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Effect of opioid sparing strategies on postoperative pain and perioperative hemodynamics in patients undergoing laparoscopic cholecystectomy: a randomized controlled study

Lei Wang[1†], Xinhua Hong[1†], Yiting Xue[1] and Zhen Su[1*]

Abstract

Background Opioid-sparing anesthesia(OSA) or opioid-free anesthesia(OFA) strategy can reduce postoperative pain, but the effect of different stratigies on postoperative pain for patients with high pain sensitivity remains unclear, and the effect of different stratigies on perioperative haemodynamic fluctuations remains controversial for patients undergoing laparoscopic cholecystectomy.

Methods A total of 173 patients scheduled for elective laparoscopic cholecystectomy were randomly assigned into three groups: opioid-free anesthesia group(Group OFA), opioid-sparing anesthesia group(Group OSA) or opioid-based anesthesia group (Group OBA). The preoperative assessment of patients' pain sensitivity was conducted using the Pain Sensitivity Questionnaire (PSQ). The visual analog scale (VAS) scores were recorded at 30 min, 1 h, 2 h, 6 h, 12 h, and 24 h postoperatively. Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and Heart Rate (HR) were recorded at baseline(T0), after admission (T1), after induction(T2), 1 min after tracheal intubation (T3), 1 min after pneumoperitoneum (T4), and calculated as the variability of blood pressure (BPV), coefficient of variation (CV) and average real variability (ARV). Time to awake, acute pain, rescue analgesia, postoperative nausea and vomiting (PONV), and time to first exhaust were also recorded.

Results Compared with Group OBA, VAS scores were significantly lower in Group OFA and OSA at 2 h, 6 h and 12 h postoperatively ($P<0.05$). BPV_{SBP}, BPV_{DBP}, BPV_{MAP}, CV_{SBP}, CV_{DBP}, CV_{MAP}, ARV_{DBP} and ARV_{MAP} were lower in both Group OSA and OBA compared to the Group OFA ($P<0.05$). Group OSA exhibited lower $BPV_{SBP,}$ CV_{DBP}, and ARV_{DBP} compared to the OBA group ($P<0.05$). In the subgroup analysis of patients with high pain sensitivity, BPV_{SBP}, BPV_{DBP}, BPV_{MAP}, CV_{DBP}, CV_{MAP}, ARV_{SBP}, ARV_{DBP} and ARV_{MAP} were lower in Group OSA compared to Group OFA ($P<0.05$). BPV_{DBP}, CV_{DBP},

[†]Lei Wang and Xinhua Hong contributed equally to the study as co-first authors.

*Correspondence:
Zhen Su
xzmcsuzhen@163.com

Full list of author information is available at the end of the article

ARV_{SBP} and ARV_{DBP} were lower in the OSA group compared to the OBA group ($P < 0.05$). The time to first exhaust was significantly reduced in patients in Group OFA compared with Group OSA and OBA ($P < 0.05$).

Conclusion OSA can effectively control patients' postoperative pain with lower perioperative haemodynamic variability. It also has lower perioperative haemodynamic variability and acute pain in patients with high pain sensitivity, making it suitable for laparoscopic cholecystectomy.

Trial registration The trial is registered with the China Clinical Trials Registry Registration Number: ChiCTR2400093036. Retrospectively registered (date of registration: 27/11/2024).

Keywords Opioid-sparing anesthesia, Opioid-free anesthesia, Pain sensitivity questionnaire, Variability of blood pressure, Coefficient of variation

Background

Opioid-sparing anaesthesia (OSA) is a strategy based on multimodal analgesia that maximises the use of non-opioids for anaesthesia and analgesia and preserves opioids for the control of severe acute pain that cannot be relieved by other medications [1]. It can be further subdivided into opioid free anesthesia (OFA) and OSA, based on whether or not intraoperative opioids are used. Currently, studies have reported that opioid-sparing strategies can control postoperative pain, reduce opioid-related adverse effects, accelerate postoperative recovery, and shorten the length of hospital stay [2]. However, some studies have shown that reducing intraoperative opioid use is not beneficial for postoperative pain management and may even lead to chronic postoperative pain [3, 4]. Whether OFA or OSA strategy can reduce perioperative haemodynamic fluctuations also remains controversial. It has been shown [5] that perioperative target organ damage is related to the patient's blood pressure variability, and it is particularly important to maintain haemodynamic stability in hypertensive patients because of the increased secretion of endogenous catecholamines, hyperexcitability of the sympathetic nervous system, increased peripheral vascular resistance, and easy fluctuation of haemodynamics, which increase the patient's risk during anaesthesia and surgery. Patients' pain sensitivity has also been shown to be strongly associated with the risk and severity of acute postoperative pain [6, 7]. However, the feasibility and safety of implementing an opioid sparing strategy in a highly pain-sensitive population has not been reported. Therefore, this study aims to provide a clinical reference by comparing the effects of different anaesthetic regimens on postoperative pain and perioperative haemodynamics in patients undergoing laparoscopic cholecystectomy.

Materials and methods

Research ethics

This prospective, randomized, controlled clinical trial (KY-2023-085-02) was approved by the Ethics Committee of Huaian First People's Hospital (Chairperson Liang Yu) on 3 July 2023 and registered in the Chinese Clinical Trial Register (ChiCTR2400093036, Registration Date: 27/11/2024), and written informed consents were obtained from all participants enrolled in the study before surgery. This manuscript adheres to the applicable Consolidated Standards of Reporting Trials (CONSORT) guidelines refer. This study started in July 2023 and ended in June 2024. Patients were randomly assigned to three groups: opioid-free anesthesia (Group OFA), opioid-sparing anesthesia (Group OSA), and opioid-based anesthesia (Group OBA) using the random number table method. The details of each patient's method of anesthesia was stored in an opaque, sealed envelope and opened only by researchers before anesthesia induction. All participants, preoperative and postoperative follow-up assessors and statisticians were blinded to the group allocation.

Patients

All male and female patients scheduled for elective laparoscopic cholecystectomy aged between 18 and 70 with an ASA grade I-II, BMI ranged 18.5 kg/m^2-30.0 kg/m^2 were included in the study. Exclusion criteria were as follows: patients had severe cardiovascular disease or liver and kidney dysfunction; history of chronic pain; history of abuse of analgesic drugs and long-term use of analgesic drugs or alcohol intake; patients with allergies or contraindications to drugs that may be used in the test; in the context of anticoagulation therapy, or in the presence of coagulation disorders; history of central nervous system and/or mental illness; hypertention; patients had chronic diabetes and other effects on pain perception. Elimination criteria were: intraoperative blood loss > 400 ml or operation time > 3 h; intraoperative change of operation mode or postoperative need for a second operation; postoperative admission to the intensive care unit; quit midway or incomplete follow-up data collection.

Anesthesia procedure

All patients were abstaining from all medications prior to the procedure, in accordance with the preoperative fasting and abstinence from food and drink recommended by the Enhanced Recovery After Surgery Guidelines.

Electrocardiogram (ECG), pulse oximetry (SpO_2), blood pressure (BP), and end-expiratory carbon dioxide pressure ($P_{ET}CO2$) were monitored routinely following admission to the room, and peripheral intravenous access was established in the upper extremities.

Patients in Group OFA and OSA underwent ultrasound-guided transabdominal plane (TAP) block prior to induction of anesthesia. A total of 20 ml of 0.375% ropivacaine was administered in a uniform manner on both sides of the abdominal wall. Patients in Group OFA were given dexmedetomidine 0.4 μg/kg intravenously for a period of 10 min, while dexamethasone 0.1 mg/kg and flurbiprofenate 50 mg intravenously for prophylactic analgesia. Subsequently, intravenous lidocaine 1 mg/kg, midazolam 0.04 mg/kg, esketamine 0.5 mg/kg, propofol 2 mg/kg, and rocuronium 0.6 mg/kg were employed for the induction of anesthesia. Patients in the Group OSA were given dexmedetomidine 0.4 μg/kg intravenously for 10 min, and dexamethasone 0.1 mg/kg and flurbiprofenac 50 mg intravenously for prophylactic analgesia followed by intravenous lidocaine 1 mg/kg, midazolam 0.04 mg/kg, propofol 2 mg/kg, sufentanil 0.3 μg/kg and rocuronium bromide 0.6 mg/kg for anesthesia induction. Group OBA was induced with intravenous administration of midazolam 0.04 mg/kg, sufentanil 0.6 μg/kg, propofol 1 mg/kg, and rocuronium 0.6 mg/kg. All three groups were maintained with propofol at a dosage of 3 mg/kg/h, administered with sevoflurane inhalation, and the depth of anesthesia was maintained at 40–60 using bispectral index (BIS) to monitor the depth of anesthesia in the patients. The OSA and OBA groups received an additional dose of sufentanil, and intraoperative vasoactive medications were used appropriately to maintain blood pressure within ± 20% of the basal value. The concentration of sevoflurane was maintained until the conclusion of the surgical procedure, at which point ropivacaine was administered for incisional infiltration anesthesia. Patients were admitted to the post-anesthesia care unit (PACU) for the purposes of undergoing postoperative awakening and extubation. Once the patients had resumed spontaneous respiration, Sugammadex Sodium 2 mg/kg was administered to antagonize the residual neuromuscular blockade. Following extubation, patients were reassessed in the PACU and subsequently transferred to the ward for further monitoring when the Aldrete awakening score reached a value of ≥ 9. The patient's pain level was assessed within 24 h postoperatively, and when the VAS score was > 3, sufentanil 5 μg IV was administered for the purpose of providing remedial analgesia.

Outcomes and data collection

The primary outcome of the study was the VAS score 1 h postoperatively. SBP, DBP, HR, and MAP were recorded at baseline (T0), following anesthesia induction (T2), 1 min after tracheal intubation (T3), and 1 min after pneumoperitoneum (T4). Blood pressure variability (BPV), coefficient of variation (CV) and average real variability (ARV) were calculated according to BP. In this study, the standard deviation of blood pressure measurements was employed as a measure of BPV. CV was calculated by dividing BPV by the mean blood pressure, while ARV was calculated by averaging the absolute difference between blood pressure measurements taken at different time points during the follow-up period. Preoperative pain sensitivity questionnaire (PSQ) was used to assess the patient's pain sensitivity. In this study, PSQ score ≥ 5 were defined as high pain sensitivity. Rescue analgesia for 24 h postoperatively, acute postoperative pain (VAS > 3 points), the time to first exhaust and the occurrence of postoperative nausea and vomiting were also recorded.

Sample size caculating

The sample size was calculated using PASS 15.0 software. This study employed a parallel randomized controlled trial design, with the 1-hour postoperative VAS score serving as the primary outcome indicator. The pretest results indicated that the VAS scores of patients in the OFA, OSA, and OBA groups were 3.5, 2.2, and 2.5, respectively, at 1 h postoperatively. Additionally, the standard deviations of each group were 1.5, 1.9, and 1.7, respectively. A two-sided test was conducted, with α set at 0.05 and 1-β at 0.9. This resulted in a calculated sample size of 51 patients per group. Considering a potential dropout rate of 10% within the study population, a minimum of 170 patients were required to be included in this study.

Statistical analysis

The data were processed using SPSS 26.0 statistical software. The measurement data used the Shapiro-Wilk test to determine the normality of the data distribution, and the Levene method was used to test the homogeneity of variance. The measurement data that meet the normal distribution were expressed as the mean ± standard deviation ($\bar{x} \pm s$) or represented by the median (M) and the interquartile range (IQR) which meets the non-normal distribution. Measurement data were subjected to multiple group comparisons using the Kruskal-Wallis H test. Nonnormally distributed data collected at multiple points in time, such as VAS scores, were analyzed using the generalized estimated equation (GEE). The analysis of variance for repeated measures (ANOVA) was employed for count data, which were expressed as percentages. The chi-square test or Fisher's exact probability method was used for count data. Two-by-two comparisons of multiple group rates were made using the Bonferroni method

of correction. A *P*-value of less than 0.05 was considered to indicate a statistically significant difference.

Results

Flow chart of the research process

A total of 185 patients were screened, and 8 were subsequently excluded from further participation. Three patients declined to sign the informed consent form, three had diabetes, and two had obesity. A total of 177 patients were ultimately included in the study. These patients were randomly assigned to three groups. One case in Group OFA resulted in a change to the surgical procedure, two cases in Group OSA underwent a surgical procedure that lasted more than three hours, and one case in Group OBA underwent a surgical procedure that lasted more than three hours. Ultimately, 173 patients were included in the statistical analysis (Fig. 1).

Characteristics of patients

No statistically significant differences were observed in the general conditions of age, gender, BMI, ASA classification, operation time, hypertension, and PSQ between the three groups ($P>0.05$)(Table 1).

VAS in different time between three groups

Using generalized estimating equation analysis, there is an interaction between groups and time (Wald $X^2_{time*group}$=48.12, $P<0.001$), therefore a separate effects analysis is conducted. The individual effects analysis of time showed that the VAS scores of the three groups of patients at different time points were statistically significant (Wald $X^2_{time}=313.96$, $P<0.001$), and showed a decreasing trend at different postoperative time points. The individual effects analysis between groups showed that compared with Group OBA, Group OFA and OSA had lower values at 2, 6, and 12 h after surgery (Wald $X^2_{group}=7.37$, $P<0.05$) (Table 2);

Hemodynamics

In comparison to the OFA group, the OSA and OBA groups exhibited lower systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) at T2 ($P<0.05$). However, no statistically significant differences were observed in SBP, DBP, MAP, and HR at the remaining time points ($P>0.05$) (Fig. 2).

Blood pressure variation index

BPV_{SBP}, BPV_{DBP}, BPV_{MAP}, CV_{SBP}, CV_{DBP}, CV_{MAP}, ARV_{DBP}, and ARV_{MAP} were found to be significantly lower in Group OSA group compared to Group OFA ($P<0.05$). Group OSA exhibited lower levels of BPV_{SBP}, CV_{DBP}, and ARV_{DBP} compared to Group OBA ($P<0.05$) (Table 3).

Subgroup analysis of patients with high pain sensitivity

In the subgroup analysis of patients with high pain sensitivity, BPV_{SBP}, BPV_{DBP}, BPV_{MAP}, CV_{DBP}, CV_{MAP}, ARV_{SBP}, ARV_{DBP}, and ARV_{MAP} were lower compared with Group OFA ($P<0.05$). BPV_{DBP}, CV_{DBP}, ARV_{SBP}, ARV_{DBP} were lower in Group OSA compared to Group OBA ($P<0.05$) (Table 4).

Postoperative events

The time to first flatus was significantly shorter in patients in the OFA group than in the OSA and OBA groups ($P<0.05$). There was no significant difference in postoperative rescue analgesia, incidence of acute pain, postoperative nausea and vomiting, and awakening time among patients in the three groups with high pain sensitivity ($P>0.05$). Subgroup analysis was conducted on patients with high sensitivity to pain, and the frequency of postoperative acute pain was significantly higher in Group OFA than in Group OSA and OBA ($P<0.05$) (Table 5).

Disscusion

The opioid sparing anesthesia strategy of anesthesia is based on multimodal analgesia to reduce opioid-related postoperative respiratory failure, nausea, vomiting, urinary retention, delirium and so on. This is achieved through the adoption of non-opioid medications, which includes non-steroidal anti-inflammatory drugs (NSAIDs), N-methyl-D-aspartate (NMDA) receptor antagonists, α2 agonists, and peripheral regional block techniques, while maintaining the use of opioids for the treatment of uncontrolled severe acute pain to rationalize their use [8]. In light of the potential benefits of opioid-sparing anesthesia, some scholars have put forth the concept of opioid-free anesthesia. This approach involves the integration of diverse opioid-sparing techniques with the aim of attaining intraoperative opioid-free anesthesia [4]. In this study, we employed a multimodal approach to anesthesia, utilizing OFA, OSA, and OBA, in patients undergoing elective laparoscopic cholecystectomy. Our findings indicate that the opioid-sparing strategy anesthesia regimen effectively managed postoperative pain, with minimal perioperative hemodynamic fluctuation and lower BPV, CV, and ARV. Additionally, this regimen demonstrated a reduced incidence of perioperative adverse events in patients with high pain sensitivity.

Previous studies have demonstrated the efficacy of OFA strategies in a range of surgical procedures. Aboalsoud [9] observed markedly diminished VAS scores in the OFA cohort whether at rest or with upper arm movement during modified radical mastectomy. Additionally, Yu [10] observed reduced VAS scores in the OFA cohort at 2 and 8 h postoperatively during laparoscopic cholecystectomy. Toleska [11] demonstrated that the use of opioid-free and

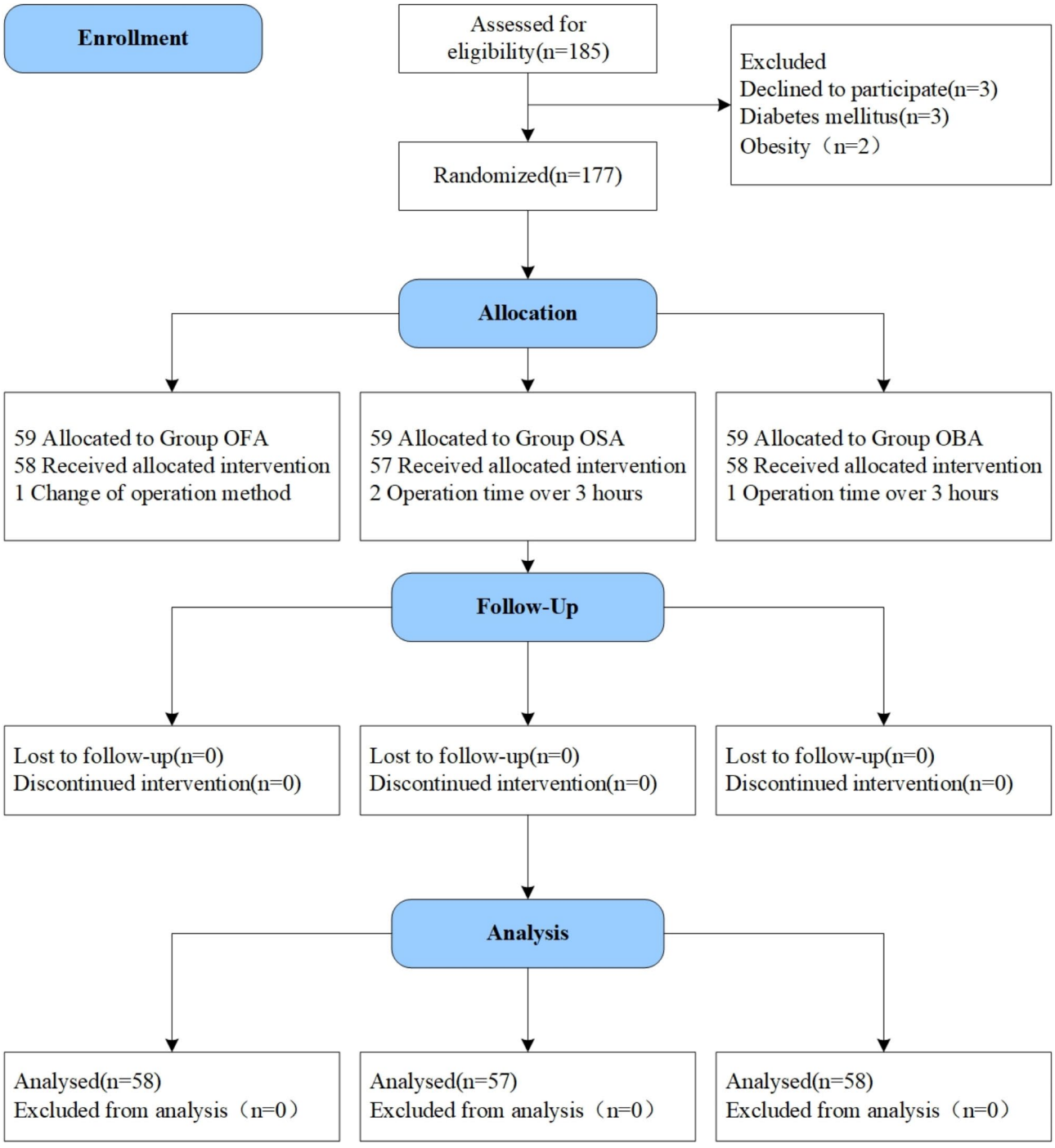

Fig. 1 The CONSORT flow diagram

opioid-sparing anesthesia reduces the incidence of postoperative pain in patients, decreases the adverse effects and shortens the length of stay in the hospital. The results of the present study are consistent with previous research findings. Jean Paul Mullier and some others [12, 13] have proposed the concept of the "Opioid Paradox" that shows that the more opioid was given intraoperatively the more opioid is required postoperatively to achieve the same level of analgesia, which is likely to be central facet. Nevertheless, a meta-analysis conducted by Feenstra [14] revealed that OSA did not result in a reduction in postoperative NRS scores or postoperative opioid consumption, indicating a lack of substantial evidence to support this hypothesis. It has been proposed that opioid sparing strategies may be advantageous in certain patient populations, while in other populations, these strategies should

Table 1 Characteristics of patients

	OFA($n=58$)	OSA($n=57$)	OBA($n=58$)	F/X^2	*P*
Age	47.16 ± 13.00	50.65 ± 14.11	51.26 ± 14.39	1.484	0.23
Gender	25/33	33/24	27/31	2.749	0.25
BMI	22.20 ± 3.42	24.80 ± 3.47	25.19 ± 2.96	0.270	0.76
ASA	35/23	29/28	30/28	1.278	0.53
Operation time	44.52 ± 22.36	42.46 ± 22.45	42.90 ± 22.49	0.135	0.87
Hypertension	46/12	41/16	49/9	2.720	0.26
PSQ	4.95 ± 1.45	5.08 ± 1.57	4.91 ± 1.44	0.206	0.81

Data are expressed as mean ± SD or median [IQR], or n (%). BMI, body mass index; ASA, American Society of Anesthesiologists; PSQ, pain sensitivity questionnaire

be tailored on an individual basis to achieve an optimal balance between adequate analgesia and reduced adverse effects.

Concurrently, the absence of adequate monitoring of adverse effects has prompted the proposition that the analgesic efficacy of opioid sparing strategies remains uncertain, with the potential for intraoperative hemodynamic fluctuations. In comparison to blood pressure and heart rate, an increasing number of studies have demonstrated that target organ damage is associated with blood pressure variability (BPV) in patients [15]. It has been shown that greater perioperative hemodynamic fluctuations are associated with perioperative cardiovascular events, acute kidney injury, and subclinical organ damage [16]. Therefore, it is of particular importance to reduce perioperative hemodynamic fluctuations in patients. BPV, CV, and ARV are commonly employed for the evaluation of hemodynamic fluctuations [17]. In this

Table 2 Comparison of VAS in different times between three groups

	T1	T2	T3	T4	T5	T6	T7	X^2-group effect simple	*P*
OFA	2(0,4)	2(0,4)	2(1,3)	2(1,3)	1(0,2)	1(0,2)	1(0,1)	99.55	<0.001
OSA	2(0,3)	2(0,3)	2(1,3)	2(1,3)	1(0,2)	1(0,2)	0(0,1)	105.12	<0.001
OBA	2(0,3)	2(1,3)	2(1,3)	3(1,3)	2(1,2)	2(1,2)	1(0,1)	155.43	<0.001
X^2-time effect simple	207.96	255.69	292.74	309.50	209.91	175.27	106.43		
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001		

Note: Wald $X^2_{group}=7.37$, $P=0.025$; Wald $X^2_{time}=313.96$, $P<0.001$; Wald $X^2_{time*group}=48.12$, $P<0.001$

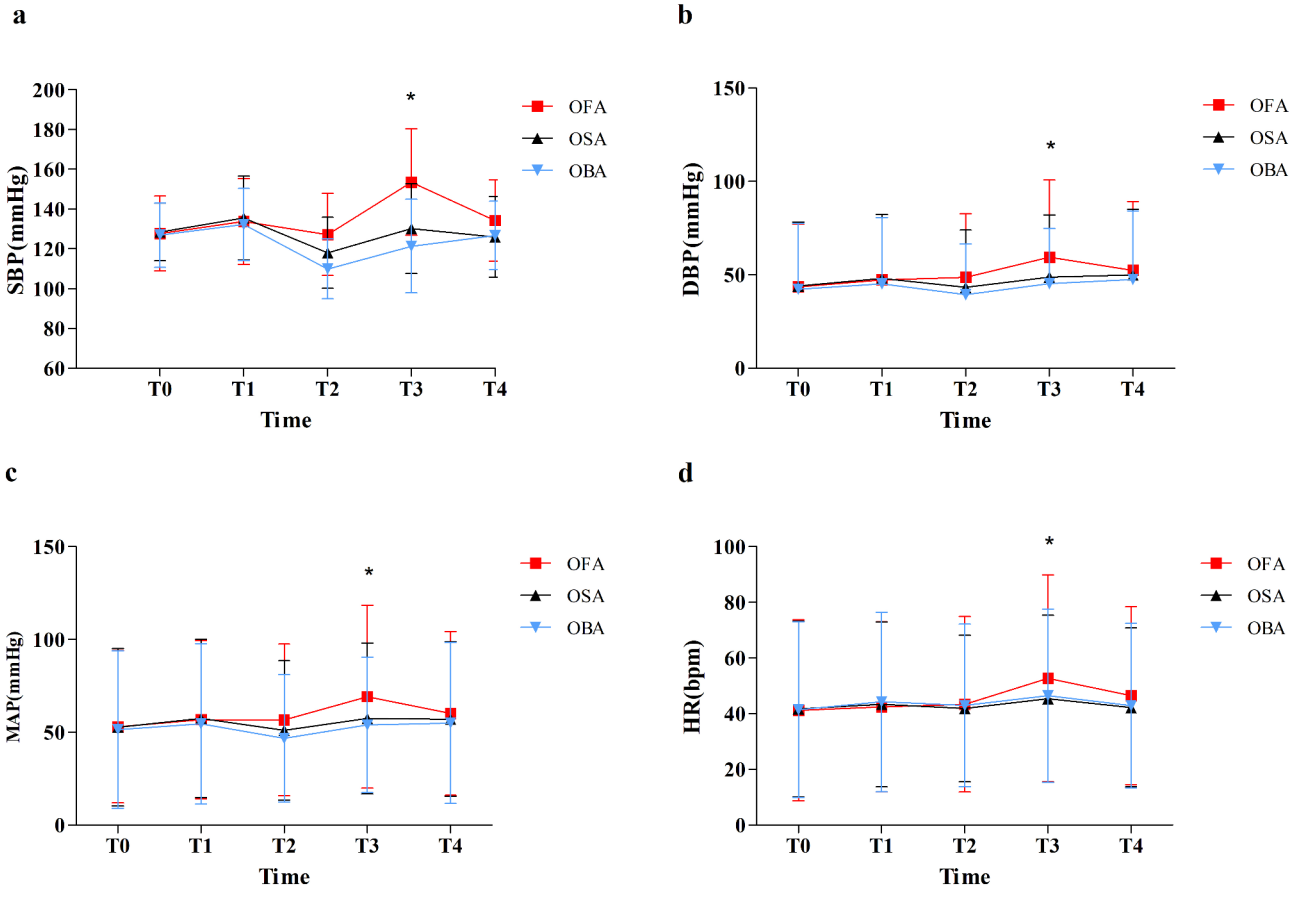

Fig. 2 Comparison of intraoperative hemodynamics between the three groups

Table 3 Comparison of blood pressure variation index

	OFA(*n* = 58)	OSA(*n* = 57)	OBA(*n* = 58)	H/F	*P*
BPV_{SBP}	16.34(11.63,22.31)	12.16(8.31,15.33)	13.58(8.66,17.53)	65.258	<0.001
CV_{SBP}	10.71(7.72,16.31)	10.10(6.14,13.03)	9.91(7.04,13.51)	8.080	0.018
ARV_{SBP}	13.40(10.20,22.60)	11.40(8.60,18.00)	12.20(8.60,15.00)	11.108	0.004
BPV_{DBP}	11.77(9.12,16.08)	8.69(6.25,12.22)	9.94(7.79,12.53)	124.25	<0.001
CV_{DBP}	13.37(11.30,18.19)	10.39(7.90,13.71)	11.43(8.84,13.54)	84.556	<0.001
ARV_{DBP}	11.20(8.40,15.40)	8.60(6.20,11.20)	9.20(6.73,12.51)	91.173	<0.001
BPV_{MAP}	13.14(10.14,16.63)	8.38(6.35,12.31)	11.05(7.95,12.98)	132.61	<0.001
CV_{MAP}	12.26(9.93,16.52)	8.78(6.94,12.53)	10.33(7.77,12.35)	59.035	<0.001
ARV_{MAP}	11.73(10.26,16.63)	8.80(6.69,12.67)	10.60(6.53,13.00)	86.894	<0.001

Data are expressed as median [IQR]. BPV, blood pressure variability; CV, coefficient of variation; ARV, average real variability

Table 4 Sub-analysis of high PSQ in different subgroups

	OFA	OSA	OBA	H/F	*P*
BPV_{SBP}	14.63(9.37,20.68)	12.92(8.49,16.94)	11.51(8.28,14.59)	69.256	<0.001
CV_{SBP}	9.86(6.89,13.66)	10.75(6.14,14.95)	9.21(6.23,11.50)	24.526	<0.001
ARV_{SBP}	15.60(10.40,21.60)	10.20(7.80,18.00)	10.40(7.10,13.40)	93.562	<0.001
BPV_{DBP}	11.49(7.34,14.02)	8.82(6.34,12.27)	10.63(7.46,11.82)	76.472	<0.001
CV_{DBP}	11.69(7.89,15.24)	10.53(7.28,14.07)	12.18(8.65,14.79)	47.913	<0.001
ARV_{DBP}	10.60(7.00,13.00)	8.20(5.40,10.40)	10.60(7.00,12.90)	78.266	<0.001
BPV_{MAP}	10.70(9.26,15.30)	8.38(6.49,12.67)	8.69(7.23,12.22)	84.690	<0.001
CV_{MAP}	10.13(8.86,12.44)	9.09(6.41,12.54)	9.05(7.52,11.88)	48.849	<0.001
ARV_{MAP}	10.40(8.80,12.92)	8.00(6.20,10.80)	10.40(6.40,12.78)	86.556	<0.001

Data are expressed as median [IQR]. BPV, blood pressure variability; CV, coefficient of variation; ARV, average real variability

Table 5 Postoperative events

	OFA(*n* = 58)	OSA(*n* = 57)	OBA(*n* = 58)	F/X^2	*P*
Rescue anagesic	30	28	42	9.00	0.342
Acute pain	23	13	22	12.00	0.285
Nausea	6	14	26	12.00	0.285
Vomiting	5	11	22	12.00	0.285
Time to awake	27.21 ± 11.21	24.42 ± 9.76	23.29 ± 9.76	2.11	0.125
Time to fist flatus	13.33 ± 2.95	18.18 ± 3.90	22.47 ± 4.46	81.47	0.000
Acute pain (High PSQ)	19	11	10	7.82	0.020

Data are expressed as mean ± SD or median [IQR], or n, n (%). PSQ, pain sensitivity questionnaire

study, we observed that the OFA group exhibited higher levels of BPV, CV, and ARV compared to both the OSA and OBA groups. This suggests that hemodynamic fluctuations were more pronounced at the onset of anesthesia and surgery in patients who underwent the OFA protocol.

Ruscheweyh [18] developed the Pain Sensitivity Questionnaire (PSQ) in 2009. Compared to traditional quantitative sensory tests, the PSQ has the advantages of being time-saving, low-cost, and non-invasive. Previous studies have demonstrated that pain sensitivity assessed by the PSQ is positively correlated with patients' postoperative pain intensity. This correlation allows for the prediction of acute postoperative pain and the guidance of postoperative analgesic regimens. In this study, patients were classified into two groups based on their PSQ scores: those with high pain sensitivity and those with low pain sensitivity. Subgroup analysis revealed that the OFA group of patients with high pain sensitivity and those with hypertension exhibited a greater propensity for hemodynamic fluctuations during anesthesia and surgery. These findings suggest that opioid-free anesthesia is an ineffective method for controlling the perception of harm in individuals with high pain sensitivity, thereby preventing satisfactory analgesia. One potential explanation is that patients with high pain sensitivity are more prone to central sensitization and are more sensitive to inflammatory stimuli from surgical incisions in the postoperative period [19]. Additionally, it is evident that medications such as NSAIDs and NMDA receptor antagonists are insufficient as replacements for opioids. In addition, Park [20] discovered a considerable risk of acute postoperative pain and a prolonged postoperative recovery period in a population with a high pain sensitivity. These findings are analogous to those of the present study. Furthermore, previous studies have indicated that OFA and OSA regimens may result in bradycardia intraoperatively [21], potentially due to the induction of dexmedetomidine. This suggests that OFA regimens compounded with dexmedetomidine should be used with caution and in accordance with the individual needs of the patient.

This study has several limitations. First, in this study, Group OFA were given dexmedetomidine 0.4 μg/kg intravenously, but findings would have changed if a great dose had been given to Group OFA. Additionally, there is a lack of widely available injury perception monitoring to guide individualized opioid dosing. Furthermore, this study only recorded patients' resting pain, and their exercise-induced pain was not observed. Additionally, the recording of hemodynamic endpoints was brief, and further validation is necessary with a larger sample and longer observation period.

In conclusion, the OSA regimen has been demonstrated to effectively control patients' postoperative pain, exhibit minimal perioperative hemodynamic fluctuations, especially in patients with high pain sensitivity and hypertension, and a relatively low incidence of perioperative adverse events.

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Author contributions
Lei Wang: designed the study and wrote manuscript. Xinhua Hong: designed the study and wrote manuscript. Lei Wang and Xinhua Hong: data collection and analysis. Yiting Xue: statistical treatment. Zhen Su: designed research and revised manuscript. All authors reviewed the manuscript.

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Data availability
All data for this study can be obtained from the corresponding author, based on reasonable reasons.

Declarations

Ethics approval and consent to participate
Ethics approval and consent to participate Ethical approval for this observational study (KY-2023-085-02) was provided by the local ethics committee of the Affiliated Huaian No.1 Hospital of Nanjing Medical University in 03/07/2023. The trial was registered with the Clinical Trial Registry of China (registrationnumber: ChiCTR2400093036,Registration Date: 27/11/2024). All patients signed informed consent. All methods were carried out in accordance with declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Anesthesiology, Affiliated Huaian No.1 Hospital of Nanjing Medical University, No. 1, Huanghe Road, Huaian, Jiangsu Province 223300, China

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