded the scores for postoperative pain and PONV, the rescue analgesics and antiemetics administered, and any adverse events in electronic medical records. Decisions to stop PCA were made by the anesthesiologists on the basis of the severity of patients’ signs and symptoms.

3.2. Continuous wound infusion analgesia

continous wound infusion analgesia was performed with placement of a multi-perforated wound catheter (Painfusor, Baxter, Maurepas, France) during

wound closure, which the surgeon inserted from the lower end of the incision. The catheter was sutured as close as possible to the intercostal nerve, and the deep surface of the serratus muscle along its full length [13]. After 10 mL (0.25% ropivacaine) at the end of the operation, the catheter was connected to a continuously infusing container (Infusor LV, Baxter, Auckland, New Zealand), which allowed a 2.5 mg/mL of ropivacaine delivery at a constant flow rate of at 2 mL/h for 5 days.

4. Outcomes

This study assessed age, sex, weight, body mass index (BMI), American Society of Anesthesiologists - Physical Status (ASA-PS), diabetic mellitus, hypertension, risk factors of PONV (smoking, motion sickness, and previous PONV), diagnosis, operation name, operation duration, anesthesia duration, and day of hospital stay.

PCA regimens (types and doses of opioids, adjuvant analgesics, and adjuvant antiemetics), type of PCA device, and operating days of each analgesia were investigated. Doses of adjuvant analgesics were converted to fentanyl-equivalent doses (μg) considering the ratios of ketorolac (mg) to fentanyl (30:100), and nefopam (mg) to fentanyl (20:100) [16]. The NRS was investigated at postoperative 0, 1, 2, 3, 4, and 5 days. Requirement of rescue analgesics and rescue antiemetics were investigated at postoperative 0, 1, 2, 3, 4, and 5 days. Meanwhile, postoperative complications were investigated during the postoperative 5 days. The presence of persistent pain was assessed at postoperative 3 and 6 months.

This study investigated the postoperative incidences of PONV, rescue analgesics and antiemetics requirement, hypotension, dizziness, headache, pruritus, sedation, urinary retention, motor weakness, respiratory difficulty, PCA stop, and pain persistence after postoperative 3 and 6 months.

5. Analysis

The primary endpoint was NRS at postoperative 0, 1, 2, 3, 4, and 5 days. The secondary endpoint was the presence of persistent pain at postoperative 3 months.

All statistical analyses were performed with SPSS Statistics for Windows, ver. 26.0 (IBM Corp., Armonk, NY, USA). All data were presented as means (95% confidence intervals [CI]), or numbers (percentage) of patients (npatients [%]).

Patients who received intravenous PCA with continous wound infusion analgesia were matched to those who received intravenous PCA alone (control group) at a 1:1 ratio and 0.1 match tolerance using propensity score matching (PSM). This matching was used to obtain groups of patients corresponding to the 2 analgesic modalities that were balanced about age, sex, body mass index, operation name, anesthesia duration, the dose of fentanyl used for intravenous PCA, kinds of adjuvant analgesics, and NRS at postoperative 0 days.

Continuous variables were tested for normality using the Shapiro-Wilk test. Variables with non-skewed distributions were reported as means (95% confidence intervals [CI]) and differences evaluated using the unpaired Student's t-test. For the analysis of time-interval data that passed Mauchly's sphericity test, the author used repeated measures ANOVA; for data that did not pass Mauchly's sphericity test, Wilk's lambda multivariate analysis of variance was used. To compare three groups in each time interval, a one-way ANOVA test was used. Nominal variables were analyzed with the $\chi 2$ test or Fisher’s exact test. Statistical significance was set at $p < 0.05$.

Ⅲ. RESULTS

This study excluded 1177 of enrolled 1658 patients into either PCA or PCA-CWA groups for the following reasons (Fig.1); operations except for thoracotomy and ORIF (1070 of PCA group and 6 of PCA-CWA group), patients under the age of 20 and over 75 years old (357 of PCA group and 43 of PCA-CWA group), opioids except fentanyl used for PCA (32 of PCA group and 2 of PCA-CWA group), and ASA-PS IV and V (31 of PCA group and 13 of PCA-CWA group). This study finally enrolled a total of 481 patients to compare the postoperative analgesic effect between the PCA group and the PCA-CWA group. The author selected 83 patients for each group for analysis after propensity score matching.

1. Demographic Data

Significant differences in age ($p = 0.008$), ASA-PS ($p = 0.001$), and operation ($p < 0.001$) were observed before performing propensity score matching (Table 1). After propensity score matching, these differences were not significant (Table 2). There were no patients with motion sickness and previous PONV in both groups.

Table 1. Demographic data before propensity score matching

	PCA group (n = 244)	PCA-CWA group (n = 237)	p Value
Age (y)	57.2 (55.7 − 58.8)	60.1 (58.7 − 61.5)	0.008 *
Sex (male/female)	188/ 56 (77/ 23)	180/ 57 (75.9/ 24.1)	0.776
Weight (kg)	64.1 (62.6 − 65.5)	63.9 (62.4 − 65.4)	0.866
Height (cm)	165.4 (164.3 − 166.6)	165.4 (164.3 − 166.5)	0.971
BMI (kg/m^2)	23.3 (22.9 − 23.8)	23.3 (22.8 − 23.7)	0.868
ASA-PS (Ⅰ/Ⅱ/Ⅲ)	49/ 142/ 53	25/ 133/ 79	0.001 *

	(20.1/ 58.2/ 21.7)	(10.5/ 56.1/ 33.3)	
Hypertension (no/yes)	177/ 67 (72.5/ 27.5)	153/ 84 (64.6/ 35.4)	0.059
Diabetic mellitus (no/yes)	199/ 45 (81.6/ 18.4)	183/ 54 (77.2/ 22.8)	0.239
Smoking (no/yes)	166/ 78 (68/ 32)	168/ 69 (70.9/ 29.1)	0.497
Anesthesia duration (min)	174.6 (165.2 − 184.1)	183 (174.2 − 191.8)	0.202
Operation duration (min)	149.5 (140.3 − 158.6)	157.7 (149 − 166.5)	0.198
Hospital stay (d)	19.5 (17.9 − 21.1)	21.7 (18.9 − 24.5)	0.172
Operations (ORIF/Thoracotomy)	119/ 125 (48.8/ 51.2)	64/ 173 (27/ 73)	<0.001 *

Values are expressed as mean (95% confidence interval) or number (percentage) of patients. ASA-PS, American Society of Anesthesiologists -physical status; BMI, body mass index; CWA, continuous wound infusion analgesia; ORIF, open reduction and internal fixation; PCA: patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

Table 2. Demographic data after propensity score matching

	PCA group (n = 83)	PCA-CWA group (n = 83)	p Value
Age (y)	56.9 (54.1 − 59.7)	58.1 (55.7 − 60.6)	0.514
Sex (male/female)	59/ 24 (71.1/ 28.9)	59/ 24 (71.1/ 28.9)	1.000
Weight (kg)	63 (60.2 − 65.8)	64.6 (62 − 67.3)	0.406
Height (cm)	164.3 (161.8 − 166.7)	166.1 (164.2 − 167.9)	0.258
BMI (kg/m^2)	23.2 (22.4 − 24.1)	23.3 (22.6 − 24.1)	0.804
ASA-PS (Ⅰ/Ⅱ/Ⅲ)	8/ 53/ 22 (9.6/ 63.9/ 26.5)	14/ 43/ 26 (16.9/ 51.8/ 31.3)	0.222
Hypertension (no/yes)	57/ 26 (68.7/ 31.3)	56/ 27 (67.5/ 32.5)	0.868
Diabetic mellitus (no/yes)	67/ 16 (80.7/ 19.3)	67/ 16 (80.7/ 19.3)	1.000
Smoking (no/yes)	57/ 26 (68.7/ 31.3)	61/ 22 (73.5/ 26.5)	0.493
Anesthesia duration (min)	181.5 (163.8 − 199.3)	183.2 (170.1 − 196.3)	0.879
Operation duration (min)	160.3 (142.8 − 177.9)	156.6 (143.5 − 169.6)	0.734

Hospital stay (d)	21.8 (18.1 − 25.5)	20.3 (17 − 23.6)	0.547
Operations (ORIF/Thoracotomy)	44/ 39 (53/ 47)	37/ 46 (44.6/ 55.4)	0.277

Values are expressed as mean (95% confidence interval) or number (percentage) of patients. ASA-PS, American Society of Anesthesiologists -physical status; BMI, body mass index; CWA, continuous wound infusion analgesia; ORIF, open reduction and internal fixation; PCA: patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

2. Postoperative Analgesia Modalities

There were significant differences in fentanyl doses used for PCA ($p <0.001$), kinds of adjuvant analgesics ($p < 0.001$), and adjuvant antiemetic doses ($p < 0.001$) before performing propensity score matching (Table 3). Fentanyl and ramosetron were used for PCA in both groups. Fentanyl dose for PCA was higher in the PCA group than in the PCA-CWA group ($p <0.001$) (Table 3). Nefopam was more used as adjuvant analgesics in the PCA-CWA group than PCA group ($p <0.001$) (Table 3). Doses of adjuvant analgesics converted to fentanyl-equivalent doses were higher in the PCA-CWA group than PCA group ($p <0.001$) (Table 3). Ramosetron dose for prevention of PONV during PCA was higher PCA-CWA group than PCA group ($p <0.001$) (Table 3). After propensity score matching, these differences were not significant except for ramosetron dose ($p <0.001$) (Table 4). Ramosetron dose for prevention of PONV during PCA was higher PCA-CWA group than PCA group ($p <0.001$) (Table 4).

Table 3. Postoperative analgesia modalities before propensity score matching

	PCA group (n = 244)	PCA-CWA group (n = 237)	p Value
Fentanyl used for PCA	244 (100)	237 (100)	1.000
Doses (μg)	1107 (1075.2 − 1138.8)	944.7 (922 − 967.5)	<0.001 *

Adjuvant analgesics (nefopam/ketorolac/none)	107/ 93/ 44 (43.9/ 38.1/ 18)	228/ 4/ 5 (96.2/ 1.7/ 2.1)	<0.001 *
Doses (μg)	526.6 (490.5 − 562.8)	705.1 (685.3 − 724.8)	<0.001 *
Adjuvant antiemetics (ramosetron)	244 (100)	237 (100)	1.000
Doses (mg)	0.9 (0.9 − 0.9)	1.2 (1.2 − 1.2)	<0.001 *

Values are expressed as mean (95% confidence interval) or number (percentage) of patients. CWA, continuous wound infusion analgesia; PCA, patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

Table 4. Postoperative analgesia modalities after propensity score matching

	PCA group (n = 83)	PCA-CWA group (n = 83)	p Value
Fentanyl used for PCA	83 (100)	83 (100)	1.000
Doses (μg)	986.7 (935.2 − 1038.3)	974.7 (936.7 − 1012.6)	0.709
Adjuvant analgesics (nefopam/ketorolac/none)	71/ 2/ 10 (85.5/ 2.4/ 12)	74/ 4/ 5 (89.2/ 4.8/ 6)	0.302
Doses (μg) †	643.4 (584.4 − 702.4)	691.6 (22.3 − 647.2)	0.196
Adjuvant antiemetics (ramosetron)	83 (100)	83 (100)	1.000
Doses (mg)	1 (1 − 1.1)	1.2 (1.2 − 1.2)	<0.001 *

Values are expressed as mean (95% confidence interval) or number (percentage) of patients. CWA, continuous wound infusion analgesia; PCA, patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance. †: Doses of fentanyl equivalents (μg) converted from doses of adjuvant analgesics with ratios of ketorolac (mg) to fentanyl (30:100), ratio of nefopam (mg) to fentanyl (1:5) [16].

3. Postoperative Analgesic effect

NRSs were lower in the PCA-CWA group than the PCA group during entire

postoperative periods, before performing propensity score matching ($p < 0.001$, Fig.2). After propensity score matching, NRSs were lower in the PCA-CWA group than the PCA group during entire postoperative periods except for NRS at postoperative 0 days (POD0) ($p < 0.001$, Fig.3).

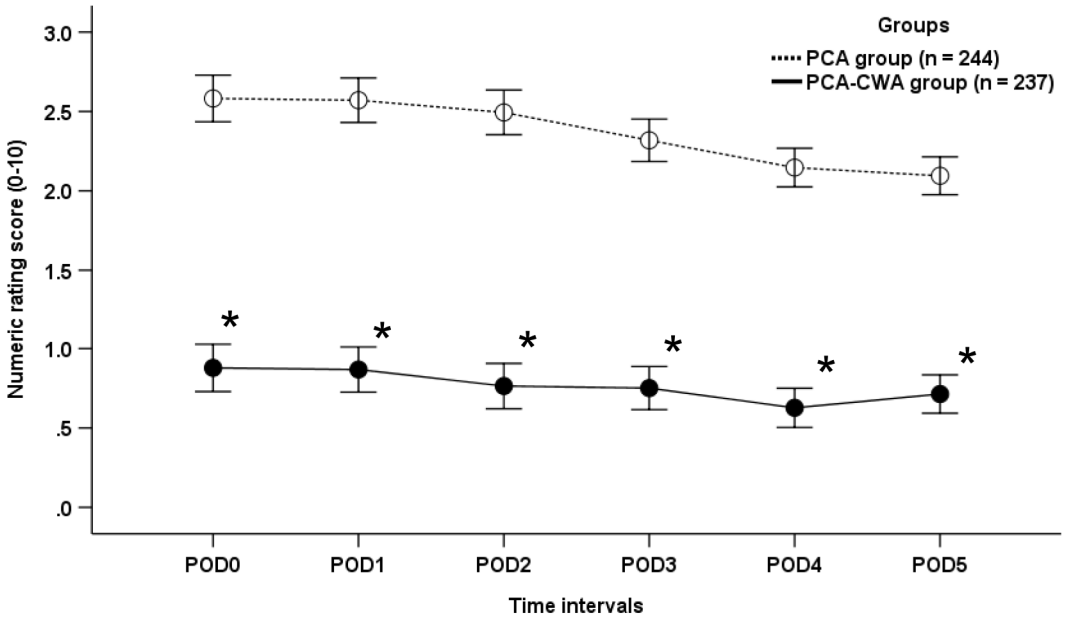

Fig. 2. Numeric rating score during postoperative 5 days, before propensity score matching. POD, postoperative day; POD0, day of surgery; POD1, postoperative 1 day; POD2, postoperative 2 days; POD3, postoperative 3 days; POD4, postoperative 4 days; POD5, postoperative 5 days. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia.

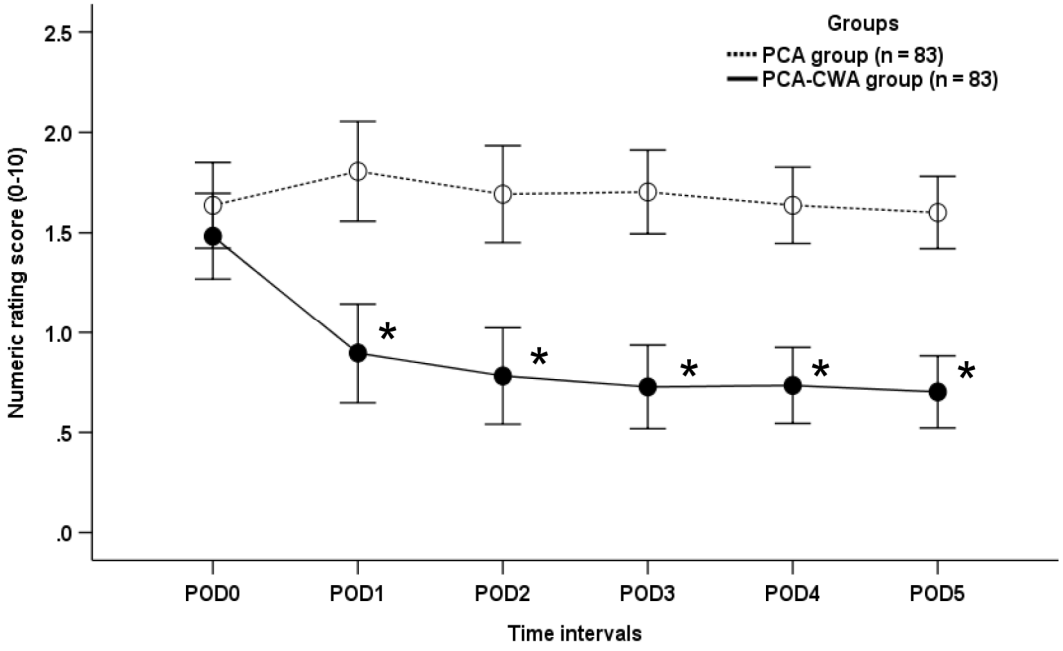

Fig. 3. Numeric rating score during postoperative 5 days, after propensity score matching. POD, postoperative day; POD0, day of surgery; POD1, postoperative 1 day; POD2, postoperative 2 days; POD3, postoperative 3 days; POD4, postoperative 4 days; POD5, postoperative 5 days. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

4. Postoperative Outcomes

There were significant differences in rescue analgesic requirement, sedation, and urinary retention before performing propensity score matching (Table 5). Incidences of rescue analgesic requirement and urinary retention were higher in the PCA-CWA group (55.7% and 28.7%) than in the PCA group (46.7% and 19.3%). Incidence of sedation was lower in the PCA-CWA group (0.8%) than in the PCA group (11.5%). After propensity score matching, these differences were not significant except for the incidence of sedation ($p = 0.034$) (Table 6). Incidence of sedation was lower in the PCA-CWA group (1.2%) than in the PCA

group (9.6%). There was no significant difference in postsurgical pain syndrome, which was persistent pain after postoperative 3 and 6 months (p = 1.000, Tables 5 and 6).

Table 5. Postoperative outcomes before propensity score matching

	PCA group (n = 244)	PCA-CWA group (n = 237)	p Value
PONV (no/yes)	229/ 15 (93.9/ 6.1)	227/ 10 (95.8/ 4.2)	0.341
Rescue analgesics (no/yes)	130/ 114 (53.3/ 46.7)	105/ 132 (44.3/ 55.7)	0.049 *
Rescue antiemetics (no/yes)	234/ 10 (95.9/ 4.1)	225/ 12 (94.9/ 5.1)	0.613
Hypotension (no/yes)	232/ 12 (95.1/ 4.9)	233/ 4 (98.3/ 1.7)	0.072
Dizziness (no/yes)	235/ 9 (96.3/ 3.7)	233/ 4 (98.3/ 1.7)	0.261
Headache (no/yes)	242/ 2 (99.2/ 0.8)	237/ 0 (100/ 0)	0.499
Pruritus (no/yes)	241/ 3 (98.8/ 1.2)	235/ 2 (99.2/ 0.8)	1.000
Sedation (no/yes)	216/ 28 (88.5/ 11.5)	235/ 2 (99.2/ 0.8)	<0.001 *
Urinary retention (no/yes)	197/ 47 (80.7/ 19.3)	169/ 68 (71.3/ 28.7)	0.015 *
Motor weakness (no/yes)	244/ 0 (100/ 0)	236/ 1 (99.6/ 0.4)	0.493
Respiratory difficulty (no/yes)	237/ 7 (97.1/ 2.9)	232/ 5 (97.9/ 2.1)	0.772
PCA stop (no/yes)	235/ 9 (96.3/ 3.7)	228/ 9 (96.2/ 3.8)	0.950
Persistent pain after postoperative 3 months (no/yes)	244/ 0 (100/ 0)	235/ 2 (99.2/ 0.8)	0.242
Persistent pain after postoperative 6 months (no/yes)	244/ 0 (100/ 0)	235/ 2 (99.2/ 0.8)	0.242

Values are expressed as number (percentage) of patients. CWA, continuous wound infusion analgesia; PCA: patient-controlled analgesia; PONV, postoperative nausea and vomiting. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

Table 6. Postoperative outcomes after propensity score matching

	PCA group (n = 83)	PCA-CWA group (n = 83)	p Value
PONV (no/yes)	79/ 4 (95.2/ 4.8)	81/ 2 (98.8/ 1.2)	0.682
Rescue analgesics (no/yes)	47/ 36 (56.6/ 43.4)	45/ 38 (54.2/ 45.8)	0.755
Rescue antiemetics (no/yes)	81/ 2 (97.6/ 2.4)	79/ 4 (95.2/ 4.8)	0.682
Hypotension (no/yes)	81/ 2 (97.6/ 2.4)	82/ 1 (98.8/ 1.2)	1.000
Dizziness (no/yes)	82/ 1 (98.8/ 1.2)	83/ 0 (100/ 0)	1.000
Headache (no/yes)	83/ 0 (100/ 0)	83/ 0 (100/ 0)	1.000
Pruritus (no/yes)	82/ 1 (98.8/ 1.2)	83/ 0 (100/ 0)	1.000
Sedation (no/yes)	75/ 8 (90.4/ 9.6)	82/ 1 (98.8/ 1.2)	0.034 *
Urinary retention (no/yes)	65/ 18 (78.3/ 21.7)	58/ 25 (69.9/ 30.1)	0.215
Motor weakness (no/yes)	83/ 0 (100/ 0)	83/ 0 (100/ 0)	1.000
Respiratory difficulty (no/yes)	77/ 6 (92.8/ 7.2)	82/ 1 (98.8/ 1.2)	0.117
PCA stop (no/yes)	80/ 3 (96.4/ 3.6)	78/ 5 (94/ 6)	0.720
Persistent pain after postoperative 3 months (no/yes)	83/ 0 (100/ 0)	82/ 1 (98.8/ 1.2)	1.000
Persistent pain after postoperative 6 months (no/yes)	83/ 0 (100/ 0)	82/ 1 (98.8/ 1.2)	1.000

Values are expressed as number (percentage) of patients. CWA, continuous wound infusion analgesia; PCA: patient-controlled analgesia; PONV, postoperative nausea and vomiting. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.

Ⅳ. DISCUSSION

This study showed that multimodal analgesia with PCA and CWA was more effective to reduce postoperative pain 1,2,3,4, and 5 postoperative days, in analysis with data after prwopensity score matching. This study also showed less incidence of sedation in patients with multimodal analgesia with PCA and CWA compared with PCA alone. The author believes that this study is meaningful in that it analyzed the postoperative analgesic and PSPS preventive effects of multimodal analgesia with PCA and CWA in patients undergoing thoracotomy and thoracic ORIF.

Most studies on postoperative analgesic effects and postoperative complications of CWA were conducted in patients with thoracotomy [2, 12-15, 17]. Liu et al. [2] investigated whether the continuous CWA with ropivacaine through a wound catheter placed below the fascia was effective to reduce postoperative pain score compared with intravenous PCA in patients undergoing non-cardiac thoracotomy. They reported that CWA showed non-significant differences in analgesic effects and rescue analgesic requirements compared with intravenous PCA [2]. Some studies were investigated the postoperative analgesics effect of the combined modality of Intravenous PCA and CWA in patients who underwent thoracotomy [13-15]. Fiorelli et al. [13] performed CWA by suturing the catheter as close as possible to the intercostal nerve in patients who underwent a standard muscle-sparing thoracotomy. They also suggested that the combined modality of intravenous PCA and CWA showed more reduction of postoperative pain and analgesic requirements, and a faster recovery of respiratory function than intravenous PCA alone [13].

Thoracic epidural analgesia and continuous thoracic paravertebral block are modalities that be comparable or superior to intravenous PCA [12]. Lenz et al.

[12] reported that continuous thoracic paravertebral block was comparable with thoracic epidural analgesia, but less than intravenous PCA in patients undergoing thoracotomy for lung transplantation. They suggested that continuous thoracic paravertebral block could be a better option than thoracic epidural analgesia for acute pain after thoracotomy. So, some authors investigated the combined modality of Intravenous PCA and CWA on the postoperative analgesia compared with thoracic epidural analgesia, continuous thoracic paravertebral block, or intravenous PCA in patients who underwent thoracotomy [14, 15]. Unfortunately, they reported that the combined modality of intravenous PCA and CWA did not show the significant benefit on reduction of postoperative pain score and opioid consumption compared with thoracic epidural analgesia, continuous thoracic paravertebral block, or intravenous PCA [14, 15]. Gebhardt et al. [14] documented that the combined modality of Intravenous PCA and CWA did not show a significant difference in the average postoperative pain scores, which was higher compared with thoracic epidural analgesia. Furthermore, the maximum postoperative pain score was higher in patients receiving the combined modality of Intravenous PCA and CWA than thoracic epidural analgesia [14]. Moreover, this combination modality improved comfort which allowed early discharge [14]. Fortier et al. [15] also reported that the combined modality of Intravenous PCA and CWA showed less postoperative pain scores compared with intravenous PCA alone, but there was no significant difference between groups. In addition, the combined modality of Intravenous PCA and CWA showed a higher postoperative pain score after coughing within postoperative 1 day compared with the combined modality of continuous thoracic paravertebral block and intravenous PCA [15]. However, there was no significant difference in postoperative pain score at rest during all postoperative periods [15].

Ultimately, these previous studies supported that the combined modality of CWA and was effective to control the acute pain after thoracotomy, even though it was not superior to thoracic epidural analgesia, combination modality of the

continuous thoracic paravertebral block with intravenous PCA, and intravenous PCA alone [2, 12-15, 17]. However, this study showed that the combined modality of Intravenous PCA and CWA was effective in significantly reducing postoperative pain than PCA alone. This discrepancy with the results of this study can be explained in that the previous studies were conducted with a small sample size, which is insufficient to confirm whether the combined modality of Intravenous PCA and CWA was effective as other analgesic modalities. On the other hand, although there are limitations in collecting data retrospectively through a review of electronic medical records, the author analyzed the data with sufficient power after adjustment of demographic data, the type and dose of opioid used for postoperative analgesia, operation types, and the postoperative pain score on the day of surgery using propensity score matching.

The complications such as drowsiness and dizziness, sedation, cardiovascular, respiratory depression, infection, and general complications were significantly lower or no-difference in patients receiving CWA compared with other analgesic modalities [2, 14, 15]. We should also pay attention to local anesthetic-related adverse effects in patients receiving CWA because the catheter for CWA is placed as close as possible to the intercostal nerve and local anesthetic is continuously infused. The risk of local anesthetic systemic toxicity is higher with continuous peripheral nerve blockade compared to single-shot techniques due to local anesthetic accumulation [18]. The plasma concentration of bupivacaine was increased continuously after 4 mg/h for postoperative 48 hours until the end of infusion, but it was less than 4 μg/mL (toxic level) [13]. The previous studies on the analgesic effect of CWA have infused at between 4 mg/h and 10 mg/h of rocuronium or bupivacaine continuously [2, 13-15], and there was no toxicity of local anesthetics [14, 15, 19]. The incidence of PSPS was not a significant difference in patients receiving CWA compared with other analgesic modalities [2, 14].

This study had several limitations as follows. First, the retrospective analysis might have influenced the results of this study even though the data was adjusted with propensity score matching [14]. Second, unlike other preview studies, the author included not only thoracotomy but also ORIF in this study, because ORIF requires a similar wound incision for thoracotomy [20]. Third, the author did not enroll the patient receiving CWA alone. So, it cannot be demonstrated if CWA alone could be effective to control acute pain after thoracic surgeries compared with other analgesic modalities, and whether it has a synergic effect with other analgesic modalities [13]. Forth, postoperative rescue analgesics requirement and opioid consumption were not investigated. Although the additional application of CWA to PCA showed a more significant postoperative pain reduction in PCA alone, this study showed that both groups provided clinically effective postoperative analgesia. However, it was shown that sedation, one of the opioid-related complications, was significantly higher in the PCA-only group than in the group that additionally used CWA for PCA. This can be explained as the possibility that more opioid was administered by pressing the bolus button of the PCA equipment at a higher frequency in the PCA-only group due to postoperative pain [2]. And fifth, this result shows only the effect of postoperative analgesia on thoracic surgeries performed by a single surgeon in a single institute, so it may not reflect the effect of postoperative analgesia on thoracotomy performed in other institutes [14].

Ⅴ. CONCLUSIONS

This study demonstrates that the combined modality of Intravenous PCA and CWA is a good option with effective, easy, and safe postoperative analgesia after thoracotomy and ORIF. However, this study as well as the previous literature suggests that there is still remained to confirm whether the combined modality of Intravenous PCA and CWA is more effective than intravenous PCA or other analgesic modalities, and it has a synergistic analgesic effect.

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Legends for Figures

Fig. 1. Flowchart of this study. . ASA-PS, American Society of Anesthesiologists - Physical Status; ORIF, open reduction and internal fixation; PCA, intravenous patient-controlled analgesia. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia.

Fig. 2. Numeric rating score during postoperative 5 days, before propensity score matching. POD, postoperative day; POD0, day of surgery; POD1, postoperative 1 day; POD2, postoperative 2 days; POD3, postoperative 3 days; POD4, postoperative 4 days; POD5, postoperative 5 days. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia.

Fig. 3. Numeric rating score during postoperative 5 days, after propensity score matching. POD, postoperative day; POD0, day of surgery; POD1, postoperative 1 day; POD2, postoperative 2 days; POD3, postoperative 3 days; POD4, postoperative 4 days; POD5, postoperative 5 days. PCA Group, postoperative intravenous PCA; PCA-CWA Group, postoperative intravenous PCA and continuous wound infusion analgesia. *: $p < 0.05$ was considered to indicate statistical significance.