

Comparison of Postoperative Pain between Patients who underwent Primary and Repeated Caesarean Section: A Prospective Cohort Study

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Research Article

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Abstract

Background: The presences of differences in post-operative pain are unclear between the primipara who underwent a primary cesarean section and multipara who underwent first repeat cesarean section. The study aimed to explore the possible difference in postoperative pain between primipara and multipara.

Methods: Women who underwent cesarean deliveries under spinal anesthesia were included, and postoperative patient-controlled intravenous analgesia was performed. Postoperative incision and visceral pain within 48 hours after the surgery were evaluated. Serum leukocyte and neutrophil counts before and 24 hours after the surgery were retrospective collected. Additionally, the patients' pain statuses on postoperative week 1 and week 4 were also assessed during follow-up via telephone.

Results: A total of 168 patients (67 primipara and 101 multipara) were included. The multipara showed less risk for experiencing moderate to severe incision pain during the 48 hours after the surgery than the primipara (15.8% vs.37.3%; $P=0.001$). In patients under 30 years old, inadequate treatment of the visceral pain in the multipara was higher than that of the primipara (22.7% vs.6.4%; $P=0.026$). There was no significant difference in the combined incidence of inadequate analgesia in both types of pain between the multipara and primipara (33.7% vs.40.2%, $P=0.381$). Additionally, a significantly higher incidence of pain at 4 weeks after the surgery was noted in the primipara compared to the multipara (55.4% vs.36.1%, $P=0.015$).

Conclusions: Individual differences between the primipara and multipara should be considered in the management of postoperative analgesia for those who have undergone Cesarean deliveries.

Background

Cesarean section is the most common inpatient surgical procedure globally. It was reported that in the United States, approximately 1.4 million women underwent a cesarean section, representing 32% of all births in 2007(1). In China, the annual rate reached 34.9% in 2014(2). Surgery is the most common and predictable source of acute pain(3), and therefore, it creates a considerable clinical challenge in the acute postoperative care of a cesarean section. However, despite the numerous measures that have been developed to manage postoperative pain, inadequate analgesia after cesarean section is common, with an incidence of nearly 50%(4-6). Inadequate postoperative pain management is associated with persistent pain, delayed functional recovery, and a longer hospital stay, which increase medical expenses, and is becoming a public health issue(7,8). Therefore, the treatment of pain after a cesarean section remains unresolved.

In China, a new clinical challenge for the treatment of pain after a cesarean section has emerged following the implementation of China's new national two-child policy(9,10). More obstetrics patients with a known history of previous cesarean section were scheduled to receive repeated cesarean section. Since

repeated cesarean sections are often associated with a more advanced age and are known to have higher operative difficulties and longer surgical times due to severe adhesions(11,12), we speculated that there would be a difference in pain control during the postoperative period between the patients who underwent repeat and primary cesarean sections, and the multipara may have a higher risk of receiving inadequate analgesia.

Currently, most female patients receive a one-size-fits-all approach for the postoperative analgesia after a cesarean section. In the recent Practice Guidelines for Obstetric Analgesia and Anesthesia, there was no specific explanation for the possible difference of postoperative pain between the patients who underwent repeat and primary cesarean sections(13,14). To the best of our knowledge, there are limited studies that focus on this issue. Additionally, exploring the inter-individual variability in the degree of pain and accurately targeting the treatment in women who will experience inadequate analgesia may improve the clinical outcome(15,16). Therefore, the current prospective cohort study aimed to include patients who were scheduled to receive a primary or repeated cesarean section in order to investigate the potential difference in postoperative pain between them.

Methods

Patients

This prospective observational study was carried out according to the STROBE recommendations(17,18). The study protocol was approved by the Institutional Ethics Committee of Xinqiao Hospital, Third Military Medical University, Chongqing, China. Prior to the enrollment of patients, Written informed consent was obtained from all patients and the study was registered on ClinicalTrial.gov (ID: NCT03009955).

From January to May 2017, a total of 168 Chinese patients, aged 20 to 40 years, who were scheduled to receive elective cesarean section with a transverse incision were recruited into the current study (Figure 1). Patients who had a gestational age of 37 to 40 weeks and singleton pregnancy, voluntarily received intravenous patient-controlled intravenous analgesia (PCIA) treatment, and were classified as having American Society of Anesthesiology physical status I-II were eligible for participation. The reasons for an elective cesarean section in a primipara included the patient's own choice, preoperative complications including malpresentation (breech and transverse positions and compound presentation), placenta previa, uterine inertia, gestational diabetes, chronic or gestational hypertension, and preeclampsia. For the multipara in this study, the indication for a cesarean section was a previously scarred uterus. Only those who were undergoing their first repeat Cesarean deliveries were included. Exclusion criteria included a history of a pain disorder, chronic opioid use, substance abuse, heavy smoking (>30 pack-years)(19) or alcohol dependence, absolute or relative contraindication to subarachnoid space block anesthesia, history of prior pelvic or abdominal surgery, or severe pregnancy complications, such as heart disease, brain disease, liver disease and kidney disease, that were life-threatening and required emergency treatment prior to the cesarean section.

Anesthetic and Analgesia Management

Cardiac rhythm via electrocardiography, mean arterial pressure, and pulse oxygen saturation were monitored after the patients entered the operating room. Standardized anesthesia was performed by the same experienced anesthetist and the operations for the study patients were conducted by a single surgical team, using the same standardized technique. Spinal anesthesia, via a subarachnoid space block at the L3–4 interspace, was performed using 0.66% ropivacaine (20 mg).

After the fetal section and once a day after the surgery, oxytocin (20 IU in 500 mL of saline) was routinely administered while the patient was admitted to the obstetrics ward. PCIA was started immediately after surgery with a mixture of hydromorphone (0.04 mg/kg), flurbiprofen (4 mg/kg), and 0.9% normal saline at a dose volume of 200 mL, using a controlled infusion pump. The pump was programmed to use a loading dose of 2 mL, background infusion rate of 2.0 mL/h, and PCIA dose of 1 mL, with a lockout period of 15 min. For the prevention of the postoperative nausea and vomiting, 3 mg of droperidol was administered at the outset of the PCIA. Patients were monitored for 6 hours in the postanesthesia care unit of the obstetrics ward after the surgery. When pain was treated inadequately, the patients were administered additional pain treatment with tramadol 50 mg in a timely manner.

Outcome Measurements

A pain visual analogue scale (VAS score; 0–100, where 0 is defined as no pain and 100 as maximum pain) was used to evaluate postoperative pain at 4, 8, 12, 24, and 48 hours. The primary outcome was the incidence of inadequate analgesia (defined as pain VAS score ≥ 40)(20) during the postoperative 48 hours. In the study, abdominal incision pain at rest and during mobilization (during coughing) was assessed using the VAS. The visceral pain induced by uterine contractions was also assessed using the VAS. The duration of pain according to the patient's self-reported time points and PCIA consumption for 48 hours after surgery were recorded.

The hospital anxiety and depression scale (HADS) before the operation was assessed in all patients. The HADS includes 14 assessment including the symptoms of anxiety and depression (seven items scored 0 to 3 in each subscale, yielding a range of 0–21) with subscale scores of 8 indicating possible anxiety or depression(21, 22). The intraoperative amount of blood loss, neonatal Apgar score, weight and height of the newborn, and surgery time were recorded. The Ramsay sedation score, respiratory rate, pulse oxygen saturation, systolic pressure, diastolic pressure and heart rate were recorded before surgery and during the postoperative 48 hours. Early walking time, determined by the time point when patients could ambulate, was also recorded. Sleep quality (rated as good or poor) on the day of and one day after surgery was also evaluated. Postoperative adverse events including nausea and vomiting and pruritus were also noted. Additionally, the patients' duration of hospital stay was recorded.

The results of routine blood examinations before and 24 hours after the surgery were retrospectively collected for all patients. The leukocyte and neutrophil counts were analyzed. One and 4 weeks after the surgery, patients were interviewed by telephone and asked the following questions from a standardized questionnaire: was there existing pain?; was the location of pain at the incision, viscera, both, or none;

was sleep affected?; were they able to perform the activities of daily life with full autonomy, **partial dependency**, or **absolute dependence**?

Sample size determination

The study sample size was calculated according to the design of chi-square test for four-fold table data in a cohort study. As previous studies reported, the incidence of postoperative moderate to severe pain under postoperative analgesia for primipara was approximately 50%. The current study hypothesized that the Relative Risk (RR) value for multipara was 1.5 compared to that of the primipara. The anticipated incidence for multipara was 75%. Therefore, based on a significance level of 0.05, power of 0.9, and an estimated ratio between number of multipara and primipara of 1.5, and considering about 3% loss of follow-up, the total required minimum sample size was determined to be 168 individuals using the sample size calculation software PASS, version 11.0 (NCSS, Kayesville, UT).

Statistical Analysis

Statistical analysis was performed using SPSS for Windows version 19.0 (SPSS Inc., Chicago, IL). A two-tailed P-value less than 0.05 was considered statistically significant. The mean \pm standard deviation (SD), median (interquartile range), and number (frequency) were used to summarize the variables. The patients who were scheduled to undergo a primary cesarean section were designated as group P in the final analysis, while the patients scheduled to undergo repeat cesarean section were designated as group R. The primary outcomes (postoperative inadequate analgesia on incision or visceral pain) were respectively described and analyzed. Logistic regression analysis was used to evaluate the role of group P or group R in the prediction of postoperative inadequate analgesia. Presence of postoperative inadequate analgesia on incisional and visceral pain was considered as the outcome variable. BMI, age, gestational age, surgery time, preoperative complications (yes/no), depression (yes/no) and anxiety (yes/no) were also considered in the model. Odds ratios (OR) with 95% confidence intervals (CIs) were determined based on the logistic regression analysis.

An independent-sample t test was used to compare the differences in age, body mass index, surgery time, weight and height of the newborn, blood loss, incision pain VAS at mobilization, time of starting to feel pain, early walking time, hospital stays and PCIA administration between groups P and R. Because of abnormal distribution, HAD scale, incision pain VAS at rest, and visceral pain VAS were compared using a Mann-Whitney U test.

Differences in the incidence of postoperative inadequate analgesia, sleep quality, adverse events, and long-term pain status between the two groups were analyzed using Pearson's chi-squared test. Furthermore, relative risk (RR) values and 95% CI for the probability of the occurrence of inadequate analgesia regarding the incision pain and visceral pain during the postoperative 48-hour follow-up were calculated, as well as the postoperative pain status at 1 and 4 weeks. Subgroup analysis according to the age group (≤ 30 years or > 30 years) was performed. Two way repeated analysis of variance (ANOVA) with post hoc LSD testing was used to compare the preoperative and postoperative systolic pressure,

diastolic pressure, heart rate, respiratory rate, and leukocyte and neutrophil counts between the two groups.

Results

General results

A total of 168 women were included in the study. Among the 67 primipara who were scheduled to receive cesarean section, 54 were due to preoperative complications (maternal or fetal factors) and 13 were due to social factors. For the 101 multiparas, all were due to the history of a previous cesarean section. Fifty-four also had accompanying preoperative complications. As shown in Figure 1, all patients completed the postoperative 48-hour follow-up. However, 6 patients (2 in group P and 4 in group R, $P=0.739$) were lost to follow-up via the telephone interview either because they could not be contacted or they refused to continue to participate in the study. The demographics and preoperative data of all patients are shown in Table 1.

Logistic regression analysis

Enter logistic regression models were applied to explore the possible predictors for postoperative inadequate analgesia on incisional pain (overall $P=0.001$) and visceral pain (overall $P=0.589$). As summarized in Table 2, patient group (OR=0.19 [95% CI, 0.07 to 0.51], $P=0.001$) and preoperative complications (OR=0.37 [95% CI, 0.15 to 0.90], $P=0.030$) were identified as significant factors for inadequate analgesia on incision pain. This showed that patients in group P or with accompanying preoperative complications would have higher odds of inadequate pain control.

Postoperative Data

The distribution of pain VAS is shown in Figure 2. The incidence of inadequate postoperative analgesia on incision or visceral pain at different times is shown in Figure 3. A total of 41 patients (41/168, 24.4%) were found to have inadequate treatment of their incision pain (Figure 3A). The total incidence of inadequate analgesia on incision pain in group P was significantly higher than that of group R (37.3% vs. 15.8%; $P=0.001$). The RR for multipara to experience inadequate analgesia on incision pain was 0.42 (95% CI: 0.25 to 0.74) compared to primipara.

As shown in Figure 3B, postoperative inadequate treatment for visceral pain was observed in 28 patients (28/168, 16.7%). The total incidence of inadequate analgesia on visceral pain in group P was lower than that of group R, but there was no statistical significance (10.4% vs. 20.8%; $P=0.078$). The RR for patients in group R to experience inadequate analgesia on incision pain was 1.75 (95% CI: 0.82 to 3.70) compared to that of patients in group P. Additionally, the total combined incidence of inadequate analgesia was 36.3% (61/168); no significant difference was found between groups P and R (40.2% vs. 33.7%, $P=0.381$, Figure 3C).

The results of subgroup analysis showed that group R was associated with a lower incidence of inadequate control on incision pain in both groups ≤ 30 and >30 years (RR, 0.47 [0.23 to 0.98], $P=0.033$ and 0.40 [0.17 to 0.96], $P=0.042$, respectively, Table 3). Group R was associated with a higher incidence of inadequate control on viscera pain in group ≤ 30 years (RR, 3.56 [1.05 to 12.04], $P=0.025$).

Other postoperative outcomes are shown in Table 4. There was no significant difference in the incidence of adverse effects between the two groups. No respiratory depression, excessive sedation, or agitation was found in the present study. In addition, no significant difference was found in the time elapsed prior to the onset of pain, early walking time, sleep quality, and PCIA administration between the two groups. The results showed a mean hospital stay for primipara was longer than that of multipara (3.6 ± 1.2 vs. 3.0 ± 0.8 , $P=0.001$).

Changes of serum leukocyte count and neutrophil count

Two-way repeated ANOVA for leukocyte count showed a group effect ($P<0.001$), time effect ($P<0.001$) and group and time interaction effect ($P=0.041$) were significant. For the neutrophil count, the group effect ($P=0.006$) and time effect ($P<0.001$) were significant, while group and time interaction effect was not significant (P value = 0.058). As shown in Figure 4, there was no difference in the absolute leukocyte ($8.89\pm 3.04\times 10^9/L$ vs. $8.22\pm 2.19\times 10^9/L$, $P=0.101$) and neutrophil ($6.73\pm 2.92\times 10^9/L$ vs. $6.23\pm 1.99\times 10^9/L$, $P=0.185$) counts between the different groups before the surgery, while both leukocyte ($10.77\pm 2.63\times 10^9/L$ vs. $9.32\pm 2.17\times 10^9/L$, $P<0.001$) and neutrophil ($8.39\pm 2.47\times 10^9/L$ vs. $7.17\pm 2.08\times 10^9/L$, $P<0.001$) counts at 24 hours after the surgery in group P were significantly higher than that in group R.

Long-term follow-up

As shown in Table 5, no significant difference of pain status was found between the two groups 1 week after the surgery. The results showed that 4 weeks after the surgery, the incidence of existing pain in group P was significantly higher than that in group R (55.4% vs. 36.1%, $P=0.015$), as was the incidence of sleep being affected (13.8% vs. 4.1%, $P=0.026$). The RR values for patients in group R to experience pain 4 weeks after the surgery was 0.65 (95% CI: 0.46 to 2.16) when compared to group P. Additionally, compared to group P, RR values for patients in group R to experience pain that affected patients' sleep 4 weeks after the surgery was 0.30 (95% CI: 0.10 to 0.92).

Discussion

Our results show that the total incidence of inadequate postoperative pain control was 36.3% using PCIA combined with hydromorphone and flurbiprofen, which was demonstrated as an effective combination for postoperative pain control(23). One previous prospective cohort study(4) demonstrated that postoperative pain after a cesarean section reached 6 (interquartile range: 4 to 8), and the incidence of moderate to severe pain or requirement of extra analgesia was reported to range from 40 to 65%(5,6). Therefore, the analgesia strategy in the study might be effective for postoperative pain control.

Nevertheless, the incidence of 36.3% remains relatively high and more effective analgesia strategies should be explored in the future.

As we know, a great proportion of female patients were scheduled to receive secondary cesarean section because of a previous cesarean section. In the United States, a repeat cesarean section due to a previous uterine scar contributed to more than 30% of all cesarean sections(24,25). Severe adhesions induced by previous surgery were often inevitable and thus would cause higher operative difficulties(26,27). In the study, surgery duration in group R was significantly longer than that in group P, which is also indicative of higher operative difficulties for patients who received repeat cesarean sections. Additionally, previous surgery history might increase the patients' pain sensitivity(28,29). Therefore, based on the above information, it was speculated that multipara might experience more postoperative pain than primipara.

For patients undergoing cesarean section, oxytocin, which can induce contraction pain, was routinely used to reduce intraoperative and postoperative hemorrhage(30,31). Thus, postoperative visceral pain induced by uterine contraction must frustrate the patients and should not be ignored. Although numerous previous studies focused on the improvement of the postoperative analgesia for cesarean section(32-35), many of these studies did not differentiate incision pain from visceral pain. However, a previous study found that the analgesic effects of same analgesics on incision and uterine cramping pain varied(36). Therefore, postoperative abdominal incision and visceral pain were evaluated in this study.

One previous study demonstrated that compared to primiparous women, analgesic effect on post-Cesarean uterine cramping pain is less in multiparous women(37). The current results also showed that the incidence of inadequate treatment on visceral pain in group R was higher than that of group P, with the RR for multipara being 3.56 (95% CI: 1.05 to 12.04) in the patients whose age ≤ 30 years. In addition, of all patients in the two groups, few were found to experience inadequate analgesia 8 hours after the surgery, indicating that visceral pain might mainly appear at an early postoperative stage. Therefore, for the multipara, the focus should be on postoperative visceral pain at the early stage, especially for young patients.

In contrast, the current study showed that multipara were less likely to experience inadequate treatment on incision pain. The RR for multipara was 0.42 (95% CI: 0.25 to 0.74), and the mean incision pain VAS in patients of group R was significantly lower than that of group P at several time points including 4, 12, and 24 hours after the surgery. Based on the results of the current study, several reasons might account for this phenomenon. First, as shown in the study, the rate of preoperative complications in group P was higher than that of group R (80.6% vs. 53.5%) and it was identified as a significant risk factor for inadequate treatment on incision pain. Second, through retrospective analysis, we found that both the leukocyte count and neutrophil count were significantly increased at postoperative 24 hours compared to that prior to surgery and the ascents for both in group P were higher than that in group R. Increases of white blood cell and neutrophil counts have been demonstrated to positively associate with inflammatory responses in previous studies(38-40). Therefore, these indicated that different physiological responses to surgery or analgesia might exist between multipara and primipara. For primipara, effective analgesia

strategy, e.g., combination of perioperative anti-inflammatory agent using, on incision pain should be further considered.

In summary, because of the differentiation between postoperative control on visceral and incision pain, there was no significant difference in the combined incidence of inadequate analgesia on both types of pain between patients in groups P and R. Regarding the other postoperative outcomes during the hospital stay, no significant difference was found in the incidence of adverse events, time to feel pain, early walking time, sleep quality, and PCIA administration between the two groups. However, we found that the mean hospital stay for primipara was longer than that of multipara. This indicated that primipara might need more care after the cesarean section. Furthermore, the current study demonstrated that primipara might experience a longer duration of pain because 4 weeks after the surgery a higher incidence of existing and affecting sleep was found in group P compared to that in group R. This might be due to the higher incidence of inadequate incision pain control in patients of group P, because a previous study has identified inadequately controlled acute postoperative pain as a risk factor for the development of chronic pain postoperatively(41).

Several limitations should be noted in the study. First, the study only included Chinese women from urban areas, thus race and socio-economic status should be considered when interpreting the current results(42,43). Second, although significant difference of postoperative pain status was found between the primipara and multipara, the current sample size was relatively small, and a multicenter study with a larger sample size might be needed in the future. Third, in the current study, all multiparas were undergoing secondary surgery; thus, whether and what the difference might be for those who received two or more Cesarean deliveries were not known.

Conclusion

In summary, multipara under 30 years of age may be more prone to experiencing moderate to severe visceral pain under PCIA with opioids during the first 48 hours after surgery compared to primipara; while primipara have a higher incidence of inadequate treatment on incision pain and possibly a higher incidence of existing pain 4 weeks after the surgery. Based on the results of the current study, individual differences between primipara and multipara should be considered in the postoperative analgesia in the future.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Ethics Committee of Xinqiao Hospital, Army Medical University. Written informed consent was obtained from all patients and the study was registered on ClinicalTrial.gov (ID: NCT03009955).

Consent to publish

Not Applicable

Availability of data and materials

All data can be acquired from the corresponding author (HL) by request.

Competing interests

The authors declare no competing interests.

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Authors' Contributions

Conceptualization, JP; Data curation, GY, JP, ZD, JL and XT; Formal analysis, GD, GY and HL; Funding acquisition, GD and HL; Investigation, ZD, JL and XT; Supervision, HL; Writing original draft, GD and GY; Writing – review & editing, HL.

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References

1. Menacker F, Hamilton BE. Recent trends in cesarean delivery in the United States. *NCHS Data Brief*. 2010;1-08.
2. Li HT, Luo S, Trasande L, et al. Geographic Variations and Temporal Trends in Cesarean Delivery Rates in China, 2008-2014. *JAMA*. 2017;**317**:69-76.
3. Raja SN, Jensen TS. Predicting postoperative pain based on preoperative pain perception: are we doing better than the weatherman? *ANESTHESIOLOGY*. 2010;**112**:1311-12.
4. Gerbershagen HJ, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *ANESTHESIOLOGY*. 2013;**118**:934-44.
5. Patel R, Carvalho JC, Downey K, Kanczuk M, Bernstein P, Siddiqui N. Intraperitoneal Instillation of Lidocaine Improves Postoperative Analgesia at Cesarean Delivery: A Randomized, Double-Blind, Placebo-Controlled Trial. *ANESTH ANALG*. 2017;**124**:554-59.

6. Ortner CM, Granot M, Richebe P, Cardoso M, Bollag L, Landau R. Preoperative scar hyperalgesia is associated with post-operative pain in women undergoing a repeat Caesarean delivery. *EUR J PAIN*. 2013;**17**:111-23.
7. Eisenach JC, Pan PH, Smiley R, Lavand'Homme P, Landau R, Houle TT. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. *PAIN*. 2008;**140**:87-94.
8. Lavand'Homme P. Chronic pain after vaginal and cesarean delivery: a reality questioning our daily practice of obstetric anesthesia. *INT J OBSTET ANESTH*. 2010;**19**:1-02.
9. Zeng Y, Hesketh T. The effects of China's universal two-child policy. *LANCET*. 2016;**388**:1930-38.
10. Wang L, Xu X, Baker P, et al. Factors associated with intention to have caesarean delivery in pregnant women in China: a cross-sectional analysis. *LANCET*. 2016;**388** Suppl 1:S2.
11. Gasim T, Al JF, Rahman MS, Rahman J. Multiple repeat cesarean sections: operative difficulties, maternal complications and outcome. *J REPROD MED*. 2013;**58**:312-18.
12. Elbohoty AE, Gomaa MF, Abdelaleim M, Abd-El-Gawad M, Elmarakby M. Diathermy versus scalpel in transverse abdominal incision in women undergoing repeated cesarean section: A randomized controlled trial. *J Obstet Gynaecol Res*. 2015;**41**:1541-46.
13. Practice Guidelines for Obstetric Anesthesia: An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. *ANESTHESIOLOGY*. 2016;**124**:270-300.
14. Practice Bulletin No. 177: Obstetric Analgesia and Anesthesia. *OBSTET GYNECOL*. 2017;**129**:e73-89.
15. Pan PH, Tonidandel AM, Aschenbrenner CA, Houle TT, Harris LC, Eisenach JC. Predicting acute pain after cesarean delivery using three simple questions. *ANESTHESIOLOGY*. 2013;**118**:1170-79.
16. Ip HY, Abrishami A, Peng PW, Wong J, Chung F. Predictors of postoperative pain and analgesic consumption: a qualitative systematic review. *ANESTHESIOLOGY*. 2009;**111**:657-77.
17. von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLOS MED*. 2007;**4**:e296.
18. Eisenach JC, Kheterpal S, Houle TT. Reporting of Observational Research in ANESTHESIOLOGY: The Importance of the Analysis Plan. *ANESTHESIOLOGY*. 2016;**124**:998-1000.
19. Pietzak EJ, Mucksavage P, Guzzo TJ, Malkowicz SB. Heavy Cigarette Smoking and Aggressive Bladder Cancer at Initial Presentation. *UROLOGY*. 2015;**86**:968-72.

20. Duan G, Xiang G, Zhang X, Yuan R, Zhan H, Qi D. A single-nucleotide polymorphism in SCN9A may decrease postoperative pain sensitivity in the general population. *ANESTHESIOLOGY*. 2013;**118**:436-42.
21. de Miranda S, Pochard F, Chaize M, et al. Postintensive care unit psychological burden in patients with chronic obstructive pulmonary disease and informal caregivers: A multicenter study. *CRIT CARE MED*. 2011;**39**:112-18.
22. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;**67**:361-70.
23. Oh E, Ahn HJ, Sim WS, Lee JY. Synergistic Effect of Intravenous Ibuprofen and Hydromorphone for Postoperative Pain: Prospective Randomized Controlled Trial. *PAIN PHYSICIAN*. 2016;**19**:341-48.
24. Zhang J, Troendle J, Reddy UM, et al. Contemporary cesarean delivery practice in the United States. *AM J OBSTET GYNECOL*. 2010;**203**:321-26.
25. Molina G, Weiser TG, Lipsitz SR, et al. Relationship Between Cesarean Delivery Rate and Maternal and Neonatal Mortality. *JAMA*. 2015;**314**:2263-70.
26. Tulandi T, Agdi M, Zarei A, Miner L, Sikirica V. Adhesion development and morbidity after repeat cesarean delivery. *AM J OBSTET GYNECOL*. 2009;**201**:51-56.
27. Arlier S, Seyfettinoglu S, Yilmaz E, et al. Incidence of adhesions and maternal and neonatal morbidity after repeat cesarean section. *ARCH GYNECOL OBSTET*. 2017;**295**:303-11.
28. Valdes AM, Suokas AK, Doherty SA, Jenkins W, Doherty M. History of knee surgery is associated with higher prevalence of neuropathic pain-like symptoms in patients with severe osteoarthritis of the knee. *Semin Arthritis Rheum*. 2014;**43**:588-92.
29. Duan G, Guo S, Zhang Y, et al. The effects of epidemiological factors and pressure pain measurement in predicting postoperative pain: A prospective survey of 1002 Chinese patients. *PAIN PHYSICIAN*. 2017.
30. De Bonis M, Torricelli M, Leoni L, et al. Carbetocin versus oxytocin after caesarean section: similar efficacy but reduced pain perception in women with high risk of postpartum haemorrhage. *J Matern Fetal Neonatal Med*. 2012;**25**:732-35.
31. Rath W. Prevention of postpartum haemorrhage with the oxytocin analogue carbetocin. *Eur J Obstet Gynecol Reprod Biol*. 2009;**147**:15-20.
32. Schewe JC, Komusin A, Zinserling J, Nadstawek J, Hoefl A, Hering R. Effects of spinal anaesthesia versus epidural anaesthesia for caesarean section on postoperative analgesic consumption and postoperative pain. *Eur J Anaesthesiol*. 2009;**26**:52-59.

33. Booth JL, Harris LC, Eisenach JC, Pan PH. A Randomized Controlled Trial Comparing Two Multimodal Analgesic Techniques in Patients Predicted to Have Severe Pain After Cesarean Delivery. *ANESTH ANALG*. 2016;**122**:1114-19.
34. Kagwa S, Hoefl MA, Firth PG, Ttendo S, Modest VE. Ultrasound guided transversus abdominis plane versus sham blocks after caesarean section in an Ugandan village hospital: a prospective, randomised, double-blinded, single-centre study. *LANCET*. 2015;**385** Suppl 2:S36.
35. Moriyama K, Ohashi Y, Motoyasu A, Ando T, Moriyama K, Yorozu T. Intrathecal Administration of Morphine Decreases Persistent Pain after Cesarean section: A Prospective Observational Study. *PLOS ONE*. 2016;**11**:e155114.
36. Hsu HW, Cheng YJ, Chen LK, et al. Differential analgesic effect of tenoxicam on the wound pain and uterine cramping pain after cesarean section. *CLIN J PAIN*. 2003;**19**:55-58.
37. Yeh YC, Chen SY, Lin CJ, Yeh HM, Sun WZ. Differential analgesic effect of tenoxicam on post-cesarean uterine cramping pain between primiparous and multiparous women. *J FORMOS MED ASSOC*. 2005;**104**:647-51.
38. Csendes A, Burgos AM, Roizblatt D, Garay C, Bezama P. Inflammatory response measured by body temperature, C-reactive protein and white blood cell count 1, 3, and 5 days after laparotomic or laparoscopic gastric bypass surgery. *OBES SURG*. 2009;**19**:890-93.
39. Chen SB, Lee YC, Ser KH, et al. Serum C-reactive protein and white blood cell count in morbidly obese surgical patients. *OBES SURG*. 2009;**19**:461-66.
40. Kim SY, Koo BN, Shin CS, Ban M, Han K, Kim MD. The effects of single-dose dexamethasone on inflammatory response and pain after uterine artery embolisation for symptomatic fibroids or adenomyosis: a randomised controlled study. *BJOG*. 2016;**123**:580-87.
41. Jin J, Peng L, Chen Q, et al. Prevalence and risk factors for chronic pain following cesarean section: a prospective study. *BMC ANESTHESIOLOGY*. 2016;**16**:99.
42. Dorner TE, Muckenhuber J, Stronegger WJ, Rasky E, Gustorff B, Freidl W. The impact of socio-economic status on pain and the perception of disability due to pain. *EUR J PAIN*. 2011;**15**:103-09.
43. Ng B, Dimsdale JE, Rollnik JD, Shapiro H. The effect of ethnicity on prescriptions for patient-controlled analgesia for post-operative pain. *PAIN*. 1996;**66**:9-12.

Tables

Table 1. Demographic, preoperative and intraoperative data.

	Group P (n=67)	Group R (n=101)	Statistics
year)	29.5±3.9	31.3±3.4	$t=3.112, P=0.002$
group (>30)	20(29.9%)	57(56.4%)	$\chi^2=11.467, P=0.001$
kg/m ²)	26.7±1.9	26.9±1.9	$t=0.820, P=0.415$
tional age (week)	38.9±0.9	38.4±0.6	$t=103, P<0.001$
erative complications	54(80.6%)	54(53.5%)	$t=12.912, P<0.001$
S-A (score)	2(0, 5)	1(0, 4)	$U=0.887, P=0.375$
S-D (score)	0(0, 2)	0(0, 2)	$U=0.129, P=0.897$
ery duration (min)	62.1±15.3	71.1±16.2	$t=3.782, P<0.001$
at of newborn (g)	3278±481	3443±1074	$t=1.185, P=0.238$
at of newborn (cm)	49.7±2.1	49.9±1.7	$t=0.820, P=0.505$
l loss (mL)	286±94	306±92	$t=0.668, P=0.889$

Group P and R mean patients who received primary and repeated cesarean delivery, respectively; Data were presented as Means±SD, median (interquartile range) or as numbers (percentage); BMI=body mass index; HADS-A=Hospital anxiety scale; HADS-D=Hospital depression scale.

Table 2. Logistic regression analysis of [inadequate analgesia on incision pain and visceral](#).

	Predictors	Wals	<i>P</i> value	OR	95% CI	
e analgesia on ain	Age(year)	0.543	0.461	1.043	0.932 to 1.169	
	BMI(kg/m ²)	0.193	0.660	1.048	0.850 to 1.293	
	Gestational age (week)	0.035	0.853	1.048	0.637 to 1.727	
	Preoperative complications(yes/no)	4.721	0.030	0.365	0.147 to 0.906	
	Surgery duration (min)	3.610	0.057	1.000	0.999 to 1.000	
	Patient group(P/R)	10.790	0.001	0.191	0.071 to 0.513	
	Anxiety(yes/no)	0.000	0.999	0.000	NA	
	Depression(yes/no)	0.000	0.999	0.000	NA	
	e analgesia on ain	Age	3.463	0.063	0.897	0.801 to 1.006
		BMI	0.002	0.968	1.005	0.804 to 1.256
Gestational age (week)		0.175	0.675	0.885	0.498 to 1.570	
Preoperative complications(yes/no)		0.277	0.599	1.273	0.519 to 3.124	
Surgery duration (min)		0.586	0.444	1.000	0.999 to 1.000	
Patient group(P/R)		0.599	0.439	1.515	0.529 to 4.340	
Anxiety(yes/no)		0.133	0.715	1.462	0.190 to 11.219	
Depression(yes/no)		0.423	0.515	0.403	0.026 to 6.228	

BMI=body mass index; CI= [confidence interval](#); OR=odds rate.

Table 3. Subgroup analysis for different age groups

Outcomes	Group P	Group R	Statistics
Inadequate control on incision pain	18(38.3%)	8(18.2%)	$\chi^2=4.506$, $P=0.033$
Inadequate control on viscera pain	3(6.4%)	10(22.7%)	$\chi^2=4.958$, $P=0.025$
Inadequate control on both incision and viscera pain	18(38.3%)	16(36.4%)	$\chi^2=0.036$, $P=0.849$
Inadequate control on incision pain	7(35.0%)	8(14.0%)	$\chi^2=4.149$, $P=0.042$
Inadequate control on viscera pain	5(25.0%)	11(19.3%)	$\chi^2=0.292$, $P=0.588$
Inadequate control on both incision and viscera pain	9(45.0%)	18(31.6%)	$\chi^2=1.171$, $P=0.279$

Group P and R mean patients who received primary and repeated cesarean delivery, respectively; Data were presented as numbers (percentage).

Table 4. The postoperative short-term outcomes in different groups.

Outcomes	Group P (n=67)	Group R (n=101)	Statistics
Time to feel pain (hour)	3 (2, 5)	4 (2, 6)	$U=0.919$, $P=0.358$
Time to walking time (hour)	29.7 ± 9.9	27.3 ± 8.7	$t=1.663$, $P=0.098$
Diarrhea or vomiting	5(7.5%)	7(6.9%)	$\chi^2=0.017$, $P=0.896$
Pruritus	3(4.5%)	4(4.0%)	$\chi^2=0.034$, $P=0.853$
PO quality PO 0d (poor)	23(34.3%)	29(28.7%)	$\chi^2=0.594$, $P=0.441$
PO quality PO 1d (poor)	5(7.5%)	4(3.9%)	$\chi^2=0.975$, $P=0.324$
PCA consumption (mL)	110.9 ± 35.7	117.3 ± 35.9	$t=1.159$, $P=0.248$
Hospital stays (day)	3.6 ± 1.2	3.0 ± 0.8	$t=3.250$, $P=0.001$

Group P and R mean patients who received primary and repeated cesarean delivery, respectively; Data were presented as means ± SD, median (interquartile range) or as numbers (percentage); PO=postoperative; PCA=patient controlled intravenous analgesia.

Table 5. The long-term postoperative outcomes in different groups.

Outcomes	Group P (n=65)	Group R (n=97)	Statistics
Experiencing pain	53(81.5%)	75(77.3%)	$\chi^2=0.418$, $P=0.518$
Location of pain (abdominal incision/viscera/both)	39(60.0%)/6(9.2%)/5(7.7%)	59(60.8%)/6(6.2%)/1(1.0%)	$\chi^2=6.236$, $P=0.101$
Affect sleep	18(27.7%)	21(21.6%)	$\chi^2=0.778$, $P=0.378$
Quality of daily life (fully autonomy/partial dependency)	41(63.1%)/24(26.9%)	57(58.8%)/40(41.2%)	$\chi^2=0.303$, $P=0.582$
Experiencing pain	36(55.4%)	35(36.1%)	$\chi^2=5.889$, $P=0.015$
Location of pain (abdominal incision/viscera/both)	22(33.8%)/12(18.5%)/1(1.5%)	23(23.7%)/10(10.3%)/0(0%)	$\chi^2=7.472$, $P=0.058$
Affect sleep	9(13.8%)	4(4.1%)	$\chi^2=4.984$, $P=0.026$
Quality of daily life (fully autonomy/partial dependency)	65(100%)/0(0%)	97(100%)/0(0%)	$\chi^2=0.000$, $P=1.000$

Group P and R mean patients who received primary and repeated cesarean delivery, respectively; Data were presented as numbers (percentage); PO=postoperative.

Figures

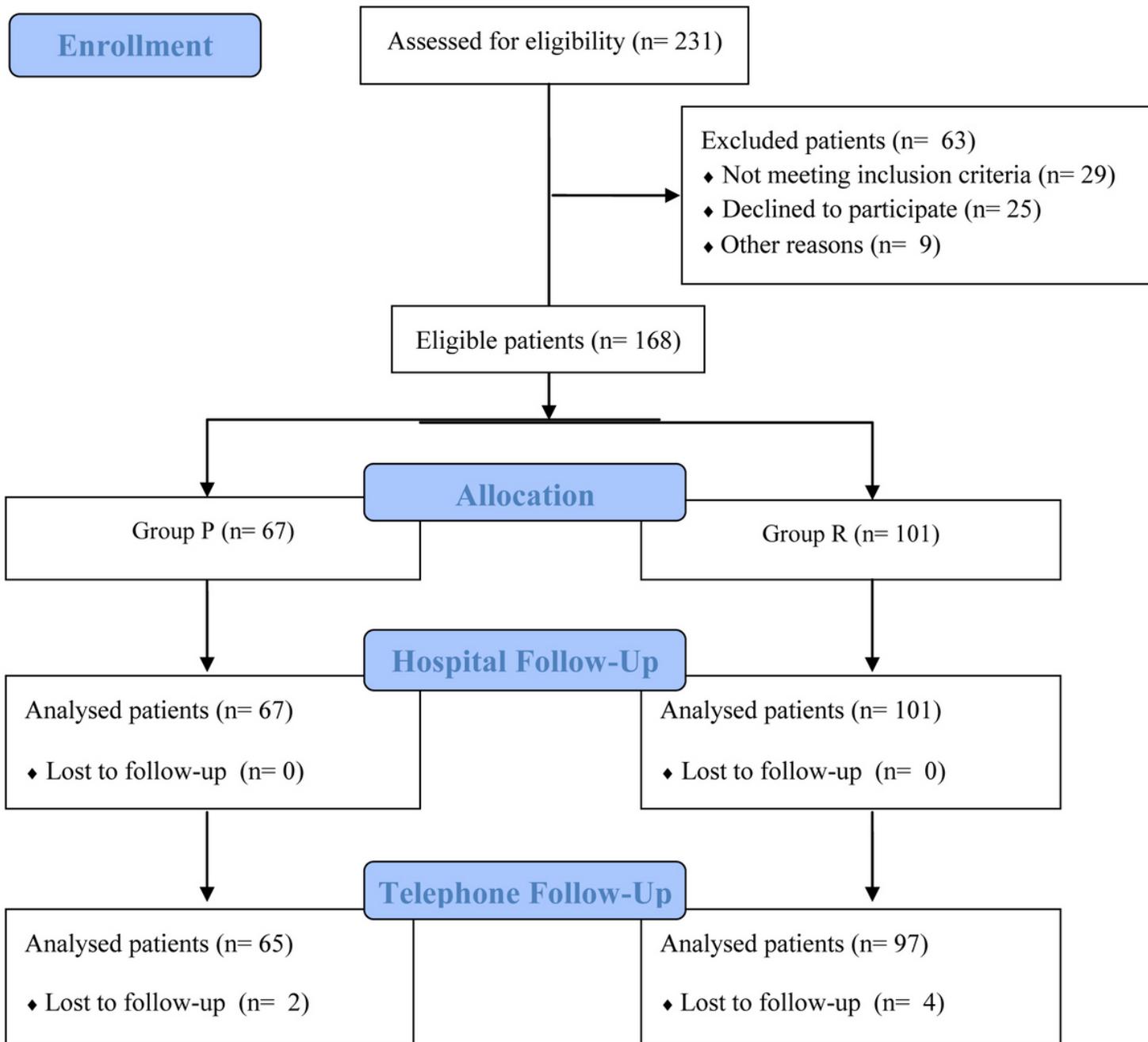


Figure 1

The flow diagram of the study.

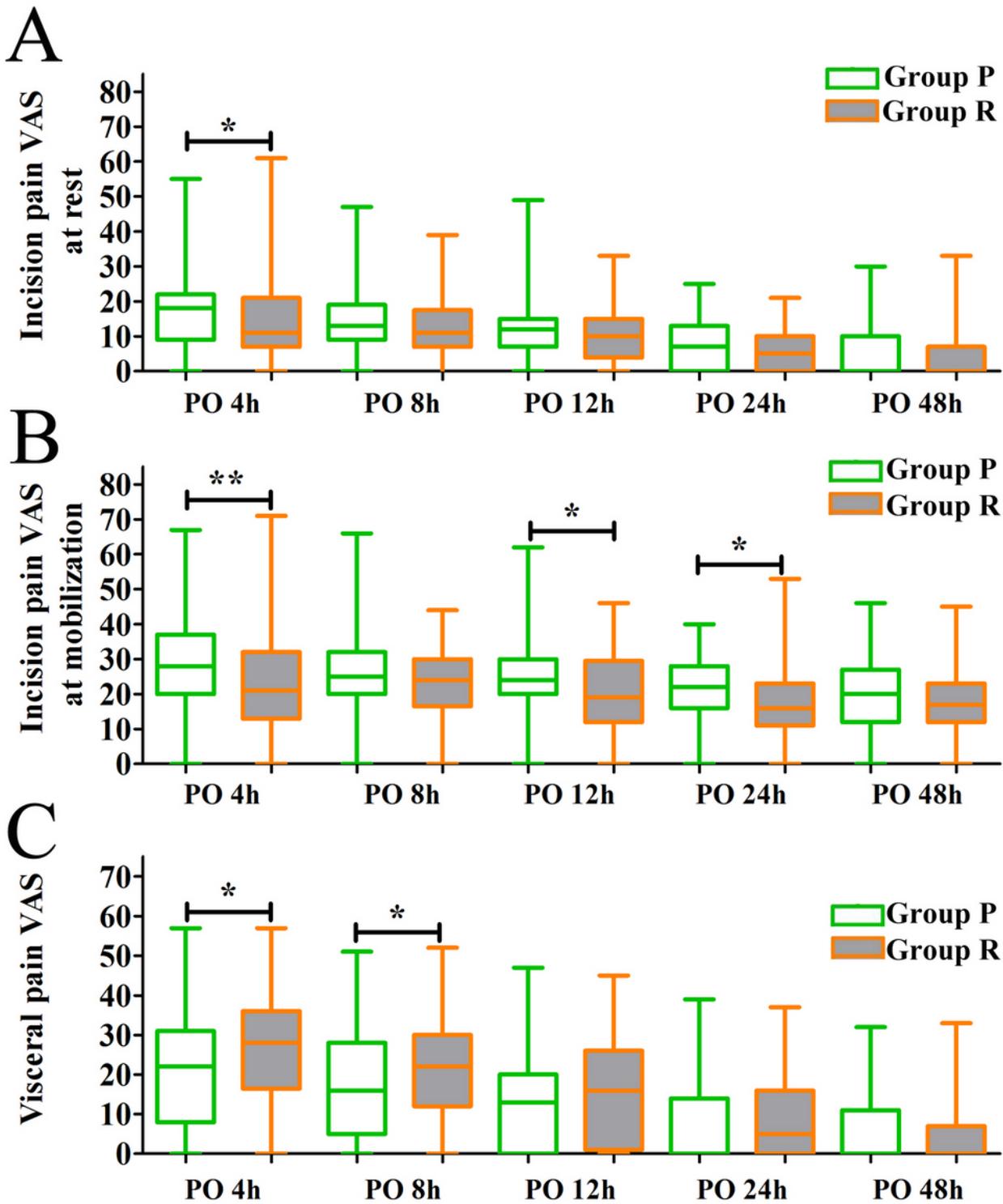


Figure 2

The distribution of postoperative pain VAS at different time points. Means of groups P and R patients who received primary and repeated cesarean section, respectively; VAS=visual analogue scale; PO=postoperative; * $P < 0.05$; ** $P < 0.01$.

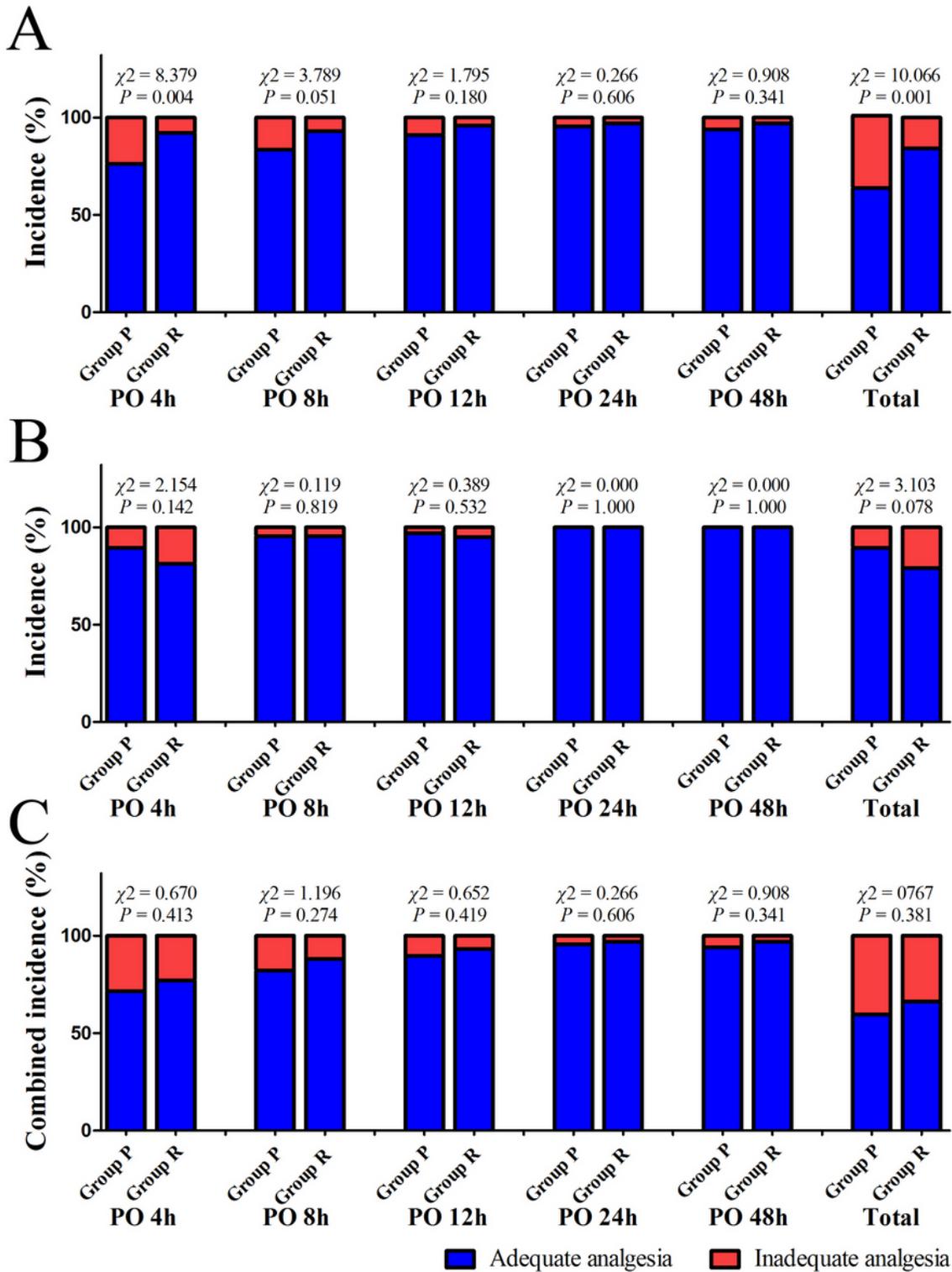


Figure 3

The incidence of postoperative inadequate treatment on incision pain (A), visceral pain (B) and the combined incidence (C). Groups P and R represent patients who received primary and repeated cesarean section; VAS=visual analogue scale; PO=postoperative.

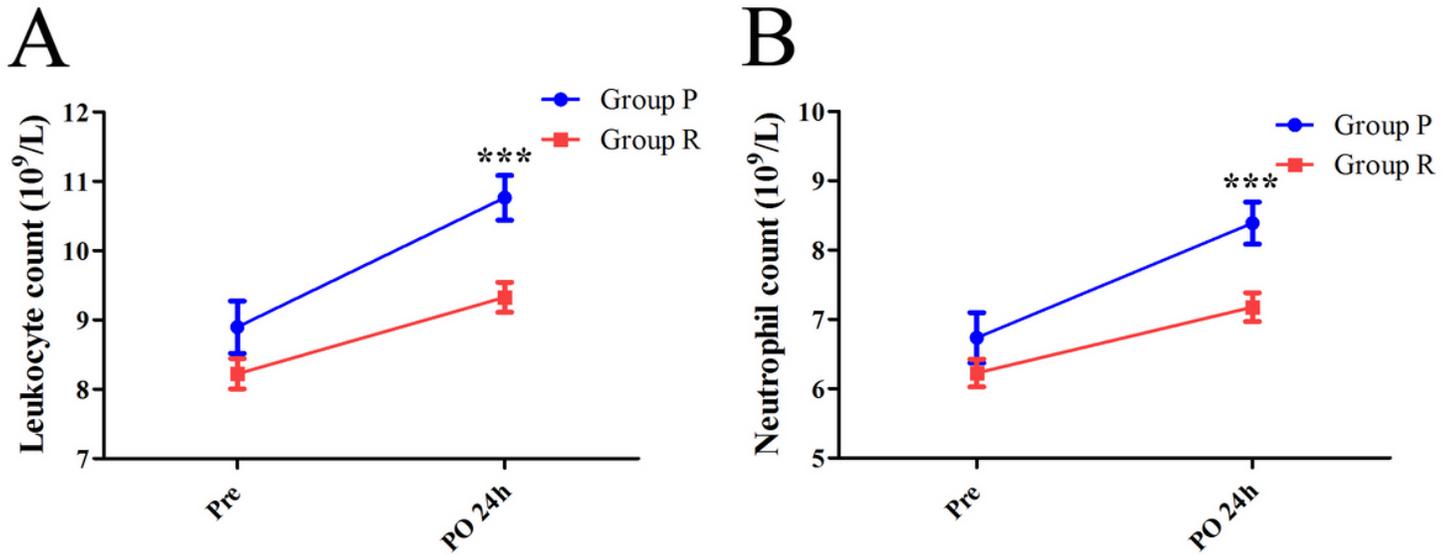


Figure 4

The changes in leukocyte count (A) and neutrophil count (B) before and after surgery. Means of groups P and R patients who received primary and repeated cesarean section, respectively; Pre=preoperative; PO=postoperative; *** compared to group R, $P < 0.001$.