

Effect of preoperative smoking cessation on postoperative pain outcomes in elderly patients with high nicotine dependence

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Abstract

Objective: To investigate the effect of smoking cessation before surgery on postoperative pain and analgesic consumption after thoracoscopic radical resection of lung cancer in elderly patients with high nicotine dependence.

Methods: A total of 107 male patients, ages 60 to 70 years, undergoing elective thoracoscopic radical lung cancer surgery from July 2017 to July 2018 were enrolled into 3 groups: group A (highly nicotine-dependent and discontinued smoking <3 weeks before surgery, n=36), group B (highly nicotine-dependent and discontinued smoking >3 weeks before surgery, n=38), and group C (nonsmokers, n=33). Postoperative sufentanil consumption, visual analog scale (VAS) pain scores at rest and during cough, rescue analgesia, opioid-related adverse events, and patient satisfaction were assessed from 0 to 48 h postoperatively.

Results: Patient characteristics were comparable among the 3 groups. Sufentanil consumption and VAS pain scores from postoperative 0 to 48 h were significantly higher in groups A and B than in group C. In addition, group B had lower sufentanil consumption and pain scores than group A. No differences in the need for rescue analgesia, patient satisfaction, or occurrence of postoperative adverse events, including nausea, vomiting, respiratory depression, and oversedation, were observed among the 3 groups.

Conclusion: Compared with nonsmokers, highly nicotine-dependent male patients who were deprived of cigarettes experienced more severe pain and required treatment with more sufentanil after thoracoscopic radical lung cancer surgery. Moreover, preoperative smoking cessation at least 3 weeks before surgery led to better postoperative pain outcomes than smoking cessation within 3 weeks of surgery.

Abbreviations: FTND = Fagerström Test of Nicotine Dependence Questionnaire, HPA = hypothalamus–pituitary–adrenal axis, PCA = patient-controlled analgesia, VAS = visual analog scale.

Keywords: analgesia, high nicotine dependence, postoperative pain, radical thoracoscopic lung cancer surgery, smoking cessation

1. Introduction

Approximately 300 million adults undergo surgical procedures worldwide each year. In the United States, 30% of surgical patients are smokers.^[1,2] Nicotine dependence increases 30-day mortality and the incidence of pulmonary complications after

surgery.^[3] Notably, postoperative pulmonary complications are more common than cardiac complications and lead to increased medical costs.^[4] Long-term smokers are more likely to develop postoperative pulmonary complications because of airway secretions and sputum retention. In addition, patients experiencing postoperative pain are not willing to breathe deeply or cough, which may increase the risk of pulmonary complications. Therefore, postoperative analgesia is of critical importance for the rehabilitation of nicotine-dependent patients who undergo surgical procedures.

Compared with thoracotomy, thoracoscopic procedures improve postoperative pain and quality of life for patients scheduled for radical resection of lung cancer.^[5] However, postoperative acute and chronic moderate-to-severe pain is still common in these patients.^[6,7] Studies have shown that surgical patients with nicotine dependence require a greater amount of postoperative opioids because of hyperalgesia.^[8,9] However, smoking cessation may help improve small airway function and reduce postoperative complications.^[10,11] Most recently, Shen et al^[12] reported that abstinent smokers showed decreased pain tolerance and needed more opioids after surgery than nonsmokers. Other studies also addressed the effects of smoking on the use of postoperative opioids.^[13,14] However, whether the time of smoking cessation has an impact on postoperative pain outcomes is still unknown.

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In this study, we investigated the effect of the time of smoking cessation on postoperative pain and analgesic consumption in elderly patients with high nicotine dependence undergoing thoracoscopic radical resection of lung cancer. Based on our preliminary observation, we hypothesized that a longer duration of smoking cessation (>3 weeks) before surgery would contribute to better postoperative pain control.

2. Patients and methods

2.1. Patients

After obtaining approval from the Institutional Ethics Committee of Jilin University (2017, 363), we conducted this study between July 2017 and July 2018. Written informed consent was obtained from all patients. This study included male patients (ages 60–70 years, ASA physical status I–II) who were scheduled to undergo thoracoscopic radical resection of lung cancer.

The exclusion criteria included alcohol abuse, allergy to opioids, opioid abuse, hyperalgesia, mental or neurological dysfunction, history of postoperative cognitive dysfunction, difficult airway, reoperation within the first 24 h after surgery, inability to understand the visual analog scale (VAS) for pain or to use patient-controlled analgesia (PCA), and refusal to participate. For the nonsmoker control group, those who had a long-term passive smoking history were also excluded. To be included in the group of patients who were highly nicotine dependent, the patients had to have a minimum score of 6 in the Fagerström Test of Nicotine Dependence Questionnaire (FTND; Table 1).

Eligible patients were divided into 3 groups according to the time of smoking cessation: group A (patients who were highly nicotine-dependent and discontinued smoking <3 weeks before surgery), group B (those who were highly nicotine-dependent and discontinued smoking >3 weeks before surgery), and group C (nonsmokers).

Table 1

The Fagerström Test of Nicotine Dependence (FTND) Questionnaire.

Questions	Answers	Points
1. How soon after you wake up do you smoke your first cigarette?	Within 5 min	3
	6–30 min	2
	31–60 min	1
	After 60 min	0
2. Do you find it difficult to refrain from smoking in places where it is forbidden?	Yes	1
	No	0
3. Which cigarette would you hate to give up?	The first one in the morning	1
	Others	0
4. How many cigarettes do you smoke a day?	10 or less	0
	11–20	1
	21–30	2
	31 or more	3
5. Do you smoke more during the first 2 h than during the rest of the day?	Yes	1
	No	0
6. Do you smoke if you are so ill that you are in bed most of the day?	Yes	1
	No	0

2.2. Anesthesia

For general anesthesia induction, patients received etomidate 0.3 mg/kg and sufentanil 0.35 µg/kg. Cisatracurium 0.15 mg/kg was injected to facilitate tracheal intubation. After intubation, the lungs were mechanically ventilated with 40% oxygen in air to maintain the end-tidal CO₂ of 30 to 40 mmHg. For general anesthesia maintenance, intravenous propofol and sevoflurane inhalation were administered, titrated to BIS 40 to 60. Remifentanil 0.1 to 0.2 µg/kg/min was used for intraoperative analgesia, and sufentanil 0.15 µg/kg was given 30 min before the end of surgery. During one-lung ventilation, 50% oxygen in air was used.

2.3. Postoperative analgesia

After surgery, patients were transferred to a postanesthesia care unit and monitored until discharge. After extubation, a PCA containing sufentanil 1 µg/mL and ondansetron 80 µg/mL in 100 mL saline was started, with a bolus dose of 3 mL and a lockout time of 10 min, without a background infusion. A maximal dose of 40 mL in 4 h was set to avoid opioid overdose. A bolus of tramadol 100 mg was given for rescue analgesia if patients reported a VAS pain score more than 6. No use of other analgesics was permitted throughout this study.

2.4. Primary and secondary outcomes

The primary outcome of interest in this study was postoperative sufentanil consumption during the first 0 to 48 h after surgery. The secondary outcomes were VAS pain scores at rest and during cough from 0 to 48 h after surgery, the incidence of adverse events, the need for rescue analgesia, and patients' satisfaction. Researchers who were responsible for postoperative follow-up and data analyses were unaware of the patient grouping.

2.5. Statistical analysis

Data analyses were performed using SPSS software (version 19.0; Chicago, IL). Continuous variables are expressed as mean ± SD and were compared with one-way analysis of variance followed by Bonferroni posthoc testing. Categorical data are expressed as number (percentage) and were compared using Pearson's chi-squared test or Fisher's exact test. A *P* value <0.05 was considered statistically significant.

3. Results

A total of 161 male patients who underwent thoracoscopic radical lung cancer surgery were screened for participation. Of the 161 patients, 54 were excluded and 107 were finally included in this study. Group A (*n*=36) and group B (*n*=38) included highly nicotine-dependent patients with FTND scores ≥6, and group C (*n*=33) included nonsmokers. A flowchart of patient selection is presented in Figure 1.

As shown in Table 2, patients' baseline characteristics including age, weight, duration of surgery, duration of anesthesia, ASA classifications, and intraoperative remifentanil consumption did not differ among the 3 groups. In addition, there was no significant difference in the FTND scores of groups A and B, whereas the duration of smoking cessation was longer in group A.

Sufentanil consumption from 0 to 48 h after surgery is shown in Table 3. Patients in groups A and B required more sufentanil at

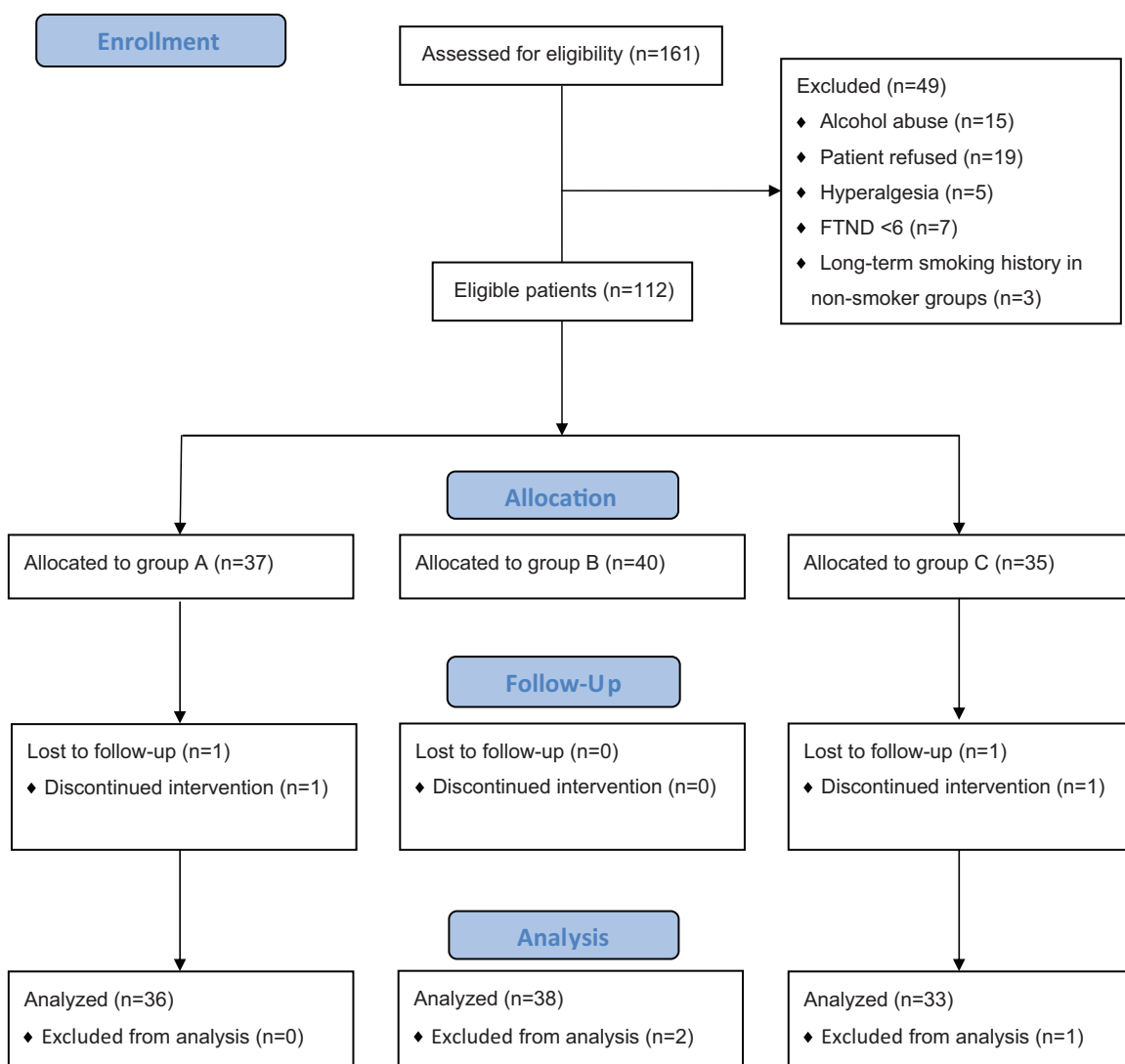


Figure 1. Flowchart of patient selection.

all time points (6, 12, 24, and 48 h postoperatively) than those in group C. In addition, sufentanil consumption in group A was the highest among the 3 groups at each time point. The number of patients who needed rescue tramadol did not differ among the 3 groups.

Postoperative VAS pain scores from 0 to 48 h after surgery are displayed in Table 4. Compared with group C, groups A and B had higher pain scores both at rest and during cough at all time points (1, 2, 4, 8, 16, 24, 36, and 48 h postoperatively). Additionally, group A had the highest pain scores at each time point.

Table 2
Patient characteristics.

Parameters	Group A (n = 36)	Group B (n = 38)	Group C (n = 33)	P value
Age (years)	64.28 ± 2.46	64.13 ± 2.12	64.64 ± 2.40	0.65
Weight (kg)	65.50 ± 1.96	66.13 ± 2.29	66.52 ± 2.61	0.18
Duration of surgery (min)	146.17 ± 7.77	147.95 ± 7.38	150.79 ± 19.27	0.30
Duration of anesthesia (min)	183.17 ± 8.34	180.66 ± 7.20	179.79 ± 7.12	0.16
ASA (I/II)	9/27	8/30	11/22	0.49
FTND score	7.47 ± 1.11	6.97 ± 1.08	NA	0.00
Smoke cessation time (days)	14.28 ± 2.88*	29.79 ± 6.20	NA	0.00
Intraoperative remifentanyl (g)	0.85 ± 0.035	0.84 ± 0.04	0.84 ± 0.04	0.62

Data are shown as mean ± SD or number.

Group A: patients who discontinued smoking <3 weeks before surgery. Group B: patients who discontinued smoking >3 weeks before surgery. Group C: nonsmokers.

FTND = Fagerström Test of Nicotine Dependence.

* P < 0.05 vs group B.

Table 3
Analgesic consumption 0–48 h postoperatively.

Parameters	Group A (n = 36)	Group B (n = 38)	Group C (n = 33)
Sufentanil consumption (μg)			
At 6 h postoperatively	31 ± 3.83 ^{*,†}	26.79 ± 3.55 [*]	22.06 ± 2.82
At 12 h postoperatively	57.08 ± 6.19 ^{*,†}	47.89 ± 4.48 [*]	34.12 ± 3.98
At 24 h postoperatively	97.33 ± 8.13 ^{*,†}	80.18 ± 5.50 [*]	68.58 ± 6.89
At 48 h postoperatively	172.31 ± 8.83 ^{*,†}	140.89 ± 6.43 [*]	124.85 ± 9.27
Patients who needed tramadol (n, %)	8 (22.22%)	7 (18.42%)	5 (15.15%)

Data are shown as mean ± SD.
Group A: patients who discontinued smoking <3 weeks before surgery.
Group B: patients who discontinued smoking >3 weeks before surgery.
Group C: nonsmokers.
^{*} P < 0.05 vs group C.
[†] P < 0.05 vs group B.

Overall, the incidence rates of adverse events in the 3 groups were relatively low (Table 5). Nausea occurred in 2 patients and vomiting in 1 patient in group A, and similar results were found in groups B and C. No patients experienced respiratory depression or oversedation. In addition, there was no significant difference in patient satisfaction.

4. Discussion

In this study, male patients with high nicotine dependence who underwent thoracoscopic radical lung cancer surgery required more sufentanil and reported higher VAS pain scores within 48 h postoperatively than nonsmokers. In addition, patients who discontinued smoking >3 weeks before surgery needed less sufentanil and had lower pain scores than those who discontinued smoking <3 weeks before surgery. Patient satisfaction, the need for rescue analgesia, and the incidence of postoperative

Table 4
Postoperative VAS pain scores during 0–48 h.

VAS pain scores	Group A (n = 36)	Group B (n = 38)	Group C (n = 33)
At rest			
At 1 h postoperatively	3.11 ± 0.32 ^{*,†}	2.55 ± 0.50 [*]	1.79 ± 0.42
At 2 h postoperatively	2.72 ± 0.45 ^{*,†}	2.24 ± 0.43 [*]	1.45 ± 0.51
At 4 h postoperatively	2.56 ± 0.50 ^{*,†}	1.89 ± 0.31 [*]	1.27 ± 0.45
At 8 h postoperatively	2.39 ± 0.49 ^{*,†}	1.71 ± 0.46 [*]	0.97 ± 0.17
At 16 h postoperatively	1.94 ± 0.23 ^{*,†}	1.29 ± 0.46 [*]	0.82 ± 0.39
At 24 h postoperatively	1.56 ± 0.50 ^{*,†}	1.08 ± 0.43 [*]	0.73 ± 0.45
At 36 h postoperatively	1.17 ± 0.38 ^{*,†}	0.76 ± 0.43 [*]	0.61 ± 0.50
At 48 h postoperatively	1.06 ± 0.23 ^{*,†}	0.71 ± 0.46 [*]	0.52 ± 0.51
During cough			
At 1 h postoperatively	5.78 ± 0.42 ^{*,†}	5.29 ± 0.46 [*]	4.97 ± 0.31
At 2 h postoperatively	5.58 ± 0.50 ^{*,†}	5.18 ± 0.39 [*]	4.76 ± 0.50
At 4 h postoperatively	5.53 ± 0.51 ^{*,†}	5.13 ± 0.41 [*]	4.70 ± 0.47
At 8 h postoperatively	5.42 ± 0.50 ^{*,†}	5.08 ± 0.54 [*]	4.52 ± 0.51
At 16 h postoperatively	5.14 ± 0.35 ^{*,†}	4.82 ± 0.39 [*]	4.48 ± 0.51
At 24 h postoperatively	5.03 ± 0.17 ^{*,†}	4.68 ± 0.47 [*]	4.15 ± 0.36
At 36 h postoperatively	4.75 ± 0.44 ^{*,†}	4.42 ± 0.55 [*]	4.09 ± 0.29
At 48 h postoperatively	4.72 ± 0.45 ^{*,†}	4.32 ± 0.47 [*]	4.06 ± 0.24

Data are shown as mean ± SD.
Group A: patients who discontinued smoking <3 weeks before surgery. Group B: patients who discontinued smoking >3 weeks before surgery. Group C: nonsmokers.
VAS = visual analog scale.
^{*} P < 0.05 vs group C.
[†] P < 0.05 vs group B.

Table 5
Adverse events and patient satisfaction.

	Group A (n = 36)	Group B (n = 38)	Group C (n = 33)
Adverse events			
Nausea	2 (5.56%)	2 (5.26%)	3 (9.09%)
Vomiting	1 (2.78%)	1 (2.63%)	1 (3.03%)
Respiratory depression	0 (0%)	0 (0%)	0 (0%)
Oversedation	0 (0%)	0 (0%)	0 (0%)
Total	3 (8.33%)	3 (7.89%)	4 (12.12%)
Satisfaction			
Very satisfied	16 (44.44%)	19 (50.0%)	21 (63.64%)
Satisfied	10 (27.78%)	13 (34.21%)	8 (24.24%)
Neutral	10 (27.78%)	6 (15.79%)	4 (12.12%)
Unsatisfied	0	0	0

Data are shown as number (%). Group A: patients who discontinued smoking <3 weeks before surgery. Group B: patients who discontinued smoking >3 weeks before surgery. Group C: nonsmokers.

nausea, vomiting, respiratory depression, and oversedation did not differ among the 3 groups.

Although enhanced recovery after surgery pathways have been shown to improve postoperative patients' outcomes, optimization of postoperative pain management is a key component.^[15–17] To accelerate postoperative recovery in elderly patients with a long-term smoking history, it is of great importance to provide well-tolerated and effective postoperative pain relief, titrated to each individual patient. Several studies have addressed the association between hyperalgesia and nicotine dependence.^[18–20] In addition, secondhand smoke may also lead to increased postoperative fentanyl consumption and more severe pain.^[21] Smoking was also found to be related to other types of pain including back pain, arthralgia, neuropathic pain, and chronic pelvic pain.^[22–25] However, other studies reported that nicotine dependence did not have a significant impact on postoperative pain.^[26,27] This inconsistency may be because of the differences in the study design, surgical procedures, and patient populations. To the best of our knowledge, this is the first study to show that a longer time of smoke cessation (>3 weeks before surgery) could lead to better pain outcomes compared with smoke cessation for <3 weeks before surgery.

There are several explanations for the possible effects of smoking in the pain nociception: in acutely abstinent tobacco smokers, beta2* nicotinic acetylcholine receptors take part in pain sensitivity but not pain tolerance;^[28] the endogenous opioid system plays an important role in nicotine-rewarding effects, nicotine-aversive responses, and the development of physical dependence to nicotine;^[29,30] nicotine is a potent activator of the hypothalamus–pituitary–adrenal axis (HPA), and long-term smoking downregulates the HPA axis;^[31] and smoking is associated with increased blood loss and transfusion use, which may increase operative times and the use of intraoperative opioids.^[32] Postoperative hyperalgesia is also associated with the amount of intraoperative remifentanyl.^[33]

Preoperative opioid use and nicotine treatment have been evaluated. Preoperative opioid use was found to be independently associated with increased costs and worse postoperative outcomes.^[34] Nicotine has been used as an adjunctive medication for postoperative pain management. However, a recent meta-analysis demonstrated that nicotine therapy did not reduce postoperative opioid consumption but may increase the risk of nausea.^[35]

The present study has some limitations. First, nicotine dependence was evaluated using the FTND scale rather than the measurement of blood nicotine concentration, which may have introduced some bias in the patient selection process. Second, we divided the smokers into 2 groups on the basis of arbitrary time threshold of 3 weeks. It remains to be explored whether pain outcomes would differ after an even shorter or longer smoke cessation time. Third, we failed to show any difference in patient satisfaction, which may possibly be because of the limited sample size. However, it is notable that the level of pain at rest was relatively low for all the 3 groups. Last, we included only male patients. It has been reported that women smokers were less likely to develop hyperalgesia than men.^[36] Further studies to determine the complete effects of smoking cessation on postoperative pain in a larger patient population are warranted.

5. Conclusion

Among cases requiring thoracoscopic radical lung cancer surgery, highly nicotine-dependent patients who are deprived of cigarettes before surgery require a larger quantity of postoperative sufentanil and experience more severe pain than nonsmokers. Furthermore, patients who discontinued smoking 3 weeks or more before surgery had better pain outcomes than those who stopped smoking within 3 weeks. Based on the current findings, preoperative smoking cessation as early as possible may contribute to postoperative pain relief in this patient population.

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