

Research Article

Predictors of Acute Postsurgical Pain following Gastrointestinal Surgery: A Prospective Cohort Study

Qing-Ren Liu ^{1,2}, Mu-Huo Ji,³ Yu-Chen Dai,⁴ Xing-Bing Sun,² Cheng-Mao Zhou,⁵ Xiao-Dong Qiu,⁴ and Jian-Jun Yang ^{1,5}

¹School of Medicine, Southeast University, Nanjing 210009, China

²Department of Anesthesiology, Xishan People's Hospital of Wuxi City, Wuxi 214105, China

³Department of Anesthesiology, The Second Affiliated Hospital, Nanjing Medical University, Nanjing 210011, China

⁴Department of Anesthesiology, Zhongda Hospital, Medical School, Southeast University, Nanjing 210009, China

⁵Department of Anesthesiology, Pain and Perioperative Medicine, The First Affiliated Hospital of Zhengzhou University, Zhengzhou 450000, China

Correspondence should be addressed to Jian-Jun Yang; yjyangjj@126.com

Received 1 December 2020; Accepted 20 January 2021; Published 29 January 2021

Academic Editor: Jian-Guo Zhou

Copyright © 2021 Qing-Ren Liu et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. Several predictors have been shown to be independently associated with chronic postsurgical pain for gastrointestinal surgery, but few studies have investigated the factors associated with acute postsurgical pain (APSP). The aim of this study was to identify the predictors of APSP intensity and severity through investigating demographic, psychological, and clinical variables. **Methods.** We performed a prospective cohort study of 282 patients undergoing gastrointestinal surgery to analyze the predictors of APSP. Psychological questionnaires were assessed 1 day before surgery. Meanwhile, demographic characteristics and perioperative data were collected. The primary outcomes are APSP intensity assessed by numeric rating scale (NRS) and APSP severity defined as a clinically meaningful pain when NRS ≥ 4 . The predictors for APSP intensity and severity were determined using multiple linear regression and multivariate logistic regression, respectively. **Results.** 112 patients (39.7%) reported a clinically meaningful pain during the first 24 hours postoperatively. Oral morphine milligram equivalent (MME) consumption (β 0.05, 95% CI 0.03–0.07, $p < 0.001$), preoperative anxiety (β 0.12, 95% CI 0.08–0.15, $p < 0.001$), and expected postsurgical pain intensity (β 0.12, 95% CI 0.06–0.18, $p < 0.001$) were positively associated with APSP intensity. Furthermore, MME consumption (OR 1.15, 95% CI 1.10–1.21, $p < 0.001$), preoperative anxiety (OR 1.33, 95% CI 1.21–1.46, $p < 0.001$), and expected postsurgical pain intensity (OR 1.36, 95% CI 1.17–1.57, $p < 0.001$) were independently associated with APSP severity. **Conclusion.** These results suggested that the predictors for APSP intensity following gastrointestinal surgery included analgesic consumption, preoperative anxiety, and expected postsurgical pain, which were also the risk factors for APSP severity.

1. Introduction

Acute postsurgical pain (APSP) is defined as pain within the first 24 hours postoperatively. Moderate or severe APSP is reported in 10% to 57% of patients undergoing various types of surgeries [1]. A larger study with 22,000 patients also showed that 28% experienced moderate–severe APSP after various types of surgeries [2]. APSP has a considerable influence on cardiovascular system, respiratory system, and immune system, which impacts postoperative early recovery [3]. Furthermore, APSP can transit to CPSP that may impair

a patient's long-term quality of life [4, 5]. It has been demonstrated that female [6], young age [2, 7, 8], preoperative anxiety [7, 9–15] and depression [10], expected postsurgical pain [9, 16–19], pain catastrophizing [7, 20, 21], preoperative pain [7, 10, 22], and type of surgery [14, 21, 23] are risk factors for APSP.

Enhanced Recovery after Surgery (ERAS) is a multimodal perioperative care pathway designed to reduce perioperative stress, maintain postoperative physiological function, and accelerate recovery after surgery. Thus, major complications can be reduced while length of stay can be

shortened after major gastrointestinal surgery [24–28]. Pain management is an integral part of ERAS protocols. Around 30% of patients reported that pain would affect mood, sleep, and enjoyment of life after gastrointestinal surgery while 12% visited the emergency department because of unendurable pain [29]. Therefore, great attention should be paid to early intervention and control of acute pain through identifying specific predictors after gastrointestinal surgery [30–32]. Currently, several studies on predictors of CPSP have been performed among patients undergoing gastrointestinal surgery, showing that the associated predictors are female gender [30], younger age [30], preoperative anxiety and depression [29], and preoperative pain [33]. However, little is known about the predictors of APSP intensity or severity for gastrointestinal surgery.

The purpose of our study was to determine the predictors of APSP intensity and severity for gastrointestinal surgery by investigating demographic, psychological, and clinical variables. The primary outcome of interest is APSP intensity assessed using the 11-point numeric rating scale (NRS, 0 = no pain at all, 10 = strongest pain imaginable) [34, 35] and APSP severity defined as a clinically meaningful pain when maximum pain NRS ≥ 4 [12, 14]. We hypothesized that analgesic consumption and certain psychological variables would be the independent risk factors for APSP after controlling the confounding factors.

2. Methods

2.1. Participants. The protocol was registered at the Chinese Clinical Trial Registry (ChiCTR1900024837). This prospective cohort study was carried out at Zhongda Hospital, Southeast University. The study was approved by IEC for Clinical Research of Zhongda Hospital Affiliated to Southeast University (No. 2019ZDSYLL084-P01). Patients eligible for participation were those scheduled for gastrointestinal surgery between August 2019 and January 2020. The study recruited 345 patients to investigate the prediction of acute pain after gastrointestinal surgery. The written informed consent was obtained as a condition to participate in the study. Inclusion criteria included patients undergoing elective gastrointestinal surgery, aged ≥ 18 years old and physical status classification of the American Society of Anesthesiologists (ASA) \leq III. Patients with self-expression disorder and hearing or visual impairment were excluded.

2.2. Demographic Characteristics. Demographic characteristics such as gender, age, height, weight, calculated body mass index (BMI), occupation status, education level, smoking (never, former, and current), alcohol drinking (never, former, and current), hypertension, diabetes, coronary heart disease, and physical status classification of ASA were collected on the day before surgery. Moreover, patients were asked to rate a history of preexisting pain. Patients who suffered from pain for more than 3 months were classified as having previous chronic pain. Simultaneously, a history of previous surgery was also attained and participants were classified as previous surgery and no previous surgery.

2.3. Psychological Questionnaires. During the preoperative visit, psychological factors were assessed with the respective standardized and validated questionnaires: Hospital Anxiety and Depression Scale (HADS) [36] and Surgical Fear Questionnaire (SFQ) [37]. The HADS consists of two seven-item subscales that measure anxiety and depression levels among patients in nonpsychiatric hospital settings. Subscale scores vary between 0 and 21, with higher scores representing higher levels of anxiety and depression. The SFQ, as a valid and reliable index of surgical fear, consists of two eight-item subscales that measure short-term consequences of surgery (SFQ-s) and fear of the long-term consequences (SFQ-l). All item scores covered the full range of 0–10. In addition, patients were asked to rate their average expected pain intensity for the first day postoperatively (on a scale from 0 = no pain at all to 10 = strongest pain imaginable) [9].

2.4. Surgery and Anesthesia. Surgery was performed by 3 surgeons according to a standardized protocol. Data regarding type, site, duration of surgery, as well as number of drainage tube and length of hospital stay, were collected. Additionally, preoperative clinical factors were attained from the medical record. The primary sites of surgery included stomach, colorectum, and small bowel. The surgery was performed using either open or laparoscopic procedure.

After standard monitoring (electrocardiogram, peripheral oxygen saturation, noninvasive blood pressure, and end-tidal carbon dioxide), a standardized anesthetic protocol was carried out by the anesthesiologists who were members of the research team. General anesthesia was induced with intravenous (IV) administration of 0.3 μ g/kg of sufentanil, 2 to 2.5 mg/kg of propofol, and 0.6 mg/kg of rocuronium. Anesthesia was maintained with sevoflurane, remifentanil, and cisatracurium. During skin closure, sufentanil (0.1 μ g/kg, IV) was given.

2.5. Acute Postoperative Pain. The primary outcome was the maximum pain intensity assessed using NRS pain scores within the first 24 h after surgery. At 6–8, 14–16, and 22–24 hours after operation, patients were asked to report their level of pain during movement (changing position to either sitting up or standing), respectively. The maximum pain intensity was identified as the highest NRS pain score at three time points within the first 24 h postoperatively. We defined NRS ≥ 4 of the maximum pain as clinically meaningful pain, indicating moderate-to-severe pain intensity.

After surgery, patients received routine postoperative pain management. In the postanesthesia care unit (PACU), patients received tramadol (50 mg, IV) or oxycodone (2 mg, IV) when NRS pain at rest > 3 . On the ward, patients received celecoxib 200 mg orally every 12 h, as well as a patient-controlled analgesia device with oxycodone or sufentanil. Furthermore, patients administered the breakthrough pain using tramadol intravenously only as needed. The analgesic consumption of 24 hours postoperatively was measured from arriving PACU. To compare the analgesic consumption, systemic opioid analgesics were converted to oral milligram morphine equivalent (MME). MME use was calculated using standard published conversion factors.

2.6. Statistical Analysis. First, descriptive statistics were calculated on all variables. Mean \pm standard deviation was used for normally distributed variables, medians (interquartile range) for nonnormally distributed variables, and number (percentage) for categorical data. $p < 0.05$ was considered statistically significant. Pearson's test was performed to investigate the correlation between preoperative anxiety and depression, expected postsurgical pain, SFQ-s, SFQ-l, and APSP intensity. Next, univariate linear regression and multiple linear regression models were used to examine whether MME consumption, preoperative anxiety, and expected postsurgical pain had an independent effect on APSP intensity. Furthermore, we also performed univariate logistic regression and multivariate logistic regression to identify whether MME consumption, preoperative anxiety, and expected postsurgical pain were independently associated with APSP severity. All analyses were performed with R (<http://www.R-project.org>) and EmpowerStats software (<http://www.empowerstats.com>, X&Y Solutions, Inc., Boston, MA, USA).

3. Results

345 patients were approached for participation in this study. 31 declined participation, and 6 withdrew consent. There were 12 patients excluded owing to incomplete questionnaires, 8 patients for surgery cancellation, and 6 patients for transferring to intensive care unit. Thus, 282 patients (81.7%) were available for analysis (Figure 1).

3.1. Demographic, Clinical, and Psychological Characteristics. Demographic and clinical characteristics of patients are shown in Table 1. 110 patients (39%) were female; 38 (13.5%) were single, separated or divorced; 183 (64.9%) had a middle-school education or above; 66 (23.4%) reported previous chronic pain; and 143 (50.7%) had a history of previous surgery. Most patients (93.2%) received gastric or colorectal surgery, but only 83 patients (29.4%) underwent laparoscopic surgery. Most patients (84.4%) had malignant tumor.

Psychological characteristics of patients are shown in Table 2. In preoperative assessment, 56 patients (19.9%) had anxiety, and 39 patients (13.8%) had depression. The median score of expected postsurgical pain intensity was 5.0 (3.0, 7.0), and 113 patients (40.1%) reported moderate-to-severe pain (NRS ≥ 4) during movement within the first 24 hours postoperatively. The median scores of SFQ-s and SFQ-l subscales were 9.0 (3.0, 15.0) and 6.0 (2.0, 14.0), respectively.

3.2. Predicting Postsurgical Pain Intensity. Table 3 presented Pearson's correlation coefficients between APSP intensity and other study variables. APSP intensity was significantly correlated with MME consumption (Pearson's $r = 0.63$, $p < 0.001$), preoperative anxiety (Pearson's $r = 0.48$, $p < 0.001$), preoperative depression (Pearson's $r = 0.36$, $p < 0.001$), and expected postsurgical pain intensity (Pearson's $r = 0.38$, $p < 0.001$). Meanwhile, it was also obviously correlated with SFQ-s (Pearson's $r = 0.31$, $p < 0.001$) and

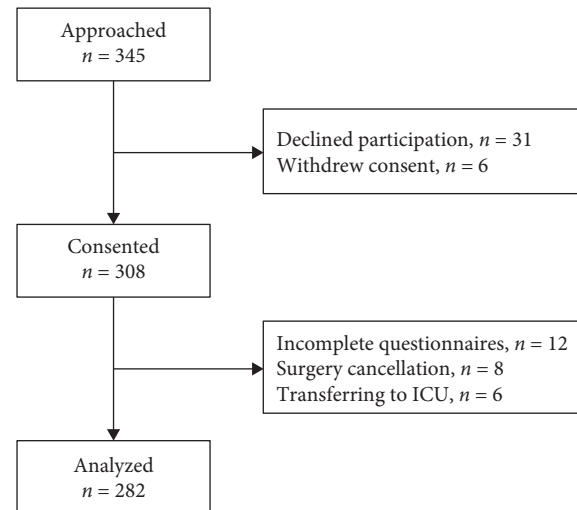


FIGURE 1: Flowchart of the study. ICU: intensive care unit.

SFQ-l (Pearson's $r = 0.32$, $p < 0.001$) but negatively correlated with age (Pearson's $r = -0.17$, $p < 0.001$).

As shown in Table 4, for the univariate analysis, APSP intensity was significantly correlated with MME consumption (β 0.07, 95% CI 0.05–0.09, $p < 0.001$), preoperative anxiety (β 0.15, 95% CI 0.12–0.18, $p < 0.001$), preoperative depression (β 0.12, 95% CI 0.08–0.15, $p < 0.001$), and expected postsurgical pain (β 0.20, 95% CI 0.15–0.26, $p < 0.001$). In addition, SFQ-s (β 0.04, 95% CI 0.03–0.05, $p < 0.001$) and SFQ-l (β 0.04, 95% CI 0.03–0.06, $p < 0.001$) were associated with APSP intensity. Meanwhile, age (β -0.02 , 95% CI: 0.03 to -0.01 , $p = 0.004$) and occupation (β 0.38, 95% CI 0.07–0.70, $p = 0.018$) might also be associated with APSP intensity.

To determine the predictors of postsurgical pain intensity, a multiple linear regression analysis was conducted (Table 4). Preoperative anxiety (β 0.12, 95% CI 0.08–0.15, $p < 0.001$), expected postsurgical pain (β 0.12, 95% CI 0.06–0.18, $p < 0.001$), and MME consumption were positively associated with APSP intensity.

3.3. Risk Factors for Postsurgical Pain Severity. 169 patients reported absence of pain or mild pain (NRS ≤ 3) on APSP severity, whereas 113 patients reported moderate-to-severe pain, regarded as clinically meaningful pain. The univariate logistic analysis showed that APSP severity was significantly correlated with MME consumption (OR 1.18, 95% CI 1.12–1.24, $p < 0.001$), preoperative anxiety (OR 1.40, 95% CI 1.28–1.53, $p < 0.001$), preoperative depression (OR 1.31, 95% CI 1.20–1.43, $p < 0.001$), and expected postsurgical pain (OR 1.55, 95% CI 1.36–1.78, $p < 0.001$). In addition, SFQ-s (OR 1.09, 95% CI 1.06–1.12, $p < 0.001$), SFQ-l (OR 1.09, 95% CI 1.05–1.12, $p < 0.001$), and age (OR 0.97, 95% CI 0.95–0.99, $p = 0.005$) were also associated with APSP severity (Table 5).

After multivariable risk adjustment for potential confounding factors, a logistic regression was performed (Table 5). MME consumption (OR 1.15, 95% CI 1.10–1.21, $p < 0.001$), preoperative anxiety (OR 1.33, 95% CI 1.21–1.46,

TABLE 1: Demographic and clinical characteristics of patients.

| Characteristics | |
|-------------------------------|--------------|
| Female | 110 (39%) |
| Age, year | 65.8 ± 12.0 |
| BMI, kg/m ² | 25.0 ± 5.0 |
| No occupation | 225 (79.8%) |
| Education level | |
| Primary | 99 (35.1%) |
| Middle or high school | 135 (47.9%) |
| College or above | 48 (17.0%) |
| Marital status | |
| Single, separated or divorced | 38 (13.5%) |
| Married | 244 (86.5%) |
| Smoking | |
| Never smoker | 157 (55.7%) |
| Former | 58 (20.6%) |
| Current | 67 (23.8%) |
| Alcohol drinking | |
| Never drinks | 156 (55.3%) |
| Former | 65 (23.0%) |
| Current | 61 (21.6%) |
| Hypertension | 131 (46.5%) |
| Diabetes | 38 (13.5%) |
| Coronary heart disease | 25 (8.9%) |
| ASA physical status | |
| ASA I | 45 (16.0%) |
| ASA II | 202 (71.6%) |
| ASA III | 35 (12.4%) |
| Preoperative chronic pain | 66 (23.4%) |
| Previous surgery | 143 (50.7%) |
| Site of surgery | |
| Stomach | 118 (41.8%) |
| Colorectum | 145 (51.4%) |
| Small bowel | 19 (6.7%) |
| Type of surgery | |
| Open | 199 (70.6%) |
| Laparoscopic | 83 (29.4%) |
| Duration of surgery, min | 180.0 ± 61.8 |
| MME consumption, mg | 48.3 ± 16.4 |
| Number of drainage tubes | |
| 1 tube | 120 (42.6%) |
| ≥2 tubes | 162 (57.4%) |
| Retention time of tube, day | 7.9 ± 3.0 |
| Length of hospital stay, day | 18.8 ± 6.8 |
| Malignant tumor | 238 (84.4%) |

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as *n* (%). BMI: body mass index; ASA: American Society of Anesthesiologists; MME: morphine milligram equivalent.

$p < 0.001$), and expected postsurgical pain (OR 1.36, 95% CI 1.17–1.57, $p < 0.001$) were independently associated with APSP severity.

4. Discussion

To the best of our knowledge, there were few predictive prospective studies on APSP for gastrointestinal surgery. In this study, we assessed possible predictors for APSP after gastrointestinal surgery. We discovered that higher preoperative anxiety and higher expected postsurgical pain score were independently associated with stronger postsurgical

TABLE 2: Psychological characteristics of patients.

| Characteristics | |
|--------------------------------------|-----------------|
| HADS: anxiety | 3.0 (1.0, 6.0) |
| HADS: anxiety | |
| No | 226 (80.1%) |
| Yes | 56 (19.9%) |
| HADS: depression | 2.0 (1.0, 5.0) |
| HADS: depression | |
| No | 243 (86.2%) |
| Yes | 39 (13.8%) |
| Expected postsurgical pain intensity | 5.0 (3.0, 7.0) |
| Expected postsurgical pain severity | |
| No or mild | 95 (33.7%) |
| Moderate | 110 (39.0%) |
| Severe | 77 (27.3%) |
| SFQ-s | 9.0 (3.0, 15.0) |
| SFQ-l | 6.0 (2.0, 14.0) |

Continuous variables are presented as median (interquartile range). Categorical variables are presented as *n* (%). HADS: Hospital Anxiety and Depression Scale; SFQ-s: Surgical Fear Questionnaire short-time consequences; and SFQ-l: Surgical Fear Questionnaire long-time consequences.

pain intensity and severity. Moreover, the study showed that more analgesics were consumed in patients undergoing moderate or severe postoperative pain during the first 24 postoperative hours. Our results confirm and extend those of previous studies focused on patients undergoing other types of surgery.

Despite uniform multimodal analgesic treatment, we discovered a large variability in pain intensity during movement. 59.9% of patients experienced moderate or severe pain during the first 24 postoperative hours, respectively. An important increase in opioid analgesic consumption was observed in the patients experiencing moderate or severe pain compared to those experiencing mild pain. Similar to previous studies on other surgery [9], cumulative analgesic consumption was a strong predictor for APSP. Furthermore, analgesic consumption has significant correlation with patients' factors such as age, depression, anxiety, and expected postsurgical pain.

We found that preoperative anxiety was significantly correlated with APSP intensity and became an independent predictor of APSP intensity and severity. These results are consistent with studies which suggested that presurgical anxiety can predict APSP intensity for hysterectomy [7], cesarean [9], inguinal hernioplasty [10], knee replacement [11], and breast cancer surgery [12–14]. Furthermore, a systematic review in women undergoing breast surgery suggested that presurgical anxiety assessed by HADS, state anxiety, or trait anxiety could predict APSP [15].

Similar to previous studies on cesarean [9, 16] and breast cancer [17, 18], expected postsurgical pain could predict APSP intensity in our study. Meanwhile, it was also a strong predictor of APSP severity. In addition, expected postsurgical pain has been used as predictor of the acute pain trajectories during the first postoperative week after breast cancer surgery. The result suggested that patients with higher expected postsurgical pain intensity had higher pain intercepts (high initial pain intensity) and more unfavorable slopes (poor resolution of pain) [19]. However, a previous

TABLE 3: Pearson's correlation between age, BMI, MME consumption, psychological characteristics, and APSP intensity.

| Variables | A | B | C | D | E | F | G | H | I |
|--------------------------------|--------------------|--------------------|-------|-------------------|-------------------|-------------------|-------------------|-------------------|-----|
| APSP intensity (A) | 1.0 | | | | | | | | |
| Age, year (B) | -1.71 [†] | 1.0 | | | | | | | |
| BMI, kg/m ² (C) | -0.13 | -0.08 | 1.0 | | | | | | |
| MME consumption (D) | 0.63 [†] | -0.14* | 0.11 | 1.0 | | | | | |
| HADS: anxiety (E) | 0.48 [†] | -0.20 [†] | 0.03 | 0.58 [†] | 1.0 | | | | |
| HADS: depression (F) | 0.36 [†] | 0.04 | -0.01 | 0.52 [†] | 0.53 [†] | 1.0 | | | |
| Expected postsurgical pain (G) | 0.38 [†] | -0.18 [†] | 0.00 | 0.56 [†] | 0.42 [†] | 0.16 [†] | 1.0 | | |
| SFQ-s (H) | 0.31 [†] | -0.13* | 0.07 | 0.25 [†] | 0.57 [†] | 0.38 [†] | 0.44 [†] | 1.0 | |
| SFQ-l (I) | 0.31 [†] | -0.11 | -0.03 | 0.22 [†] | 0.55 [†] | 0.40 [†] | 0.34 [†] | 0.75 [†] | 1.0 |

* $p < 0.05$, [†] $p < 0.01$. APSP: acute postsurgical pain; BMI: body mass index; MME: morphine milligram milligram equivalent; HADS: Hospital Anxiety and Depression Scale; SFQ-s: Surgical Fear Questionnaire short-time consequences; and SFQ-l: Surgical Fear Questionnaire long-time consequences.

TABLE 4: Univariate and multivariate analyses of predictors for APSP intensity.

| Variables | Unadjusted β (95% CI) | p value | Adjusted β (95% CI) | p value |
|----------------------------|-----------------------------|-----------|---------------------------|-----------|
| Gender | | | | |
| Male | Reference | | 0 | |
| Female | 0.15 (-0.11-0.42) | 0.247 | -0.11 (-0.46-0.23) | 0.518 |
| Age, year | -0.02 (-0.03 to -0.01) | 0.004 | -0.01 (-0.03 to -0.01) | 0.317 |
| BMI | -0.00 (-0.03-0.02) | 0.775 | -0.04 (-0.09-0.01) | 0.096 |
| Occupation status | | | | |
| No occupation | Reference | | 0 | 0.152 |
| Occupation | 0.38 (0.07-0.70) | 0.018 | 0.28 (-0.10-0.66) | |
| ASA physical status | | | | |
| ASA I | Reference | | 0 | |
| ASA II | -0.53 (-0.88 to -0.1) | 0.003 | 0.14 (-0.32-0.6) | 0.547 |
| ASA III | -0.42 (-0.89-0.06) | 0.088 | 0.35 (-0.29-0.98) | 0.285 |
| Preoperative chronic pain | | | | |
| Yes | Reference | | 0 | |
| No | 0.29 (-0.01-0.59) | 0.059 | 0.05 (-0.24-0.34) | 0.735 |
| Previous surgery | | | | |
| Yes | Reference | | 0 | |
| No | -0.17 (-0.43-0.08) | 0.179 | -0.05 (-0.30-0.20) | 0.694 |
| Site of surgery | | | | |
| Stomach | Reference | | 0 | |
| Colorectum | -0.17 (-0.44-0.09) | 0.204 | -0.25 (-0.52-0.02) | 0.071 |
| Small bowel | -0.20 (-0.73-0.33) | 0.457 | -0.25 (-0.79-0.29) | 0.365 |
| Type of surgery | | | | |
| Open | Reference | | 0 | |
| Laparoscopic | -0.16 (-0.44-0.12) | 0.259 | 0.21 (-0.10-0.52) | 0.189 |
| MME consumption, mg | 0.07 (0.05-0.09) | <0.001 | 0.05 (0.03-0.07) | <0.001 |
| HADS: anxiety | 0.15 (0.12-0.18) | <0.001 | 0.12 (0.08-0.15) | <0.001 |
| HADS: depression | 0.12 (0.08-0.15) | <0.001 | 0.11 (-0.04-0.07) | 0.565 |
| Expected postsurgical pain | 0.20 (0.15-0.26) | <0.001 | 0.12 (0.06-0.18) | <0.001 |
| SFQ-s | 0.04 (0.03-0.05) | <0.001 | 0.55 (-1.43-2.52) | 0.589 |
| SFQ-l | 0.04 (0.03-0.06) | <0.001 | 0.56 (-1.42-2.54) | 0.582 |

BMI: body mass index; ASA: American Society of Anesthesiologists; MME: morphine milligram equivalent; HADS: Hospital Anxiety and Depression Scale; SFQ-s: Surgical Fear Questionnaire short-time consequences; and SFQ-l: Surgical Fear Questionnaire long-time consequences.

trial that explored prediction of APSP following breast cancer surgery showed that expected postsurgical pain was not a risk factor for APSP severity [14]. The reason was probably that the variables included stronger confounding factors such as pain sensitivity, anxiety, and axillary dissection.

Our results did not support an independent association between preoperative depression and APSP, although preoperative depression was correlated with APSP intensity by

Pearson's test or univariable analysis. As previously stated, depression was not predictive of APSP severity at 2 days in women with breast cancer surgery, and only body image score emerged as an independent predictor [38]. In addition, a systematic review [15] did not find an association between preoperative depression and APSP in women undergoing breast surgery. But it had an association with CPSP at 3, 6, or 12 months [39, 40]. Thus, the preoperative depression might better predict CPSP compared to APSP.

TABLE 5: Univariate and multivariate analyses of predictors for APSP severity.

| Variables | Unadjusted OR (95% CI) | <i>p</i> value | Adjusted OR (95% CI) | <i>p</i> value |
|----------------------------|------------------------|----------------|----------------------|----------------|
| Gender | | | | |
| Male | Reference | | Reference | |
| Female | 1.44 (0.89–2.35) | 0.141 | 1.31 (0.49–3.48) | 0.589 |
| Age, year | 0.97 (0.95–0.99) | 0.005 | 0.95 (0.91–1.01) | 0.093 |
| BMI | 1.0 (0.95–1.05) | 0.992 | 0.91 (0.80–1.03) | 0.124 |
| Occupation status | | | | |
| No occupation | Reference | | Reference | |
| Occupation | 1.59 (0.89–2.85) | 0.120 | 1.15 (0.42–3.18) | 0.786 |
| ASA physical status | | | | |
| ASA I | Reference | | Reference | |
| ASA II | 0.44 (0.23–0.85) | 0.015 | 1.08 (0.33–3.54) | 0.905 |
| ASA III | 0.67 (0.28–1.64) | 0.383 | 2.84 (0.49–16.50) | 0.244 |
| Preoperative chronic pain | | | | |
| Yes | Reference | | Reference | |
| No | 1.45 (0.83–2.52) | 0.193 | 0.79 (0.37–1.70) | 0.541 |
| Previous surgery | | | | |
| Yes | Reference | | Reference | |
| No | 0.73 (0.45–1.18) | 0.198 | 0.95 (0.48–1.87) | 0.871 |
| Site of surgery | | | | |
| Stomach | Reference | | Reference | |
| Colorectum | 0.8 (0.49–1.32) | 0.385 | 0.52 (0.26–1.08) | 0.079 |
| Small bowel | 0.77 (0.28–2.08) | 0.602 | 0.61 (0.12–2.99) | 0.539 |
| Type of surgery | | | | |
| Open | Reference | | Reference | |
| Laparoscopic | 0.74 (0.43–1.25) | 0.257 | 1.34 (0.60–3.01) | 0.480 |
| MME consumption, mg | 1.18 (1.12–1.24) | <0.001 | 1.15 (1.10–1.21) | <0.001 |
| HADS: anxiety | 1.40 (1.28–1.53) | <0.001 | 1.33 (1.21–1.46) | <0.001 |
| HADS: depression | 1.31 (1.20–1.43) | <0.001 | 1.03 (0.90–1.18) | 0.675 |
| Expected postsurgical pain | 1.55 (1.36–1.78) | <0.001 | 1.36 (1.17–1.57) | <0.001 |
| SFQ-s | 1.09 (1.06–1.12) | <0.001 | 1.00 (0.94–1.06) | 0.928 |
| SFQ-l | 1.09 (1.05–1.12) | <0.001 | 1.00 (0.95–1.06) | 0.922 |

BMI: body mass index; ASA: American Society of Anesthesiologists; MME: morphine milligram equivalent; HADS: Hospital Anxiety and Depression Scale; SFQ-s: Surgical Fear Questionnaire short-time consequences; and SFQ-l: Surgical Fear Questionnaire long-time consequences.

A significant increase in postsurgical pain intensity was observed with the elevation of SFQ-s and SFQ-l. In addition, SFQ-s and SFQ-l could increase the incidence rate of the clinically meaningful postsurgical pain. However, after adjusting the confounding factors, they both could not independently predict the APSP intensity or severity. Unlike previous study [22], SFQ-s was an important predictor of APSP for day-case surgery, but SFQ-l could not predict APSP. The different outcomes probably came from the different criterion of SFQ, definition of APSP, and type of surgery.

Previous trials showed that preoperative chronic pain was a clinical factor of interest in predicting APSP [7, 10, 22]. However, unlike the previous trials, our study found that there was not relationship between preoperative chronic pain and APSP. The reason may lie in the different way of defining or assessing preoperative chronic pain. Our study used NRS to assess chronic pain. In a previous study, however, it was assessed through brief pain inventory. We defined the preoperative chronic pain as pain in any part of body for 3 months. But in the previous study, the chronic pain was preoperative pain in the surgical area or related to the cause of surgery. Other potential predictors such as female [6], young age [2, 7, 8], type of surgery [17, 18, 21],

and duration of surgery [23] were strongly associated with APSP in several studies, respectively. But we could not find their predictive effect for APSP intensity or severity in our study.

According to our study, despite negative correlation with APSP intensity, age was not independently associated with APSP after controlling confounding factors. This may be explained by the uneven distribution of age, because most participants were elderly. In addition, there was no significant difference on APSP in different sites of surgery (stomach, colorectum, and small bowel) and types of surgery (laparotomy and laparoscopy). However, in some studies for breast cancer, type of surgery could predict APSP, because axillary lymph nodes dissection caused potential injuries to the sensory intercostobrachial as compared with other types of surgery.

Our study had several methodological limitations. First, our subjects were patients undergoing gastrointestinal surgery. Whether the results are applicable to other surgeries remains unknown. Second, all psychological predictor variables were assessed at the first day before surgery when the threatening surgical event might influence these variables and their relations to each other. Thus, the results should be considered with caution when compared with

studies assessing the risk factors several days or even weeks before surgery. Third, the outcome variable, APSP intensity or severity, was assessed only within the first 24 hours after surgery. We did not frequently assess the pain over several days, so we did not make a clinically meaningful assessment of different pain trajectories among patients. Finally, as we investigated the predictors of APSP only in one single hospital, whether the results can be generalized to other countries should be considered cautiously. As a result, a larger multicenter study is needed.

5. Conclusion

In conclusion, this study has shown that cumulative analgesic consumption, preoperative anxiety, and expected postsurgical pain were independently associated with APSP intensity following gastrointestinal surgery. Meanwhile, the predictors were highly associated with APSP severity. Further study is needed to confirm these findings in participants of multicenter clinical trials and different surgical procedures. Future strategies to relieve APSP may start from preoperative psychological interventions.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this paper.

Authors' Contributions

All authors contributed to data analysis, drafting, or revising the article, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Acknowledgments

This study was supported by the Wuxi Municipal Health Commission (no. T202035). The authors would like to express their appreciation to all the collaborators and participants of this study.

References

- [1] M. Sommer, J. M. De Rijke, M. Van Kleef et al., "The prevalence of postoperative pain in a sample of 1490 surgical inpatients," *European Journal of Anaesthesiology*, vol. 25, no. 4, pp. 267–274, 2008.
- [2] H. J. Gerbershagen, E. Pogatzki-Zahn, S. Aduckathil et al., "Procedure-specific risk factor analysis for the development of severe postoperative pain," *Anesthesiology*, vol. 120, no. 5, pp. 1237–1245, 2014.
- [3] N. Peelen, "Current issues in Postoperative pain management," *European Journal of Anaesthesiology*, vol. 33, no. 3, pp. 160–171, 2016.
- [4] T. J. Price, A. I. Basbaum, J. Bresnahan et al., "Transition to chronic pain: opportunities for novel therapeutics," *Nature Reviews Neuroscience*, vol. 19, no. 7, pp. 383–384, 2018.
- [5] A. Buvanendran, C. J. Della Valle, J. S. Kroin et al., "Acute postoperative pain is an independent predictor of chronic postsurgical pain following total knee arthroplasty at 6 months: a prospective cohort study," *Regional Anesthesia & Pain Medicine*, vol. 44, no. 1, 2019.
- [6] C. Edgley, M. Hogg, A. De Silva, S. Braat, A. Bucknill, and K. Leslie, "Severe acute pain and persistent post-surgical pain in orthopaedic trauma patients: a cohort study," *British Journal of Anaesthesiology*, vol. 123, no. 3, pp. 350–359, 2019.
- [7] P. R. Pinto, T. McIntyre, A. Almeida, and V. Araújo-Soares, "The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy," *Pain*, vol. 153, no. 1, pp. 218–226, 2012.
- [8] B. A. Rakel, N. P. Blodgett, B. M. Zimmerman et al., "Predictors of postoperative movement and resting pain following total knee replacement," *Pain*, vol. 153, no. 11, pp. 2192–2203, 2012.
- [9] P. H. Pan, A. M. Tonidandel, C. A. Aschenbrenner, T. T. Houle, L. C. Harris, and J. C. Eisenach, "Predicting acute pain after cesarean delivery using three simple questions," *Anesthesiology*, vol. 118, no. 5, pp. 1170–1179, 2013.
- [10] P. R. Pinto, A. Vieira, D. Pereira, and A. Almeida, "Predictors of acute postsurgical pain after inguinal hernioplasty," *The Journal of Pain*, vol. 18, no. 8, pp. 947–955, 2017.
- [11] J. Thomazeau, A. Rouquette, V. Martinez et al., "Acute pain Factors predictive of post-operative pain and opioid requirement in multimodal analgesia following knee replacement," *European Journal of Pain*, vol. 20, no. 5, pp. 822–832, 2015.
- [12] J. Katz, E. L. Poleshuck, C. H. Andrus et al., "Risk factors for acute pain and its persistence following breast cancer surgery," *Pain*, vol. 119, no. 1–3, pp. 16–25, 2005.
- [13] M. A. Kaunisto, R. Jokela, M. Tallgren et al., "Pain in 1,000 women treated for breast cancer," *Anesthesiology*, vol. 119, no. 6, pp. 1410–1421, 2013.
- [14] B. Rehberg, S. Mathivon, C. Combescure, Y. Mercier, and G. L. Savoldelli, "Prediction of acute postoperative pain following breast cancer surgery using the pain sensitivity questionnaire," *The Clinical Journal of Pain*, vol. 33, no. 1, pp. 57–66, 2017.
- [15] M. McCowat, L. Fleming, J. Vibholm, and D. Dixon, "The psychological predictors of acute and chronic pain in women following breast cancer surgery," *The Clinical Journal of Pain*, vol. 35, no. 3, pp. 261–271, 2019.
- [16] P. H. Pan, R. Coghill, T. T. Houle et al., "Multifactorial preoperative predictors for postcesarean section pain and analgesic requirement," *Anesthesiology*, vol. 104, no. 3, pp. 417–425, 2006.
- [17] G. H. Montgomery, J. B. Schnur, J. Erblich, M. A. Diefenbach, D. H. Bovbjerg, and D. H. Bovbjerg, "Presurgery psychological factors predict pain, nausea, and fatigue one week after breast cancer surgery," *Journal of Pain and Symptom Management*, vol. 39, no. 6, pp. 1043–1052, 2010.
- [18] G. H. Montgomery and D. H. Bovbjerg, "Presurgery distress and specific response expectancies predict postsurgery outcomes in surgery patients confronting breast cancer," *Health Psychology*, vol. 23, no. 4, pp. 381–387, 2004.
- [19] R. M. Sipilä, L. Haasio, T. J. Meretoja, S. Ripatti, A.-M. Estlander, and E. A. Kalso, "Does expecting more pain make it more intense? Factors associated with the first week pain trajectories after breast cancer surgery," *Pain*, vol. 158, no. 5, pp. 922–930, 2017.

- [20] R. S. Khan, K. Ahmed, E. Blakeway et al., "Catastrophizing: a predictive factor for postoperative pain," *The American Journal of Surgery*, vol. 201, no. 1, pp. 122–131, 2011.
- [21] P. R. Pinto, T. McIntyre, V. Araújo-Soares, P. Costa, and A. Almeida, "Differential predictors of acute post-surgical pain intensity after abdominal hysterectomy and major joint arthroplasty," *Annals of Behavioral Medicine*, vol. 49, no. 3, pp. 384–397, 2015.
- [22] H.-F. Gramke, J. M. De Rijke, M. V. Kleef et al., "Predictive factors of postoperative pain after day-case surgery," *The Clinical Journal of Pain*, vol. 25, no. 6, pp. 455–460, 2009.
- [23] A. S. Habib, M. D. Kertai, M. Cooter, R. A. Greenup, and S. Hwang, "Risk factors for severe acute pain and persistent pain after surgery for breast cancer: a prospective observational study," *Regional Anesthesia & Pain Medicine*, vol. 44, no. 2, pp. 192–199, 2019.
- [24] L. Basse, M. Werner, and H. Kehlet, "Is urinary drainage necessary during continuous epidural analgesia after colonic resection?" *Regional Anesthesia and Pain Medicine*, vol. 25, no. 5, pp. 498–501, 2000.
- [25] Z. Serclová, P. Dytrych, J. Marvan et al., "Fast-track in open intestinal surgery: prospective randomized study (Clinical trials gov identifier no. NCT00123456)," *Clinical Nutrition (Edinburgh, Scotland)*, vol. 28, no. 6, pp. 618–624, 2009.
- [26] J. Wind, S. W. Polle, P. H. P. Fung Kon Jin et al., "Systematic review of enhanced recovery programmes in colonic surgery," *British Journal of Surgery*, vol. 93, no. 7, pp. 800–809, 2006.
- [27] M. Greco, G. Capretti, L. Beretta, M. Gemma, N. Pecorelli, and M. Braga, "Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials," *World Journal of Surgery*, vol. 38, no. 6, pp. 1531–1541, 2014.
- [28] A. Feldheiser, O. Aziz, G. Baldini et al., "Enhanced recovery after surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice," *Acta Anaesthesiologica Scandinavica*, vol. 60, no. 3, pp. 289–334, 2016.
- [29] E. G. Cox, W. M. Hopman, M. L. Reitsma et al., "Chronic pain, healthcare utilization, and quality of life following gastrointestinal surgery," *Canadian Journal of Anesthesia/ Journal Canadien D'anesthésie*, vol. 59, no. 7, pp. 670–680, 2012.
- [30] J. Bruce and Z. H. Krukowski, "Quality of life and chronic pain four years after gastrointestinal surgery," *Diseases of the Colon & Rectum*, vol. 49, no. 9, pp. 1362–1370, 2006.
- [31] M. E. Chemali and G. D. Eslick, "A meta-analysis," *The Clinical Journal of Pain*, vol. 33, no. 1, pp. 87–92, 2017.
- [32] J. Simpson, X. Bao, and A. Agarwala, "Pain management in enhanced recovery after surgery (ERAS) protocols," *Clinics in Colon and Rectal Surgery*, vol. 32, no. 02, pp. 121–128, 2019.
- [33] J. L. Joris, M. J. Georges, K. Medjahed et al., "Prevalence, characteristics and risk factors of chronic postsurgical pain after laparoscopic colorectal surgery," *European Journal of Anaesthesiology*, vol. 32, no. 10, pp. 712–717, 2015.
- [34] H. J. Gerbershagen, S. Aduckathil, A. J. M. Van Wijck, L. M. Peelen, C. J. Kalkman, and W. Meissner, "Pain intensity on the first day after surgery," *Anesthesiology*, vol. 118, no. 4, pp. 934–944, 2013.
- [35] J. Rothaug, T. Weiss, and W. Meissner, "How simple can it get? Measuring pain with NRS items or binary items," *The Clinical Journal of Pain*, vol. 29, no. 3, pp. 224–232, 2013.
- [36] A. S. Zigmond and R. P. Snaith, "The hospital anxiety and depression scale," *Acta Psychiatrica Scandinavica*, vol. 67, no. 6, pp. 361–370, 1983.
- [37] M. Theunissen, M. L. Peters, E. G. Schouten et al., "Validation of the surgical fear questionnaire in adult patients waiting for elective surgery," *PLoS One*, vol. 9, no. 6, Article ID e100225, 2014.
- [38] S. Baudic, C. Jayr, A. Albi-Feldzer et al., "Effect of alexithymia and emotional repression on postsurgical pain in women with breast cancer: a prospective longitudinal 12-month study," *The Journal of Pain*, vol. 17, no. 1, pp. 90–100, 2016.
- [39] E. L. Poleshuck, J. Katz, C. H. Andrus et al., "Risk factors for chronic pain following breast cancer surgery: a prospective study," *The Journal of Pain*, vol. 7, no. 9, pp. 626–634, 2006.
- [40] K. G. Andersen, H. M. Duriaud, H. E. Jensen, N. Kroman, and H. Kehlet, "Predictive factors for the development of persistent pain after breast cancer surgery," *Pain*, vol. 156, no. 12, pp. 2413–2422, 2015.