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ORIGINAL RESEARCH

Effects of Dexmedetomidine as an Adjuvant in Preoperative Ultrasound-Guided Internal Branch of Superior Laryngeal Nerve Block on Postoperative Sore Throat and Hemodynamics in Patients With Double-Lumen Endotracheal Intubation: A Randomized Controlled Trial

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Background: Postoperative sore throat (POST) is a significant adverse effect after endotracheal intubation, especially with double-lumen endotracheal tubes (DLTs). Ultrasound-guided internal branch of the superior laryngeal nerve block (US-guided iSLNB) presents a potential intervention for POST. In this first randomized controlled trial to date, we aimed to investigate the effects of US-guided iSLNB, with or without perineural dexmedetomidine, on the incidence and severity of POST following DLTs.

Methods: A total of 159 patients were randomly assigned to three groups: control, bilateral US-guided iSLNB (2 mL 0.20% ropivacaine + 1 mL saline on each side), and bilateral US-guided iSLNB combined with perineural dexmedetomidine group (2 mL 0.20% ropivacaine + 1 mL 0.5 $\mu g \cdot kg^{-1}$ dexmedetomidine on each side). The incidence and severity of POST, hemodynamic fluctuations during intubation and extubation, the incidence and severity of cough and agitation during extubation, and perioperative complications were assessed. The primary outcome was the incidence of POST at 6 h after surgery.

Results: Compared with the control group, preoperative US-guided iSLNB significantly reduced the incidence and severity of POST at 1 and 6 h after surgery, mitigated the incidence and severity of cough during extubation, and attenuated hemodynamic responses, including heart rate, mean arterial pressure, and rate-pressure product during intubation, 1 min after intubation, and 1 min after extubation (all $P < 0.01$). Compared with US-guided iSLNB alone, the combination of US-guided iSLNB with perineural dexmedetomidine reduced the incidence and severity of POST at 1, 6, and 12 h, as well as coughing during extubation (all $P < 0.01$). However, it demonstrated little effect on hemodynamics (all $P > 0.05$). No significant perioperative complications were observed in the three groups (all $P > 0.05$).

Conclusion: Preoperative US-guided iSLNB combined with perineural dexmedetomidine effectively reduced the incidence, severity, and duration of POST and cough during extubation. No additional hemodynamic benefits were observed.

Clinical Trial Registration: Chinese Clinical Trial Registry (ChiCTR2200061001).

Keywords: dexmedetomidine, superior laryngeal nerve, sore throat, cough, hemodynamics

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Introduction

Postoperative sore throat (POST) is a nociceptive pain caused by trauma to the pharyngeal and tracheal mucosa during endotracheal intubation following general anesthesia (GA) induction for surgical procedures.[1] Although this POST symptom is limited and self-limiting, it considerably impacts patient postoperative rehabilitation and satisfaction during hospitalization, potentially leading to severe cough and aspiration pneumonia.[1,2] Consequently, the high incidence of POST following tracheal intubation, particularly with double-lumen endotracheal tube (DLT) intubation, has garnered substantial research interest.[3–5] The incidence of POST after double-lumen endotracheal intubation is as high as 34.7%–70%.[2,6–8]

Currently, several strategies have been employed to mitigate POST following DLT intubation, including pharmacological interventions such as non-steroidal anti-inflammatory drugs and N-methyl-D-aspartic acid receptor antagonists, as well as non-pharmacological approaches such as thermal softening and two-handed jaw thrust technique.[2,9–11] Ultrasound-guided internal branch of the superior laryngeal nerve block (US-guided iSLNB) has been demonstrated to be effective in treating POST.[12,13] In a previous study, we demonstrated that preoperative US-guided iSLNB effectively reduced the incidence and severity of POST for up to 6 h following surgery.[14] However, other reports suggest that POST may persist beyond 24–48 h after surgery.[9,15]

Dexmedetomidine, an α_2-adrenergic receptor agonist, has emerged as a significant area of research for its role as an adjunctive agent in peripheral nerve block (PNB).[16,17] The analgesic mechanism of dexmedetomidine in PNB involves both central and peripheral actions.[16] Dexmedetomidine can act on the presynaptic terminals of dorsal horn neurons, postsynaptic membranes of intermediate neurons in the spinal cord, and α_2-adrenergic receptors in the locus coeruleus of the brainstem, altering spinal and supraspinal action potentials.[16] It can also inhibit the release of excitatory neurotransmitters, such as glutamate (Glu) and substance P, in the spinal cord, inhibit Aδ and C fibers, and suppress hyperpolarization-activated cation current (I_h current, the inwardly directed mixed cation current activated by the hyperpolarization of the cell membrane) that mediates pain.[16,18,19] Previous studies have demonstrated that the perineural dexmedetomidine can effectively prolong both the duration of analgesia and the onset time in procedures involving brachial plexus block (BPB), thoracic paravertebral nerve block (TPVB), and other PNBs.[20–23] However, clinical evidence on its efficacy is limited, particularly in PNBs for the head and neck.

We hypothesized that preoperative US-guided iSLNB combined with perineural dexmedetomidine would reduce the incidence, severity, and duration of POST while also mitigating hemodynamic fluctuations during intubation and extubation, as well as agitation and coughing at extubation.

Methods

Study Design and Participants

This single-center, double-blind, randomized controlled study was prospectively registered with the Chinese Clinical Trial Registry (https://www.chictr.org.cn, ChiCTR2200061001; date of registration: June 15, 2022). It was approved by the institutional ethics committee of the Second Hospital of Shandong University (No: KYLL-2022LW051). The study followed the principles stated in the Declaration of Helsinki and adhered to the relevant Consolidated Standards of Reporting Trials (CONSORT) guidelines. Patients provided informed consent before participation.

Inclusion criteria included the following: (1) American Society of Anesthesiologists physical status I–III; (2) age ≥ 18 years, no gender limitation; (3) body mass index (BMI) 18–35; and (4) patients scheduled for thoracoscopic lobectomy under GA, with or without US-guided iSLNB.

Exclusion criteria included the following: (1) patient refusal; (2) contraindications to GA or US-guided iSLNB, including coagulopathy and local and systemic infection. Coagulopathy was defined as a prothrombin time or activated partial prothrombin time exceeding standard values, an international normalized ratio ≥ 1.4, or a platelet count < 80×10^9 L^{-1}; (3) history of mental disorders or excessive opioid analgesic use; (4) history of hypertension, coronary heart disease, and long-term use of medications influencing blood pressure and heart rate (HR); (5) history of long-term poor preoperative glycemic control or combined with diabetes; (6) history of metabolic abnormal diseases affecting cortisol levels; (7) history of POST and cough; (8) heart, liver, or kidney insufficiency, and electrolyte disorder; (9) history of surgery or anesthesia within 6 months; (10) predicted as difficult airway; and (11) severe cognitive impairment or language problems.

Randomization and Blinding

Patients were randomly assigned in a 1:1:1 ratio to one of three groups using a computer-generated random number table: C group, GA alone; S group, GA with US-guided bilateral iSLNB (2 mL 0.20% ropivacaine + 1 mL saline on each side); and SD group, GA with US-guided bilateral iSLNB (2 mL 0.20% ropivacaine + 1 mL 0.5 $\mu g \cdot kg^{-1}$ dexmedetomidine on each side).

On the day of the surgery, a study coordinator, who was not involved in patient recruitment, data collection, or postoperative follow-up, sealed the randomization results in sequentially numbered opaque envelopes. The injection mixture for iSLNB, identical in appearance across groups, was prepared by the coordinator using sterile techniques. The anesthesiologist (DXZ) opened the envelopes, and each patient received the corresponding protocol. Before surgery, US-guided iSLNB was performed in the preoperative room by an experienced anesthesiologist (GDL). General anesthesia was administered in the operating room by another anesthesiologist (LZ), who was blinded to patient group assignment. Postoperative follow-up was conducted by two registered nurses and an anesthesiologist (HZ), who were also blinded to patient group assignment. This ensured that the group allocation was hidden from the study coordinator, anesthesia team, and surgical team.

Anesthesia, Perioperative Care, and Intervention

Before performing the nerve block, all patients received intravenous (IV) 0.02 $mg \cdot kg^{-1}$ midazolam or 0.08 $\mu g \cdot kg^{-1}$ sufentanil for anxiolysis and analgesia.[20] We used a traditional US-guided posterior iSLNB, consistent with our previous study, in which the iSLN was precisely located on the SLN space and superior laryngeal artery (SLA).[14,24–26] Before anesthesia induction, patients in S and SD groups were positioned supine with their necks fully extended. Under ultrasound guidance, a high-frequency linear probe (11 MHz; Vivid S70 N, GE Healthcare) was placed in the parasagittal position to identify the thyroid cartilage on the head and tail sides. Subsequently, the thyrohyoid membrane (THM), thyrohyoid muscle, preepiglottic space, SLA, and iSLN adjacent to SLA were identified.

After confirming iSLN localization, a plane-outside puncture technique was employed to penetrate the THM using a 23-gauge needle tip, leaving a deep surface within the SLA and iSLN space for the injection of local anesthetic (LA). To allow sufficient time for US-iSLNB efficacy, a minimum of 30 min was allowed between block completion and anesthesia induction. The procedure was repeated on the contralateral side using the same technique. The blocking procedure was conducted by an experienced anesthesiologist, while another experienced anesthesiologist assessed the effectiveness of US-iSLNB using a previously reported methodology.[24] The performance time of US-iSLNB was defined as the combined duration of imaging and needling.[27]

Upon entering the operating room, patients were monitored for invasive blood pressure (IBP), mean arterial pressure (MAP), HR, electrocardiogram, oxygen saturation (SpO_2), temperature, and entropy index (EI) using multichannel monitors (Datex-Ohmeda S/5 Avance). A peripheral vein was cannulated in the upper limb. After administering IV midazolam (0.02 $mg \cdot kg^{-1}$), baseline blood pressure was recorded. GA was induced with IV sufentanil (0.3 $\mu g \cdot kg^{-1}$) and propofol (1.5–3.0 $mg \cdot kg^{-1}$), and the neuromuscular block was achieved using cisatracurium (0.2 $mg \cdot kg^{-1}$). During the induction phase, all patients received pure oxygen inhalation with assisted ventilation. Subsequently, DLT intubation was performed after complete muscle relaxation, denitrogenation, and oxygenation.

Appropriate DLTs were selected based on patient height, gender, tracheal transverse diameter, and vocal cord distance derived from computed tomography imaging data.[28] The insertion of DLTs and establishment of the airway followed established protocols described in previous literature.[14] Visualization of the vocal cords was achieved using a Macintosh blade 3# or 4# laryngoscope mirror, followed by a gradual clockwise or counterclockwise rotation of the DLT through the vocal cords by 90° or 180° until reaching the desired depth.[9,29,30] Accurate DLT positioning was confirmed via fiberoptic bronchoscope examination to ensure proper alignment. One-lung ventilation (OLV) was performed with a tidal volume (TV) of 5 to 7 $mL \cdot kg^{-1}$, respiratory rate of 14 to 16 $times \cdot min^{-1}$, and positive end-expiratory pressure of 3 to 10 cmH_2O.

Anesthesia was maintained with 1% sevoflurane, propofol (3–12 $mg \cdot kg^{-1} \cdot h^{-1}$), and remifentanil (0.1–0.3 $kg^{-1} \cdot h^{-1}$). The EI was kept between 40 and 60, and additional balanced fluids were administered to maintain blood volume. Sufentanil (5 μg) was administered intravenously every 30 min as required to keep fluctuations in IBP and HR within 20% of the baseline value upon admission. Vasoactive agents, including ephedrine and nitroglycerin, were used as

needed to maintain hemodynamic stability. Approximately 30 min before the end of surgery, all patients received 30 mg IV ketorolac and 8 mg IV serotonin antagonist ondansetron.

After surgery, all patients received neostigmine (0.3 $mg \cdot kg^{-1}$) and glycopyrronium (0.01 $mg \cdot kg^{-1}$) to reverse the residual neuromuscular blockade. The DLT was removed at the end of the surgical procedure when the patient's spontaneous respiration was restored, with TV > 6 mL/kg, SpO_2 > 95%, EI > 90, and muscle strength recovered to grade IV. Following extubation, cough severity and agitation score were immediately assessed, and the patient-controlled intravenous analgesia (PCIA) pump was started. Once patients' vital signs stabilized, they were admitted to the thoracic surgery postoperative observational unit (a combination of the postanesthesia care unit and level two surgical step-down unit) for observation for the first 24 h after surgery before being transferred to a regular hospital floor. All patients received a paravertebral nerve block before iSLNB.[14]

Data Collection and Measurements

Patient demographics, operative characteristics, and factors related to DLTs were assessed. Patient characteristics included smoking history and preoperative evaluation of anxiety, depression, and sleep quality. Factors related to DLT included Cormack and Lehane grade, DLT size, and time to achieve endotracheal intubation. Anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale (HADS).[31,32] Sleep quality over the previous month was evaluated using the Pittsburgh Sleep Quality Index.[33,34]

The primary outcome of our study was the incidence of POST at 6 h after surgery in the three groups.[14] Secondary outcomes included the following: (1) the incidence and severity of POST at 1 and 12 h after surgery; (2) the incidence and severity of cough during extubation; (3) the incidence and severity of sedation-agitation, as assessed by the Riker Sedation-Agitation Scale (SAS) during extubation; and (4) intraoperative hemodynamics. The severity of POST was evaluated using a 4-grade scale: none (no sore throat); mild (pain with swallowing); moderate (constant pain, increasing with swallowing); severe (pain interfering with eating and requiring analgesic medication).[14,35] Cough severity was classified into four levels: none (no cough); mild (single cough); moderate (more than mild, lasting less than 5 s); severe (sustained for longer than 5 s).[36–38] The SAS was used to evaluate sedation-agitation levels during eye opening.[39–41] The HR, SpO_2, and MAP were continuously measured and recorded before induction (baseline, T0), immediately after intubation (T1), 1 min after intubation (T2), 5 min after intubation (T3), 5 min before extubation (T4), 1 min before extubation (T5), 1 min after extubation (T6), and 5 min after extubation (T7). The rate-pressure product (RPP) was calculated as HR × systolic blood pressure (SBP).

Perioperative complications were recorded from the beginning of anesthesia until 24 h after surgery. Specifically, nausea and vomiting were defined as any retching, vomiting, or need for antiemetics; hypoxemia was defined as SpO_2 < 90% for more than 10s or a PaO_2 : FiO_2 ratio < 300 mmHg; bradycardia was defined as HR < 40 beats per minute; and hypotension was defined as SBP < 90 mmHg or a decrease of > 30% from baseline.[42,43] The occurrence of delirium, hoarseness, aspiration, and other symptoms was also recorded.

Sample Size Calculation

According to our pilot study, the incidence of POST at 6 h after surgery in the C, S, and SD groups was 60%, 35%, and 20%, respectively. Assuming a two-tailed α error of 0.05, β error of 0.1, a power of 0.90, and a 20% dropout rate, 53 patients were enrolled per group. Sample size calculations were performed using the Power Exploration and Sample Size program (PASS) (version 15.0. NCSS, LLC., Kaysville, UT, United States).

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows statistical package (version 18.0; SPSS Inc., IBM, Chicago, IL, USA) and R software (version 4.2, R Foundation for Statistical Computing). The normality of continuous variables was evaluated using the Kolmogorov–Smirnov test. The results are expressed as mean (standard deviation) or median (interquartile range). A one-way analysis of variance (ANOVA) was used for data with a normal distribution. For cardinal variables with a non-normal distribution, differences were evaluated using the Kruskal–Wallis *H*-test. Categorical variables were analyzed using χ^2 or Fisher's exact test, as appropriate, and are

presented as frequencies (n/%). The Wilcoxon rank-sum test was used to evaluate grade data. The threshold for statistical significance of the two-tailed P value in the one-way ANOVA and χ^2 test comparison among groups was set at 0.017, following Bonferroni correction. Generalized estimating equations (GEEs) were used to evaluate trend differences in repeated measures of longitudinal data at different times, and Bonferroni correction was used to adjust the threshold for tests at multiple time points.[44–47] A $P < 0.05$ was considered statistically significant. All reported P values are two-sided.

Results

Patients, Baseline Data, and Preoperative Evaluation

A total of 215 patients were screened between July 6, 2022, and November 26, 2023. Of these, 56 were deemed ineligible, declined to participate, or met an exclusion criterion. Consequently, 159 patients were included and randomized into three groups: C (n = 53), S (n = 53), and SD (n = 53). Among them, 137 patients completed the study, as presented in the CONSORT flowchart (Figure 1). Baseline characteristics, operative characteristics, preoperative evaluation of patients, and DLT-related factors were comparable between groups (Table 1).

Primary Outcome

Compared with the C group, the total incidence of POST in S and SD groups was significantly reduced, with the SD group exhibiting a lower total incidence than the S group (Table 2). At 1 and 6 h after surgery, the incidence and severity of POST were significantly lower in S and SD groups compared with the C group (Table 2 and Figure 2). At 12 h after surgery, no significant differences in the incidence or severity of POST were observed between the S and C groups; however, the SD group exhibited a lower incidence and severity of POST than the other two groups (Table 2 and Figure 2).

Secondary Outcomes and Others

Compared with the C group, the incidence and severity of coughing during extubation were reduced in S and SD groups, with the SD group exhibiting lower values than the S group (Table 3). No significant differences in the Riker SAS score during extubation were observed among the three groups (Table 3).

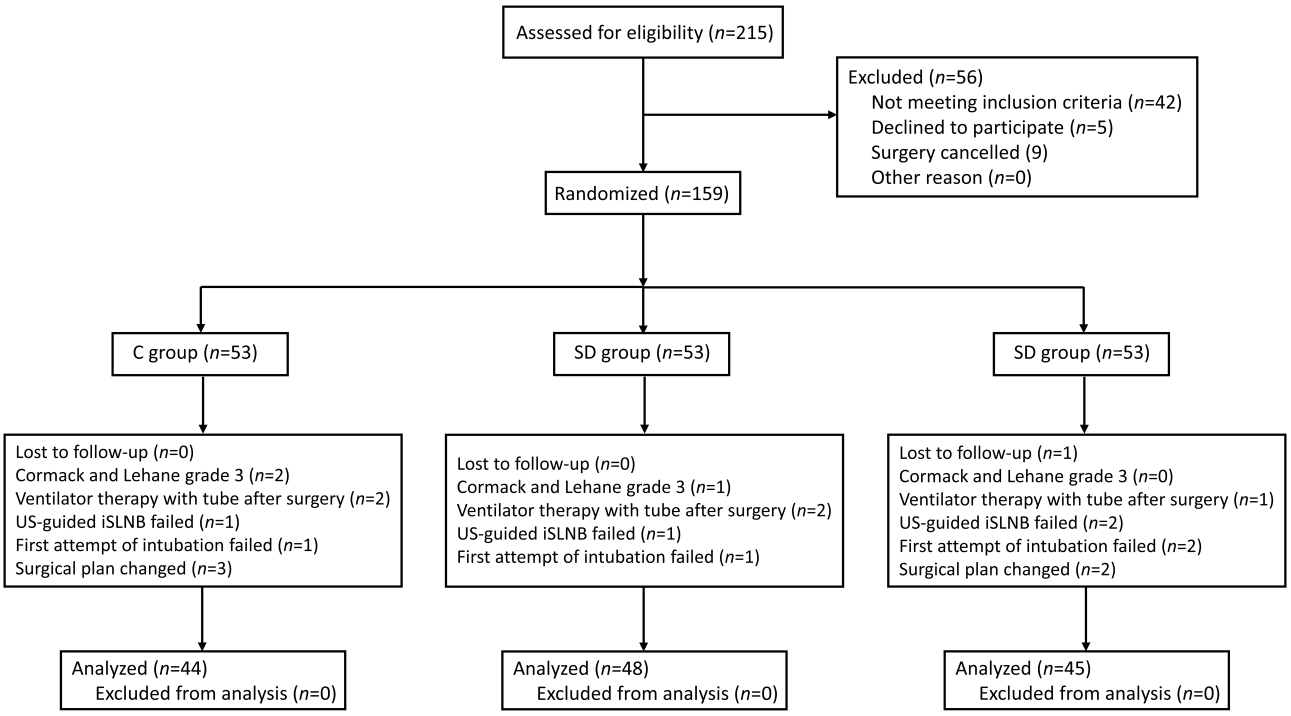

Figure 1 CONSORT flow diagram of participants.

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Table 1 Patient Demographic, Operative Characteristics and Factors Related to DLTs

Characteristic	C Group (n = 44)	S Group (n = 48)	SD Group (n = 45)
Sex (M/F)	19/25	24/24	25/20
Patient specifications			
Age, yr	54.5 (49.5, 58.0)	55.0 (50.0, 63.3)	55.0 (51.0, 59.0)
Height, m	1.6 (1.6, 1.7)	1.7 (1.6, 1.7)	1.6 (1.6, 1.7)
Weight, kg	68.0 (60.0–72.5)	66.0 (61.0–71.0)	65.0 (60.0–72.0)
BMI, kg/m^2	25.1 (24.0, 27.3)	24.0 (22.3, 25.8)	24.2 (22.7, 26.4)
ASA status 1/2/3	7/34/3	3/36/9	4/38/3
NYHA Status Norm/I/II	12/30/2	9/36/3	8/32/5
Smoking history, (%)*	12 (27.3)	14 (29.2)	15 (33.3)
Performance time of US-iSLNB, min[#]	10.0 (8.8, 11.0)	9.0 (8.0, 10.0)	9.0 (8.0, 11.0)
General anesthesia duration, min	150.0 (120.0, 182.5)	150.0 (120.0, 176.3)	140.0 (110.0, 180.0)
Surgical duration, min	125.0 (95.0, 161.3)	125.0 (93.8, 140.0)	110.0 (85.0, 140.0)
Factors related to DLT			
Cormack and Lehane grade (1/2)	29/15	30/18	32/13
DLT size (35/37)	25/19	24/24	20/25
Side of surgery (left/right)	24/20	27/21	21/24
Time to achieve endotracheal intubation (s)	81.5 (69.5, 92.8)	85.5 (71.0, 96.3)	82.0 (71.0, 92.0)
Pre-operative evaluation			
Anxiety[†]	3.5 (3.0, 5.0)	3.5 (2.0, 5.3)	4.0 (2.0, 5.0)
Depression[†]	2.0 (1.0, 3.0)	3.0 (1.8, 5.0)	2.0 (1.0, 3.0)
Sleep quality[‡]	6.0 (4.8, 7.0)	6.0 (4.0, 7.0)	7.0 (4.0, 8.0)

Notes: Values are means (SD), median (IQR) or number of patients. *Smoking 10 cigarettes per day for at least 1year, either former or current smoker; [#]The performance time of US-iSLNB was defined as the sum of imaging and needling times; [†]Anxiety and depression were evaluated using Hospital Anxiety and Depression Scale; [‡]Sleep quality were evaluated using Pittsburgh Sleep Quality Index.
Abbreviations: ASA, American Society of Anesthesiologists; US-iSLNB, Ultrasound-guided internal branch of the superior laryngeal nerve block; NYHA, New York Heart Association; BMI, Body mass index; DLT, double-lumen endotracheal tube.

Table 2 Incidence and Severity of POST

POST	C Group (n = 44)	S Group (n = 48)	SD Group (n = 45)	*P* value
1 h after surgery				
Incidence, (%)	26 (59.1)	16 (33.3)[a]	5 (11.1)[ab]	<0.001
Severity (none/mild/moderate/severe)	18/11/10/5	32/10/5/1[a]	40/4/1/0[ab]	<0.001
6 h after surgery				
Incidence, (%)	27 (61.4)	14 (29.2)[a]	4 (8.9)[ab]	<0.001
Severity (none/mild/moderate/severe)	17/14/10/3	34/9/5/0[a]	41/4/0/0[ab]	<0.001

(*Continued*)

Table 2 (Continued).

POST	C Group (n = 44)	S Group (n = 48)	SD Group (n = 45)	*P* value
12 h after surgery				
Incidence, (%)	16 (36.4)	10 (20.8)	1 (2.2)[ab]	<0.001
Severity (none/mild/moderate/severe)	28/13/2/1	38/9/1/0	44/1/0/0[ab]	0.008
Total incidence, (%)	27 (61.4)	16 (33.3)[a]	5 (11.1)[ab]	<0.001

Notes: Values are patient numbers. No patients developed new symptoms at 6 h and 12 h after surgery. [a]Compare with C group, $P < 0.017$; [b]Compare with S group, $P < 0.017$.
Abbreviation: POST, Postoperative sore throat.

At T1, T2, and T6, HR, MAP, and RPP were significantly lower in the S and SD groups than in the C group; however, no significant differences were observed at other time points (Figure 3). A similar trend was observed for SpO_2 (Figure 3). Furthermore, no significant differences in HR, MAP, and RPP were observed between S and SD groups across all measured time points.

Safety Outcomes

No significant differences in perioperative complications were observed among the three groups within 24 h after surgery (Table 4).

Discussion

This randomized controlled study represents the first investigation into the effect of preoperative US-guided iSLNB with or without dexmedetomidine on DLTs. Our findings demonstrate that preoperative US-guided iSLNB effectively reduces the incidence and severity of POST, mitigates coughing during extubation, and minimizes hemodynamic fluctuations during intubation and extubation. Additionally, our results indicate that perineural dexmedetomidine significantly decreases POST occurrence, severity, and duration, as well as cough occurrence and severity; however, no additional hemodynamic benefits were observed.

Postoperative sore throat is a common complication following tracheal intubation, particularly after DLTs. Although DLTs are widely considered the gold standard for achieving OLV in thoracic surgery, their larger diameter and frequent repositioning present significant challenges in preventing POST.[6,35,48] The mechanism of POST involves secondary inflammation caused by repetitive stimulation and cuff inflation during DLT intubation.[49]

Multiple risk factors for POST have been identified, several of which have been highlighted in previous studies on females. These factors contribute to a significantly higher incidence of POST in females compared with males owing to narrower laryngeal anatomy and female-specific cyclical hormonal changes.[50,51] Moreover, factors such as operation

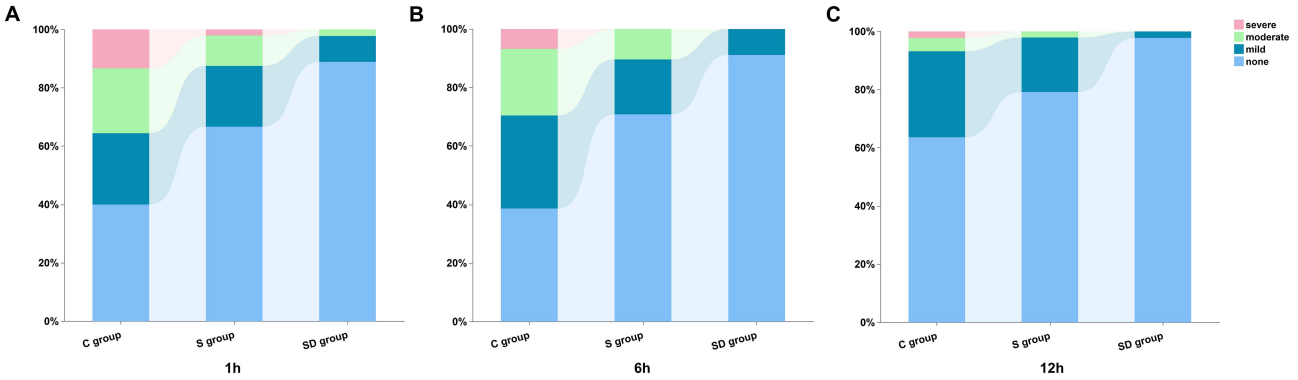

Figure 2 Severity of POST. (**A**) 1 h after surgery; (**B**) 6 h after surgery; (**C**) 12 h after surgery.

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Table 3 Cough and Riker SAS

Secondary Outcomes	C Group (n = 44)	S Group (n = 48)	SD Group (n = 45)	*P* value
Cough				
Incidence, (%)	29 (65.9)	17 (35.4)[a]	6 (13.3)[ab]	<0.001
Severity (none/mild/moderate/severe)	15/15/9/5	31/13/4/0[a]	39/5/1/0[ab]	<0.001
Riker SAS				
Incidence, (%)	8 (18.2)	3 (6.3)	4 (8.9)	0.181
Severity (4/5/6/7)	35/5/2/1	45/2/1/0	41/2/2/0	0.574

Notes: Values are patient numbers. [a]Compare with C group, $P < 0.017$; [b]Compare with S group, $P < 0.017$.
Abbreviation: SAS, Sedation-Agitation Scale.

time, anesthesia duration, and age are significantly associated with POST.[52] In this study, we assessed the preoperative state of patients, including their sleep quality and anxiety levels. Recent studies have increasingly focused on the psychological and overall life status of patients before surgery, highlighting correlations between these psychological factors and primary endpoints of clinical trials.[53,54] After adjusting for the aforementioned confounding factors, no significant differences in demographic baseline or preoperative general statuses were observed among the three groups, ensuring the reliability of our study results.

The first finding of our study was that preoperative US-guided iSLNB reduced the incidence and severity of POST in the first 6 h after surgery, consistent with the results of previous studies that the analgesic effect of ropivacaine alleviated POST occurrence in the first 6 h after surgery.[12,14,55] Consequently, US-guided iSLNB exerts a similar preventive effect on POST to other pharmacological or non-pharmacological interventions.[9,29]

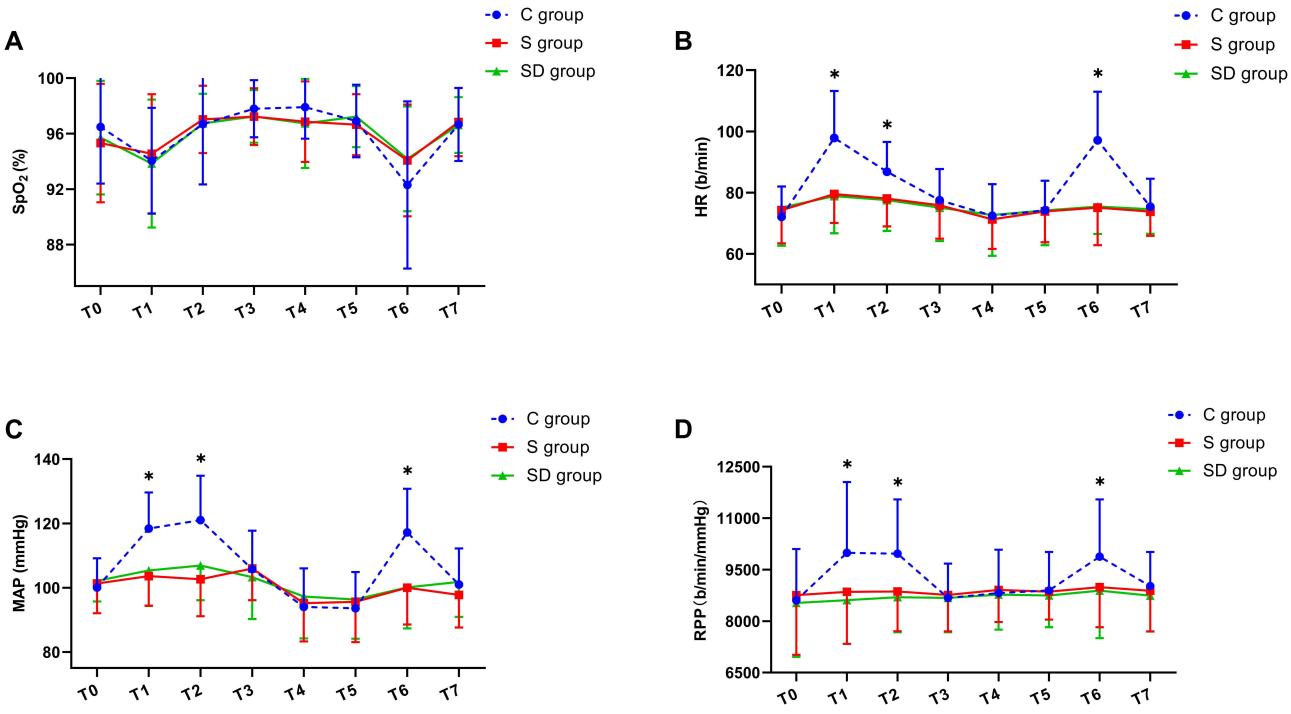

Figure 3 Perioperative hemodynamics. (**A**) SpO_2; (**B**) HR; (**C**) MAP; (**D**) RPP. *Compare with C group, $P < 0.001$.
Abbreviations: HR, Heart rate; MAP, Mean arterial pressure; RPP, rate-pressure product; T0, Baseline; T1, immediately after intubation; T2, 1 min after intubation; T3, 5 min after intubation; T4, 5 min before extubation; T5, 1 min before extubation; T6, 1 min after extubation; T7, 5 min after extubation.

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Table 4 Perioperative Complications Within 24 h After Surgery

Postoperative Adverse Reactions	C Group (n = 44)	S Group (n = 48)	SD Group (n = 45)	*P* value
Nausea and vomiting, n (%)[a]	10 (22.7)	7 (14.6)	9 (20.0)	0.605
Hypoxemia, n (%)[b]	4 (9.1)	2 (4.2)	3 (6.7)	0.570
Bradycardia, n (%)[c]	0	0	0	–
Hypotension, n (%)[d]	0	0	0	–
Delirium, n (%)	0	0	0	–
Hoarseness, n (%)	1 (2.3)	4 (8.3)	5 (11.1)	0.296
Dyspnea, n (%)	0	0	0	–
Aspiration, n (%)	0	0	0	–

Notes: Values are patient numbers. [a]Nausea and vomiting as any retching, vomiting, or requirement for antiemetics. [b]Hypoxemia was defined as defined as SpO2 < 90% for more than 10 seconds or PaO_2 : FiO_2 ratio < 300 mm Hg. [c]Bradycardia was defined as heart rate less than 40 beats per minute. [d]Hypotension was defined as systolic blood pressure < 90 mmHg or a decrease of >30% from baseline.

Secondly, preoperative US-guided iSLNB reduced the incidence and severity of cough during extubation. Coughing during extubation is an airway complication that anesthesiologists must pay attention to. It is potentially caused by tracheal stretch stimulation from DLTs and cuff pressure.[56] The SLN, a nerve in the larynx and neck, is essential for sound production, laryngeal muscle movement, and laryngeal sensation.[26] Ultrasound-guided iSLNB can inhibit reflex responses to stimuli in the laryngopharynx and glottis, thereby reducing cough occurrence. Ultrasound-guided iSLNB has been used to manage refractory and neurogenic cough. It effectively prevented coughing during bronchoscopy,[57–59] consistent with our finding. However, we observed no benefits of US-guided iSLNB on agitation during extubation.

Thirdly, our findings demonstrate the efficacy of US-guided iSLNB in mitigating mechanical stimulation during intubation and extubation, thereby reducing hemodynamic fluctuations, including HR, MAP, and RPP. Wang et al[12] discovered that postoperative US-guided iSLNB can reduce the incidence of POST. However, hemodynamic fluctuations during intubation require equal attention as those during extubation. Therefore, preoperative US-guided iSLNB offers greater advantages over postoperative block by addressing both phases of airway management. The RPP is an indicator for assessing myocardial oxygen consumption, thus suggesting that US-guided iSLNB may better preserve myocardial oxygen consumption in patients with hypertension and coronary heart disease.

Dexmedetomidine, an imidazole compound and the right-handed isomer of metomidate, was approved by the US Food and Drug Administration (FDA) in 1999 for short-term sedation in adult patients in the intensive care unit (ICU) undergoing mechanical ventilation. Recently, dexmedetomidine has gained attention as an adjuvant in PNB, where it prolongs nerve block duration and enhances local anesthetic analgesia through several mechanisms. In a previous review, we summarized this mechanism, encompassing peripheral, spinal, and supraspinal levels.[16] At the peripheral level, dexmedetomidine can enhance the effect of local anesthetics by keeping the cell hyperpolarized by inhibiting I_h current.[19] Besides, dexmedetomidine may exert central effects via systemic absorption at the neuraxial site.[18]

In this study, perineural dexmedetomidine (1 mL, 0.5 $\mu g \cdot kg^{-1}$), when used as an adjuvant to ropivacaine (2 mL, 0.20%), effectively mitigated the occurrence, severity, and duration of POST and cough during extubation. Perineural dexmedetomidine is more effective than IV dexmedetomidine, and it can induce varying degrees of absorption to exert a central effect.[18,20–23] Currently, research on perineural dexmedetomidine mostly focuses on the limbs and trunk, with limited studies conducted on the head and neck. Using dexmedetomidine as an adjuvant to ropivacaine in cervical plexus block can improve analgesic efficacy.[60] We hypothesize that dexmedetomidine may prolong the duration of US-guided iSLNB effects up to 12 h after surgery and significantly reduce the incidence of POST by inhibiting I_h current and Aδ and C-type fibers while exhibiting vasoconstrictor and local anti-inflammatory properties.[16] Perineural dexmedetomidine provided no hemodynamic benefits, although IV dexmedetomidine ensured hemodynamic stability.

Perineural dexmedetomidine can induce hypotension and bradycardia.[61] The effect of perineural dexmedetomidine is dose-dependent, and excessively high concentrations of dexmedetomidine can cause significant adverse effects. Consequently, we selected a lower dose of dexmedetomidine. We discovered that peripheral dexmedetomidine was safer and capable of prolonging analgesia, attaining a balance between analgesia and safety. A recent study investigated the diffusion range of LA in iSLNB and discovered that a volume of 2–3 mL of LA is safe.[62] Administering excessive amounts of LA may result in LA extrusion from the SLN space, causing significant complications.[62] In our study, we used well-established landmarks such as SLA and THM for iSLN localization, ensuring precise administration of LA (3 mL) within the safe range without observed complications.

Another concern is the safety of US-guided iSLNB. The SLN, a branch of the vagus nerve, divides into internal and external branches. The iSLN provides the sensory innervation of the larynx. SLNB can lead to increased fluid viscosity, resulting in a significant rise in the incidence of aspiration.[63,64] With advancements in nerve block and the development of ultrasound technology, numerous studies have indicated that US-guided iSLNB is safe, without occurrences of choking, aspiration, or regurgitation.[12,13,25,65,66] In our study, we used the recently established US-guided iSLNB technique, which we had previously used for awake tracheal intubation, and once again confirmed its safety and efficacy.[67]

Our study has some limitations. First, we did not compare perineural and IV dexmedetomidine to ascertain the superior benefits of perineural dexmedetomidine. Secondly, we did not evaluate additional dose gradients for dexmedetomidine or use a lower volume of LA. However, our combination of 3 mL of LA and 0.5 $\mu g \cdot kg^{-1}$ of dexmedetomidine proved safe. Thirdly, follow-up on POST was limited to 12 h after surgery because the pilot experiment indicated negligible POST incidence in the SD group after this period. Additional large-scale trials are necessary to validate our findings, given that US-guided iSLNB is an invasive procedure requiring anesthesiologists to carefully assess its benefits against potential risks.

Conclusion

Preoperative US-guided iSLNB combined with perineural dexmedetomidine effectively reduced the incidence, severity, and duration of POST and cough during extubation; however, no additional hemodynamic benefits were observed.

Abbreviations

POST, Postoperative sore throat; US-guided iSLNB, Ultrasound-guided internal branch block of superior laryngeal nerve; HR, Heart rate; MAP, Mean arterial pressure; RPP, rate-pressure product; DLT, Double-lumen endotracheal tube; NSAIDs, Non-steroidal anti-inflammatory drugs; NMDA, N-Methyl-D-aspartic acid; PNB, Peripheral nerve block; BPB, Brachial plexus block; TPVB, Thoracic paravertebral nerve block; ASA, American Society of Anesthesiologists; GA, General anesthesia; BMI, Body mass index; IV, Intravenous; SLA, Superior laryngeal artery; THM, Thyrohyoid membrane; TM, thyrohyoid muscle; LA, Local anesthetic; IBP, Invasive blood pressure; ECG, Electrocardiogram; SpO_2, Oxygen saturation; EI, Entropy index; TV, Tidal volume; RR, Respiratory rate; PEEP, Positive end-expiratory pressure; PCIA, Patient-controlled intravenous analgesia; SAS, Sedation-Agitation Scale; HADS, Hospital Anxiety and Depression Scale; GEE, Generalized estimating equation; OLV, One-lung ventilation; CPB, Cervical plexus block; FDA, Food and Drug Administration; ICU, Intensive care unit.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

The study was conducted with Institutional Review Board approval from the Second Hospital of Shandong University in China (No: KYLL-2022LW051), and the guidelines outlined in the Declaration of Helsinki were followed. Written informed consent was obtained from all study participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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