

Prospective Survey

Effects of Epidemiological Factors and Pressure Pain Measurements in Predicting Postoperative Pain: A Prospective Survey of 1,002 Chinese Patients

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Background: A high degree of inter-individual differences was noted in human basal pain as well as the reporting of clinical pain, such as postoperative pain. Understanding the effects of common epidemiological variations and preoperative experimental methods of human pain perception may contribute to individualized pain treatment for patients.

Objectives: The current study was aimed to assess the role of epidemiological factors and preoperative experimental pain sensitivity for predicting postoperative pain and to analyze the potential effects of epidemiological factors on experimental pain sensitivity.

Study Design: A prospective survey of patients who were scheduled for selective surgery under general anesthesia.

Setting: Department of Anesthesiology at a teaching hospital in a medical college in a major metropolitan city in China.

Methods: One thousand two Chinese patients who were scheduled for selective surgery under general anesthesia were included. The preoperative epidemiology data of all patients were collected by the investigator through face-to-face interviews, and pressure pain, including the pressure pain threshold and tolerance, was tested. Next, the pain intensity and consumption of patient-controlled analgesia during the 48 hours after surgery were followed up.

Results: Through regression analysis of the current prospective study, epidemiological factors, including current smoker ($P = 0.002$), history of surgery ($P = 0.038$), and lower preoperative pressure pain tolerance ($P = 0.001$), were identified as independent risk factors for the incidence of postoperative inadequate analgesia. Additionally, from the perspective of the postoperative analgesia outcome, minimally invasive surgery and procedure-specific pain-treatment should be encouraged. Furthermore, several factors, including gender and smoking status, were found to be associated with the postoperative analgesic requirement or basal pressure pain threshold.

Limitations: The limitations of this study include that preoperative psychological tests were not performed.

Conclusions: Preoperatively determining the smoking status and history of surgery might serve as predictors for postoperative analgesia in the Chinese population. Additional preoperative pressure pain measurements might be an effective experimental method for predicting postoperative pain.

Key words: Epidemiologic, pressure pain, smoking, predicting, surgery, postoperative pain, inadequate analgesia, Chinese population

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It is estimated that in the US, there are 126.1 million adults reporting some pain in the previous 3 months (1). A high degree of inter-individual differences was noted in human basal pain and the reporting of clinical pain such as postoperative pain (2,3). Such differences in individual pain perception are likely due to the complex interactions among environmental and demographic factors (4-7). Therefore, understanding the effect of common epidemiological variations on human pain perception may contribute to individualized pain treatment for patients (8,9). However, large-scale prospective studies, especially in the Chinese population, on the evaluation of those factors for predicting clinical pain have seldom been reported.

As we know, surgery is one of the most common and predictable sources of acute pain (10,11). However, although much effort, such as providing patient-controlled analgesia (PCA), has been made for postoperative pain treatment, inadequate postoperative pain control is still a clinical issue that urgently needs to be addressed (12). Indeed, preoperatively determining risk predictors in postoperative inadequate pain treatment might enable personalized postoperative pain therapies and improve postoperative pain control (13-15). Therefore, we were encouraged to seek direct evidence that can be quoted for predicting postoperative pain using epidemiological factors.

Beyond that, in many recent studies, preoperative experimental pain measurement has been demonstrated to be an effective predictor for clinical postoperative pain treatment (13,16,17). Among those experimental pain measurements, mechanical pressure pain stimulation is one of the most commonly used methods for predicting postoperative pain treatment or analgesia consumption. However, it remains unclear that whether this method could be applied to predict the patients' postoperative pain sensitivity in a relatively large Chinese population. In addition, inter-individual differences were also found in experimental pain sensitivity in some healthy volunteers or patients under clinical pain conditions (18-20). Therefore, in this study, experimental pain measurement was also applied to evaluate its possible association with patients' postoperative pain intensity and analgesia consumption, and this made it possible to investigate the possible effect of epidemiological factors on experimental pain.

Based on the above information, this study included a relatively large Chinese population sample to investigate the possible role of some common epidemiological factors and preoperative pain sensitivity in pre-

dicting postoperative pain. We collected epidemiological factors and the basal experimental pain sensitivity for all patients prior to surgery, and the postoperative pain intensity and the patients' PCA requirements were recorded. Through these measurements, the current study aimed to assess the role of epidemiological factors as well as preoperative experimental pain sensitivity for predicting postoperative pain and to analyze the potential effects of epidemiological factors on the experimental pain sensitivity.

METHODS

Patients

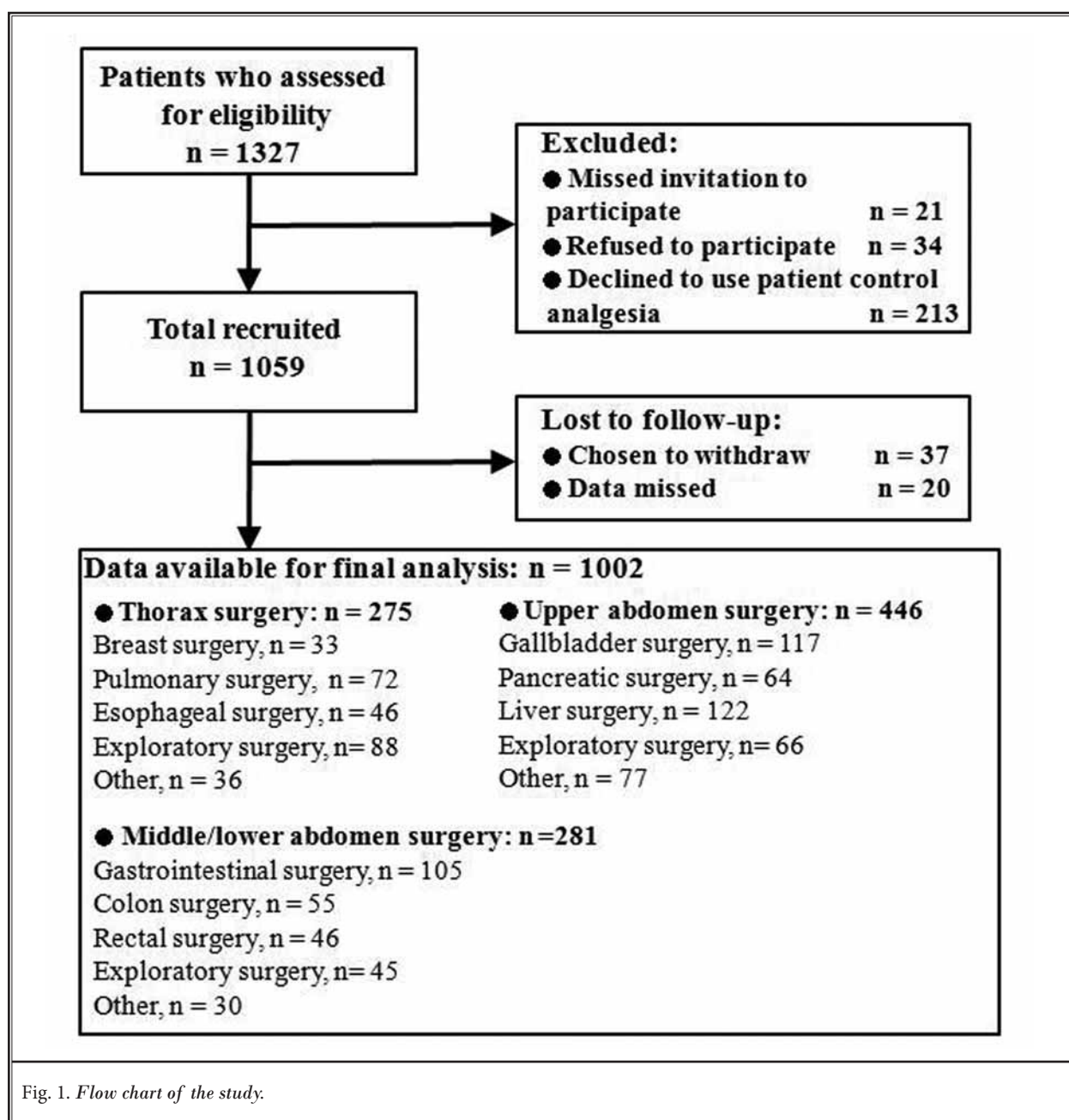
From October 2012 to April 2014, 1,327 patients (age range, 18 – 70 years) who were scheduled for selective surgery under general anesthesia were interviewed, and 1,059 of them who voluntarily received intravenous PCA treatment were included in the current prospective study (Fig. 1). The study was approved by Huazhong University of Science and Technology Tongji Hospital Ethics Committee, and informed consent was obtained from all patients prior to study enrollment. The study was also registered at clinicaltrials.gov (ID: NCT01750047) prior to the recruitment.

The inclusion criteria were as follows: American Society of Anesthesiologists physical status I ~III and right-hand dominance. The exclusion criteria were as follows: the presence of dermatitis or damaged, red, or swelling skin at the selected testing locations; use of any analgesic medication over the last 4 weeks; a known history of chronic pain; and a known history of psychiatric diseases, communication disorders, diabetes mellitus, severe cardiovascular diseases, kidney, or liver diseases with compromised hepatic function.

Preoperative Management and Demographic Data Collection

On the day before the operation, patients received information to minimize their anxiety related to the surgery. All of the patients were also trained to use the analgesic pump and numerical rating scale (NRS, 0 = no pain, 10 = unbearable pain) for postoperative pain assessment.

Epidemiology data of all patients were collected by investigator through face-to-face interviews. The collected data included 1) gender (male or female), age and age group (young, < 45 years; middle, 45 – 59 years; old, ≥ 60 years), height, weight, body mass index (BMI) and BMI group (underweight, < 18.5; normal weight, 18.5 ~



24; overweight, ≥ 24); 2) residence location (city or non-city), years of education (lack, ≤ 6 ; middle, 6 ~ 12; more, > 12), occupation (mental or manual laborer); 3) smoking status (yes, current smokers; quit, former smokers; no, never smokers), smoking years and packs/day; 4) alcohol drinking status (yes, current alcohol drinker; quit, former drinker; no, never drinker), drinking years and alcohol consumption/day; and 5) history of surgery (yes or no).

Preoperative Pressure Pain Threshold Measurement

As in our previous studies (21), a hand-held electronic pressure algometer (YISIDADS2; Hong Kong, China) was used to evaluate the pressure pain threshold (PPT) and pressure pain tolerance (PTO). The 1-cm²-sized probe was positioned perpendicularly to the skin surface, and the investigator applied continuous

pressure at approximately the same rate (1 kg/s) according to the visual LCD display on the algometer. Furthermore, to prevent unnecessary tissue damage, the maximum force was limited to 10 kg, and the maximum force was recorded as a cut-off value.

Standardized instructions of the study procedure were given, and the mechanical pain sensitivity tests were performed using the left forearm to familiarize the patients with the testing procedure at the outset of each testing session. The patients were asked to inform the investigator when they started to feel pain, and when pain became intolerable; these values were recorded. This procedure was repeated 10 minutes later, and the average of the 2 measurements was calculated.

In addition, as described in our previous studies, when women's PPT was higher than 3.63 kg/cm², men's PPT was higher than 4.63 kg/cm² or the PTO was higher than 8.50 kg/cm², we defined that as high PPT or high PTO (22,23). Otherwise, it was defined as low PPT or low PTO.

Anesthetic and Analgesia Technique

On the day of their scheduled surgeries, in the operating room, the patients were monitored via an electrocardiogram, blood pressure, heart rate (HR), and pulse oxygen saturation. Standardized general anesthesia was performed for all patients using 0.04 – 0.06 mg/kg midazolam, 1.5 – 2.5 mg/kg propofol, 0.4 – 0.6 µg/kg sufentanil, and 0.5 – 0.7 mg/kg rocuronium for anesthesia induction. Central venous pressure and arterial pressure were monitored invasively when needed. Anesthesia was maintained with a combined intravenous and inhalation anesthesia approach: inhalation of 1.0% – 2.0% sevoflurane, infusion of remifentanyl (0.2 – 0.4 µg·kg⁻¹·min⁻¹) and propofol (6 – 10 mg·kg⁻¹·h⁻¹), and intravenous boluses of 0.2 mg/kg rocuronium. The depth of anesthesia was maintained using Narcotrend (MonitorTechnik, Bad Bramstedt, Germany).

At 15 minutes prior to the incision, 40 mg of parecoxib sodium was given intravenously for pre-emptive analgesia, and 2 mg of tropisetron hydrochloride was administered for the prevention of postoperative nausea and vomiting. Using a controlled infusion pump (BCM, BCDB-150, Shanghai, China), PCA was started immediately after surgery, with sufentanil at 0.6 µg/mL and tramadol at 4 mg/mL for middle/lower abdomen and upper abdomen surgery, and butorphanol at 0.1 mg/mL for thorax surgery. The pump was programmed to use a loading dose of 2 mL, a background infusion at 1 – 2.5 mL/h, a PCA dose of 0.5 – 1.5 mL, a lockout pe-

riod of 10 minutes, and a maximal dose of 12 mL within a one-hour period.

Postoperative Pain and Analgesic Consumption Evaluation

Postoperative follow-up was carried out by investigators in the acute pain service group. The rest pain NRS scores at postoperative 0 to 6, 18 to 24, and 42 – 48 hours were evaluated. When the patients presented at rest an NRS ≥ 4 at these time points, they were given extra timely treatment and were recorded as particular patients who presented postoperative inadequate analgesia (moderate to severe pain) for final statistical analysis. In addition, the common adverse effect—i.e., postoperative nausea and vomiting (PONV)—was recorded for the analysis, and the data of PCA consumption from PCA pump were recorded at 48 hours after surgery.

Statistical Analysis

In the study, 14 independent variables were included in the final regression analysis. Therefore, a sample size of 1,002 was considered sufficient for the study. All of the statistical analyses were performed using SPSS for Windows version 17.0 (SPSS, Inc., Chicago, IL, USA). A two-tailed *P*-value less than 0.05 was considered to be statistically significant. All of the variables were summarized using standard descriptive statistics, such as the mean, standard deviation, and frequency. ANOVA with LSD post-hoc test was used to compare the difference among 3 groups, and the difference between 2 groups was compared using independent sample *t*-test.

Logistic regression analysis was used to evaluate the role of the preoperative factors in the prediction of postoperative inadequate analgesia (NRS ≥ 4) (2,24). Surgical types (middle/lower abdomen, upper abdomen, thorax), the absence or presence of high PPT or high PTO, and surgical methods (endoscopic or non-endoscopic) were also considered in the model. The criterion for inclusion into the regression equation was *P* < 0.05. Odds ratios (OR) with 95% confidence intervals (CIs) were determined based on the logistic regression analysis.

A multivariate linear stepwise regression model was used to explore the effects of those preoperative factors in the prediction of postoperative PCA consumption. Because different postoperative analgesics were used in the different types of surgery, subgroup analyses were applied for middle/lower abdomen, upper abdomen, and thorax surgery, respectively. Ad-

ditionally, in the linear regression model, categorical variables were converted to dummy variables. Furthermore, we used multivariate linear stepwise regression analysis to evaluate the effects of the epidemiological factors on the prediction of preoperative PPT and PTO. For all regression analyses in the current study, collinearity diagnostics were applied to exclude possible correlated independent variables before the models were performed.

RESULTS

General Results

As shown in Fig. 1, in this study, 37 patients chose to withdraw during the follow-up, and 20 patients were excluded because of missing data. Thus, 1,002 surgery patients were included in the final analysis. Patients were also grouped according to anatomic site and surgical method with or without the application of endoscopy. Breast, pulmonary, and esophageal surgery were categorized as thorax surgery; gallbladder, pancreatic, and liver surgery were categorized as upper abdomen surgery; and gastrointestinal, colon, and rectal surgery were categorized as middle/lower abdomen surgery. All of the patients' data are shown in Table 1. One hundred fifty-five patients (15.5%) presented with moderate-to-severe postoperative pain at rest during the 48-hour postoperative follow-up. Regarding the adverse effects, 85 patients were found to have PONV, and the incidence of PONV in women was 14.3% (61/426), which was significantly higher than that in men (24/576, 4.2%, $P < 0.001$).

Logistical Regression Analysis for Postoperative Inadequate Analgesia

A forward stepwise logistic regression model was applied to explore the possible predictors for postoperative inadequate analgesia. As summarized in Table 2, this overall model was significant ($P = 0.001$), and the ORs were determined based on the probability of occurrence of postoperative inadequate analgesia in patients with different effect factors. The results showed that the surgery method using an endoscope (OR = 0.57, 95% CI: 0.34 to 0.97, $P = 0.042$), former smoker status (OR = 0.54, 95% CI: 0.37 to 0.80, $P = 0.002$), and never smoker status (OR = 0.44, 95% CI: 0.19 to 1.04, $P = 0.063$) were protective factors for the occurrence of postoperative inadequate analgesia compared with non-endoscope surgery and current smokers.

Surgery type and surgery history were identified

Table 1. Patient characteristics.

	N = 1002
Gender (Male/Female)	576 (57.5%)/426 (42.5%)
Age (years)	49.5 ± 11.6
Age group (<45/45~60/≥60)	295 (29.4%)/492 (49.1%)/215 (21.5%)
BMI (kg/m ²)	21.8 ± 3.1
BMI group (<18.5/18.5~24/≥24)	141(14.1%)/623 (62.2%)/238(23.7%)
Living place (city/ non-city)	541 (54.0%)/461 (46.0%)
Years of education (≤6/6~12/>12)	305 (30.4%)/533 (53.2%)/164 (16.4%)
Occupation (mental / manual laborer)	362 (36.1%)/640 (63.9%)
Smoking (yes/quit/no)	310 (30.9%)/68 (6.8%)/624 (62.3%)
Alcohol drinking (yes/quit/no)	263 (26.2%)/57 (5.7%)/682 (68.1%)
Surgery history (yes/no)	387 (38.6%)/615 (61.4%)
ASA score (I / II / III)	41 (4.1%)/896 (89.4%)/65 (6.5%)
Surgical types (T/U/ML)	275 (27.4%)/446 (44.5%)/281(28.1%)
Surgical methods (E/non-E)	229(22.9%)/773 (77.1%)
PPT (kg/cm ²)	3.87 ± 1.83
PTO (kg/cm ²)	7.05 ± 2.89
PCA consumption (mL)	83.6 ± 33.7
PONV (yes/no)	85 (8.5%)/917 (91.5%)
Inadequate analgesia (yes/no)	155 (15.5%)/847 (84.5%)

BMI = body mass index; E = endoscopic; ML = middle/lower abdomen; PCA = patient controlled analgesia; PONV = postoperative nausea and vomiting; PPT = pressure pain threshold; PTO = pressure pain tolerance; T = thorax; U = upper abdomen.

as having the potential to predict the incidence of postoperative inadequate analgesia. Compared with thoracic surgery, middle/lower abdomen surgery (OR = 1.87, 95% CI: 1.05 to 3.30, $P = 0.032$) and upper abdomen surgery (OR = 2.49, 95% CI: 1.55 to 4.01, $P < 0.001$) were risk factors for postoperative inadequate analgesia. In addition, surgery history was also found to be a risk factor (OR = 1.54, 95% CI: 1.06 to 2.22, $P = 0.038$) for postoperative inadequate analgesia. The actual incidences of postoperative inadequate analgesia for these factors are shown in Fig. 2. These results indicated that the likelihood of patients undergoing endoscope surgery and former and never smokers presenting with inadequate analgesia was lower than that in non-endoscope surgery patients and current smokers, respectively; however, patients with a history

Table 2. Logistic regression model for postoperative inadequate analgesia.

Predictors	Chi-Square	P values	OR	Lower 95% CI	Upper 95% CI
Intercept	17.79	< 0.001			
Surgical type	14.243	0.001			
Surgical type = U	14.193	< 0.001	2.49	1.55	4.01
Surgical type = ML	4.587	0.032	1.87	1.05	3.30
Surgery method = E	4.154	0.042	0.57	0.34	0.97
Smoking status	10.271	0.006			
Smoking status = quit	9.193	0.002	0.54	0.37	0.80
Smoking status = no	3.463	0.063	0.44	0.19	1.04
Surgery history = yes	4.326	0.038	1.54	1.06	2.22
Preoperative basal pain sensitivity = low PTO	11.706	0.001	2.19	1.40	3.42

CI = confidence interval; E = endoscopic; ML = middle/lower abdomen; OR = odds ratio; U = upper abdomen.

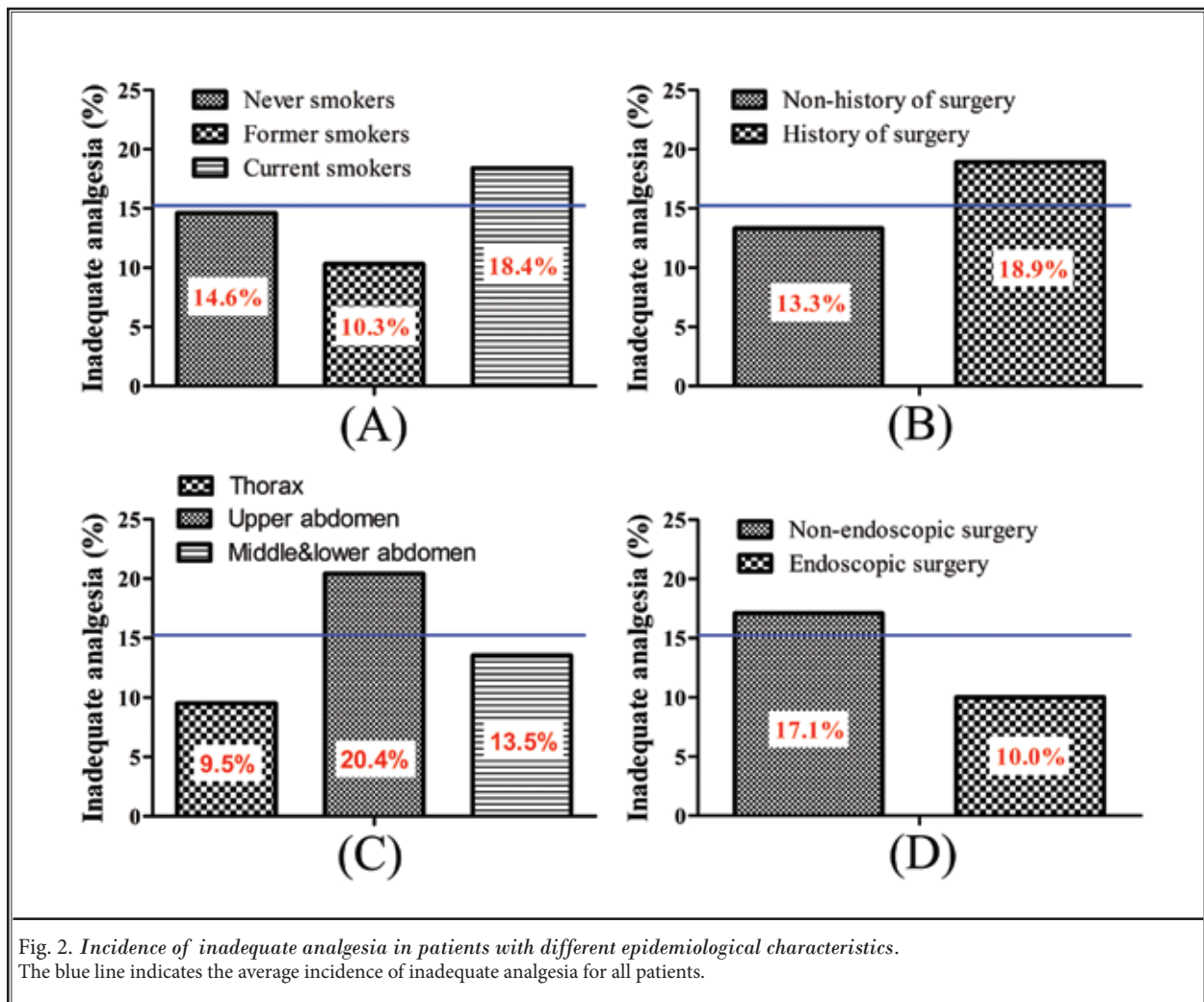


Fig. 2. Incidence of inadequate analgesia in patients with different epidemiological characteristics. The blue line indicates the average incidence of inadequate analgesia for all patients.

of surgery and patients receiving upper abdomen surgery or middle/lower abdomen surgery was higher than other patients.

Beyond those common epidemiologic and surgical factors, preoperative basal pain measurement was also found to have a significant effect on the incidence of postoperative inadequate analgesia. The OR for low PTO was 2.19 (95% CI: 1.40 to 3.42, $P = 0.001$), indicating that, compared with patients with a high PTO, patients with a low PTO would have a higher risk to present with postoperative inadequate analgesia (Fig. 3A). We also compared the basal PPT and PTO measurement values between the patients with or without postoperative inadequate analgesia. As shown in Fig. 3B, we found that the PTO values in patients with postoperative inadequate analgesia ($6.33 \pm 2.63 \text{ kg/cm}^2$) were significantly higher than those without inadequate analgesia ($7.18 \pm 2.92 \text{ kg/cm}^2$, $P < 0.001$). However, there was no significant difference ($3.61 \pm 1.71 \text{ kg/cm}^2$ vs. $3.92 \pm 1.85 \text{ kg/cm}^2$, $P = 0.056$) in the PPT between the patient group patients.

Factors for Predicting Postoperative PCA Consumption

As shown in Table 3, multiple regression analysis showed that gender and BMI provided the best predictive model for PCA consumption in all 3 types of surgery, including middle/lower abdomen (adjusted $r^2 = 0.205$, $P < 0.001$), upper abdomen (adjusted $r^2 = 0.101$, $P < 0.211$),

and thorax surgery (adjusted $r^2 = 0.133$, $P < 0.001$). All of the regression coefficients for gender were negative (-0.214, -0.390, and -0.196), indicating that women required less PCA consumption in postoperative pain control. In addition, the regression coefficients for BMI were positive (0.370, 0.570, and 0.315), indicating that patients with a higher BMI required more PCA consumption. Independent t-test also showed that women required less PCA consumption in middle/lower abdomen (63.2 ± 27.9 vs. 75.3 ± 30.6 , $P = 0.001$), upper abdomen (81.1 ± 30.7 vs. 99.1 ± 33.8 , $P < 0.001$), and thorax surgery (67.8 ± 30.2 vs. 95.0 ± 31.1 , $P < 0.001$).

As analyzed by the above logistical regression model, gender was not a significant predictor for the incidence of postoperative inadequate analgesia, and chi-squared test showed that, in women, it was 17.3%; however, in men, it was 14.1% ($P = 0.152$). Next, we compared both the total PCA consumption and PCA consumption per weight of all patients, and the results showed that women consumed less total PCA consumption ($72.9 \pm 30.8 \text{ mL}$ vs. $91.5 \pm 33.6 \text{ mL}$, $P < 0.001$) and less PCA consumption per weight ($1.33 \pm 0.54 \text{ mL/kg}$ vs. $1.44 \pm 0.52 \text{ mL/kg}$, $P = 0.001$) during the postoperative analgesia.

Multiple Regression Analysis for Pressure Pain Aensitivity

As shown in Table 4, 5 predictive factors—gender, age, BMI, living place, and smoking status—provided

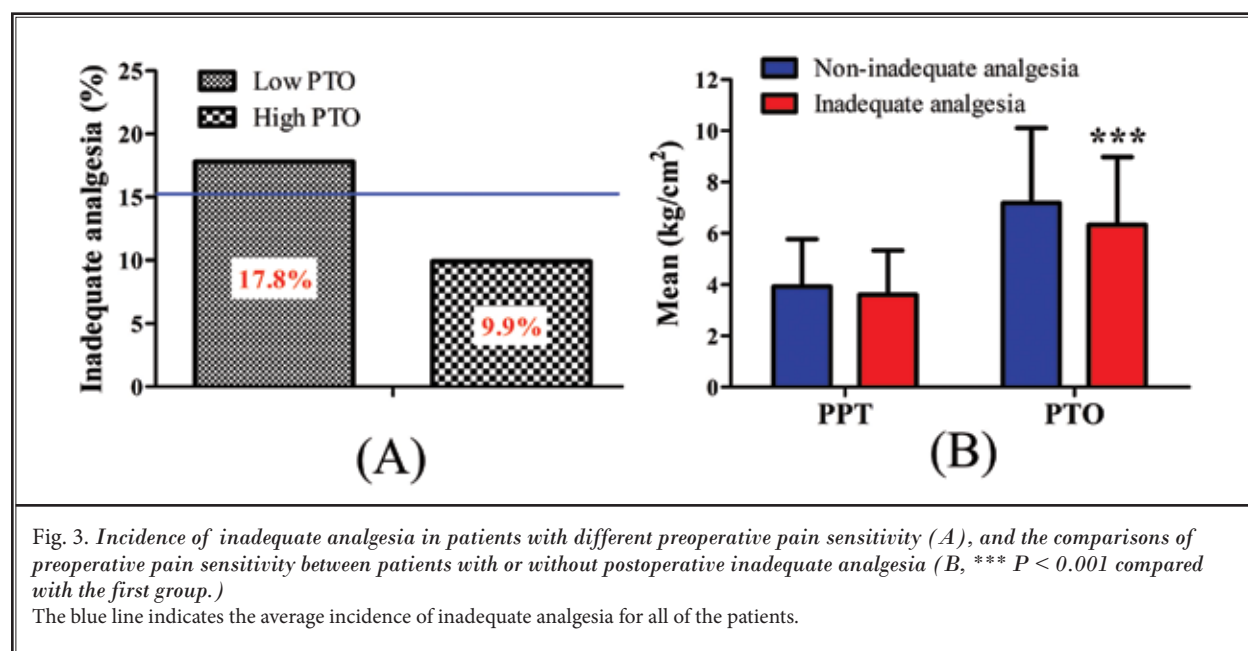


Table 3. Multiple regression analysis of PCA consumption for different types of surgery.

Outcome	Predictors	B	β	t	P value	Model			
						F	P Value	r ²	Adjusted r ²
ML surgery						55.236	< 0.001	0.211	0.205
	Gender =female	-14.861	-0.214	-4.969	< 0.001				
	BMI	3.948	0.370	8.603	< 0.001				
U surgery						37.551	< 0.001	0.217	0.211
	Gender = female	-27.078	-0.390	-7.264	< 0.001				
	BMI	2.672	0.570	4.686	< 0.001				
T surgery						22.547	< 0.001	0.140	0.133
	Gender = female	-11.811	-0.196	-3.532	< 0.001				
	BMI	3.208	0.315	5.661	< 0.001				

ML = middle/lower abdomen; U = upper abdomen; T = thorax.

Table 4. Multiple regression analysis of pressure pain sensitivity.

Outcome	Predictors	B	β	t	P value	Model			
						F	P Value	r ²	Adjusted r ²
PPT						19.755	< 0.001	0.106	0.101
	Gender = female	-0.430	-0.116	-3.025	0.003				
	Age	0.011	0.067	2.164	0.031				
	BMI	0.087	0.147	4.819	< 0.001				
	Living place = city	-0.554	-0.151	-5.002	< 0.001				
	Smoking status = yes	0.396	0.100	2.606	0.009				
	Smoking status = quit	0.786	0.108	3.237	0.001				
PTO						33.818	< 0.001	0.145	0.141
	Gender = female	-1.390	-0.237	-6.334	< 0.001				
	BMI	0.145	0.155	5.230	< 0.001				
	Living place = city	-0.790	-0.136	-4.620	< 0.001				
	Smoking status = yes	0.648	0.103	2.784	0.005				
	Smoking status = quit	0.832	0.072	2.247	0.025				

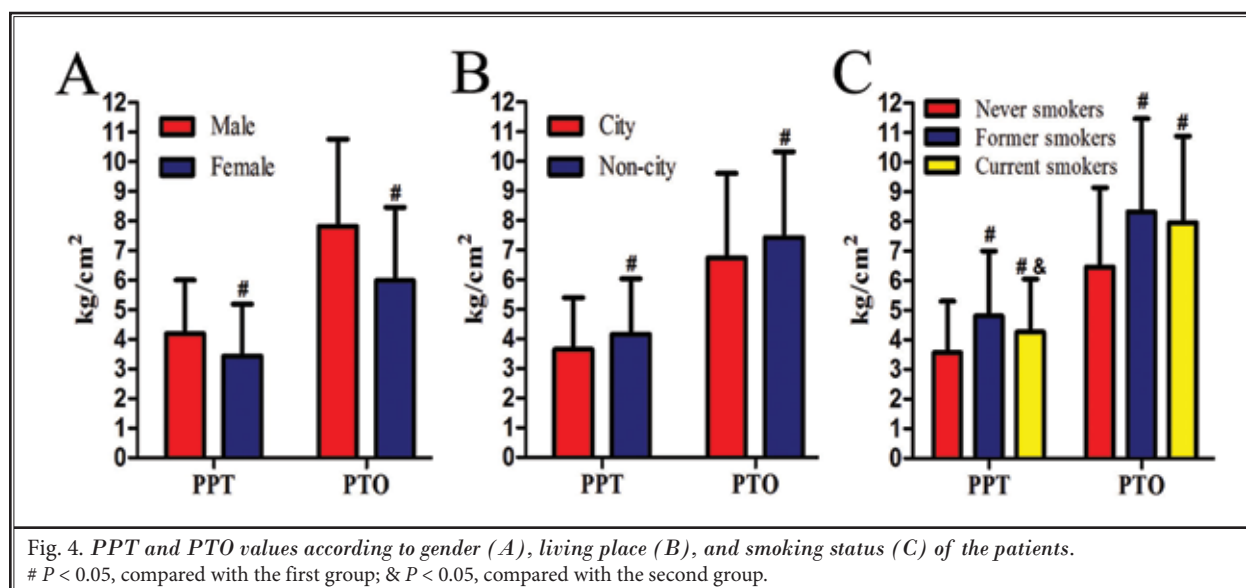
B = unstandardized coefficients; β =standardized coefficients.

the best predictive model for PPT (adjusted r² = 0.101, *P* < 0.001). In the model for PTO, 4 factors (gender, BMI, living place, and smoking status) provided the best predictive effect (adjusted r² = 0.141, *P* < 0.001).

Regression coefficients for gender and living place were negative (-0.116 and -0.151 for PPT; -0.237 and -0.136 for PTO), indicating that women and patients who lived in the city showed lower PPT and PTO values than men and non-city patients, respectively. The regression coefficients for age (0.067 for PPT) and BMI (0.147 for PPT; 0.155 for PTO) were positive, and these results indicated that patients with more advance age and higher BMI showed higher pressure pain measurement values. In addition, the regression coefficients for

former and current smokers were positive (0.100 and 0.108 for PPT; 0.103 and 0.072 for PTO), indicating that these patients showed higher PPT and PTO values than the never smokers.

Next, the patients' PPT and PTO values were compared among gender, living place, and smoking status. As shown in Fig. 4A, the men's PPT (4.20 ± 1.82 vs. 3.43 ± 1.76, *P* < 0.001) and PTO (7.83 ± 2.93 vs. 5.99 ± 2.48, *P* < 0.001) values were higher than those in women, and the city patients' PPT (3.64 ± 1.75 vs. 4.15 ± 1.88, *P* < 0.001) and PTO (6.74 ± 2.85 vs. 7.42 ± 2.90, *P* < 0.001) values were lower than those in non-city patients (Fig. 4B). ANOVA showed that there was a significant difference (*P* < 0.001) between patients of different smoking



statuses. As shown in Fig. 4C, never smokers' PPT (3.57 ± 1.73 vs. 4.81 ± 2.19 and 4.27 ± 1.79 , $P < 0.001$) and PTO (6.46 ± 2.69 vs. 8.33 ± 3.15 and 7.97 ± 2.91 , $P < 0.001$) values were significantly lower than those in former and current smokers, and former smokers' PPT values were higher than those in current smokers (4.81 ± 2.19 vs. 4.27 ± 1.79 , $P = 0.025$). However, no significant difference in the PTO was found between former and current smokers (8.33 ± 3.15 vs. 7.97 ± 2.91 , $P = 0.339$).

Discussion

In the current prospective study, we investigated the possible effects of some epidemiologic factors and preoperative pressure pain measurement on clinical postoperative pain sensitivity in a relative large Chinese population including a sample of 1,002 surgery patients. For all of these patients, we provided pre-emptive analgesia combined with postoperative PCA treatment for surgery pain control. However, there were still 15.5% of these patients presenting with moderate-to-severe postoperative pain at rest. This indicated that, even if perioperative analgesic measures were applied, a considerable portion of these surgery patients remained at the risk of postoperative inadequate analgesia. Next, through regression analysis, several different factors were identified as having a significant effect on postoperative pain intensity and analgesia requirements for postoperative pain control, and also for the patients' mechanical basal pain sensitivity.

Regarding the effect of the smoking status on the pain phenotype, an interesting phenomenon should be

noted in the current study. Patients who were current or former smokers exhibited lower pressure pain sensitivity in both higher PPT and PTO than never smokers. These results suggested that the patients' basal pressure pain sensitivity was positively associated with their exposure level to cigarettes. This led to the hypothesis that cigarettes might contribute to increasing the patients' ability to tolerate pain. However, in previous studies, the possibility that systemic nicotine could be used to provide postoperative analgesia remained controversial (25-27).

The current logistic regression analysis showed that smoking status could significantly deteriorate the patients' postoperative analgesia outcome, which was opposite to the above results regarding the basal pressure pain. The patients in the current smoking status were identified as having a higher risk than other patients to present postoperative inadequate analgesia. A recent study also found that current smokers reported higher pain intensity on day one after surgery than nonsmokers and past-smokers (28). These results demonstrated that smoking led a negative contribution to the postoperative outcome, and it was beneficial for surgery patients from the perspective of postoperative pain treatment to quit smoking before receiving an operation, which has been proven to improve the patients' postoperative outcome (29). Additionally, the effect of nicotine in postoperative analgesia might need further study clinically, especially for current or former smokers. Nevertheless, most importantly, the current results supported that preoperatively determining the surgery

patients' smoking status would be helpful for predicting their possible postoperative analgesia outcome.

Additionally, surgery history was identified as a risk factor for postoperative inadequate analgesia. This demonstrated that whether the patients have a surgery history or not might be another effective epidemiological factor that should be preoperatively determined for predicting and guiding postoperative analgesia. Except for these epidemiological factors, surgery factors, including surgery sites and methods, were also found to have a significant effect on the postoperative pain intensity. The results regarding different postoperative pain associated with different surgery types were in agreement with some previous studies (30,31); thus, postoperative pain treatment needs to comply with the existing procedure-specific pain-treatment recommendations. In addition, based on patients who received endoscopic surgery experiencing less risk of postoperative inadequate analgesia, minimally invasive surgery should be encouraged (12).

Beyond the above epidemiological and surgery factors, we found that preoperative pressure pain measurement could also predict the postoperative pain intensity. Mechanical pressure pain measurement has been shown to be a reliable quantitative sensory testing measure (32-34) and has been widely used in many experimental and clinical pain studies (14,35-37). Additionally, pressure stimulation is easily applied to evaluate pain sensitivity and is typically a more acceptable method to patients. Thus a pressure algometer was preferentially applied to evaluate the patients' basal pain sensitivity in the current study. However, in the study, we found that only PTO but not PPT showed a significant association with the incidence of postoperative inadequate analgesia. The comparison between patients with or without inadequate analgesia also showed that those patients without inadequate analgesia exhibited significantly higher PTO values, but the difference in PPT did not reach statistical significance. Therefore, these findings suggest that important differences might exist between stimulation modalities (13); in the current study, the suprathreshold stimulate—i.e., PTO—seemed to have a much greater predictive potential than PPT.

In the analysis for postoperative PCA consumption, only BMI and gender factors were identified. Actually, the effect of gender on various pain phenotypes has been demonstrated in many previous studies, but there were some inconsistent or absent results observed in

some studies (38-40). In the current study, we found that women presented with higher basal pressure pain sensitivity, and the incidence of postoperative inadequate analgesia in women was slightly higher (17.4% vs. 14.1%, Pearson $P = 0.152$) than that in men. However, our results showed that, during the postoperative analgesia, women consumed significantly less analgesic, including total and per weight PCA volume, than men. This might be caused by the specific adverse effect that has a high incidence in women because the incidence of PONV in women was significantly higher than that in men (14.3% vs. 4.2%, $P < 0.001$) in the current study. Therefore, based on the current study, the effect of gender factors on postoperative pain treatment needs to be further studied, and, clinically, a better method or analgesic should be considered for the prevention of PONV in women.

Several limitations should be noted in the current study. First, that the study did not apply psychological tests might be a potential limitation. However, in the study, all of the patients were given information to minimize their anxiety related to the surgery and the experimental pain test on the day prior to the operation. Second, in the current study, the normal reference values of PPT and PTO were cited from our previous healthy volunteer study. Although this ensured the pressure pain data came from the same investigators using the same test instrument and procedure, the difference between the 2 population groups should not be ignored. In addition, the patients examined in the current study were all from the Chinese Han population, and the demographic factors such as BMI in diverse racial populations are different. Thus the possible impact of race should be considered when interpreting the current results.

CONCLUSION

Through the current prospective study, epidemiological factors, including current smokers and history of surgery, were identified as independent risk factors for the incidence of postoperative inadequate analgesia. Additionally, from the perspective of the postoperative analgesia outcome, minimally invasive surgery and procedure-specific pain-treatment should be encouraged. In addition, preoperative PTO measurement could effectively predict postoperative inadequate analgesia. These factors have the potential to serve as predictors for postoperative analgesia in the Chinese population.

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