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Opioid-free anesthesia with esketamine-dexmedetomidine versus opioid-based anesthesia with propofol-remifentanil in shoulder arthroscopy: a randomized controlled trial

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Abstract

Background OFA (Opioid-free anesthesia) has the potential to reduce the occurrence of opioid-related adverse events and enhance postoperative recovery. Our research aimed to investigate whether OFA, combining esketamine and dexmedetomidine, could serve as an alternative protocol to traditional OBA (opioid-based anesthesia) in shoulder arthroscopy, particularly in terms of reducing PONV (postoperative nausea and vomiting).

Methods A total of 60 patients treated with shoulder arthroscopy from September 2021 to September 2022 were recruited. Patients were randomly assigned to the OBA group ($n=30$) and OFA group ($n=30$), receiving propofol-remifentanil TIVA (total intravenous anesthesia) and esketamine-dexmedetomidine intravenous anesthesia, respectively. Both groups received ultrasound-guided ISBPB(interscalene brachial plexus block)for postoperative analgesia.

Results The incidence of PONV on the first postoperative day in the ward (13.3% vs. 40%, $P<0.05$) was significantly lower in the OFA group than in the OBA group. Moreover, the severity of PONV was less severe in the OFA group than in the OBA group in PACU (post-anesthesia care unit) (0 [0, 0] vs. 0 [0, 3], $P<0.05$) and in the ward 24 h postoperatively (0 [0, 0] vs. 0 [0, 2.25], $P<0.05$). Additionally, the OFA group experienced a significantly shorter length of stay in the PACU compared to the OBA group (39.4 ± 6.76 min vs. 48.7 ± 7.90 min, $P<0.001$).

Conclusions Compared to the OBA with propofol-remifentanil, the OFA with esketamine- dexmedetomidine proved to be feasible for shoulder arthroscopy, resulting in a reduced incidence of PONV and a shorter duration of stay in the PACU.

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Keywords Opioid-free anesthesia, Esketamine, Dexmedetomidine, Shoulder arthroscopy

Introduction

Shoulder arthroscopy, a common orthopedic surgery to treat rotator cuff tears, shoulder instability, and stiff shoulders, is characterized by its minimal invasiveness, clear surgical field, reduced postoperative complications, and expedited recovery [1]. In shoulder arthroscopy, patients are positioned in either the LDP (lateral decubitus position) or the BCP (beach-chair position). When comparing cerebral oxygenation saturation in patients undergoing shoulder arthroscopic surgery in the BCP or LDP, it was noted that oxygen saturation decreased more significantly in the BCP than in the LDP, and a higher incidence of PONV (postoperative nausea and vomiting) was observed in patients experiencing cerebral desaturation events [2].

General anesthesia combines with brachial plexus block, which is extensively adopted for shoulder arthroscopy, can stabilize intraoperative hemodynamics, alleviate postoperative pain, reduce the postoperative use of remedial analgesics, and lower the incidences of opioid-related adverse events [3–5]. Opioid-related side effects, including PONV, itching, respiratory depression, hyperalgesia, and drug addiction, provide significant difficulties for patients [6–8]. PONV is a prevalent postoperative adverse event, occurring in approximately 30% of surgical patients and in up to 80% of those at high risk [9]. Moreover, the occurrence of PONV is associated with significantly prolonged stays in the PACU and considerable patient dissatisfaction [9, 10]. PONV still occurs in 30% of surgical patients despite the perioperative prophylactic use of antiemetics [11]. Studies have suggested that the combination of two or three drugs or even five drugs does not fully alleviate PONV in high-risk patients [12], which also greatly hinders the promotion of ERAS (enhanced recovery after surgery). These findings suggest that additional measures should be taken in addition to prophylactic antiemetic drugs in high-risk PONV patients.

OFA can effectively reduce perioperative opioid use and opioid-related adverse events through the administration of nonopioid medications and regional blocks [13, 14]. Nonopioid medications include alpha-2 agonists, NMDA (N-methyl-d-aspartate) receptor antagonists, gabapentioids, NSAID (nonsteroidal anti-inflammatory drugs), magnesiu, antidepressants [15, 16]. Esketamine, acting as the S-enantiomer of ketamine, is an antagonist of the NMDA receptor and has been proven effective in augmenting analgesia [17, 18]. Recent studies have shown that esketamine, when combined with other general anesthetics, can facilitate opioid-free anesthesia and reduce the incidence of PONV [19–21]. Dexmedetomidine, a highly selective alpha-2 receptor agonist, is utilized for perioperative sedation and has been shown to reduce the probability of PONV [22, 23].

OFA is known to lower the rate of PONV [24], yet its application in shoulder arthroscopy has not been extensively explored. Consequently, we hypothesized that OFA, when combined with esketamine and dexmedetomidine, may be an ideal strategy to reduce the incidence of PONV during shoulder arthroscopy.

Methods

Randomization and blinding

From September 2021 to September 2022, a total of 60 patients were prospectively enrolled and randomized using a computerized randomization software in The First People's Hospital of Yancheng. The study assignments were allocated to opaque envelopes, numbered from 1 to 60, and sealed by a nurse. These patients were randomly assigned to either the OBA group ($n=30$) or the OFA group ($n=30$), receiving interventions through TIVA with propofol-remifentanil and esketamine-dexmedetomidine. Prior to anesthesia induction, an interscalene brachial plexus block was administered to both groups. Before the patients' arrival in the operative room, the chief anesthesiologist gained access to the envelope. All anesthesia procedures were performed by experienced anesthesiologists holding senior titles, while the same surgical team carried out all operations. Relevant intraoperative anesthesia data was recorded by the chief anesthesiologist, and the postoperative follow-up was conducted by anesthesiologists not involved in the surgery.

Patient selection

Inclusion criteria: (*i*) 30–65 years old; (*ii*) body mass index (BMI): 18–30 kg/m^2 (*iii*) ASA (American Society of Anesthesiologists) classification: I–II.

Exclusion criteria: (*i*) allergic to esketamine, dexmedetomidine or local anesthetics; (*ii*) combined with obstructive or restrictive pulmonary disease, coagulopathy, uncontrolled or untreated hypertension (SBP [systolic blood pressure] /DBP [diastolic blood pressure] >180/100 mmHg), puncture site infection, liver or renal failure, psychiatric disease; (*iii*) pregnant; (*iv*) using opioids for chronic pain (v) having a history of shoulder and neck surgery.

Anesthesia protocol

All patients adhered to ERAS guidelines [19], involving fasting from solid food for 6 h and clear fluids for 2 h. Monitoring of ECG (Electrocardiogram), SpO_2 (oxygen saturation), and invasive blood pressure was conducted.

Midazolam (1–2 mg) was administered to alleviate anxiety prior to the block. Following oxygen inhalation, patients were instructed to turn their heads to the contralateral side. Local anesthesia with 1–3 ml of 1% lidocaine was administered, followed by positioning the 3-5 MHz Philips Sparq ultrasound transducer (22100 Bothell-Everett Hwy Bothell, WA 98021 USA) near the clavicle for cephalad scanning up to the level of the cricoid cartilage in a sterile manner. After clear visualization of C5-C7 between the anterior and middle scalene muscles, the block was achieved by administering 20 ml of 0.375% ropivacaine using a 50 mm 22G stimulating needle (Stimuplex®, B. Braun Melsungen AG) with an in-plane technique and a lateral-to-medial direction [5]. Sensory and motor functions were assessed at 5-minute intervals for 30 min by the chief anesthesiologist. Sensory function testing included assessments of both the supraclavicular and axillary nerves, which innervate the cutaneous area overlying the clavicle and the lateral surface of the deltoid. Sensory block grading was based on a cold test: 0 (no block), 1 (feels touch, not cold), and 2 (cannot feel touch). Motor block evaluation involved shoulder abduction and external shoulder rotation using a scale of: 0 (no block), 1 (paresis), 2 (paralysis). If the overall score reached or exceeded 6 points (out of a maximum of 8 points), the block was considered successful [5].

All patients were administered TIVA without the use of volatile anaesthetics. Anesthesia induction in the OBA group involved administering propofol 2 mg/kg, cis-atracurium 0.2 mg/kg, and fentanyl 3–4 μg/kg. Following endotracheal intubation, propofol 5–8 mg/kg/h and remifentanil 5–10 μg/kg/h were administered to maintain a specific depth of anesthesia, with the MOAA/S (Modified Observer Assessment of Alertness/Sedation Scale) score maintained at 0–1. Intermittent intravenous infusion of cis-atracurium was used intraoperatively to maintain muscle relaxation. Ventilator parameters were established as follows: fresh gas flow rate at 2 L/min (FiO_2 0.5), tidal volume of 6–8 ml/kg, respiratory rate of 10–14 times/min, a suction/breathing ratio of 1:2, and maintenance of $PETCO_2$ (patient end-tidal carbon dioxide) between 35-45mmHg. Patients in the OFA group received anesthesia through an infusion pump administering dexmedetomidine at 0.8–1 μg/kg for 10 min, subsequently followed by a continuous infusion of dexmedetomidine at 0.3–0.5 μg/kg/h to ensure the MOAA/S score remained between 0 and 1. Prior to the surgical incision, esketamine was administered intravenously at a dosage of 0.3 mg/kg, and an infusion of 0.15 mg/kg/h esketamine was maintained throughout the operation. Patients who received a MOAA/S score of 2 or higher were excluded from the OFA group and given tracheal intubation for general anesthesia. After the commencement of the operation, urapidil or nitroglycerin were administered to maintain the MAP (mean arterial pressure) approximately at 70% of the baseline using controlled hypotension technology. Hypotension (MAP < 55 mmHg) was managed with an intravenous administration of ephedrine 12 mg, and bradycardia (HR [heart rate] < 50 bpm) was addressed with an intravenous administration of atropine 0.5 mg. Prior to the operation, all patients were positioned in the LDP.

All patients received dexamethasone 5 mg and ondansetron 5 mg for the prevention of PONV, in accordance with Apfel's simplified PONV risk score [25]. Postoperative analgesic medications and their respective dosages were prescribed based on VAS scores. Adhering to the analgesic ladder, NSAIDs were initially prescribed, followed by a gradual transition to strong opioids. Diclofenac sodium (50 mg) was initially administered to patients exhibiting VAS scores > 3, and subsequently, dezocine (5 mg) was administered if the pain did not show significant relief within 30 min. We employed the modified Aldrete score to assess patients' conditions, including: movements (2- ability to autonomously move arms and legs and raise the head, either autonomously or as directed; 1- capability to move two limbs and limited head movement, either autonomously or based on medical advice; 0- inability to move limbs or raise the head), breathing (2- ability to breathe deeply and cough effectively with a normal breathing rate and amplitude; 1- experiencing breathing difficulties or limited shallow and slow spontaneous breathing, possibly requiring the use of an oropharyngeal airway; 0- apnea or weak breathing, necessitating assisted breathing or a ventilator), blood pressure (2- deviation within ±20% before anesthesia; 1- deviation within ±20–49% before anesthesia; 0- deviation of ±50% or more before anesthesia), consciousness (2- fully awake; 1- able to awaken but lethargic; 0- no response), and transcutaneous oxygen saturation (2- oxygen saturation ≥ 92% while breathing air; 1- oxygen intake ≥ 90%; 0- oxygen intake < 90%). Each item scored from 0 to 2 points, resulting in a total score of 10 points. Patients were eligible for discharge from the PACU when their score was ≥ 9 [26].

Primary end points

The primary outcomes encompassed the occurrence of PONV in either the PACU or during the initial day following surgery in the ward between two groups. PONV is defined as any episode of nausea, dry-retching or vomiting and assessed by simplified PONV impact scale (Q1: Have you vomited or had dry-retching? 0- no; 1- once;

2- twice; 3- three or more times. Q2: Have you experienced a feeling of nausea? 0- not at all; 1- sometimes; 2- often or most of the time; 3- all of the time) [27].

Second end points

Secondary outcomes included the severity of PONV, the incidences of nausea or vomiting, the requirement for antiemetics, the PONV risk score, block score, modified Aldrete score, the length of stay in PACU, the incidence of hallucination, nightmare, bradycardia, excessive oral secretion, VAS score at post-anesthesia recovery in PACU, and postoperative 6 h, 12 h and 24 h and the number of rescue analgesia required within 24 h, MAP and HR before anesthesia (T_0), at the time points of making surgical incision (T_1), 0.5 h after surgical incision (T_2), 1 h after surgical incision (T_3) and end of shoulder arthroscopy (T_4).

Statistical analysis

Considering a detection rate of 30% ($\alpha=0.05$, Power=0.8) in the reduced incidence of PONV in the ward within 24 h, including a 5% rate of loss to follow-up, the sample size per group was estimated at 30 with the PASS software (version15; NCSS, Kaysville, UT, USA).

Statistical analysis was performed using IBM SPSS Statistics for Windows (Version 22.0; IBM Corp., Armonk, NY, USA). Continuous data were tested for normality using Shapiro-Wilk test. Continuous variables in normal distribution such as age, BMI, operative time, PACU stay time, MAP and HR were expressed as mean±standard deviation, and their differences were analyzed by the independent sample t test. Non-normally distributed continuous variables such as VAS score, block score, modified Aldrete score and the severity of PONV were presented as median (IQR [interquartile range]) and compared using a Mann-Whitney U-test. Pearson χ^2 test, continuity correction χ^2 test or Fisher's exact test for categorical variables such as gender, ASA classification, surgical site, type of shoulder diseases, the incidences of PONV, nausea, vomiting or rescue antiemetics, number of analgesic required and adverse events were used to compare between two groups. $P<0.05$ was considered as statistically significant.

Results

Demographic data and clinical characteristics

A total of 69 patients were initially recruited, with 9 patients subsequently excluded from the study. The reasons for exclusion encompassed 3 patients with obstructive or restrictive pulmonary disease, 2 patients with renal failure, 1 patient who was using opioids for chronic pain management, and 3 patients with a history of shoulder and neck surgery. Consequently, a cohort of 60 patients were included in the final analysis, with no loss to follow-up. For statistical analysis, the OBA group and OFA group each received 30 patients finally (Fig. 1). Clinical characteristics exhibited comparability between the two groups, with no statistically significant distinctions identified in terms of gender, age, ASA classification, BMI, surgical site, type of shoulder diseases, operative duration, block score, and modified Aldrete score (Table 1). Additionally, Apfel's PONV risk score did not differ significantly between both groups ($p=0.101$), with approximately 50% of all patients carrying a 60–80% risk of developing PONV (Table 1).

Primary outcome

The incidences of PONV in PACU (10% vs. 33.3%, $P<0.05$ [asymptotic-only]; $P>0.05$ [exact]) and on the first day after the operation in the ward (13.3% vs. 40%, $P<0.05$) among patients in the OFA group were lower than that in the OBA group (Table 2).

Secondary outcomes

Although the OFA group's antiemetics requirement in PACU was lower than that of the OBA group (6.7% vs. 26.7%, $P<0.05$ [asymptotic-only]; $P>0.05$ [exact]), there was no statistically significant difference (3.3% vs. 23.3%, $P>0.05$) in antiemetics requirement between the two groups in the ward on the first day after surgery. Whether in the PACU (0 [0, 0] vs. 0 [0, 3], $P<0.05$) or in the ward on the first postoperative day (0 [0, 0] vs. 0 [0, 2.25], $P<0.05$), the OFA group experienced less severe PONV than the OBA group. Excessive oral secretion was defined as secretion that required an aspirator to be removed. The incidences of excessive oral secretion, hallucination, nightmare, and bradycardia were not significantly different between the two groups (Table 3). Respiratory depression was characterized by a drop in SpO_2 to below 90% for more than 10 s, necessitating manual ventilation. There were no reports of respiratory depression, local anesthetic toxicity, Horner syndrome or pneumothorax. In the OFA group, the length of stay in PACU was significantly shorter than in the OBA group (39.4±6.76 min vs. 48.7±7.90 min, $P<0.001$) (Table 1). There were no significant differences in the VAS scores at PACU, and at 6, 12, and 24 h postoperatively, or in the number of rescue analgesics required within the first 24 h (Table 4). We did not detect significant differences in MAP and HR before anesthesia (T_0), at the time points of making surgical incision (T_1), 0.5 h after shoulder arthroscopy (T_2), 1 h after shoulder arthroscopy (T_3) and end of shoulder arthroscopy (T_4) between OBA group and OFA group (Fig. 2-A and -B).

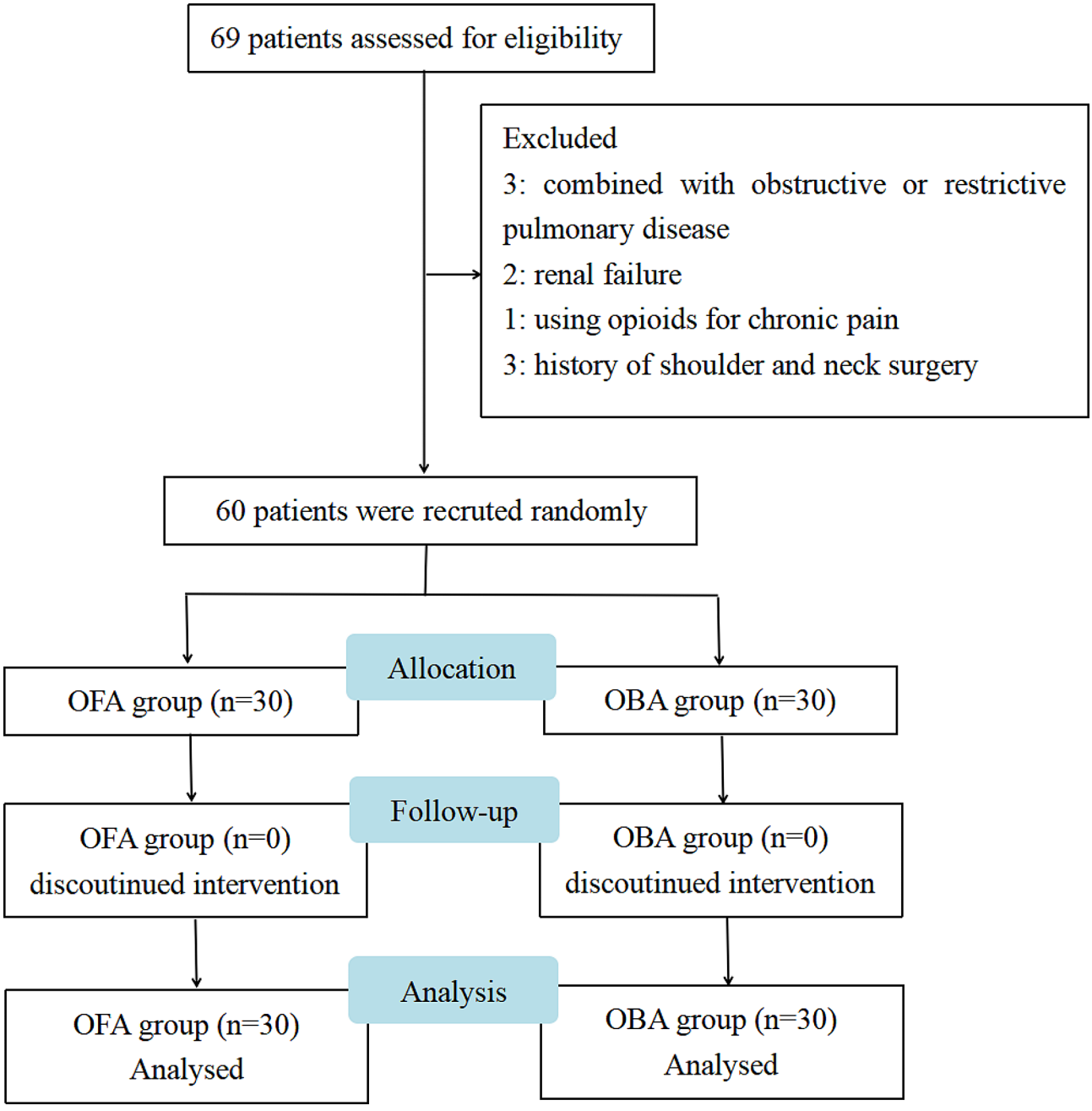

Fig. 1 Flowchart based on Consolidated Standards of Reporting Trials (CONSORT) statement

Discussion

The opioid crisis in the United States, stemming from opioid abuse and misuse, has consistently presented a significant challenge for anesthesiologists [7]. Consequently, the concepts of multimodal anesthesia and OFA have been proposed, with the objective of utilizing a broader spectrum of drugs in minimal dosages to maximize efficacy and minimize patient adverse effects [28, 29]. In addition to gynecological laparoscopic surgery and general surgery [20, 21], OFA has been extensively utilized in a variety of surgical procedures, such as spinal surgery, thoracoscopic pneumonectomy and cardiac surgery [30–32]. However, its application in shoulder arthroscopy has not yet been documented. Shoulder arthroscopy is anticipated to provide adequate analgesia, reduce postoperative adverse events, and enable early discharge for day surgery, aligning well with ERAS recommendations.

Common risk factors for PONV include gender, age, smoking history, surgical type, history of motion sickness, and opioid usage [10]. A heightened risk of PONV is often associated with specific types of surgical procedures, including laparoscopic, bariatric, gynecological

Table 1 Demographic data and clinical characteristics ($n=60$)

	OFA group ($n=30$)	OBA group ($n=30$)	*P* value
Male/female (n, %)	18 (60%)/ 12 (40%)	20 (67.7%)/ 10 (33.3%)	0.592
Age (years)	57.9 ± 6.3	59.6 ± 6.9	0.343
ASA I/II (n, %)	17 (56.7%)/ 13 (43.3%)	14 (46.7%)/ 16 (53.3%)	0.438
BMI (kg/m^2)	25.5 ± 3.0	24.7 ± 3.1	0.308
Surgical site (Left/Right, n, %)	9 (30%)/ 21 (70%)	11 (36.7%)/ 19 (63.3%)	0.584
Type of shoulder diseases (n, %)			0.810
rotator cuff tears	14 (46.7%)	15 (50%)	
instability	7 (23.3%)	5 (16.7%)	
stiffness	9 (30%)	10 (33.3%)	
PONV risk score			0.101
1	2 (6.7%)	4 (13.3%)	
2	13 (43.3%)	11 (36.7%)	
3	8 (26.7%)	9 (30%)	
4	7 (23.3%)	6 (20%)	
Block score	7 (7,8)	8 (7,8)	0.24
Operative time (min)	106.8 ± 17.2	105.3 ± 17.4	0.727
PACU stay time (min)	39.4 ± 6.8***	48.7 ± 7.9	0.000
Modified Aldrete score	10 (9,10)	10 (9,10)	0.674

Note: Data are presented as total number (n, %) or mean ± standard deviation

Abbreviation: OFA, opioid-free anesthesia; OBA, opioid-based anesthesia; ASA, American Society of Anesthesiologists; BMI, body mass index; PACU, post-anesthesia care unit. *** $P<0.001$

Table 2 Incidences of PONV in PACU and the first day after operation ($n=60$)

	OFA group ($n=30$)	OBA group ($n=30$)	*P* value (Asymptotic Sig.)	*P* value (Exact Sig.)
PACU				
nausea	2 (6.7%)	6 (20%)	0.255	0.254
vomiting	1 (3.33%)	4 (13.3%)	0.35	0.353
PONV	3 (10%)	10 (33.3%)	0.028*	0.057
severity of PONV	0 [0, 0]	0 [0, 3]	0.027*	0.029*
antiemetics	2 (6.7%)	8 (26.7%)	0.038*	0.08
postoperative day 1 in the ward				
nausea	2 (6.7%)	7 (23.3%)	0.148	0.145
vomiting	2 (6.7%)	5 (16.7%)	0.421	0.424
PONV	4 (13.3%)	12 (40%)	0.02*	0.039*
severity of PONV	0 [0,0]	0 [0, 2.25]	0.012*	0.10*
antiemetics	1 (3.3%)	7 (23.3%)	0.058	0.052

Note: Data are presented as total number (n, %) or median (interquartile range, IQR)

Abbreviation: OFA, opioid-free anesthesia; OBA, opioid-based anesthesia; PACU, post-anesthesia care unit; PONV, postoperative nausea and vomiting. *$P<0.05$

surgery, and cholecystectomy [33]. Nevertheless, limited research existed on PONV in patients following shoulder arthroscopy. Indeed, our study found that participants undergoing shoulder arthroscopy exhibited a risk ratio

Table 3 Adverse events in patients treated with shoulder arthroscopy ($n=60$)

	OFA group ($n=30$)	OBA group ($n=30$)	*P* value
Hallucination	6 (20%)	2 (6.7%)	0.255
Nightmare	3 (10%)	0 (0%)	0.236
Bradycardia	8 (26.7%)	5 (16.7%)	0.347
Excessive oral secretion	11 (36.7%)	6 (20%)	0.152

Note: Data are presented as total number (n, %)

Abbreviation: OFA, opioid-free anesthesia; OBA, opioid-based anesthesia. *$P<0.05$

Table 4 VAS scores of patients treated with shoulder arthroscopy at each time point ($n=60$)

	OFA group ($n=30$)	OBA group ($n=30$)	*P* value
Post-anesthesia recovery in PACU	0 (0, 1)	0 (0, 1)	0.334
6 h postoperatively	1(0, 1.25)	1(0, 1)	0.868
12 h postoperatively	2 (1, 2.25)	2 (1, 2)	0.806
24 h postoperatively	3 (2, 4)	3 (2, 3.25)	0.215
Number of rescue analgesia required within 24 h (n,%)	9 (30%)	11 (36.7%)	0.584

Note: Data are presented as median (interquartile range, IQR) or total number (n, %)

Abbreviation: VAS, visual analog scale; PACU, post-anesthesia care unit; OFA, opioid-free anesthesia OBA; opioid-based anesthesia. * $P<0.05$

of nearly 50% for moderate to severe PONV. Studies have shown that PONV was a primary factor in readmissions and delayed discharges among post-shoulder arthroscopy patients [34, 35].

Feng discovered that the incidence of PONV in the OFA group was lower than that in the OBA group within 24 h post-thoracoscopic pneumonectomy [31], and Chen reported similar results in laparoscopic gynecological surgery [19]. Our research findings were consistent with the aforementioned results. However, this contradicts the study by Massoth, which revealed that there was no difference in PONV incidence between the OFA group and the OBA group at any time after laparoscopic gynecological surgery in patients [36]. We believed that the following factors could explain the conflicting outcomes mentioned above: (1) Limited comparability arose from variations in drug dosages, methods of combination, and surgical procedures across clinical trials, which led to inconsistent results. (2) Chen strictly adhered to the ERAS protocol, whereas Massoth did not mention it in their article, even though both groups studied patients undergoing laparoscopic gynecological surgery. An analysis of 41,260 pediatric surgical patients demonstrated that OFA is suitable for most ambulatory and selected inpatient surgeries, potentially reducing PONV and the length of stay in the PACU [37]. In conclusion, we still believe that OFA can mitigate PONV in shoulder arthroscopy patients; however, larger sample sizes in prospective

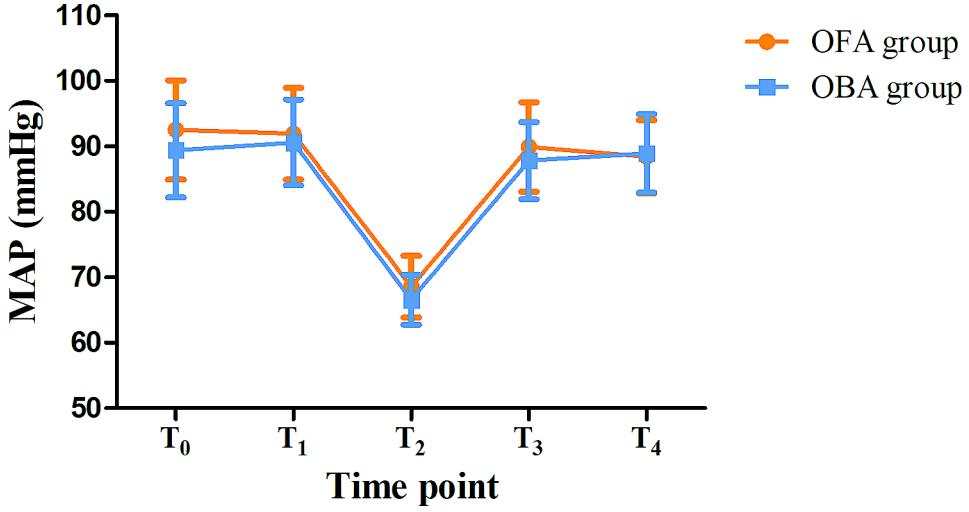

Fig. 2A MAP from T_0 to T_4 in two groups

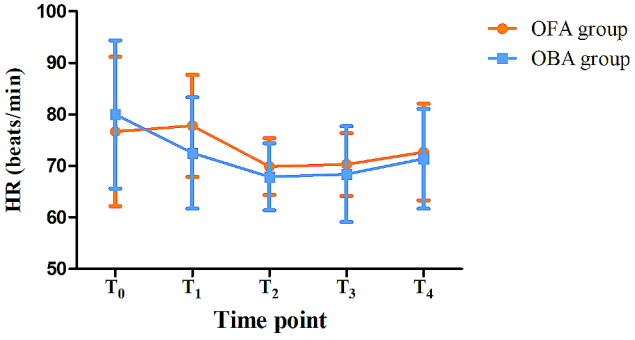

Fig. 2B HR from T_0 to T_4 in two groups. $P<0.05$ is defined statistically signifcant. There were no significant differences in MAP and HR at all the timepoints between two groups. Abbreviations: MAP, mean arterial pressure; HR, heart rate; T_0, before anesthesia; T_1, at the time point of making surgical incision; T_2, 0.5 h after shoulder arthroscopy; T_3, 1 h after shoulder arthroscopy; T_4, at the end of shoulder arthroscopy; OBA, opioid-based anesthesia; OFA, opioid-free anesthesia

clinical trials and more rigorous scientific methodologies are needed to strengthen this assertion.

OFA has been shown to reduce PACU stay times in patients undergoing spinal surgery and laparoscopic urological operation, leading to shorter hospital stays and enhanced patient outcomes [38, 39]. This conclusion was supported by our data (OFA: 39.4±6.76 min vs. OBA: 48.7±7.90 min, $P<0.001$). However, Chen's study presented a contrasting view, indicating that the awakening and orientation recovery times were longer in the OFA group than in the OBA group during gynecological laparoscopy [19]. Firstly, this may be attributed to the fact that in our trial, OFA comprised only esketamine and dexmedetomidine, with no other anesthetics used, unlike Chen's approach, which incorporated propofol. Secondly, the majority of research indicated a correlation between the use of dexmedetomidine and excessive sedation in the PACU [31]. During major or intermediate noncardiac surgery, lasting 169±83 min, the OFA group received a dosage of 1.2±2 μg/kg/h of dexmedetomidine, which was a relatively higher total dosage [40]. However, dexmedetomidine was used at a relatively lower dose (0.3–0.5 μg/kg/h) during shoulder arthroscopy, which was a day surgery with a short operating duration (106.8±17.2 min). Perhaps the patient was not oversedated in the PACU because of the relatively lower overall dosage of dexmedetomidine. Finally, we speculated that it might also be related to the absence of tracheal intubation in the OFA group.

OFA aims to utilize non-opioid medications and regional nerve block techniques to mitigate the adverse effects of opioids. In our study, the non-opioid drugs employed were esketamine and dexmedetomidine. Ketamine provides pain relief as it reduces secondary hyperalgesia mediated by NMDA receptors and mitigates opioid-induced hyperalgesia through interaction with opioid receptors [41]. Esketamine has a 3–4 times greater affinity for NMDA receptors compared to ketamine, and a 2–3 times higher affinity for opioid receptors [42]. Besides its sedative and analgesic properties, dexmedetomidine was also employed in OFA to diminish the risk of PONV [43]. However, a meta-analysis indicated that intravenous administration of esketamine in adults provided effective for assisting analgesia, though caution is advised due to the risk of psychotomimetic adverse events [44]. No significant differences were observed in the incidences of hallucination and nightmare between the OFA and OBA groups. The implementation of OFA, comprising esketamine and dexmedetomidine for shoulder arthroscopy, marked a pioneering effort. It not only facilitated successful operations but also diminished the incidence of PONV, reduced PACU stay times, and eliminated the need for intubation due to OFA failure.

Several limitations should be noted. First of all, the experiment had a limited sample size. We used the Pearson Chi-square test to compare the probability of PONV and the usage of antiemetics between the two groups in PACU. The p values were 0.028 and 0.038 using the asymptotic-only analysis, but p values were 0.057 and 0.08 using the exact analysis. We believe that the small sample size is the cause of the contradictory results observed above. Future research may reduce the disparity between the two algorithms by including a larger number of patients. Seccondly, we have not purchased NIRS (near infrared spectroscopy) due to financial constraints, which could monitor the regional cerebral tissue oxygen saturation. According to a research on shoulder arthroscopy, cerebral oxygen saturation and MAP have a correlation (P<0.05), which makes MAP a trustworthy monitoring indicator when NIRS is not available [45].

Conclusion

Compared to the OBA with propofol-remifentanil, the OFA with esketamine-dexmedetomidine was feasible in shoulder arthroscopy and resulted in a lower incidence of PONV and shorter PACU stay time.

Abbreviations

OFA	Opioid-free anesthesia
OBA	Opioid-based anesthesia
PONV	Postoperative nausea and vomiting
ERAS	Enhanced recovery after surgery
TIVA	Total intravenous anesthesia
ISBPB	Interscalene brachial plexus block
PACU	Post-anesthesia care unit
LDP	Lateral decubitus position
BCP	Beach-chair position
NMDA	N-methyl-d-aspartate
NSAID	Nonsteroidal anti-inflammatory drugs
ASA	American Society of Anesthesiologists
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
ECG	Electrocardiogram
SpO_2	Oxygen saturation
MOAA/S	Modified Observer Assessment of Alertness/Sedation Scale
$PETCO_2$	patient end-tidal carbon dioxide
MAP	Mean arterial pressure
HR	Heart rate
IQR	Interquartile range
NIRS	Near infrared spectroscopy

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Author contributions

XL and ZYX designed the project. XL, ZYX, CY and YL completed the methodology and collected all medical records. ZYX, CY, YL, NY and GQZ prepared all the data analysis and figures. ZYX wrote the original manuscript and WSQ, BQ reviewed the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This randomized prospective controlled study was approved by the Ethics Committee of The First People's Hospital of Yancheng (2021-K023), and the clinical trial was registered in the Chinese Clinical Trial Registry (No: ChiCTR2100047355, 12/06/2021). The written informed consents were provided by all participants prior to enrollment, and our present research followed the Helsinki Declaration.

Consent for publication

All authors approved the publication of the manuscript.

Competing interests

The authors declare no competing interests.

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