

A comparison of 2 intravenous patient-controlled analgesia modes after spinal fusion surgery

Constant-rate background infusion versus variable-rate feedback infusion, a randomized controlled trial

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Abstract

Background: Conventional intravenous patient-controlled analgesia (PCA), which usually involves constant-rate background infusion plus demand dosing, may cause adverse effects or insufficient analgesia. When variable-rate feedback infusion plus demand dosing mode is used, the infusion rate can be changed according to the patient's needs.

Methods: In this prospective randomized double-blind study, 78 adults who were undergoing spinal fusion surgery were randomly allocated to either the constant-rate background infusion plus demand dosing group (group C) or the variable-rate feedback infusion plus demand dosing group (group V). The number of demands, volume delivered, numerical rating scale (NRS) score, adverse effects and the use of rescue analgesics were examined at 30 minutes after the operation in the post-anesthesia care unit, and at 6, 12, 24, and 48 hours.

Results: The number of demands was significantly lower in group V than in group C at 12-24 hours (4.59 ± 4.31 vs 9.21 ± 6.79 times, $P = .001$) and over the total period. The volume delivered via PCA was significantly lower in group V than in group C at 12 to 24 hours (13.96 ± 13.45 vs 21.19 ± 8.66 mL, $P = .006$), 24 to 48 hours (13.39 ± 12.44 vs 33.6 ± 12.49 mL, $P = .000$), and over the total period. NRS scores, administration of rescue analgesics, and postoperative nausea and vomiting showed no between-group differences.

Conclusions: Variable-rate feedback infusion plus the demand dosing mode can control postoperative pain more efficiently, with lower dosages of analgesics, than constant-rate background infusion plus demand dosing in patients who undergo spinal fusion surgery.

Abbreviations: IV = intravenous, NRS = numerical rating scale, PACU = post-anesthesia care unit, PCA = patient-controlled analgesia, PONV = postoperative nausea and vomiting, SSII = surgical spine invasiveness index.

Keywords: background infusion, patient-controlled analgesia, postoperative pain, spinal fusion

1. Introduction

Patient-controlled analgesia (PCA) provides individual analgesics to meet patient needs for pain control.^[1] For this reason, it has

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The authors report no conflicts of interest.

We can provide available data upon request, through institutional review board, and reviewers. If anyone requires our data of this study, please do not hesitate to contact the corresponding author.

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become one of the best strategies for acute pain management over the last quarter century, and opioid-based intravenous (IV) PCA is widely used to control postoperative pain.^[2]

It is well known that patients who undergo spinal fusion surgery report high-severity postoperative pain.^[3,4] The adequate management of postoperative pain is essential to facilitate early rehabilitation and recovery.^[5] Furthermore, spinal fusion surgery produces characteristic pain patterns postoperatively, with severe pain on the first postoperative day, with the pain decreasing steeply on the following day.^[6-8] PCA is an essential, safe, and effective method for postoperative pain management in patients undergoing painful spinal fusion surgery.^[7]

In the conventional PCA mode, demand dose with or without continuous background infusion is commonly used.^[9] When a relatively low background infusion is set, analgesic effects may be inadequate. Conversely, when the background infusion rate is set higher than required to treat the patient's pain, adverse effects such as postoperative nausea and vomiting (PONV), sedation, dizziness, and potentially dangerous respiratory depression can occur.^[10,11] Therefore, conventional PCA with a continuous background infusion may not be suitable for the postoperative pain patterns associated with spinal fusion surgery. If the background infusion rate changes according to the patient's pain level and needs, the pain can be managed more efficiently, and the adverse effects of excessive opioids would be expected to be reduced.

Therefore, this study compared the variable-rate feedback infusion mode, in which the background infusion rate increases

or decreases according to the patient's demand, with the conventional constant rate background infusion plus demand dosing mode.

2. Materials and methods

This study was approved by the institutional review board of Chung-Ang University Hospital (ref: 1610-004-258) and was registered with ClinicalTrials.gov (ref: NCT03102333). The subjects included patients aged 20 to 70 years who were categorized as ASA class I-III and underwent general anesthesia for elective spinal fusion surgery between December 30, 2016 and December 29, 2017. Patients with severe cardiopulmonary disease, neurological or psychological disorders, and those who could not understand Korean were excluded. All patients were provided with a thorough explanation of the purpose of this study and PCA (PS-1000, Unimedics, Korea), including instructions to push the demand button whenever they feel pain. Following this, written informed consent was obtained from all participants. Seventy-eight patients were allocated to either the constant-rate background infusion plus demand dosing group (group C, $n=39$) or the variable-rate feedback infusion plus demand dosing group (group V, $n=39$). Randomization was based on a computer-generated random table. Patients' group allocations were sealed in serially numbered envelopes, and the patients were unaware of their assigned group.

No premedication was used before the induction of anesthesia. Anesthesia was induced with propofol and rocuronium and maintained with remifentanyl and desflurane, as appropriate, by an anesthesiologist who was unaware of the patient group allocations. When drainage was applied and the suturing was started, about 30 minutes before the end of surgery, fentanyl ($1 \mu\text{g kg}^{-1}$) was injected intravenously and ibuprofen 400 mg, diluted in 100 mL normal saline, was initiated and administered until 15 minutes after arrival to the post-anesthesia care unit (PACU). Simultaneously, another investigator opened the allocation envelope and set and started PCA according to the patient's group allocation.

The total PCA volume for all patients comprised 100 mL normal saline, with fentanyl ($20 \mu\text{g kg}^{-1}$) and ramosetron (0.3 mg). In group C, the PCA was set to administer a bolus of 1.5 mL ($0.3 \mu\text{g kg}^{-1}$) with a lock out interval of 15 minutes and background infusion rate of 1 mL h^{-1} ($0.2 \mu\text{g kg}^{-1} \text{ h}^{-1}$). In group V, a bolus of 1.5 mL ($0.3 \mu\text{g kg}^{-1}$) with a lock out interval of 15 minutes and background infusion rate of 1 mL h^{-1} ($0.2 \mu\text{g kg}^{-1} \text{ h}^{-1}$), which increased by 0.2 mL h^{-1} ($0.04 \mu\text{g kg}^{-1} \text{ h}^{-1}$), was used whenever the demand dose was administered. The background infusion rate was limited to a maximum of 3.0 mL h^{-1} ($0.6 \mu\text{g kg}^{-1} \text{ h}^{-1}$) and automatically decreased by 0.2 mL h^{-1} ($0.04 \mu\text{g kg}^{-1} \text{ h}^{-1}$) when the bolus button was not pressed for 1 hour.

At the completion of surgery, patients were awakened and transferred to the PACU. A trained study investigator who was not involved in patient allocation, intraoperative anesthetic management, and PCA setting, and was blinded to the patient's group, continuously evaluated the patients' conditions, including the intensity of pain and adverse effects such as PONV, dizziness, and sedation in the PACU. This clinician collected all the data throughout the study period. When the patient was still in the PACU and complained of pain, the PACU nurse, who was also not involved in this study, pushed the demand button. If patients requested analgesics other than those being administered through PCA, either ibuprofen 400 mg or nefopam 20 mg, diluted in 100

mL of saline, was administered for 30 minutes as a rescue analgesic. There were no important harms or unintended effects in each group by this study.

The aim of our study was to compare the efficiency of postoperative pain management between 2 different PCA modes. The primary outcome of this study was the difference in the number of demands, which were counted whenever patients pushed the demand button. The secondary outcomes were the differences in the numerical rating scale (NRS: 0=no pain, 10=worst pain imaginable) score, volume delivered via PCA, incidence of adverse effects such as PONV, dizziness, and sedation, and the need of additional IV rescue analgesics. We obtained these values at 30 minutes in the PACU, and postoperatively at 6, 12, 24, and 48 hours.

A surgical spine invasiveness index (SSII), based on the number of vertebral levels of decompression, fusion, and instrumentation from an anterior or posterior approach, was calculated to examine spinal fusion surgery invasiveness.^[12]

To estimate the group size, we conducted a pilot study to measure the total number of demands after surgery in 10 patients in group C. The mean and standard deviation of the number of demands were 31.0 ± 8.7 times for 24 hours after surgery. For our power calculation, we assumed an equal standard deviation in groups C and V. We wanted to show a 20% decrease in the total number of demands for 24 hours after surgery. With $\alpha=0.05$, 2-tailed, and a power of 80%, we required 35 patients per group. Considering a drop-out rate of 10%, we allocated 78 patients to this study. The number of samples was calculated using PASS software version 11 (NCSS, Kaysville, UT).

For intergroup comparisons of continuous variables, the data distribution was first evaluated for normality using the Kolmogorov–Smirnov test. Normally distributed data were presented as means \pm standard deviations, and the groups were compared using Student *t* tests. Non-normally distributed data were expressed as medians (P_{25} – P_{75}), and these data were analyzed using Mann–Whitney *U* tests. As height, weight, and total volume delivered for 48 hours after surgery passed the Kolmogorov–Smirnov test, they were analyzed using Student *t* tests. As age, SSII, number of demands for 24 hours after surgery, volume delivered for 24 hours after surgery, and total number of demands for 48 hours after surgery did not pass the Kolmogorov–Smirnov test, they were analyzed using Mann–Whitney *U* tests.

While analyzing the data according to time periods, the number of demands, volume delivered, NRS, and rescue analgesics did not pass the Kolmogorov–Smirnov test. Therefore, we also used a q–q plot, which did not indicate significant deviation from linearity, allowing normal assumptions for the repeated measured analysis of variance (ANOVA). Because the number of demands indicated significant deviation from linearity in the q–q plot, it was log transformed. Mauchly's sphericity test indicated that the assumption of sphericity had been violated for NRS [$\chi^2(9)=27.962$, $P=.001$, $W=0.687$], number of demands [$\chi^2(5)=18.122$, $P=.003$, $W=0.785$], and volume delivered [$\chi^2(5)=40.630$, $P<.001$, $W=0.526$]. Therefore, we used a Wilk's lambda multivariate analysis of variance (MANOVA). Rescue analgesics passed Mauchly's sphericity test [$\chi^2(2)=2.344$, $P=.310$, $W=0.945$], and were analyzed using repeated-measured ANOVA. To compare the data in each time period, Student *t* tests with Bonferroni corrections were performed.

Descriptive variables were analyzed using χ^2 analyses or Fisher exact tests, as appropriate, and *P* values $<.05$ were considered statistically significant. Statistical analyses were conducted using SPSS 21.0 (IBM Corp., Armonk, NY).

3. Results

Seventy-eight of 85 consecutive patients assessed for eligibility were allocated into either group and finished this study (Fig. 1). The patients' basic demographic and characteristics were not significantly different between groups V and C (Table 1).

There were statistically significant differences between the 2 groups in number of demands [15.0 (9.0–23.0), 22.0 (15.0–37.0) times in group V and C, respectively, $P = .011$] for 24 hours and total number of demands [20.0 (12.0–31.0), 28.0 (18.0–44.0) times in groups V and C, respectively, $P = .017$] for 48 hours after surgery (Table 2). And there was no difference [42.50 (25.50–64.00), 50.00 (37.50–63.00) mL in groups V and C, respectively, $P = .146$] between the 2 groups in the volume delivered for 24 hours after surgery, but that for 48 hours after surgery was lower (59.5 ± 34.1 , 86.3 ± 27.8 mL in groups V and C, respectively, $P < .001$) in group V than group C (Table 2). When analyzing the difference in these data according to the time periods in detail, we found statistically significant differences between the 2 groups in the number of demands [$F(3,74) = 23.121$, $P < .001$; $\lambda = 0.516$, partial $\eta^2 = 0.484$] and volume delivered [$F(3,74) = 22.255$, $P < .001$; $\lambda = 0.526$, partial $\eta^2 = 0.474$]. The number of demands

in group V was 4.59 ± 4.31 times at postoperative 12 to 24 hours, which was lower than the corresponding 9.21 ± 6.79 times in group C ($P = .001$; Fig. 2 and Table 3). The volume delivered in group V was 13.96 ± 13.45 mL at postoperative 12 to 24 hours and 13.39 ± 12.44 mL at postoperative 24 to 48 hours, which were lower than the 21.19 ± 8.66 mL and 33.6 ± 12.49 mL values noted in group C ($P = .006$ and $.000$, respectively; Fig. 3 and Table 3).

NRS showed no significant difference between the groups [$F(5,72) = 0.557$, $P = .732$; $\lambda = 0.963$, partial $\eta^2 = 0.037$; Fig. 4 and Table 3]. Rescue analgesics also showed no significant difference between the groups [$F(2,75) = 2.164$, $P = .122$; $\lambda = 0.945$, partial $\eta^2 = 0.055$; Table 3]. The number of patients who complained of PONV was 7/39 (18%) and 13/39 (33%) in groups V and C, respectively; there were no significant differences in these values between the groups ($P = .12$, Table 2).

4. Discussion

In this prospective, double-blind, randomized controlled study, the number of demands and the volume delivered via PCA were significantly lower in group V than in group C. Therefore,

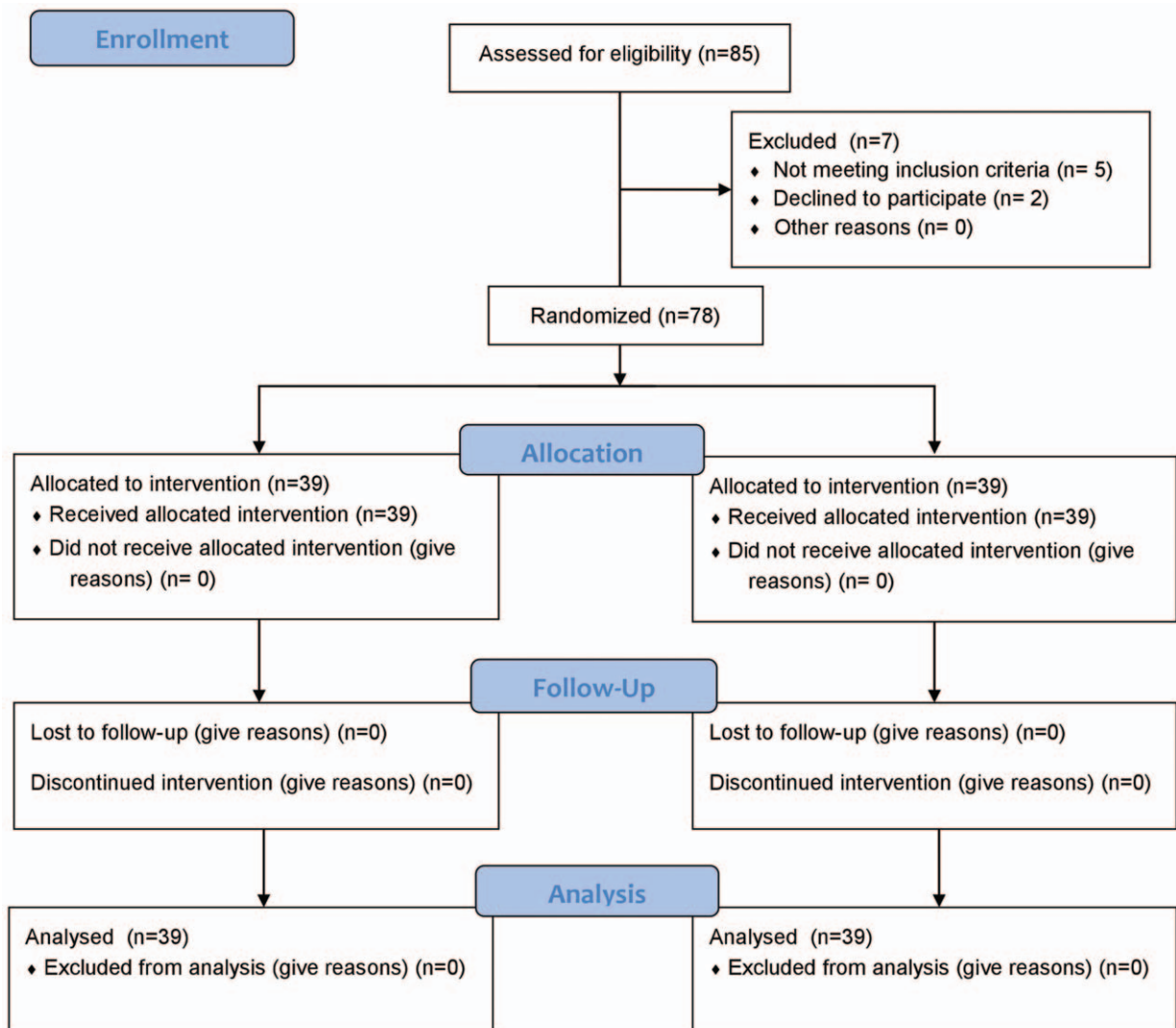


Figure 1. CONSORT diagram. CONSORT = Consolidated Standards of Reporting Trials.

Table 1
Demographic data and surgical characteristics.

	Group C (n = 39)	Group V (n = 39)	P value
Age, yr	63.0 (59.0–66.0)	62.0 (59.0–65.0)	.718
Sex, M/F	18/21 (46.2%/53.8%)	14/25 (35.9%/64.1%)	.357
Height, cm	160.0 ± 8.6	156.9 ± 9.6	.133
Weight, kg	63.2 ± 12.6	60.1 ± 8.6	.212
ASA, n	10/23/6	6/26/7	.532
Operation time, min	165.0 (120.0–220.0)	165.0 (125.0–230.0)	.503
SSII	6.0 (5.0–8.0)	6.0 (5.0–9.0)	1.000

Values are expressed as the mean ± SD, medians (Q₁-Q₃), or number (%), ASA (class I/class II/class III). *P* < .05 means a statistically significant difference. Group C: constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group. SSII = spine surgical invasiveness index.

Table 2
Postoperative outcomes for 24 and 48 hours in the 2 groups.

Hours after surgery	Group C (n = 39)	Group V (n = 39)	P value
Number of demands, times			
0–24	22.0 (15.0–37.0)	15.0 (9.0–23.0)	.011
0–48	28.0 (18.0–44.0)	20.0 (12.0–31.0)	.017
Volume delivered, mL/Fentanyl administered, µg kg ⁻¹			
0–24	50.00 (37.50–63.00)/8.44 (5.1–12.8)	42.50 (25.50–64.00)/10 (7.5–12.6)	.146
0–48	86.30 ± 27.80/11.9 ± 6.82	59.50 ± 34.10/17.26 ± 5.56	<.001
PONV			
0–48	13 (33%)	7 (18%)	.120

Values are expressed as the mean ± SD, medians (Q₁-Q₃), or number (%). *P* < .05 means a statistically significant difference. Group C constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group. PONV = postoperative nausea and vomiting.

variable-rate feedback infusion mode PCA may be more helpful than constant-rate background infusion mode PCA to control postoperative pain in patients who undergo spinal fusion surgery.

The 2 most commonly used PCA modes are demand only (i.e., a fixed-size dose is self-administered intermittently) and continuous infusion plus demand dosing (i.e., a constant-rate background infusion is supplemented by patient demand dose).^[9] There have been many comparative studies on these PCA modes.

Background infusion rate may increase daily opioid consumption and the incidence of adverse effects, including respiratory depression.^[11,13,14] It does not always result in better analgesic effects and improved sleep patterns.^[15] Therefore, the routine use of the background infusion PCA mode is controversial.^[9] However, some studies have shown that using a low dose background infusion had several benefits,^[14,16,17] including better pain relief, lower opioid consumption, and minimal

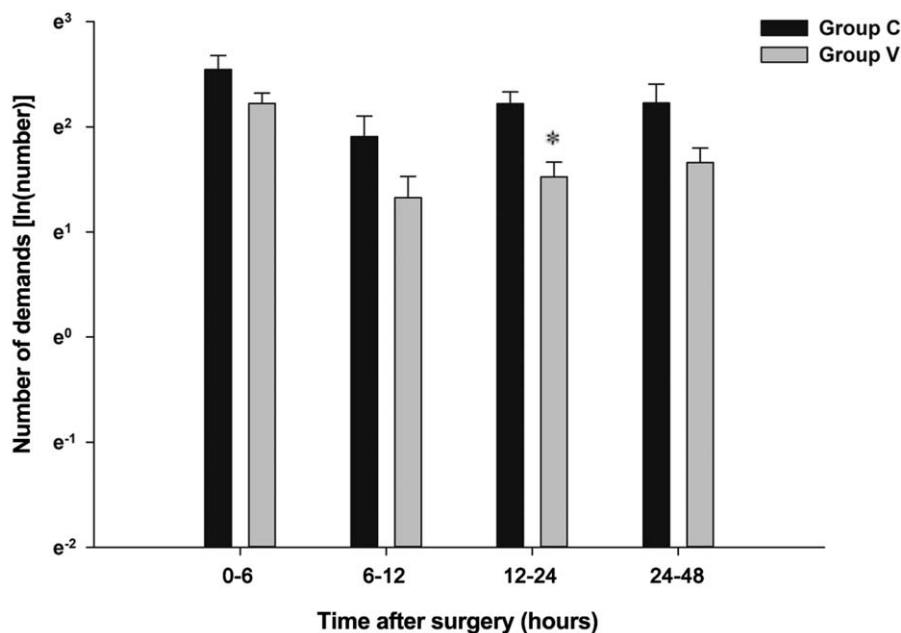


Figure 2. The comparison of the number of demands between the 2 groups. Values are expressed as mean ± standard error, * refers to a statistically significant difference compared to group C (*P* < .05). Group C: constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group.

Table 3
Postoperative outcomes according to time periods 48 hours after surgery in the 2 groups.

	Hours after surgery	Group C (n=39)	Group V (n=39)	P value
Number of demands, times	0-6	12.74 ± 11.41	9.23 ± 5.91	<.001
	6-12	6.74 ± 8.98	3.77 ± 5.26	
	12-24	9.21 ± 6.79	4.59 ± 4.31	
	24-48	9.25 ± 11.48	5.26 ± 4.86	
Volume delivered, mL	0-6	19.54 ± 7.59	20.62 ± 8.23	<.001
	6-12	12.01 ± 6.41	11.53 ± 8.79	
	12-24	21.19 ± 8.66	13.96 ± 13.45	
	24-48	33.6 ± 12.49	13.39 ± 12.44	
NRS	0	6.08 ± 1.53	5.77 ± 1.55	.732
	6	5.23 ± 1.75	4.77 ± 1.68	
	12	4.48 ± 1.64	4.03 ± 1.53	
	24	3.92 ± 1.58	3.90 ± 1.47	
	48	3.13 ± 1.56	3.00 ± 1.21	
Rescue analgesics, times	0-12	1.13 ± 0.95	1.08 ± 1.06	.122
	12-24	1.36 ± 1.22	1.87 ± 1.19	
	24-48	0.90 ± 0.99	1.10 ± 1.17	

Values are expressed as the mean ± SD, *P* < .05 means a statistically significant difference. NRS: numerical rating scale. Group C: constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group.

complication rate.^[16,18] So, low dose of constant-rate background infusion plus demand dosing has been widely applied to control postoperative pain for PCA.^[19]

However, it is still not easy for the low dose background infusion rate PCA mode to appropriately cope with postoperative pain with a steep slope in intensity, like that in patients who underwent spinal fusion surgery. Because of the nature of constant-rate background infusion, pain control is often insufficient immediately after surgery. The pain can be controlled by increasing the infusion rate or concentration of PCA. However, the day after the surgery, as the intensity of pain steeply reduces, adverse effects like nausea, vomiting, dizziness, sedation, and respiratory depression may occur. With variable-rate feedback infusion plus the demand dosing mode, the background infusion rate is changed according to the patient's need. Therefore, it is expected to control pain more efficiently on

the first postoperative day and reduce adverse effects from unnecessary opioid infusion thereafter.

In this study, the number of demands was only lower in group V than in group C at postoperative 12 to 24 hours. However, the volume delivered was significantly lower in group V than in group C at postoperative 12 to 24 and 24 to 48 hours. Regarding both differences in the number of demands and volume delivered at postoperative 12 to 24 hours, we can tell that the number of demands affects the volume delivered. This also means that PCA was delivered efficiently, changing background infusion rates according to patients' demand and showing better analgesic effects in group V.

At postoperative 24 to 48 hours, there was a significant difference only in the volume delivered, And not in the number of demands. The decrease in volume delivered in group V was achieved by slowing the background infusion rate due to the

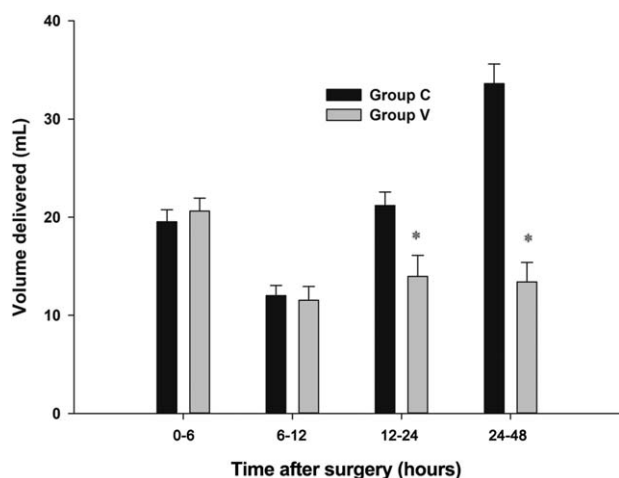


Figure 3. Comparison of the volume delivered via PCA between 2 groups. Values are expressed as mean ± standard error, * refers to a statistically significant difference compared to group C (*P* < .05). Group C: constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group.

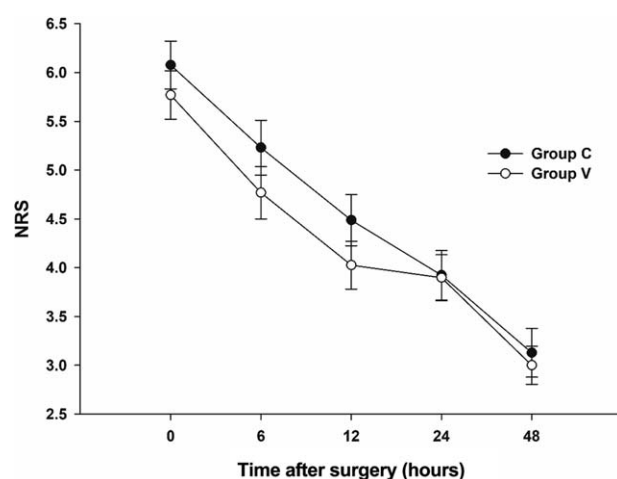


Figure 4. Comparison of the numerical rating scale between the 2 groups. Values are expressed as mean ± standard error. NRS: Numerical rating scale. Group C: constant-rate background infusion plus demand dosing group. Group V: variable-rate feedback infusion plus demand dosing group.

decrease in the number of demands as the patient's pain eased, unlike that observed postoperatively, at 12 to 24 hours. More volume than that delivered at 24 to 48 hours in group C translates into the unnecessary infusion of opioids and may cause adverse effects.

There was no difference in adverse effects between both groups. However, the number of patients having PONV was 13/39, and 7/39 in groups C and V, respectively, although this difference was statistically insignificant. The sample size of our study was calculated based on the number of demands. Future studies with a large number of patients may be expected to yield significantly lower PONV in the variable-rate feedback infusion plus demand dosing mode.

There are several ways to assess patient pain, such as NRS, verbal rating scales, and visual analog scales.^[20] These pain scales have been used in assessing acute, chronic, and changing pain patterns.^[21–23] Those values expressed by patients might be subjective. As patients pushed the demand button whenever they feel pain, we thought that the number of demands as a primary outcome of this study could reflect the pain intensity more objectively. When it comes to NRS, there were no differences between 2 groups in this study. Because patients could get the same NRS with a smaller volume delivered in group V, we can suppose that analgesic medication was administered cost-effectively.

There are a few things to be considered in this study. First, opioid alone could be insufficient to control postoperative pain effectively. Therefore, multimodal pain management that refers to the use of various kinds of analgesics that target different mechanisms together, has been recommended.^[24–26] It can also reduce opioid needs and unwanted side effects. In this study, there were no statistically significant differences in the administration of rescue analgesics between the 2 groups. However, given the frequency of rescue analgesics that was administered once or twice a day in both groups, PCA regimen with opioids alone were not enough to completely control pain. If studies with PCA regimens that add non-opioid analgesics to PCA opioids were conducted, better pain relief to patients would be obtained and the results might be different from this study.

Second, the variable-rate feedback infusion mode required additional inputs for several variables, such as increment, decrement, maximum, and minimum rates other than total volume, bolus dose, lockout, and infusion rate in constant-rate background infusion mode, which are already known well. When the unfamiliar PCA mode was first encountered during the course of our research, it required time to learn because there were more data values to input. We examined the variable-rate feedback infusion mode to determine our inputs in advance of this study. The combination of variable inputs could provide different results when investigating variable-rate feedback infusion modes, especially depending on the nature and severity of the surgery.

Third, we only compared variable-rate feedback infusion with constant-rate background infusion. As mentioned before, some studies recommend that background infusion should not be used routinely. The variable-rate feedback infusion mode needs to be compared with the demand only mode in order to ensure its effectiveness.

In conclusion, variable-rate feedback infusion plus demand dosing can control postoperative pain more efficiently, with lower dosages of analgesics, than constant-rate background infusion plus demand dosing in patients who undergo spinal fusion surgery.

Author contributions

Study conception and design and drafting of manuscript by SHL; study conception and design and drafting and review of manuscript by CWB; study conception and design and analysis and interpretation of data by HK; conduct of anesthesia by YHP; manipulation of PCA by GJC; acquisition of data by YHJ; study conception and design and review of manuscript YCW.

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Data curation: Yong Hun Jung.

Formal analysis: Hyun Kang.

Funding acquisition: Chong Wha Baek.

Investigation: Seung Hyuk Lee.

Methodology: Yong-Hee Park, Geun Joo Choi.

Supervision: Chong Wha Baek.

Writing – original draft: Seung Hyuk Lee.

Writing – review & editing: Chong Wha Baek, Young Cheol Woo.

References

- [1] Ratrout HF, Hamdan-Mansour AM, Seder SS, et al. Patient satisfaction about using patient controlled analgesia in managing pain post surgical intervention. *Clin Nurs Res* 2014;23:353–68.
- [2] Lehmann KA. Recent developments in patient-controlled analgesia. *J Pain Symptom Manage* 2005;29(suppl 5):S72–89.
- [3] Bianconi M, Ferraro L, Ricci R, et al. The pharmacokinetics and efficacy of ropivacaine continuous wound instillation after spine fusion surgery. *Anesth Analg* 2004;98:166–72.
- [4] Cohen BE, Hartman MB, Wade JT, et al. Postoperative pain control after lumbar spine fusion. Patient-controlled analgesia versus continuous epidural analgesia. *Spine* 1997;22:1892–6.
- [5] Bonnet F, Marret E. Postoperative pain management and outcome after surgery. *Best Pract Res Clin Anaesthesiol* 2007;21:99–107.
- [6] Ortiz-Cardona J, Bendo AA. Perioperative pain management in the neurosurgical patient. *Anesthesiol Clin* 2007;25:655–74.
- [7] Gepstein R, Arinzon Z, Folman Y, et al. Efficacy and complications of patient-controlled analgesia treatment after spinal surgery. *Surg Neurol* 2007;67:360–6.
- [8] Schenk MR, Putzier M, Kugler B, et al. Postoperative analgesia after major spine surgery: patient-controlled epidural analgesia versus patient-controlled intravenous analgesia. *Anesth Analg* 2006;103:1311–7.
- [9] Grass JA. Patient-controlled analgesia. *Anesth Analg* 2005;101(5S):S44–61.
- [10] Smythe MA, Zak MB, O'Donnell MP, et al. Patient-controlled analgesia versus patient-controlled analgesia plus continuous infusion after hip replacement surgery. *Ann Pharmacother* 1996;30:224–7.
- [11] Chen WH, Liu K, Tan PH, et al. Effects of postoperative background PCA morphine infusion on pain management and related side effects in patients undergoing abdominal hysterectomy. *J Clin Anesth* 2011;23:124–9.
- [12] Mirza SK, Deyo RA, Heagerty PJ, et al. Towards standardized measurement of adverse events in spine surgery: conceptual model and pilot evaluation. *BMC Musculoskelet Disord* 2006;7:53.
- [13] Owen H, Szekely SM, Plummer JL, et al. Variables of patient-controlled analgesia. 2. Concurrent infusion. *Anaesthesia* 1989;44:11–3.
- [14] McCoy EP, Furness G, Wright PM. Patient-controlled analgesia with and without background infusion. Analgesia assessed using the demand: delivery ratio. *Anaesthesia* 1993;48:256–60.
- [15] Parker RK, Holtmann B, White PF. Effects of a nighttime opioid infusion with PCA therapy on patient comfort and analgesic requirements after abdominal hysterectomy. *Anesthesiology* 1992;76:362–7.
- [16] Wu H-L, Tsou M-Y, Chao P-W, et al. Evaluation of the relationships between intravenous patient-controlled analgesia settings and morphine requirements among patients after lumbar spine surgery. *Acta Anaesthesiol Taiwanica* 2010;48:75–9.
- [17] Doyle E, Harper I, Morton NS. Patient-controlled analgesia with low dose background infusions after lower abdominal surgery in children. *Br J Anaesth* 1993;71:818–22.
- [18] White I, Ghinea R, Avital S, et al. Morphine at “sub-analgesic” background infusion rate plus low-dose PCA bolus control pain better and is as safe as twice a bolus-only PCA regimen: a randomized, double blind study. *Pharmacol Res* 2012;66:185–91.
- [19] Kim K. Analysis of the current state of postoperative patient-controlled analgesia in Korea. *Anesth Pain Med* 2016;11:28–35.

- [20] Hjermstad MJ, Fayers PM, Haugen DF, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage* 2011;41:1073–93.
- [21] Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. *Acad Emerg Med Off J Soc Acad Emerg Med* 2001;8:1153–7.
- [22] Boonstra AM, Schiphorst Preuper HR, Reneman MF, et al. Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. *Int J Rehabil Res* 2008;31:165–9.
- [23] Gallagher EJ, Bijur PE, Latimer C, et al. Reliability and validity of a visual analog scale for acute abdominal pain in the ED. *Am J Emerg Med* 2002;20:287–90.
- [24] Hartrick CT. Multimodal postoperative pain management. *Am J Health Syst Pharm* 2004;61(suppl 1):S4–10.
- [25] Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. *JAMA Surg* 2017;152:691–7.
- [26] Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American pain society, the American society of regional anesthesia and pain medicine, and the American society of anesthesiologists' committee on regional anesthesia, executive committee, and administrative council. *J Pain Off J Am Pain Soc* 2016;17:131–57.