Journal of Anesthesia (2025) 39:545–554
https://doi.org/10.1007/s00540-025-03494-x

ORIGINAL ARTICLE

Prevalence and risk factors of chronic postsurgical pain after lung cancer surgery and knee arthroplasty: a prospective multicenter cohort study in Japan

Yoko Sugiyama[1,2] · Hiroki Iida[1,2] · Mariko Sugimoto[3] · Hiroshi Sekiyama[3] · Hisakatsu Ito[4] · Mitsuaki Yamazaki[4] · Atsuko Hara[5] · Masako Iseki[5] · Satoshi Tanaka[6] · Mikito Kawamata[6] · Akihiro Otsuki[7] · Yoshimi Inagaki[7] · Yoshiyasu Hattanmaru[8] · Takayuki Hamaguchi[8] · Ryoko Nakata[9] · Tomoyuki Kawamata[9] · Hiroyuki Nishie[10] · Hideki Nakatsuka[10] · Yuko Sato[11] · Yoshihiro Fujiwara[11]

Received: 4 October 2024 / Accepted: 22 March 2025 / Published online: 13 April 2025

Abstract

Purpose Chronic postsurgical pain (CPSP) is being increasingly recognized as an important clinical problem. The purpose of this prospective multicenter study was to evaluate the prevalence and risk factors of CPSP at 3 months after surgery in a Japanese population.

Methods Adult patients who underwent lung cancer surgery (L) or knee arthroplasty (K) at university hospitals in Japan and provided informed consent were included. Perioperative demographic, clinical, and psychological data were collected. Postsurgical pain scores were assessed via face-to-face interviews at each time point. We also investigated analgesic use at each time point in patients with CPSP.

Results A total of 494 (L) and 194 (K) patients completed our interviews at all visits up to 3 months after surgery. The prevalence of clinically relevant CPSP was 10% (L) and 28% (K), respectively. In both cohorts, pain intensity at 1 month after surgery was moderately correlated with pain intensity at 3 months after surgery. Multivariate logistic regression analysis revealed significant associations between preoperative chronic pain, current smoking status, and open thoracotomy with CPSP in the lung cohort. However, no pre- or intraoperative risk factors were identified in the knee cohort. None of the CPSP patients used strong opioids.

Conclusions The prevalence of CPSP after lung cancer surgery and knee arthroplasty among Japanese patients was comparable with prevalences previously reported in other countries. Subacute pain was significantly correlated with CPSP; however, further studies are needed to determine whether intensive treatment of subacute postsurgical pain can prevent the development of CPSP.

Keywords Chronic postsurgical pain · Subacute postsurgical pain · Thoracic surgery · Knee arthroplasty · Risk factors

✉ Yoko Sugiyama
yohshi@wb4.so-net.ne.jp

[1] Department of Anesthesiology and Pain Medicine, Gifu University Graduate School of Medicine, Gifu, Japan

[2] Anesthesiology and Pain Relief Center, Central Japan International Medical Center, Kenkonomachi 1-1, Minokamo City, Gifu 505-8510, Japan

[3] Department of Anesthesia, Teikyo University, Tokyo, Japan

[4] Department of Anesthesiology, Graduate School of Medicine and Pharmaceutical Sciences for Research, University of Toyama, Toyama, Japan

[5] Department of Anesthesiology and Pain Medicine, Juntendo University School of Medicine, Tokyo, Japan

[6] Department of Anesthesiology and Resuscitology, Shinshu University School of Medicine, Matsumoto, Japan

[7] Department of Anesthesiology and Critical Care Medicine, Faculty of Medicine, Tottori University, Yonago, Japan

[8] Department of Anesthesiology, The Jikei University School of Medicine, Tokyo, Japan

[9] Department of Anesthesiology, Wakayama Medical University, Wakayama, Japan

[10] Department of Anesthesiology and Intensive Care Medicine, Kawasaki Medical School, Kurashiki, Japan

[11] Department of Anesthesiology, Aichi Medical University, Nagakute, Japan

Introduction

Chronic postsurgical pain (CPSP) is defined as pain that develops after surgical procedures and persists for at least three months after surgery [1]. CPSP is being increasingly recognized as an important clinical problem that may have a significant impact on the quality of life (QOL) of postoperative patients. In addition, especially in North America, the persistent use of opioids in postoperative patients is a serious problem, regardless of the severity of CPSP [2–4]. Previous studies have shown that the prevalence of CPSP is quite high, ranging from 5 to 85%, depending on the surgery and survey [5]. We previously conducted a retrospective chart review to investigate the prevalence of CPSP in Japan [6], and the percentage of patients whose medical records indicated that they still had pain at the surgical site at the 3-month postoperative visit was 18% for lung cancer surgery and 48% for total knee arthroplasty (TKA). However, a prospective study is needed to confirm the exact prevalence and risk factors. Several risk factors for CPSP have been reported in various countries [7], and the intensity and duration of acute postsurgical pain are significantly associated with CPSP [8, 9]. For the present study, however, we focused on the association between CPSP and subacute postsurgical pain (SAPSP). Since the subacute phase begins when postoperative patients are discharged from the hospital, it is possible that adequate pain management is not being provided in Japan today.

The aim of this prospective multicenter trial was to investigate the prevalence of and risk factors for CPSP in Japanese patients after lung cancer surgery and knee arthroplasty, both of which are regarded as high-risk surgeries for CPSP [5, 10]. We also investigated the types of analgesics used in Japan during the subacute and chronic postoperative periods to ascertain the actual status of postoperative pain management in Japan.

Methods

Study design and participants

This study was a multicenter, prospective observational study involving ten university hospitals in Japan: Gifu University Hospital in Gifu, Teikyo University Hospital, Juntendo University Hospital, Jikei University Hospital in Tokyo, Toyama University Hospital in Toyama, Shinshu University Hospital in Matsumoto, Wakayama Medical University Hospital in Wakayama, Tottori University Hospital in Yonago, Kawasaki Medical University Hospital in Kurashiki, and Aichi Medical University Hospital in Nagakute. The study protocol was approved by the institutional review board (29-208) and was registered with the University Hospital Medical Information Network Clinical Trials Registry (registered ID: UMIN000028759). Adult patients who underwent elective lung cancer surgery (the lung cohort) or knee arthroplasty (the knee cohort) between 2017 and 2019 and who provided written consent for the study were enrolled. The exclusion criteria were as follows: bilateral surgery, additional surgery within 3 months, chest wall resection (the lung cohort), the presence of cancer recurrence (the lung cohort) or infection at the surgical site, and lack of follow-up for at least 3 months after surgery.

Preoperative questionnaire

The following data were collected: age, sex, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), smoking status, and history of diabetes. Current smokers were defined as patients who continued to smoke during the one month prior to surgery. During the preoperative visit, the anesthesiologist also asked the patients to complete the Hospital Anxiety and Depression Scale (HADS, Japanese version) questionnaire. Both the anxiety subscale (HADS-A) and the depression subscale (HADS-D) are four-point Likert scales with scores ranging between 0 and 3 and a maximum attainable score of 21 points. After the literature review, a score ≥ 8 points was defined as clinically relevant anxiety or depression [11]. Anxiety and depression are known to be associated with CPSP [7]. The HADS-A and HADS-D have been widely used in CPSP studies to assess these psychological factors [12] and a systematic review has recommended using HADS for the assessment of psychosocial factors [13]. Accordingly, we used HADS to evaluate preoperative anxiety and depression as potential risk factors for CPSP. In addition, we checked for preoperative knee pain (in the knee cohort), chronic pain in other body parts, and a history of preoperative analgesic use.

Anesthesia and surgery

The type of anesthesia and analgesia used at each institution was determined by the anesthesiologists based on their preference. The perioperative use of regional anesthesia, such as epidural anesthesia and peripheral nerve blocks, and postoperative analgesic use during the first 48 h were recorded. The type of surgery was also determined according to the protocol of each institution: open thoracotomy or video-assisted thoracoscopic surgery (VATS) for the lung cohort and total knee arthroplasty (TKA) or unicompartmental knee

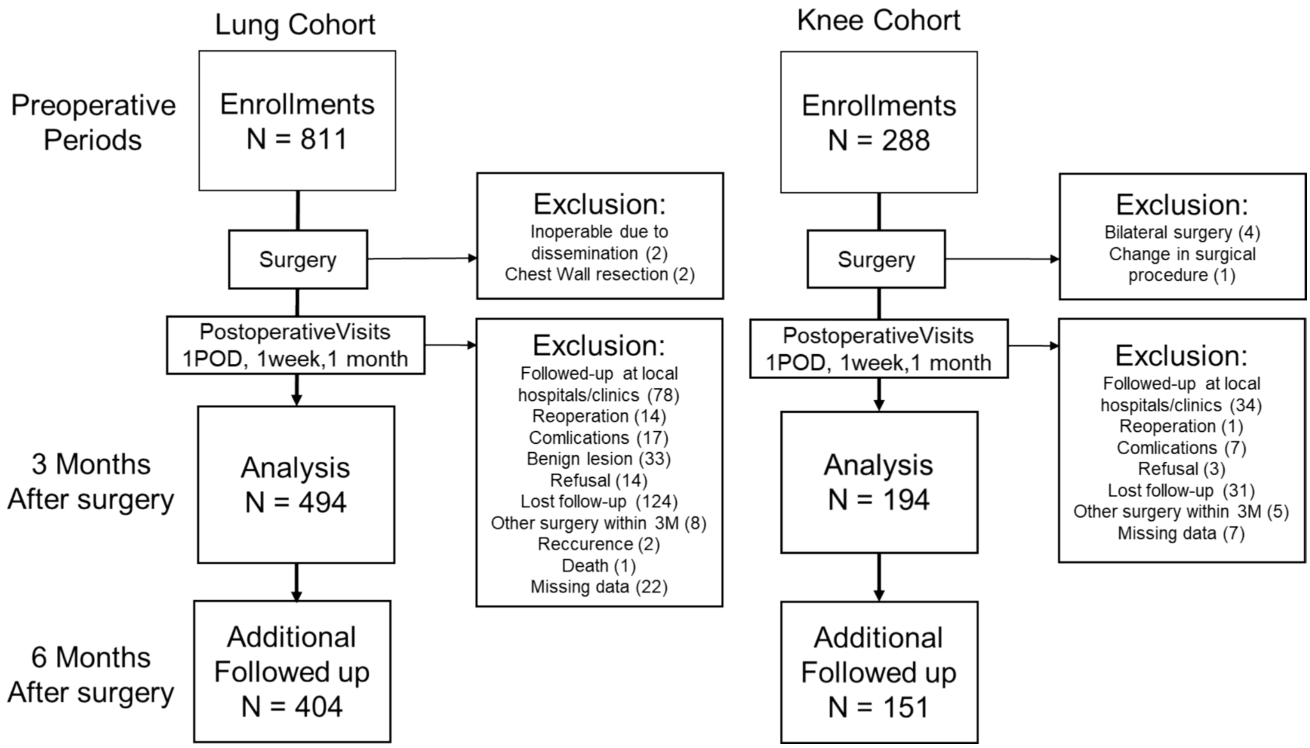

Fig. 1 A flow chart of this study shows the enrollment process

arthroplasty (UKA) for the knee cohort. The duration of surgery, amount of bleeding, and duration of tourniquet use (in the knee cohort) were also recorded.

Postoperative visit

Postoperative pain at the surgical site was assessed by the research anesthesiologists at each institution through five follow-up visits and face-to-face interviews at 1 day, 4–7 days (1 week), 3–5 weeks (1 month), and 3 months after surgery. Optionally, if possible, pain intensity was also assessed at the 6-month postoperative visit. The average daily pain intensity both at rest and with movement was evaluated using a numerical rating scale (NRS; 0 to 10, 0 = no pain, 10 = worst possible pain). Neuropathic pain at the surgical site was assessed according to the Douleur Neuropathic 4 (DN4) score [14] at 1 week, 1 month, and 3 months after surgery. The impact of CPSP on patients' QOL was assessed via the Japanese version of the EQ5D-5L at the 3-month postoperative visit [15]. The analgesics prescribed at each time point after surgery were also recorded.

Definition of CPSP

Clinically relevant CPSP was defined as positive if either NRS at rest or NRS with movement was greater than 3 at 3 months after surgery, according to previous studies [16, 17].

Statistical analyses

The primary endpoints of the current study were the prevalence of and risk factors for clinically relevant CPSP at 3 months after surgery. The secondary endpoint was the prevalence of SAPSP (NRS > 3) at 1 month after surgery and the correlation between acute to subacute postsurgical pain and CPSP. Continuous variables are presented as the means ± SDs or medians and interquartile ranges (IQRs), and categorical variables are presented as counts and percentages. To identify the risk factors for CPSP, a multivariate logistic regression analysis was performed using the shrink method to avoid overfitting the model. A nonparametric Spearman's correlation matrix was created to analyze the association between pain intensity at each postoperative time point. All the statistical analyses were performed with SPSS II for Windows (version 11, IBM, Armonk, NY, USA) and R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided p value < 0.05 was considered to indicate statistical significance.

Table 1 Patient characteristics and perioperative factors

Variables	Lung cohort N = 494	Knee cohort N = 194
Age (years)	68.0 ± 9.7	71.9 ± 8.5
Female	210 (42.5%)	152 (78.4%)
Height (cm)	160.4 ± 8.7	154.0 ± 8.8
Weight (kg)	59.0 ± 11.3	61.4 ± 12.4
BMI (kg/m^2)	22.9 ± 3.6	25.8 ± 4.4
ASA (I/II/III)	90/353/51 (18.2/71.5/10.3%)	21/156/17 (10.8/80.4/8.8%)
DM	104 (21.1%)	33 (17.1%)
Current Smoker	34 (6.9%)	12 (6.3%)
Chronic pain	167 (33.8)	104 (54.5)
Preoperative severe (NRS > 6) knee pain	–	80 (41.7%)
Preoperative analgesic use for knee pain	–	98 (50.5%)
Preoperative HADSD≧ 8	56 (11.3%)	25 (12.9%)
Preoperative HADSA≧ 8	55 (11.1%)	26 (13.4%)
Anesthesia method G/Ep-G or CSE/PNB-G	46/395/53 (9.3/80.0/10.7%)	119/53/22 (61.3/27.3/11.3%)
Surgical procedure	275 (55.7%) VATS (vs. open)	165 (85.1%) TKA (vs. UKA)
Surgery time (min)	184.9 ± 83.6	117.3 ± 44.3
Tourniquet (min)	–	87.9 ± 44.3
Blood loss (mL)	56.3 ± 173.2	91.2 ± 52.8
Analgesics used within 48 h after surgery		
Acetaminophen	256 (51.8)	99 (51.0)
NSAIDs	432 (87.4)	163 (84.0)
Epidural opioid + LA	393 (79.6)	53 (27.3)
IV-fentanyl/morphine	60 (12.1)/2 (0.4)	134 (69.1)/0 (0)
Tramadol or codeine or buprenorphine	50 (10.1)	18 (9.3)
Pregabalin	155 (31.4)	1 (0.5)
Periarticular cocktail		131 (67.5)

The values are presented as the means ± standard deviations (SDs) or numbers unless otherwise mentioned. *BMI* body mass index, *ASA* American Society of Anesthesiology physical status, *DM* diabetes mellitus, *HADSD* hospital anxiety depression scale depression subscale, *HADSA* HADS anxiety subscale, *G* general anesthesia only, *Ep-G* general + epidural anesthesia, *CSE* combined spinal and epidural anesthesia, *PNB-G* general anesthesia + peripheral nerve block, *VATS* video assisted thoracotomy surgery, *TKA* total knee arthroplasty, *UKA* unicompartmental knee arthroplasty, *NSAIDs* nonsteroidal anti-inflammatory drugs, *LA* local anesthetics, *IV* intravenous

Results

The lung cohort

A total of 811 patients who underwent lung cancer surgery were enrolled; 494 patients completed follow-up interviews up to 3 months after surgery, and 404 patients completed follow-up interviews up to 6 months after surgery (Fig. 1). Patient demographics and intraoperative factors are displayed in Table 1. The pain intensity and percentage of patients with neuropathic pain after surgery are shown in Table 2. A total of 46% and 29% of patients had CPSP (NRS > 0) at 3 and 6 months after surgery, respectively. A total of 10% and 6% of patients had clinically relevant CPSP (NRS > 3) at 3 and 6 months after surgery, respectively. Logistic regression analysis with the shrinkage method was used to determine the risk factors for clinically relevant CPSP at 3 months after surgery (Table 3). Current smoking status (odds ratio (OR) = 3.8 [95% confidence interval (CI) 1.5–9.1]) and preoperative chronic pain (OR = 2.8 [1.5–5.0]) were risk factors for CPSP at 3 months. On the other hand, VATS was a more protective factor for CPSP at 3 months than was open thoracotomy (OR = 0.5 [0.3–0.9]). The current study revealed that preoperative psychiatric factors, such as HADS scores, and anesthesia methods were not associated with CPSP. There was a significant positive correlation between pain intensity at each postoperative time point (Fig. 2). In particular,

Table 2 Postsurgical pain intensity

	Postoperative visits	NRS at rest median [IQR]	NRS with movement median [IQR]	NRS > 0 N (%)	NRS > 3 N (%)	DN4 > 3 N (%)
The lung cohort N = 494 (~ 3 months) N = 404 (6 months)	1 day	2 [0–3]	4 [2–6]	455 (92.1)	274 (55.5)	–
	1 week	2 [13]	3 [2–5]	441 (89.3)	205 (41.5)	66 (13.4)
	1 month	2 [1–4]	2 [0–4]	467 (94.5)	154 (31.2)	100 (20.2)
	3 months	0 [0–1]	0 [0–1.25]	229 (46.4)	51 (10.3)	45 (9.1)
	6 months	0 [0–0]	0 [0–0]	117 (29.0)	26 (6.4)	22 (5.5)
The knee cohort N = 194 (~ 3 months) N = 151 (6 months)	1 day	2 [0–5]	6 [3–8]	179 (92.3)	130 (67.0)	–
	1 week	1 [0–3]	4.5 [3–6]	187 (96.4)	127 (65.5)	31 (15.9)
	1 month	1 [0–2]	3 [2–5]	167 (86.1)	97 (50.0)	39 (20.1)
	3 months	0 [0–1]	2 [0–3]	134 (69.1)	54 (27.8)	34 (17.5)
	6 months	0 [0–0]	0 [0–0]	75 (50.0)	24 (15.9)	15 (9.9)

NRS numerical rating scale, *IQR* interquartile range, *DN4* douleur neuropathique 4 questionnaire

pain intensity at 1 month after surgery was moderately correlated with pain intensity at 3 months after surgery for both pain at rest and pain during movement. Twenty-three percent of patients in the lung cohort received analgesics at 3 months after surgery. Among CPSP patients with NRS scores > 3, 64% of those in the lung cohort were using analgesics at 3 months after surgery. Among the 51 patients with CPSP (NRS score > 3), 16% received acetaminophen, 35% received nonsteroidal anti-inflammatory drugs (NSAIDs) or celecoxib, 18% received weak opioids (tramadol or codeine), 31% received gabapentinoids, and 6% received antidepressants (Fig. 3).

Table 3 Adjusted odds ratios of risk factors for CPSP (the lung cohort). Multivariate logistic regression analysis with the shrinkage method

Factor	Odds ratio	95% CI		p value
		Lower	Upper	
Age	0.98	0.95	1.01	0.148
Sex female vs. male	0.94	0.51	1.75	0.85
BMI	1.03	0.95	1.11	0.54
ASA-PS – 2 vs. 1	0.79	0.4	1.58	0.507
ASA-PS – 3 vs. 1	0.94	0.38	2.31	0.889
DM	0.74	0.34	1.62	0.45
Current smoker	**3.75**	**1.54**	**9.12**	**0.004**
Preoperative chronic pain	**2.75**	**1.5**	**5.04**	**0.001**
Preoperative HADSD≧8	0.99	0.89	1.1	0.849
Preoperative HADSA≧8	1.06	0.95	1.18	0.294
Epidural-G vs. G	0.98	0.41	2.33	0.961
PNB-G vs. G	1.62	0.61	4.25	0.33
Surgery (VATS vs. open)	**0.48**	**0.26**	**0.89**	**0.02**
Surgery time	1	1	1.01	0.415
Blood loss	1	1	1	0.481

Bold indicates statistical significance ($p < 0.05$)

CPSP chronic postsurgical pain, *CI* confidence interval, *BMI* body mass index, *ASA-PS* American Society of Anesthesiology physical status, *DM* diabetes mellitus, *HADSD* Hospital Anxiety Depression Scale Depression subscale, *HADSA* HADS anxiety subscale, *G* general anesthesia, *PNB* peripheral nerve block, *VATS* video-assisted thoracotomy surgery

The knee cohort

A total of 288 patients who underwent knee arthroplasty were enrolled; 194 patients completed follow-up interviews up to 3 months after surgery, and 151 patients completed follow-up interviews up to 6 months after surgery (Fig. 1). Patient demographics and intraoperative factors are displayed in Table 1. Sixty-nine percent and 50% of patients had CPSP (NRS score > 0) at 3 and 6 months after surgery, respectively. Twenty-eight percent and 16% of patients had clinically relevant CPSP (NRS > 3) at 3 and 6 months after surgery, respectively (Table 2). The proportion of patients who underwent UKA was 15% in both the CPSP-positive and CPSP-negative groups, indicating no difference between UKA and TKA in terms of CPSP incidence. Logistic regression analysis with the shrinkage method did not reveal any preoperative or intraoperative factors that were significantly associated with CPSP in the knee cohort (Table 4). Pain intensity at 1 month after surgery was moderately correlated with pain intensity at 3 months after surgery for both pain at rest and pain during movement (Fig. 2). Fifty percent of patients in the knee cohort received analgesics at 3 months after surgery. Among CPSP patients with NRS scores > 3, 56% of those in the knee cohort were using analgesics at 3 months after surgery. Of the 54 patients with CPSP (NRS score > 3), 18% received acetaminophen, 38% received NSAIDs or celecoxib, 25% received weak opioids, 6% received gabapentinoids, and 6% received antidepressants (Fig. 3). No

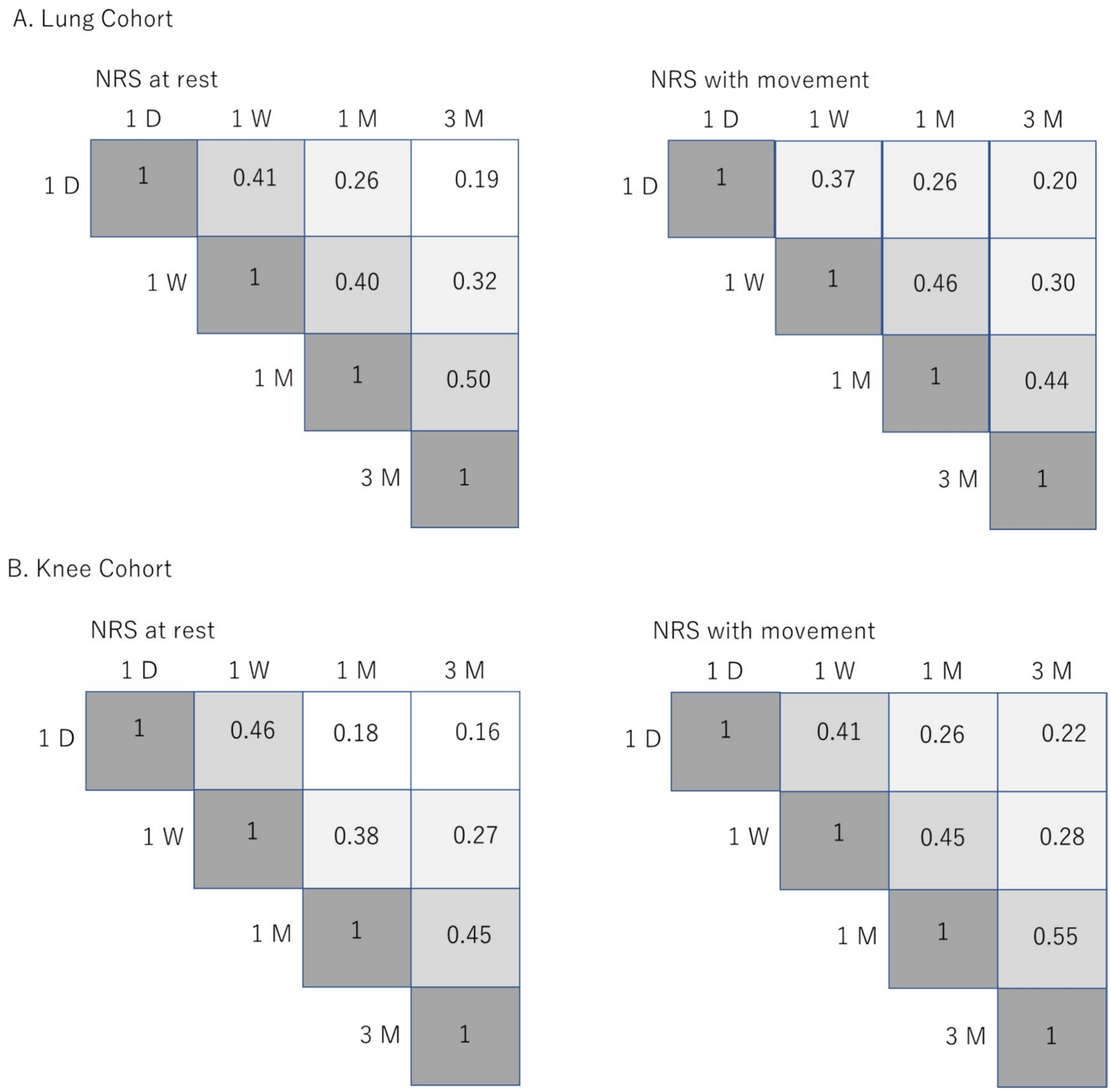

Fig. 2 Correlation Matrix of Pain Severity (NRS) at Different Postoperative Time Points. The correlation matrix displays the Pearson correlation coefficients between the NRS at various postoperative time points (1D, 1 day after surgery; 1 W, 1 week; 1 M, 1 month; and 3 M, 3 months), with all correlations reaching statistical significance ($P < 0.05$). The strength of the correlation is indicated by the color intensity

patients used strong opioids during the entire postoperative period.

QOL impairment

According to the EQ5D-5L results, patients with clinically significant CPSP reported not only significantly higher rates of pain and discomfort but also significantly higher rates of problems with mobility, self-care, usual activity, and anxiety in both cohorts (Table 5).

Discussion

The present prospective study indicated that the prevalence of clinically relevant CPSP at 3 and 6 months after lung cancer surgery (10%, 6%) and knee arthroplasty (28%, 16%) in Japanese patients was generally comparable to that recently reported in other countries. Yoon S et al. reported that 14% of patients in a Korean hospital had a pain intensity score greater than 3 on the NRS at 3 months after thoracic surgery[18]. Kampe S et al. reported that the prevalence of CPSP at 6 months after thoracotomy in a German hospital was 39% for NRS > 0 and 13% for NRS > 3, respectively

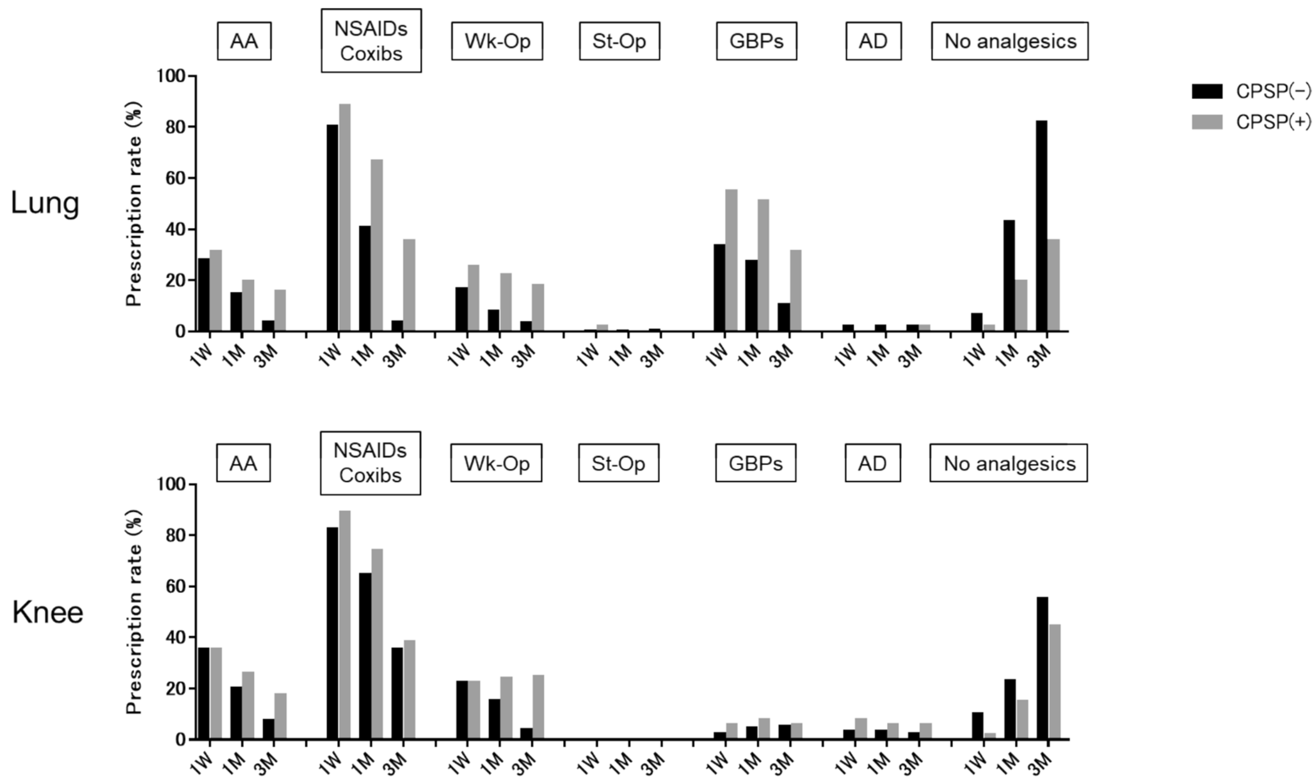

Fig. 3 Proportion of Prescribed Analgesics in Each Cohort. *AA* acetaminophen, *NSAIDs* nonsteroidal anti-inflammatory drugs, *Wk-Op* weak opioids, *St-Op* Strong opioids, *GBPs* gabapentinoids, *AD* antidepressants, *1W* 1 week after surgery, *1 M* 1 month after surgery, *3 M* 3 months after surgery

Table 4 Adjusted odds ratios of risk factors for CPSP (the Knee cohort). Multivariate logistic regression analysis with the shrinkage method

Factor	Odds ratio	95% CI		p value
		Lower	Upper	
Age	1	0.97	1.02	0.881
Sex female vs. male	0.91	0.53	1.56	0.742
BMI	1	0.95	1.05	0.959
Current smoker	1.55	0.61	3.93	0.36
Preoperative chronic pain	1.04	0.67	1.62	0.864
Preoperative analgesic use for knee pain	1.04	0.67	1.63	0.848
Preoperative HADSD≧8	0.78	0.39	1.55	0.47
Preoperative HADSA≧8	1.04	0.53	2.05	0.901
Epidural-G vs. G alone	1.05	0.72	1.53	0.792
PNB-G vs. G alone	1.07	0.72	1.59	0.721
Surgery time	1	0.99	1	0.417

CPSP chronic postsurgical pain, *CI* confidence interval, *BMI* body mass index, *HADSD* hospital anxiety depression scale depression subscale, *HADSA* HADS anxiety subscale, *G* general anesthesia, *PNB* peripheral nerve block, *VATS* video-assisted thoracotomy surgery

[19]. Recent reports, including the results of the present study, show a decreasing trend in the incidence of CPSP compared to the results of a meta-analysis by Bayman et al. using studies published between 1993 and 2013 (i.e., 57% incidence at 3 months and 47% incidence at 6 months after thoracotomy) [20]. One possible reason for their higher incidence is their broad definition of CPSP as any pain with NRS > 0. However, even when compared to the NRS > 0 proportions in our study (as shown in Table 2) and in Reference 19, their reported incidence may still be slightly higher. This may reflect recent advances in minimally invasive surgical techniques and improved perioperative pain management. However, further research is needed to clarify this. In a European multicenter prospective study, the incidence of CPSP (NRS > 3) at 3 and 6 months after TKA was 15% and 13%, respectively [21]. In Japan, the incidence of CPSP (visual analogue scale > 30 mm) at 6 months after TKA was 10% in a single-center prospective study by Aso K et al. [17]. Comparisons of CPSP prevalence in the current literature may be problematic because previous reports have defined CPSP differently with regard to duration and intensity, which is reflected in the variability in prevalence [9]. In this study, clinically relevant CPSP was defined as moderate to severe

Table 5 Impact of clinically relevant CPSP on QOL (EQ5D-5L) at 3 months after surgery

	EQ5D-5L-J 3 months	CPSP (-) NRS ≤ 3 N = 443 N (%)	CPSP (+) NRS > 3 N = 51 N (%)	P
The Lung Cohort N = 494 (~3 months)	Mobility > 1	91 (20.5)	25 (49.0)	< 0.0001
	Self-care > 1	29 (6.6)	15 (29.4)	< 0.0001
	Usual activity > 1	86 (19.4)	23 (45.1)	< 0.0001
	Pain/discomfort > 1	172 (38.8)	50 (98)	< 0.0001
	Anxiety/depression > 1	76 (17.2)	17 (33.3)	0.008
		NRS < = 3 N = 140	NRS > 3 N = 54	
The Knee Cohort N = 194 (~3 months)	Mobility > 1	82 (59.0)	41 (75.9)	0.03
	Self-care > 1	31 (22.3)	22 (40.7)	0.01
	Usual activity > 1	62 (44.6)	34 (63.0)	0.03
	Pain/discomfort > 1	84 (60.4)	52 (96.3)	< 0.0001
	Anxiety/depression > 1	21 (15.1)	23 (42.6)	< 0.0001

pain (NRS > 3) related to the surgical site at 3 months. The clinical relevance of pain should not be judged solely by the cutoff NRS but rather by its impact on quality of life and interference with activities of daily living [22]. However, in the present study, the CPSP (NRS > 3) group had significantly higher rates of impairment in mobility, self-care, and activities of daily living on the EQ-5D questionnaire, a measure of quality of life.

Identification of risk factors for CPSP and the strength of their effect on outcomes is desirable because interventions designed to influence these factors may prevent CPSP. The present study revealed that preexisting chronic pain and current smoking status were independent risk factors and that VATS (vs. open thoracotomy) was a protective factor against CPSP after lung cancer surgery. This finding supports previous reports [9, 23, 24]. Although UKA is generally considered less invasive than TKA, there was no significant difference in CPSP prevalence. Similarly, the proportion of patients experiencing significant postsurgical pain (NRS score > 3) on postoperative day 1, week 1, and month 1 did not significantly differ between the two procedures (data not shown), further supporting this finding. Furthermore, our results align with a recent systematic review and meta-analysis of randomized controlled trials comparing UKA and TKA [25]. The study demonstrated that although UKA showed statistically significant advantages in terms of knee recovery, function, and pain relief, these differences were not clinically meaningful when considering the minimal clinically important difference (MCID). Additionally, the study reported no significant differences in patient satisfaction between the two procedures. These results support our findings that the difference between TKA and UKA in terms of CPSP incidence may not be substantial. Previous meta-analyses have suggested that regional anesthesia is a protective factor for CPSP [23]; however, there were no significant differences according to anesthesia type in either cohort in the present study. This might be attributed to the prevalent use of thoracic epidural anesthesia in lung cancer surgeries across many participating centers, thereby hindering a thorough comparison with general anesthesia alone. In addition, most peripheral nerve blocks, such as intercostal nerve blocks for lung cancer surgery and femoral nerve blocks for TKA, were administered as single doses rather than being administered continuously, which may have affected outcomes. We could not identify any risk factors for CPSP in the knee cohort. A possible explanation for the failure to identify such risk factors is that fewer TKA patients could be followed during the study period than anticipated, and furthermore, the incidence of CPSP was lower than expected, resulting in a lack of power.

In both cohorts, pain intensity at 1 month after surgery was significantly correlated with pain intensity at 3 months. The postoperative subacute period is called the "grey zone" because most postoperative patients have been discharged from the hospital, and any residual postoperative pain cannot be adequately addressed [26]. Saporito A et al. reported that all patients who experienced chronic postmastectomy pain had post-discharge pain, although their acute pain was relatively well controlled [22]. As shown above, there was a moderate to high correlation between CPSP and post-discharge pain, indicating that effective pain management during the subacute phase may prevent the development of CPSP. Further research is warranted to fully understand the preventive impact of subacute analgesia on CPSP development.

In both cohorts in this study, NSAIDs were used more frequently for postsurgical pain in the acute to subacute phase (Table 1, Fig. 3). Gabapentinoids, which are recognized as first-line therapeutic agents for neuropathic pain [27], were used less frequently in the knee cohort than in the lung cohort during the subacute to chronic postoperative phase. This is despite the fact that the percentage of DN4-positive patients in the knee cohort was similar to that in the lung cohort. This suggests that the choice of analgesics may have been based on the nature of the surgery rather than on an individualized assessment of the patient's pain. Furthermore, the continued use of NSAIDs in the chronic postoperative phase, when surgical site inflammation is expected to have resolved, may reflect suboptimal pain evaluation. One possible reason for this is that, in Japan, postoperative pain management is commonly handled by surgeons rather than pain specialists throughout the entire postoperative period. Additionally, the fact that approximately 40% of CPSP patients were not receiving any analgesics suggests a lack of awareness and attention to CPSP among surgeons and other healthcare professionals. These findings highlight the need to raise awareness of the importance of CPSP management and prevention in Japan. A seamless approach to postoperative pain management, from the acute to chronic phase, should involve not only surgeons but also pain specialists to ensure optimal patient outcomes.

Interestingly, despite the low rate of opioid use in the postoperative subacute phase (i.e., post-discharge) in Japan [28–30], the incidence of CPSP was not particularly high compared to that in reports from Western countries. This raises questions about the role of opioids in postoperative pain management.

This study has several limitations. First, approximately half of the patients in the study were unable to complete the follow-up. Many patients returned to local hospitals or clinics during the follow-up period and were subsequently excluded from the analysis, which may have led to an overestimation of the incidence of CPSP in this study. However, we prioritized face-to-face surveys over telephone or mail surveys to obtain more detailed and objective CPSP information. Second, the study was initially planned to include 1000 patients in the pulmonary cohort and 400 patients in the knee cohort. These were approximated for multivariate analysis of 10–15 explanatory variables, which were set up assuming the incidence of CPSP from previous retrospective studies (i.e., 18% for the lung cohort and 48% for the knee cohort) and a dropout rate of 25%. However, the sample size was consequently inadequate as the actual number of cases collected within the specified study period was lower than expected and the drop-out rate was considerably higher than expected. Nevertheless, this is one of the larger prospective studies reported thus far [31–33]. In addition, following the advice of our statistician, we avoided overfitting the multivariate analysis by using the shrinkage method. Finally, there is a possibility that unmeasured factors were not included in the analysis.

Conclusions

The prevalence of CPSP after lung cancer surgery and knee arthroplasty among Japanese patients was comparable with previous results in other countries. Chronic use of strong opioids was not observed in Japanese patients with CPSP. Pain in the subacute phase was significantly correlated with CPSP; however, further studies are needed to determine whether intensive treatment of subacute postsurgical pain can prevent the development of CPSP.

Acknowledgements The authors express their sincere gratitude to Dr. T Ishihara, a statistician at the Gifu University Graduate School of Medicine, for his invaluable assistance and expertise in statistical analysis throughout the course of this study.

Data availability The datasets used and analyzed during this study are available from the corresponding author upon reasonable request.

References

1. Schug SA, Lavand'homme P, Barke A, Korwisi B, Rief W, Treede RD. The IASP classification of chronic pain for ICD-11: chronic postsurgical or posttraumatic pain. Pain. 2019;160(1):45–52.
2. Neuman MD, Bateman BT, Wunsch H. Inappropriate opioid prescription after surgery. Lancet. 2019;393(10180):1547–57.
3. Sun EC, Darnall BD, Baker LC, Mackey S. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. JAMA Intern Med. 2016;176(9):1286–93.
4. Carroll I, Barelka P, Wang CKM, Wang BM, Gillespie MJ, McCue R, Younger JW, Trafton J, Humphreys K, Goodman SB, Dirbas F, Whyte RI, Donington JS, Cannon WB, Mackey SC. A pilot cohort study of the determinants of longitudinal opioid use after surgery. Anesth Analg. 2012;115(3):694–702.
5. Macrae WA. Chronic post-surgical pain: 10 years on. Br J Anaesth. 2008;101(1):77–86.
6. Sugiyama Y, Iida H, Amaya F, Matsuo K, Matsuoka Y, Kojima K, Matsuno F, Hamaguchi T, Iseki M, Yamaguchi K, Takahashi Y, Hara A, Sugasawa Y, Kawamata M, Tanaka S, Inagaki Y, Otsuki A, Yamazaki M, Ito H. Prevalence of chronic postsurgical pain after thoracotomy and total knee arthroplasty: a retrospective multicenter study in Japan (Japanese Study Group of Subacute Postoperative Pain). J Anesth. 2018;32(3):434–8.
7. Rosenberger DC, Pogatzki-Zahn EM. Chronic post-surgical pain - update on incidence, risk factors and preventive treatment options. BJA Educ. 2022;22(5):190–6.
8. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006;367(9522):1618–25.
9. Glare P, Aubrey KR, Myles PS. Transition from acute to chronic pain after surgery. Lancet. 2019;393(10180):1537–46.
10. Grosu I, Lavand'homme P, Thienpont E. Pain after knee arthroplasty: an unresolved issue. Knee Surg Sports Traumatol Arthrosc. 2014;22(8):1744–58.
11. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–70.
12. Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis. Pain. 2021;162(1):10–30.

13. Hinrichs-Rocker A, Schulz K, Jarvinen I, Lefering R, Simanski C, Neugebauer EA. Psychosocial predictors and correlates for chronic post-surgical pain (CPSP) - a systematic review. Eur J Pain. 2009;13(7):719–30.
14. Bouhassira D, Attal N, Alchaar H, Boureau F, Brochet B, Bruxelle J, Cunin G, Fermanian J, Ginies P, Grun-Overdyking A, Jafari-Schluep H. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain. 2005;114(1–2):29–36.
15. Yoshii I, Kondo M. Clinical characteristics of frailty in Japanese rheumatoid arthritis patients. J Frailty Aging. 2020;9(3):158–64.
16. Wildgaard K, Ravn J, Nikolajsen L, Jakobsen E, Jensen TS, Kehlet H. Consequences of persistent pain after lung cancer surgery: a nationwide questionnaire study. Acta Anaesthesiol Scand. 2011;55(1):60–8.
17. Aso K, Ikeuchi M, Takaya S, Sugimura N, Izumi M, Wada H, Okanoue Y, Dan J. Chronic postsurgical pain after total knee arthroplasty: a prospective cohort study in Japanese population. Mod Rheumatol. 2021;31(5):1038–44.
18. Yoon S, Hong WP, Joo H, Kim H, Park S, Bahk J-H, Lee H-J. Long-term incidence of chronic postsurgical pain after thoracic surgery for lung cancer: a 10-year single-center retrospective study. Reg Anesth Pain Med. 2020;45(5):331–6.
19. Kampe S, Geismann B, Weinreich G, Stamatis G, Ebmeyer U, Gerbershagen HJ. The influence of type of anesthesia, perioperative pain, and preoperative health status on chronic pain six months after thoracotomy-a prospective cohort study. Pain Med. 2017;18(11):2208–13.
20. Bayman EO, Brennan TJ. Incidence and severity of chronic pain at 3 and 6 months after thoracotomy: meta-analysis. J Pain. 2014;15(9):887–97.
21. Martinez V, Lehman T, Lavand'homme P, Harkouk H, Kalso E, Pogatzki-Zahn EM, Komann M, Meissner W, Weinmann C, Fletcher D. Chronic postsurgical pain. Eur J Anaesthesiol. 2024;41(5):351–62.
22. Stamer UM, Ehrler M, Lehmann T, Meissner W, Fletcher D. Pain-related functional interference in patients with chronic neuropathic postsurgical pain: an analysis of registry data. Pain. 2019;160(8):1856–65.
23. Clephas PRD, Hoeks SE, Singh PM, Guay CS, Trivella M, Klimek M, Heesen M. Prognostic factors for chronic post-surgical pain after lung and pleural surgery: a systematic review with meta-analysis, meta-regression and trial sequential analysis. Anaesthesia. 2023;78(8):1005–19.
24. Khan JS, Sessler DI, Matthew TV, Chan CY, Wang IG, Szczeklik W, Turan A, Busse JW, Norman Buckley D, Paul J, McGillion M, Fernández-Riveira C, Srinathan SK, Shanthanna H, Gilron I, Jacka M, Jackson P, Hankinson J, Paniagua P, Pettit S, Devereaux. PJ. Persistent incisional pain after noncardiac surgery: an international prospective cohort study. Anesthesiology. 2021;135(4):711–23.
25. Xia K, Min L, Xie W, Yang G, Yon DK, Lee SW, Koyanagi A, Jacob L, Smith L, Shin JI, Rahmati M. Is unicompartmental knee arthroplasty a better choice than total knee arthroplasty for unicompartmental osteoarthritis? A systematic review and meta-analysis of randomized controlled trials. Chin Med J. 2024. https://doi.org/10.1097/CM9.0000000000003193.
26. Lavand'homme P. "Why me?" The problem of chronic pain after surgery. Br J Pain. 2017;11(4):162–5.
27. Bates D, Schultheis BC, Hanes MC, Jolly SM, Chakravarthy KV, Deer TR, Levy RM, Hunter CW. A comprehensive algorithm for management of neuropathic pain. Pain Med. 2019;20(1):S2-12.
28. Mondoñedo JR, Brescia AA, Clark MJ, Chang ML, Jiang S, He C, Welsh RJ, Popoff AM, Kulkarni MG, Lall SC, Pratt JW, Adams KN, Alnajjar RM, Martin JR, Gandhi DB, Brummett CM, Chang AC, Lagisetty KH. Evidence-based opioid prescribing guidelines after lung resection: a prospective, multicenter analysis. J Thorac Dis. 2023;15(6):3285–94.
29. Chalmers BP, Lebowitz J, Chiu Y-F, Joseph AD, Padgett DE, Bostrom MPG, Valle AGD. Changes in opioid discharge prescriptions after primary total hip and total knee arthroplasty affect opioid refill rates and morphine milligram equivalents: an institutional experience of 20,000 patients. Bone Joint J. 2021;103(7):103–10.
30. Ladha KS, Neuman MD, Broms G, Bethell J, Bateman BT, Wijeysundera DN, Bell M, Hallqvist L, Svensson T, Newcomb CW, Brensinger CM. Opioid prescribing after surgery in the United States, Canada, and Sweden. JAMA Netw Open. 2019;2(9):e1910734.
31. Tang S, Jin Y, Hou Y, Wang W, Zhang J, Zhu W, Zhang W, Gu X, Ma Z. Predictors of chronic pain in elderly patients undergoing total knee and hip arthroplasty: a prospective observational study. J Arthroplasty. 2023;38(9):1693–9.
32. Danielsen AV, Andreasen JJ, Dinesen B, Hansen J, Kjær-Staal Petersen K, Simonsen C, Arendt-Nielsen L. Chronic post-thoracotomy pain after lung cancer surgery: a prospective study of preoperative risk factors. Scand J Pain. 2023;23(3):501–10.
33. Bayman EO, Parekh KR, Keech J, Selte A, Brennan TJ. A prospective study of chronic pain after thoracic surgery. Anesthesiology. 2017;126(5):938–51.