

Effect of preoperative anxiety, depression, and insomnia on acute postoperative pain after non-cardiac surgery

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Abstract

Background

The mental diseases especially anxiety, depression, and insomnia are common in patients at perioperative period. This study aims to investigate the association of preoperative mental diseases with acute postoperative pain of patients undergoing non-cardiac surgery.

Method:

The patients undergoing non-cardiac surgery from August 1, 2019 to January 23, 2020 at Capital Medical University, Beijing Chao-Yang Hospital were included in this retrospective study. The demographics, clinical data and assessments of depression, anxiety, and insomnia by Insomnia Severity Index (ISI), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7) were collected and analyzed. The patients with any of depression, anxiety or insomnia were divided into mental disease group, and others were in non-mental disease group according to the. We compared the postoperative visual analog score between patients in mental diseases group with propensity score matching cohort from patients in non-mental diseases. The primary outcome was acute postoperative pain according to the Visual Analog Scale (VAS) 24h after surgery. Secondary outcomes included VAS at other time points and incidence of postoperative nausea and vomiting (PONV), rescue analgesia, and length of hospital stay (LOS).

Results

The analysis included 397 patients (274 in the group and 123 in the mental disease group). Patients in mental disease group (anxiety, depression and insomnia) were associated with higher VAS scores and increased times of rescue analgesia. Each of the 3 mental diseases was associated with higher VAS scores independently.

Conclusion

In this retrospective study, preoperative anxiety, depression and insomnia were associated with increased the level of acute postoperative pain and increased times of rescue analgesia of patients undergoing non-cardiac surgery.

Plain English Summary

The mental diseases including anxiety, depression and insomnia are common in patients at perioperative period. And the association between the mental disease and postoperative acute pain remains unclear. We conduct this cohort study to assess the association of mental disease and postoperative acute pain

in patients undergoing non-cardiac surgery. We hypothesize the patients with mental disease will tolerate severe postoperative pain at 24h after surgery. The results are that patients in mental disease group (anxiety, depression and insomnia) were associated with higher VAS scores at 24h, 48h and 72h after surgery, and increased times of rescue analgesia. Each of the 3 mental diseases was associated with higher VAS scores independently. These indicate that patients with mental diseases suffered more severe postoperative pain than patients without mental disease. The funding of this study inspire that physicians should pay more attention and give enough rescue analgesia to these patients.

Background

Mental disease is a disorder leading to different degrees of impairment in cognitive behavior and other mental activities as clinical manifestations[1, 2]. More than 1 billion people worldwide were affected by the mental disease in 2016, and they contributed to 7% of the global burden of all diseases[3]. About 14.3% of deaths worldwide, or about 8 million people per year, can be attributed to mental disorders[4]. In recent years, the prevalence of mental diseases in perioperative patients increased over time [5]. The most common mental disease in the perioperative period are anxiety, depression and insomnia and the prevalence of them are 21.9%, 14.1%, and 17.8%[6, 7]. Mental disease in surgical patients could lead to negative short-term and long-term outcomes after surgery and a significant decrease in quality of life [8, 6]. Surgical patients with severe mental disease present a significant challenge to clinicians.

Pain harms the quality of life[9, 10], and adequate analgesia is essential to improve postoperative recovery[11, 12]. Risk factors for postoperative pain include genetic susceptibility, preceding pain, psychosocial factors, age and gender[13]. Psychological factors play an important role in non-surgical causes of pain[14]. Memories of pain, fear and related emotions such as anxiety, depression and insomnia can influence the response to noxious stimuli. And pain may be the result of the interaction of biological and psychological variables. Kain et al. showed preoperative anxiety in young children increased incidence of postoperative pain and sleep problems[15]. However, another study conducted by Wong et al. found that the presence of preoperative psychiatric disease did not worsen postoperative outcomes[16]. The results of a meta-analysis showed that preoperative pain, mental disease, anxiety, depression, and somatoform disorders had a detrimental effect on postoperative pain and function after total knee arthroplasty (TKA) [17]. Although some relevant studies exist, there is controversy regarding the impact of preoperative mental disease on pain. And the effect of preoperative mental disease on acute postoperative pain in non-cardiac patients remains unclear. Due to the adverse effects of mental illness on surgical outcomes, we hypothesize that patients with preoperative mental disease will tolerate more severe acute postoperative pain. Therefore, we conducted this cohort study to assess the association of mental disease and postoperative acute pain in surgical patients.

Methods

Patient selection and data extraction

The patients were enrolled between September 2019 and January 2020. The study was approved by the Regional Ethical Review Committee at the Beijing Chao-Yang Hospital, Capital Medical University approved this retrospective study (2019-ke-273).

Patients were included according to the following inclusion criteria: (1) 18 years or older;(2) American Society of Anesthesiologists (ASA) physical status I-II;(3) undergoing elective non-cardiac surgery with general anesthesia at Beijing Chao-Yang Hospital. Exclusion criteria were as follows: (1) history of dementia or severe cognitive impairment;(2) history of the psychiatric disease;(3) history of organic sleep disorder ;(4) taking antipsychotic medication; (4) history of drug abuse.

Data collection

We collected the patient's general information and preoperative clinical data including gender, age, body mass index (BMI), smoking history, alcohol consumption, years of education, preoperative comorbidities (coronary artery disease, hypertension, diabetes), preoperative Visual Analog Scale (VAS) score. We also reviewed and analyzed patients' assessment of depression, anxiety, and insomnia using the Insomnia Severity Index (ISI), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7) respectively one day before surgery.

The surgery and anesthesia data including ASA physical status classification, type of surgery, duration of surgery, anesthesia types, and postoperative analgesia were also collected. We included postoperative data including VAS scores in the postoperative anesthesia recovery room (PACU), 24, 36, 48, 60, 72, and 84 hours after surgery respectively. Besides, we recorded postoperative nausea and vomiting (PONV), rescue analgesia, and length of hospital stay (LOS). The assessments of ISI, PHQ-9 and GAD-7 were extracted from the paper-based questionnaire. Other data were extracted from electronic medical records.

Exposure of interest

For this study, we identified the mental disease according to the scores of ISI, PHQ-9 and GAD-7. The ISI used a cut-off value of 8 points, with a score ≥ 8 points being insomnia and less than 8 points being normal[18]. And 5 points was used as the cut-off value for both the PHQ-9 and GAD-7, with a higher score indicating moderate to severe depression or anxiety[19,20]. Patients were separated into non-mental diseases group and mental diseases group (with anxiety, depression or insomnia) based on the assessments.

Outcomes

We compared the effect of preoperative mental disease on postoperative pain. And propensity score matching (PSM) analysis was performed to reduce selection bias. The primary outcome was postoperative pain according to VAS 24h after surgery. Secondary outcomes included VAS at other time points and incidence of PONV, rescue analgesia, and LOS.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as a median and interquartile range for non-normal distribution variables and mean values with standard deviation for normal distribution variable. Categorical variables were expressed as counts and percentages. We compared the categorical variables with the chi-square test or Fisher's exact test. Levene's test was used to test for equality of variances of continuous variables. Independent t-tests were performed for continuous variables with symmetric distributions. And the Mann-Whitney U test was used to compare continuous data with the asymmetric distribution.

We performed PSM analysis using multivariable logistic regression model by R (R Foundation for Statistical Computing, version 3.5.1) to build matched groups of patients to compare postoperative acute pain between patients with or without any of mental diseases. Variables were identified in the present study. These variables used for matching included ASA physician status, surgery site, preoperative pain. The matched group of patients from non-mental disease group were in Group A and the matched patients from mental disease group were in Group B. To investigate the effect of each mental diseases (anxiety, depression and insomnia), PSM were used which variables were also included ASA physician status, surgery site, preoperative pain. When we analyzed 1 mental disease, the other 2 mental diseases were also included in variables in order to minimize their effects. Matching analysis was performed based on each patient's estimated propensity score using a nearest neighbor 1:1 matching with a caliper range of 0.2. We tested the patients demographic and perioperative characteristics of patients before and after matching to ensure well-matching. Two-sided *P* values of less than 0.05 were regarded to be of statistical significance.

Results

From August 1, 2019 to January 23, 2020, a total of 400 patients' electronic medical records were screened. Among these patients, 3 patients were excluded because of their incompletely medical records. Then, 397 patients undergoing non-cardiac surgery were enrolled and analyzed. The flow diagram was shown in Fig. 1.

The demographic and perioperative characteristics of the 397 enrolled patients were listed in Table 1. There were 170 males and 227 females enrolled. Of these, 40 underwent head and neck surgery, 80 underwent thoracic surgery, 211 underwent abdominal surgery and 67 underwent joint replacement and spinal surgery. And all of the patients were used general anesthesia.

Table 1
Demographic characteristics and perioperative data of the patients enrolled

| | Total | Non-mental disease | Mental disease | |
|------------------------------------|------------------|---------------------------|-----------------------|----------|
| Characteristic | (n = 397) | (n = 274) | (n = 123) | P |
| Demographic characteristics | | | | |
| Male, n (%) | 170 (42.1) | 125 (45.6) | 45 (36.5) | 0.080 |
| Age (y) | 55.2 ± 14.0 | 54.6 ± 14.1 | 56.4 ± 13.7 | 0.233 |
| BMI (kg/m ²) | 24.7 ± 3.7 | 24.9 ± 3.7 | 24.2 ± 3.7 | 0.094 |
| History of smoking, n (%) | 110 (27.7) | 77 (28.1) | 31 (25.2) | 0.816 |
| Alcohol consumption, n (%) | 81 (20.4) | 58 (21.1) | 23 (18.7) | 0.815 |
| Education year, (y) | 11.2 ± 3.7 | 10.6 ± 3.7 | 11.5 ± 3.6 | 0.083 |
| Medical history | | | | |
| CAD, n (%) | 7 (1.7) | 4 (1.4) | 3 (2.4) | 0.422 |
| Hypertension, n (%) | 137 (34.5) | 92 (33.7) | 45 (36.5) | 0.611 |
| DM, n (%) | 64 (16.1) | 38(13.9) | 26 (21.1) | 0.079 |
| Preoperative VAS | 0(0,0) | 0(0,0) | 0(0,1) | 0.005 |
| ASA | | | | 0.031 |
| □ | 53(13.3) | 45(16.4) | 8(6.5) | |
| □ | 255(64.2) | 173(63.4) | 82(66.7) | |
| □ | 89(22.5) | 56(20.4) | 33(26.8) | |
| Surgical characteristics | | | | |
| Surgical site, n (%) | | | | 0.009 |
| Head and neck | 40(10.1) | 26(9.5) | 14(11.4) | |
| Chest | 80(20.2) | 47(17.2) | 33(26.8) | |
| Abdomen | 211(53.1) | 160(58.6) | 51(41.5) | |

Legend of Table 1. BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; ASA, American Society of Anesthesiologists; TIVA, total intravenous anesthesia; PCIA, patient-controlled intravenous analgesia; PCEA, patient-controlled epidural analgesia.

| | Total | Non-mental disease | Mental disease | |
|---|--------------|--------------------|----------------|-------|
| Arms and legs | 67(13.4) | 41(15.0) | 25(20.3) | |
| Surgery duration (min) | 139.8 ± 85.5 | 135.3 ± 83.0 | 149.8 ± 90.3 | 0.211 |
| Anesthesia | | | | 0.308 |
| TIVA | 254(64.0) | 178(65.0) | 76(61.8) | |
| Intravenous and inhalational balanced anesthesia | 110(27.8) | 76(27.7) | 35(28.5) | |
| Intravenous and nerve block | 15(3.9) | 8(2.9) | 7(5.7) | |
| Intravenous and intraspinal anesthesia | 18(4.3) | 12(4.4) | 5(4.0) | |
| Analgesia | | | | 0.575 |
| PCIA | 198(49.9) | 131(47.8) | 67(54.5) | |
| PCEA | 29(7.3) | 22(8.0) | 7(5.7) | |
| None | 172(42.8) | 121(44.2) | 49(39.8) | |
| Legend of Table 1. BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; ASA, American Society of Anesthesiologists; TIVA, total intravenous anesthesia; PCIA, patient-controlled intravenous analgesia; PCEA, patient-controlled epidural analgesia. | | | | |

The incidence of anxiety, depression and insomnia was 13.4%, 13.6% and 15.1% respectively. Patients were divided into two groups according to the preoperative assessments of mental disease (274 in non-mental disease group with mental disease and 123 in mental disease group without any mental disease). The demographic and perioperative characteristics were shown in Table 1. No significant differences were found between the two groups in basic characteristics, including gender, age, BMI, history of smoking, alcohol consumption, education years, comorbidities, preoperative VAS score, surgery duration, anesthesia and postoperative analgesia. In mental disease group, there were 8 patients in ASA I, 82 in ASA II and 33 in ASA III. In non-mental disease group, there were 53 in ASA I, 255 in ASA II and 89 in ASA III.

And postoperative outcomes after PSM were shown in Table 2. Compared with group A, the VAS score was higher in PACU, 24, 48 and 72 hours after surgery in group B ($P < 0.05$). There were no significant differences in the incidence of PONV and LOS. The times of rescue analgesia was higher in group B than that of group A ($P < 0.05$).

Table 2
Postoperative outcomes of 2 groups

| | Group A (n = 119) | Group B (n = 123) |
|--|----------------------|----------------------|
| Postoperative VAS | | |
| PACU | 2(0,3) | 2(1,3)* |
| 24h | 2(1,3) | 3(1,4)* |
| 36h | 2(1,3) | 2(0,4) |
| 48h | 2(0,3) | 2(0,3)* |
| 60h | 1(0,3) | 2(0,3) |
| 72h | 1(0,2) | 2(0,3)* |
| 84h | 1(0,2) | 1(0,3) |
| PONV | 51 | 25 |
| Rescue analgesia | 64 | 42 |
| LOS | 9(6,13) | 8(6,12) |
| Legend of Table 2. VAS, visual analog scale; PACU, postoperative anesthesia recovery room; PONV, postoperative nausea and vomiting; LOS, length of hospital stays. *compared with group A, $P < 0.05$. | | |

According to the propensity scored matched, the patients were divided into 3 pair groups, anxiety and non-anxiety group, depression and non-depression group, insomnia and non-insomnia group. The postoperative VAS scores were shown in Fig. 2. Compared with the non-anxiety group, the VAS score was higher in PACU ($P < 0.05$). Compared with the non-depression group, the VAS score was higher in PACU and 24 hours after surgery ($P < 0.05$). Compared with the non-insomnia group, the VAS score was higher in PACU, 48 and 72 hours after surgery in the insomnia group ($P < 0.05$).

Discussion

In this study, we found that mental diseases were negative associated with acute postoperative pain on patients undergoing non-cardiac surgery after matching the ASA physical status, surgery site and preoperative pain level. Furthermore, anxiety, depression and insomnia could increase the pain postoperative pain level at different time points. The association was held after propensity score matching. Besides, the mental diseases would increase the times of rescue analgesia.

Consistent with the previous study, psychological diseases are associated with higher pain levels[21]. Various psychological mechanisms may play an important role in central sensitization[22]. An

association between anxiety and depression and postoperative pain was described by Gravani, where an increased intensity and higher level of pain at 1 and 4 hours after surgery were found for patients with anxiety and depression undergoing bariatric surgery[23]. But contrasted with our study, no significance was found in pain level 24 hours after surgery. In this study, we found the VAS scores were still higher in 24, 48 and 72 hours after surgery in patients with anxiety, depression and insomnia when compared with non-mental diseases patients. And the effect of mental diseases on acute postoperative pain could last longer after surgery. Kulkarni reported anxiety and depression were associated with postoperative pain 1 week after surgery[24].

Furthermore, in our study, we were first to include insomnia as one of the essential perioperative mental diseases with anxiety and depression and to analyze the association with acute postoperative pain. Previously, insomnia was thought to be a symptom of anxiety and depression. However, insomnia plays an important role in surgical patients' short-term and long-term outcomes[25, 26]. Consistent with Orbach-Zinger's study, insomnia increased the severe pain upon movement[27]. A limitation of the study is that the included patients were all female undergoing cesarean surgery, which might be affected by multiple factors including family factors, disturbance of taking care of babies. We also found the negative effect of insomnia on postoperative pain after carefully propensity matching of ASA, preoperative pain, surgery site, anxiety, and depression. And in Luo's study, they reported, the effect of insomnia on postoperative pain could last to 12 weeks after surgery for patients undergoing total joint arthroplasty [28].

Besides, in group A, the pain level decreased significantly after 24 hours after surgery. But this trend was slowly and moved to longer than 72 hours after surgery. We were the first to report the VAS scores at consistent time points after surgery. The results will help clinicians make better analgesia management of patients who will benefit from sufficient analgesia and increase hospitalization satisfaction.

Previously, there was evidence of increased risk of postoperative nausea in surgical patients with depression symptoms[29]. In contrast with the previous study, we didn't find differences in the incidence of PONV between the two groups. NSAIDs drug in rescue analgesia treatment may be more pronounced among high-need rescue analgesia patients undergoing non-cardiac surgery. In our study, the times of rescue analgesia in the mental diseases group were more than that of group A after PSM. This was also indicated that the patients suffered more pain after surgery.

Besides, we found that the length of LOS in the mental diseases group was shorter than that of group A. The patients who we included were found the psychiatric change in the perioperative period. Lots of hospital-related risk factors contributed to this change and patients might find it difficult to adapt hospital environment[5]. After the surgery, patients would be more likely to discharge early.

Our study has several limitations. First, this study was a single-center retrospective observational study. Second, although the propensity scores balanced ASA, surgery site, preoperative pain and mental diseases, there might be other unbalanced confounding factors about the mental disease. These included the duration and severity of the mental disease. In this study, we simply assessed patients for preoperative anxiety, depression, or insomnia as having a mental disease. We understand that mental

disease can present with other psychological states that are not limited to the above three. However, we believe that anxiety, depression, and insomnia are common in surgical patients, and studying their effects with acute postoperative pain may also serve as a basis for future research. And further studies are needed to explore the correlation between the different severity, types, and duration of mental disease and acute postoperative pain.

Conclusion

In summary, we found an association between the preoperative mental diseases with the increased level of acute postoperative pain of patients undergoing non-cardiac surgery. Further work should focus on the potential mechanisms and how to identify the patients at high risk of mental diseases. And more investigations are required the physicians should take more attention to the perioperative pain management of patients with mental diseases to improve their postoperative recovery quality and satisfaction of hospitalization.

Abbreviations

ASA: American Society of Anesthesiologists; BMI: Body Mass Index; GAD-7: Generalized Anxiety Disorder-7; ISI: Insomnia Severity Index; LOS: Length of Hospital Stay; PACU: Postoperative Anesthesia Recovery Room; PHQ-9: Patient Health Questionnaire-9; PONV: Postoperative Nausea and Vomiting; PSM: propensity score matching; TKA: Total Knee Arthroplasty; VAS, Visual Analog Scale.

Declarations

Ethics approval and consent to participate

The study was approved by the Regional Ethical Review Committee at the Beijing Chao-Yang Hospital, Capital Medical University approved this retrospective study (2019-ke-273). The written informed consents were obtained from participants if the participants meet the inclusion criteria.

Consent to publish

Not applicable.

Availability of data and material

The data could be acquired from corresponding author by reasonable requirements.

Competing interest

The authors declare that they have no conflict of interest.

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Authors' contribution:

Study design: all authors; Collect data: JW, MG; Analysis of data: XH, DL; Result interpretation: JW, YH, DL, XH; Drafting of the manuscript: DL, XH; Critical revision of the manuscript: ASW, WCW.

Authors' information

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Figures

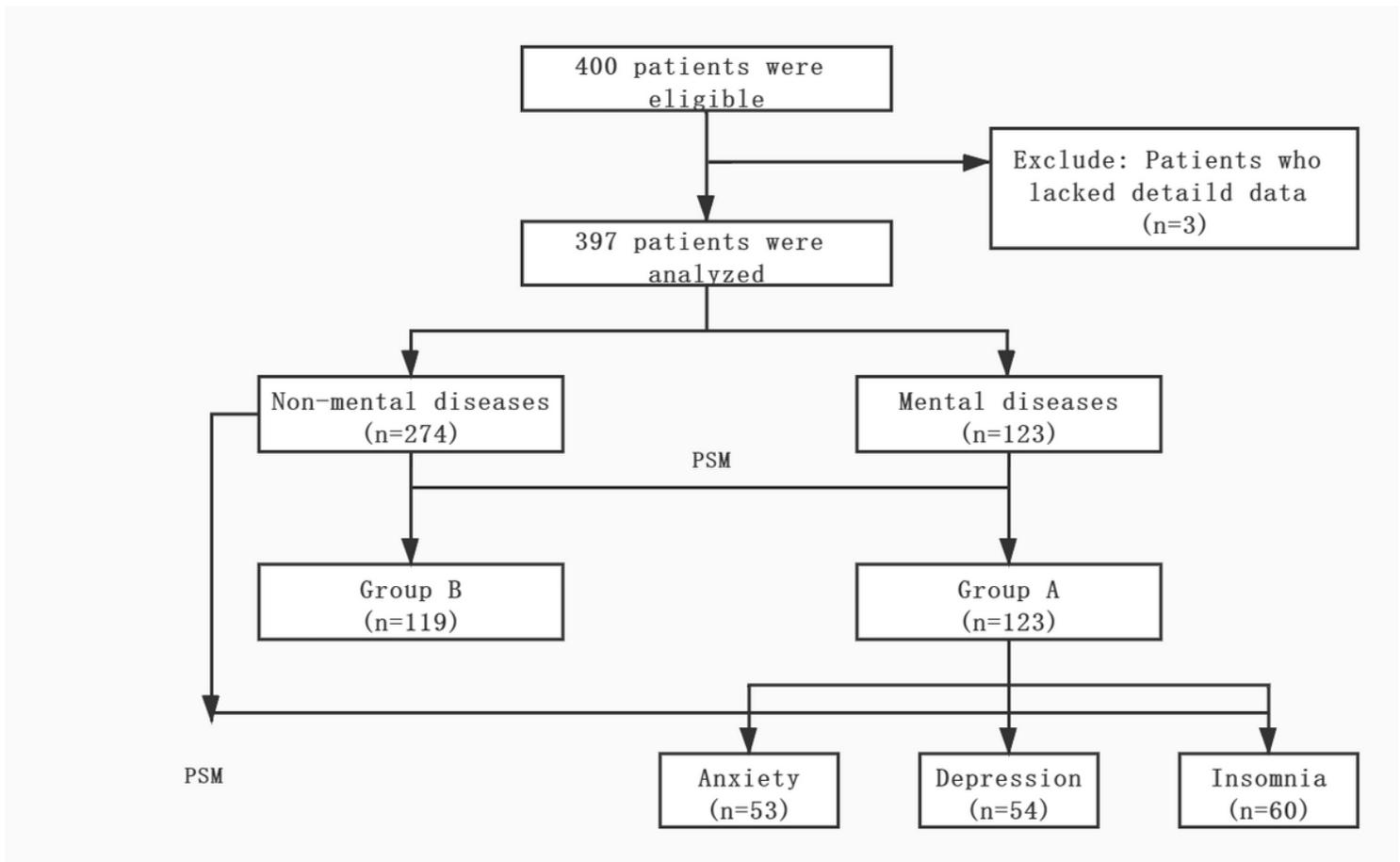


Figure 1

Flow diagram of the study. PSM: propensity score matching.

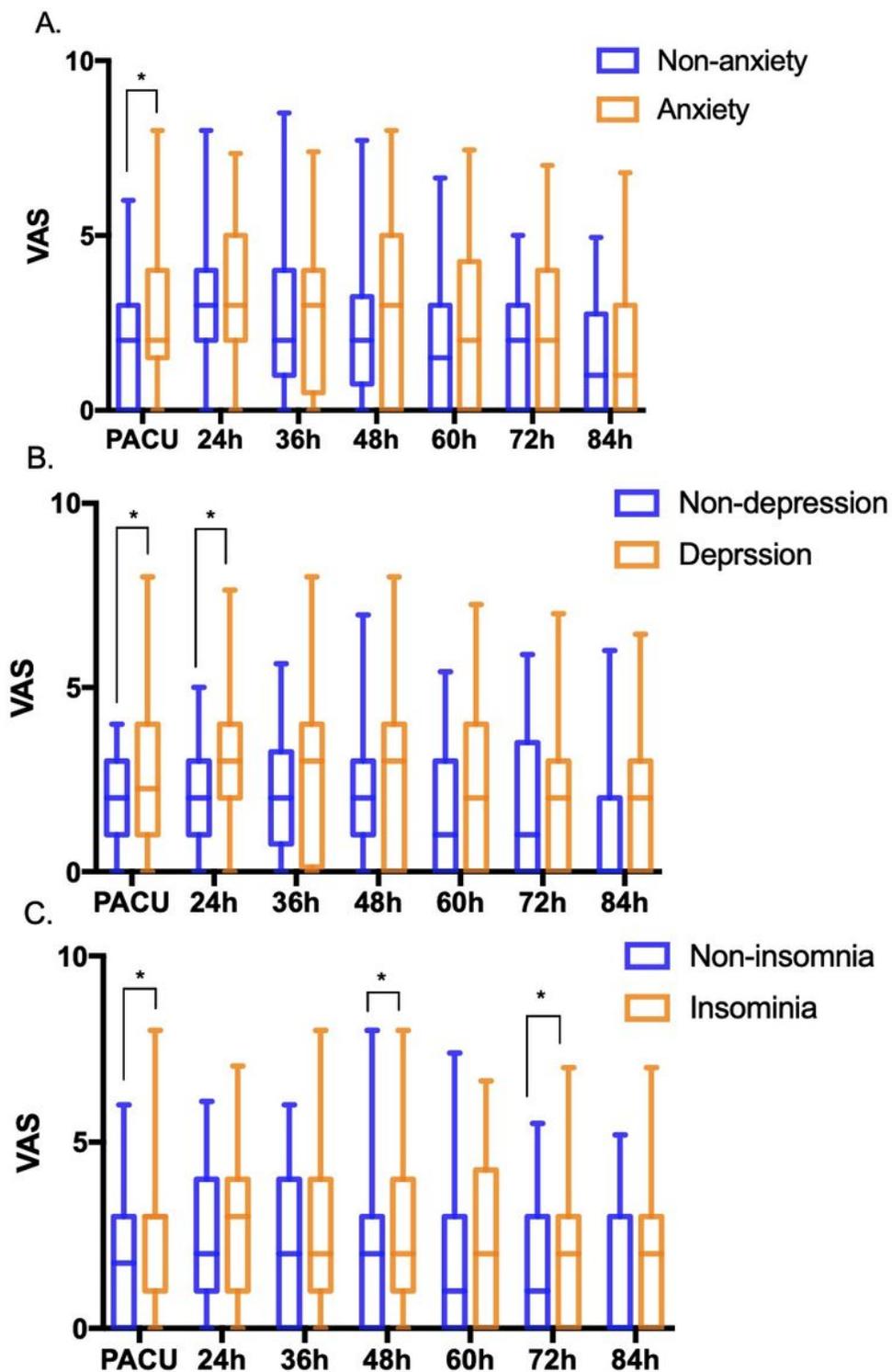


Figure 2

Comparison of postoperative VAS of patients after PSM. A. Comparison of postoperative pain between patients with and without anxiety after PSM. B. Comparison of postoperative pain between patients with and without depression after PSM. C. Comparison of postoperative pain between patients with and without insomnia after PSM. Data were expressed as median with interquartile range, and non-parametric

tests were used. *P < 0.05 compared with patients without anxiety, depression or insomnia. VAS, visual analog scale; PSM: propensity score matching; PACU, postoperative anesthesia recovery room.

Supplementary Files

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- [plainenglishsummary.docx](#)