Article

Intrapulmonary Shunt and Oxygenation During One-Lung Ventilation: Influence of Dexmedetomidine Combined with Transcutaneous Acupoint Electrical Stimulation

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Abstract: Background: One-lung ventilation (OLV) often causes hypoxemia due to intrapulmonary shunting. This study investigated how combining dexmedetomidine with transcutaneous acupoint electrical stimulation (TAES) affects intrapulmonary shunt and oxygenation during OLV. **Methods:** Eighty thoracoscopic lobectomy patients were randomized into four groups: control (Group A, saline), dexmedetomidine (Group B, 1 $\mu g \cdot kg^{-1}$ loading, 0.4 $\mu g \cdot kg^{-1} \cdot h^{-1}$ maintenance), TAES (Group C, bilateral stimulation at five acupoints), and combination (Group D, both interventions). Measurements were taken at five timepoints: before anesthesia (T_0), 15 min after two-lung ventilation (T_1), 30 min after OLV (T_2), one h after OLV (T_3), and 15 min after resuming two-lung ventilation (T_4). Oxygenation parameters (PaO_2, OI, A-aDO_2, Q_s/Q_t, RI) and hemodynamics were assessed. **Results:** During OLV (T_2, T_3), Groups B and C showed significantly improved oxygenation parameters compared to Group A ($p < 0.05$), while Group D demonstrated superior improvement compared to all other groups ($p < 0.05$). All groups experienced decreased OI and increased Q_s/Q_t and A-aDO_2 during OLV compared to baseline, with Group A showing the most pronounced changes and Group D the least. **Conclusion:** Both dexmedetomidine and TAES individually improve intrapulmonary shunt and oxygenation during OLV, but their combination provides superior results compared to either intervention alone.

Keywords: one-lung ventilation; transcutaneous acupoint electrical stimulation; dexmedetomidine; intrapulmonary shunt; oxygenation

Introduction

One-lung ventilation (OLV) is a specialized ventilation technique used during thoracic surgeries where one lung is collapsed to provide optimal surgical exposure while ventilation is maintained in the contralateral lung. This approach prevents secretions and blood from entering the ventilated lung, and allows for different ventilation strategies according to surgical requirements while maintaining appropriate airway pressure [1,2]. Despite its clinical advantages, OLV represents a non-physiological ventilation state that can lead to significant pathophysiological changes such as ventilation/perfusion mismatch [3]. This ventilation/perfusion imbalance can lead to increased intrapulmonary shunting and a higher risk of hypoxemia, and futhermore, potentially increase patient mortality [4,5].

Hypoxic pulmonary vasoconstriction (HPV) serves as a critical protective mechanism regulating intrapulmonary shunting to avoid ventilation/perfusion mismatch during OLV [6,6,7]. This physiological response occurs when alveolar hypoxia triggers localized vasoconstriction in pulmonary vessels, effectively redirecting blood flow from poorly ventilated areas to well-ventilated regions of the lung. By improving ventilation/perfusion matching and decreasing shunting in the non-ventilated lung, HPV optimizes arterial oxygenation. However, despite effective HPV, some degree of intrapulmonary shunting inevitably persists, compromising systemic oxygenation. Consequently, clinical interven-

tions that either prevent HPV suppression or enhance its effectiveness during OLV have significant therapeutic potential.

Dexmedetomidine (DEX), a highly selective α_2-adrenergic receptor agonist, has gained widespread clinical use as an anesthetic adjuvant due to its sedative, analgesic, and anxiolytic properties through central sympatholytic effects [8]. Recent basic and clinical research has demonstrated DEX's protective effects on multiple organ systems, including the nervous system, heart, lungs, and kidneys. In pulmonary applications specifically, numerous studies have confirmed DEX's lung-protective effects through anti-inflammatory mechanisms and stress response modulation so that to enhance HPV and improve intrapulmonary shunting and oxygenation during OLV [9]. For example, foundational studies have shown that DEX can effectively inhibit histamine-induced bronchospasm and mitigate OLV-associated lung injury through upregulation of aquaporin-1 expression and reduction of intrapulmonary shunting [10]. Furthermore, studies have reported that DEX can decrease intrapulmonary shunting and oxidative stress and improve arterial oxygenation and HPV during OLV while also reducing the requirement for inhaled anesthetics [9].

Acupuncture is one of China's traditional medical therapies, recognized for its simplicity, effectiveness, and wide clinical application. Transcutaneous acupoint electrical stimulation (TAES) is a non-invasive electro-acupuncture method that combines the advantages of transcutaneous electrical nerve stimulation with acupoint therapy. Both basic and clinical research have demonstrated TAES's protective effects on lung function, particularly in reducing perioperative intrapulmonary shunting and improving oxygenation [11–15].

Although, effects of DEX and TAES on intrapulmonary shunting and oxygenation during OLV have been widely studied before. Most studies have focused on the effects of these interventions used independently on intrapulmonary shunting during OLV, with few investigations examining the impact of combined DEX and TAES. And also, no clinical studies have yet examined the effects of the combination of different acupoints on intrapulmonary shunting during OLV. Therefore, this study aims to investigate whether transcutaneous electrical stimulation of combinations of the four different acupoints (Kongzui (LU6), Feishu (BL13), Hegu (LI4), and Zusanli (ST36)) improves intrapulmonary shunting and oxygenation during OLV and whether the combination of DEX and TAES provides greater improvement than either intervention alone, offering reference guidance for clinical practice.

Materials and Methods

Study design, setting, and participants

This study was conducted at the Department of Thoracic Surgery of Ningxia Medical University General Hospital. The study protocol was approved by the hospital's Ethics Committee (KYLL 2021-387), and written informed consent was obtained from all participants. The following inclusion criteria were implemented: (1) American Society of Anesthesiologists (ASA) physical status class II or III; (2) age between 18 and 65 years; (3) body mass index (BMI) between 18 and 24.9 kg/m^2; (4) expected surgery duration between 1 and 3 hours; (5) patients with no obvious abnormalities in cardiac, cerebral, hepatic, and renal function; and (6) patients with no obvious abnormalities in pulmonary function.

Patients were excluded if they had previous surgery at acupoint meridian pathways or local skin infections at acupoints, contraindications for dexmedetomidine, previous thoracotomy history, or preoperative anemia (hemoglobin < 120 g/L for males, < 110 g/L for females).

Patients were withdrawn from the study if they experienced any of the following during one-lung ventilation (OLV): $SpO_2 < 92\%$ for more than 30 seconds requiring conversion to two-lung ventilation; mean arterial pressure < 55 mmHg; peak airway pressure > 35 cmH_2O; development of respiratory or metabolic acidosis; severe cardiac arrhythmias; or intraoperative blood loss exceeding 400 mL.

Randomization and Grouping

Eighty eligible patients scheduled for thoracoscopic lobectomy were randomized using a random number table into four groups with a 1:1:1:1 allocation ratio: control group (Group A), dexmedetomi-

dine group (Group B), transcutaneous acupoint electrical stimulation group (Group C), and combined dexmedetomidine with transcutaneous acupoint electrical stimulation group (Group D).

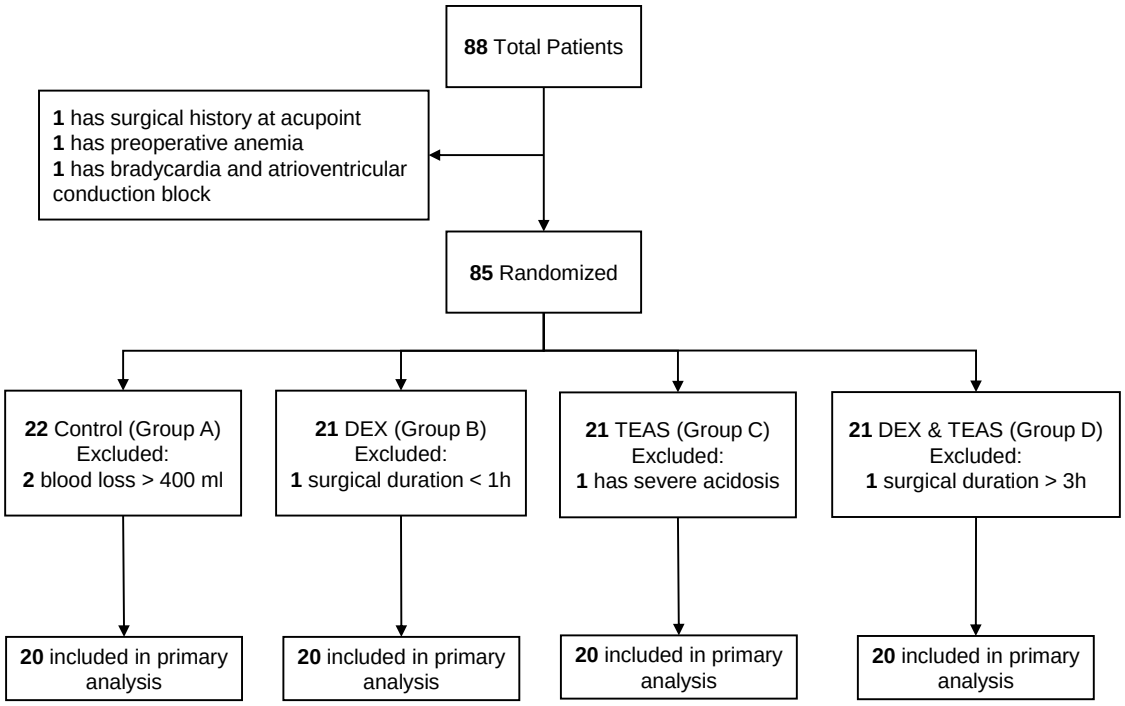

Figure 1. Flow Chart

Anesthetic Protocol and Intervention

Anesthetic Preparation: Patients underwent comprehensive preoperative evaluations before surgery. In the operating room, standard monitoring was established with a multifunction monitor (GE Healthcare, USA) for electrocardiogram (ECG), heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2).Anesthetic depth was monitored via bispectral index (BIS) (Vista 3.0, Aspect Medical Systems). After establishing peripheral venous access, patients with normal Allen's test results received left radial artery catheterization under local anesthesia for continuous blood pressure monitoring and arterial blood sampling.

Group Interventions: The four groups received specific interventions as follows:

(1) **Group A (Control):** Patients received intravenous normal saline 10 minutes before anesthesia induction with no transcutaneous acupoint electrical stimulation (TAES).

(2) **Group B (Dexmedetomidine):** Patients received intravenous dexmedetomidine at a loading dose of 1 $\mu g \cdot kg^{-1}$ 10 minutes before anesthesia induction, followed by continuous infusion at 0.4 $\mu g \cdot kg^{-1} \cdot h^{-1}$ until 30 minutes before the end of surgery, with no TAES.

(3) **Group C (TAES):** Patients received intravenous normal saline 10 minutes before anesthesia induction, with concurrent bilateral TAES at Kongzui (LU6), Feishu (BL13), Hegu (LI4), and Zusanli (ST36) acupoints. TAES was continued throughout surgery until wound closure.

(4) **Group D (Dexmedetomidine & TAES):** Patients received both dexmedetomidine administration as in Group B and TAES as in Group C.

Anesthesia Induction: Total intravenous anesthesia was administered using midazolam (0.05-0.1 $mg \cdot kg^{-1}$), sufentanil (0.3-0.5 $\mu g \cdot kg^{-1}$), etomidate (0.2-0.3 $mg \cdot kg^{-1}$), and rocuronium (0.6-0.9 $mg \cdot kg^{-1}$). After pre-oxygenation and confirmed neuromuscular blockade, a double-lumen endobronchial tube

(37# males, 35# females) was inserted under direct laryngoscopy. Proper positioning was verified by fiberoptic bronchoscopy.

During two-lung ventilation, parameters were set as: FiO_2 = 100%, tidal volume (V_T) 6-8 mL·kg^{-1}, respiratory rate 12-18 breaths/min, and I:E ratio 1:2. For OLV, parameters were adjusted to: V_T 4-6 mL·kg^{-1}, FiO_2 = 100%, and I:E ratio 1:2. Respiratory rate was adjusted to maintain $P_{ET}CO_2$ between 35-45 mmHg, with peak airway pressure limited to 30 cmH_2O.

Anesthesia Maintenance: Anesthesia was maintained using propofol (4-12 mg·kg^{-1}·h^{-1}) and remifentanil (0.2-0.5 μg·kg^{-1}·min^{-1}). These infusion rates were titrated to maintain BIS values of 40-60 and keep blood pressure within ±20% of baseline. Rocuronium boluses were administered as needed for muscle relaxation, with vasoactive drugs used to maintain hemodynamic stability. Normal saline (Groups A, C) or dexmedetomidine (Groups B, D) was discontinued 30 minutes before surgery ended. TAES (Groups C and D) were stopped after wound closure. All anesthetic infusions were terminated at procedure completion.

Anesthesia Recovery: Residual neuromuscular blockade was antagonized with neostigmine, and flumazenil was administered to reverse the effects of midazolam. Upon meeting extubation criteria, thorough suctioning of the trachea and oral cavity was performed before removing the endobronchial tube. After confirmation of stable vital signs, patients were transferred to the post-anesthesia care unit (PACU) for continued monitoring. Postoperative analgesia was managed via patient-controlled intravenous analgesia (PCIA) for all groups, with the analgesic pump containing sufentanil (2 μg·kg^{-1}) diluted to 100 mL with normal saline.

Transcutaneous Acupoint Electrical Stimulation Method

Acupoint Localization: Acupoints were located strictly according to the National Standard of the People's Republic of China GB12346-90 "Location of Acupoints." The following bilateral acupoints were selected:

(1) **Kongzui (LU6):** Located on the palmar side of the forearm on the radial side, 7 cm proximal to the transverse wrist crease on the line connecting Chize (LU5) and Taiyuan (LU9).

(2) **Feishu (BL13):** Located approximately 1.5 inches lateral to the lower border of the spinous process of the third thoracic vertebra.

(3) **Hegu (LI4):** Located between the first and second metacarpal bones, at the midpoint of the radial side of the second metacarpal bone.

(4) **Zusanli (ST36):** Located 3 inches below the lower border of the patella, one finger-breadth lateral to the anterior crest of the tibia.

TAES Parameters and Application: We used the following parameters for transcutaneous electrical stimulation: pulse width 100 μs, waveform dense-disperse wave, frequency $2 - 100Hz$, and electrical current intensity generally between $6 - 12mA$, adjusted to patient tolerance with sensations of soreness, numbness, distension, heaviness, or mild pain. After cleansing the skin at each acupoint with alcohol, $30mm \times 30mm$ electrode pads were placed bilaterally at the LU6, BL13, LI4, and ST36 acupoints and secured with sterile adhesive film. TAES was initiated 10 minutes before anesthesia induction using an electronic acupuncture device and continued throughout surgery until wound closure.

Outcomes

The primary outcome consists of hemodynamic, blood gas analysis, and Oxygenation parameters measured for each patient throughout the intraoperative period. All values were recorded at five time points: before anesthesia (T_0), 15 min after two-lung ventilation (T_1), 30 min after OLV (T_2), one h after OLV (T_3), and 15 min after resuming two-lung ventilation (T_4). Hemodynamic parameters include systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), and bispectral index (BIS). Blood gas analysis parameters include $PaCO_2$, PaO_2, hemoglobin (Hb), and hematocrit (HCT). Oxygenation parameters include alveolar-arterial oxygen difference (A-aDO_2), oxygenation index (OI), respiratory index (RI), and intrapulmonary shunt fraction (Q_s/Q_t).

We also measured the baseline characteristics (patient demographic and clinical characteristics), including patient demographic and clinical characteristics, such as gender, age, weight, height, BMI, ASA classification, preoperative pulmonary function indicators (FEV1, FVC, FEV1/FVC), OLV duration, surgical duration, surgical site, and number of resected lobes.

Statistical Analysis

Statistical analysis was performed in this study using R statistical software. Normally distributed quantitative data were expressed as mean ± standard deviation ($\bar{x} \pm s$). Intergroup differences were analyzed using one-way analysis of variance (ANOVA), with post-hoc LSD-t tests for pairwise comparisons. Repeated measures data were analyzed using repeated measures ANOVA. Categorical data were expressed as frequency (percentage) and compared using chi-square tests. The significance level was set at $\alpha = 0.05$.

Results

A total of 88 patients were initially assessed for eligibility. Flow chart are shown in Figure 2. Specifically, three patients were excluded preoperatively: one with previous surgery at acupoint locations, one with preoperative anemia, and one with preoperative bradycardia and atrioventricular block. As a consequence, 85 patients entered the study (Group A: 22 patients, Group B: 21 patients, Group C: 21 patients, Group D: 21 patients). Five patients were subsequently withdrawn: two patients in Group A with intraoperative blood loss $> 400mL$, one patient in Group B with surgery duration < 1 hour, one patient in Group C who developed severe acidosis, and one patient in Group D with surgery duration > 3 hours. Ultimately, 20 patients in each group completed the study and were included in the final analysis.

Table 1. Baseline Characteristics

Variable	Group A n = 20	Group B n = 20	Group C n = 20	Group D n = 20
Gender (Male/Female)	11/9	14/7	7/13	11/9
Age (years)	53.90 ± 7.62	57.10 ± 7.82	56.45 ± 6.40	55.85 ± 7.90
Height (cm)	166.15 ± 7.66	168.00 ± 6.67	165.25 ± 4.98	167.45 ± 7.03
Weight (kg)	63.85 ± 8.85	62.98 ± 8.72	61.65 ± 6.75	64.00 ± 5.40
BMI (kg/m^2)	23.05 ± 1.90	22.26 ± 2.34	22.55 ± 2.05	22.83 ± 1.50
ASA Classification (II/III)	12/8	10/10	9/11	11/9
FEV_1 (L)	2.44 ± 0.45	2.69 ± 0.53	2.52 ± 0.42	2.60 ± 0.41
FVC (L)	3.07 ± 0.53	3.22 ± 0.55	3.13 ± 0.52	3.23 ± 0.52
FEV_1/FVC (%)	82.28 ± 1.11	82.85 ± 2.60	83.02 ± 1.67	82.64 ± 2.25
Left/Right OLV Ratio	11/9	12/8	12/8	10/10
Resected Lobes (1/2/3)	20/0/0	20/0/0	20/0/0	20/0/0
Surgery Duration (min)	141.65 ± 38.89	131.50 ± 41.64	138.20 ± 41.60	127.65 ± 47.80
OLV Duration (min)	118.70 ± 34.52	105.05 ± 38.75	115.40 ± 37.60	117.30 ± 46.06
Anesthesia Duration (min)	170.50 ± 46.51	165.70 ± 43.00	166.40 ± 45.89	166.81 ± 44.44

The patient demographic and clinical characteristics across groups are comparable, as shown in Table 1. No statistically significant differences were observed among the four groups over gender, age, weight, height, BMI, ASA classification, preoperative pulmonary function indicators, left/right OLV ratio, number of resected lobes, surgical duration, OLV duration, or anesthesia duration ($p > 0.05$).

Comparisons of Hemodynamic Parameters

A comparison of the hemodynamic outcomes between the four groups is presented in Table 2. Our analysis encompassed both the temporal changes within each group and the between-group differences at corresponding time points. Compared with T_0, all four groups showed significant decreases in HR, SBP, DBP, MAP, and BIS values at time points T_1-T_4 ($p < 0.05$). However, no statistically significant differences were observed among the four groups in HR, SBP, DBP, MAP, or BIS values at any timepoint ($p > 0.05$).

Table 2. Comparison of Hemodynamic Parameters

Parameter	Time	Group A n = 20	Group B n = 20	Group C n = 20	Group D n = 20
HR	T_0	77.70 ± 10.27	80.00 ± 15.52	75.35 ± 10.01	77.05 ± 10.86
	T_1	71.40 ± 11.07*	67.00 ± 10.29*	67.00 ± 8.86*	69.95 ± 9.67*
	T_2	70.60 ± 9.95*	71.45 ± 14.38*	67.85 ± 6.83*	67.60 ± 7.96*
	T_3	68.55 ± 9.31*	68.90 ± 11.86*	68.55 ± 8.95*	67.45 ± 8.43*
	T_4	67.85 ± 9.30*	65.75 ± 7.61*	69.70 ± 5.82*	68.50 ± 6.91*
SBP	T_0	135.10 ± 15.31	135.90 ± 15.91	127.70 ± 15.17	133.80 ± 17.11
	T_1	117.45 ± 15.74*	115.50 ± 14.36*	118.25 ± 17.08*	118.25 ± 12.39*
	T_2	111.25 ± 15.99*	115.45 ± 15.31*	107.00 ± 13.83*	108.65 ± 10.21*
	T_3	109.65 ± 14.58*	109.10 ± 11.39*	105.35 ± 12.39*	107.00 ± 9.93*
	T_4	114.60 ± 10.54*	116.90 ± 11.41*	112.10 ± 9.40*	111.35 ± 12.06*
DBP	T_0	79.40 ± 7.07	80.10 ± 9.21	77.10 ± 10.49	79.20 ± 11.56
	T_1	69.45 ± 6.99*	72.00 ± 8.72*	70.30 ± 6.86*	69.60 ± 5.85*
	T_2	70.35 ± 11.12*	72.35 ± 9.53*	70.00 ± 5.29*	70.95 ± 8.67*
	T_3	70.10 ± 8.84*	69.05 ± 7.24*	69.45 ± 6.84*	69.40 ± 6.70*
	T_4	72.85 ± 6.66*	74.40 ± 9.14*	69.85 ± 4.45*	72.55 ± 7.79*
MAP	T_0	97.97 ± 7.27	98.70 ± 10.75	93.97 ± 9.55	97.40 ± 12.15
	T_1	85.45 ± 6.79*	86.50 ± 8.97*	86.28 ± 7.99*	85.82 ± 6.42*
	T_2	83.98 ± 11.64*	86.71 ± 9.46*	82.33 ± 6.97*	83.52 ± 8.51*
	T_3	83.28 ± 9.47*	82.40 ± 6.26*	81.42 ± 7.40*	81.93 ± 6.22*
	T_4	86.77 ± 6.94*	88.57 ± 8.48*	83.93 ± 5.11*	85.48 ± 8.38*
BIS	T_0	97.45 ± 0.95	97.00 ± 0.86	97.30 ± 1.42	97.45 ± 0.95
	T_1	50.25 ± 4.41*	49.70 ± 4.14*	50.35 ± 5.19*	51.05 ± 5.74*
	T_2	50.75 ± 4.47*	50.00 ± 4.52*	51.20 ± 5.14*	52.80 ± 5.84*
	T_3	51.15 ± 4.26*	50.65 ± 3.88*	52.40 ± 4.50*	52.95 ± 4.69*
	T_4	52.00 ± 4.27*	51.00 ± 3.76*	52.60 ± 3.66*	52.65 ± 3.77*

* $p < 0.05$ compared with T_0 within the same group.
No statistically significant differences were observed between groups at any time point ($p > 0.05$).

Comparisons of Blood Gas Analysis Parameters

The comparison of the blood gas analysis parameters between the four groups is presented in Table 3. No statistically significant differences were observed within or between groups regarding pH, $PaCO_2$, Hb, or HCT at any timepoint (p > 0.05).

Comparisons of Oxygenation Parameters

A comparison of the oxygenation parameters between the four groups is presented in Table **??**. Similarly, we analyzed the temporal changes within each group and the differences between groups at corresponding time points.

For comparison between temporal points, relative to T_0, all groups showed significant increases in PaO_2, Q_s/Q_t, RI, and A-aDO_2 at timepoints T_1-T_4. PaO_2 and RI increases were greater at T_1 and T_4 than at T_2 and T_3, with Group A showing the smallest increase and Group D the largest ($p < 0.05$). Conversely, Q_s/Q_t and A-aDO_2 increases were greater at T_2 and T_3 than at T_1 and T_4, with Group A showing the largest increase and Group D the smallest ($p < 0.05$). OI increased at T_1 and T_4 but decreased at T_2 and T_3 in all groups, with Group A showing the largest decrease and Group D the smallest ($p < 0.05$).

For intergroup comparisons, at timepoint T_2, Groups B and C showed significantly higher PaO_2 and OI, along with lower A-aDO_2, Q_s/Q_t, and RI compared to Group A ($p < 0.05$). Group D demonstrated further improvements in these parameters compared to Groups B and C ($p < 0.05$). Similarly, at timepoint T_3, Groups B and C exhibited significantly higher PaO_2 and OI, with lower A-aDO_2, Q_s/Q_t, and RI compared to Group A ($p < 0.05$). Again, Group D showed superior improvements in these parameters compared to Groups B and C ($p < 0.05$).

Discussion

In this study, we evaluated the effects of dexmedetomidine (DEX), transcutaneous acupoint electrical stimulation (TAES), and their combination on intrapulmonary shunting and oxygenation

Table 3. Comparison of Blood Gas Analysis Parameters Between Groups

Parameter	Time	Group A n = 20	Group B n = 20	Group C n = 20	Group D n = 20
pH	T_0	7.39 ± 0.02	7.39 ± 0.02	7.39 ± 0.02	7.39 ± 0.02
	T_1	7.39 ± 0.02	7.38 ± 0.03	7.39 ± 0.02	7.39 ± 0.03
	T_2	7.39 ± 0.02	7.39 ± 0.04	7.39 ± 0.02	7.39 ± 0.02
	T_3	7.38 ± 0.02	7.38 ± 0.03	7.38 ± 0.02	7.38 ± 0.03
	T_4	7.38 ± 0.02	7.38 ± 0.02	7.38 ± 0.02	7.38 ± 0.02
$PaCO_2$	T_0	38.63 ± 1.97	38.84 ± 2.35	38.48 ± 1.96	38.67 ± 2.17
	T_1	38.59 ± 2.03	38.64 ± 2.66	38.34 ± 2.45	38.92 ± 2.57
	T_2	38.98 ± 2.86	38.48 ± 2.16	38.81 ± 2.47	38.69 ± 2.26
	T_3	38.61 ± 2.17	38.72 ± 2.39	38.68 ± 2.28	38.88 ± 2.31
	T_4	38.74 ± 2.58	38.86 ± 2.29	38.76 ± 2.39	38.83 ± 2.72
Hb	T_0	14.39 ± 2.02	14.54 ± 2.00	14.47 ± 1.69	14.52 ± 2.58
	T_1	14.50 ± 2.14	14.53 ± 1.79	14.05 ± 1.38	14.44 ± 2.13
	T_2	14.38 ± 2.08	14.73 ± 2.03	14.08 ± 1.36	14.13 ± 1.96
	T_3	14.60 ± 2.02	14.66 ± 2.05	14.11 ± 1.29	14.10 ± 1.87
	T_4	14.69 ± 2.11	14.86 ± 1.98	14.78 ± 1.42	14.56 ± 1.75
HCT	T_0	41.77 ± 9.58	41.95 ± 5.98	41.53 ± 7.99	41.95 ± 5.86
	T_1	41.50 ± 9.12	41.55 ± 5.88	41.65 ± 6.97	41.70 ± 7.11
	T_2	41.05 ± 10.27	41.65 ± 6.80	41.40 ± 4.41	41.35 ± 6.23
	T_3	41.30 ± 7.04	41.05 ± 6.07	41.35 ± 6.34	41.20 ± 4.64
	T_4	41.10 ± 7.77	41.25 ± 6.10	41.60 ± 6.31	41.90 ± 4.75

No statistically significant differences were observed within or between groups at any time point ($p > 0.05$).

during one-lung ventilation (OLV) in patients undergoing thoracoscopic surgery. Our primary finding is that the combination of DEX and TAES provided superior improvement in intrapulmonary shunting and oxygenation during OLV compared to either intervention alone, suggesting a synergistic effect that could significantly benefit patients undergoing thoracic procedures requiring OLV.

To exclude confounding factors, first, we carefully controlled for patient demographics, preoperative pulmonary function, surgical characteristics, and anesthesia management across all groups. Statistical analysis confirmed no significant differences between groups for any of these parameters as shown in Table 1. Second, as previous research suggests, intrapulmonary shunting peaks approximately $30 - 40$ minutes after initiating one-lung ventilation (coinciding with lowest PaO_2), as hypoxic pulmonary vasoconstriction gradually redirects blood flow from the non-ventilated to the ventilated lung before reaching relative stability [16,17]; therefore, we verified double-lumen tube positioning bronchoscopically before and after positional changes, measured lung function parameters at five specific time points (T_0 through T_4), and employed total intravenous anesthesia to eliminate anesthetic technique as a confounding factor for intrapulmonary shunting. Additionally, we continuously monitored end-tidal carbon dioxide and adjusted respiratory parameters to maintain normal carbon dioxide levels, avoiding hypercapnia or hyperventilation that could influence HPV and intrapulmonary shunting [18]. We also strictly limited intraoperative blood loss across all groups to prevent excessive hemorrhage from causing inadequate perfusion and multi-organ ischemia-hypoxia [74]. Our results showed no significant differences in pH, $PaCO_2$, Hb, or HCT within or between groups at any time point as shown in Table 3. This comprehensive control of potential confounding variables ensures the comparability of the four groups, thereby minimizing potential confounding effects on our primary outcomes.

We want to discuss several points from our primary results. Firstly, regarding effects on oxygenation parameters, our results showed that DEX administration in Group B decreased intrapulmonary shunt (Q_s/Q_t), respiratory index (RI), and alveolar-arterial oxygen difference (A-aDO_2) while increasing arterial oxygen partial pressure (PaO_2) and oxygenation index (OI) compared to Group A. These findings align with previous studies demonstrating DEX's pulmonary protective effects during one-lung ventilation (OLV) [8,19–21]. The physiological mechanisms underlying DEX's improvements may occur through: (1) enhancement of hypoxic pulmonary vasoconstriction through reduced oxidative stress and increased nitric oxide release; (2) inhibition of inflammatory responses and promotion of pul-

Table 4. Comparison of Oxygenation Parameters Between Groups

Parameter	Time	Group A n = 20	Group B n = 20	Group C n = 20	Group D n = 20
PaO_2	T_0	73.50 ± 5.85	74.06 ± 7.77	75.27 ± 5.78	74.81 ± 6.16
	T_1	448.06 ± 28.10	449.83 ± 26.54	447.66 ± 24.17	444.12 ± 20.05
	T_2	128.46 ± 14.67	171.94 ± 23.63*	166.67 ± 23.54*	206.17 ± 32.10*†‡
	T_3	138.38 ± 19.35	180.82 ± 32.85*	170.16 ± 37.61*	217.62 ± 32.88*†‡
	T_4	452.39 ± 26.84	440.14 ± 29.23	453.82 ± 26.76	451.59 ± 22.29
OI	T_0	350.00 ± 27.85	352.64 ± 37.00	358.43 ± 27.52	356.24 ± 29.33
	T_1	448.06 ± 28.10	449.83 ± 26.54	447.66 ± 24.17	444.12 ± 20.05
	T_2	128.46 ± 14.67	171.94 ± 23.63*	166.67 ± 23.54*	206.17 ± 32.10*†‡
	T_3	138.38 ± 19.35	180.82 ± 32.85*	170.16 ± 37.61*	217.62 ± 32.88*†‡
	T_4	452.39 ± 26.84	440.14 ± 29.23*	454.82 ± 27.61*	451.60 ± 22.29*†‡
RI	T_0	0.39 ± 0.12	0.38 ± 0.13	0.36 ± 0.11	0.36 ± 0.12
	T_1	0.49 ± 0.09	0.48 ± 0.09*	0.49 ± 0.08*	0.50 ± 0.07*†‡
	T_2	4.24 ± 0.62	2.95 ± 0.64*	3.07 ± 0.63*	2.30 ± 0.54*†‡
	T_3	3.89 ± 0.69	2.80 ± 0.72*	3.11 ± 1.01*	2.12 ± 0.51*†‡
	T_4	0.47 ± 0.09	0.52 ± 0.10*	0.47 ± 0.09*	0.47 ± 0.07*†‡
Q_s/Q_t	T_0	1.70 ± 0.40	1.65 ± 0.45	1.61 ± 0.38	1.62 ± 0.40
	T_1	11.82 ± 1.36	11.74 ± 1.32*	11.87 ± 1.14*	12.00 ± 0.96*†‡
	T_2	24.93 ± 0.55	23.40 ± 0.89*	23.58 ± 0.88*	22.12 ± 1.20*†‡
	T_3	24.60 ± 0.68	23.06 ± 1.17*	23.44 ± 1.37*	21.67 ± 1.25*†‡
	T_4	11.61 ± 1.33	12.19 ± 1.42*	11.49 ± 1.33*	11.65 ± 1.06*†‡
$A\text{-}aDO_2$	T_0	27.95 ± 6.75	27.13 ± 7.53	26.37 ± 6.34	26.58 ± 6.72
	T_1	216.70 ± 28.09	214.88 ± 27.34*	217.43 ± 23.73*	220.23 ± 20.02*†‡
	T_2	535.82 ± 15.74	492.96 ± 24.65*	497.82 ± 24.30*	458.47 ± 31.99*†‡
	T_3	526.36 ± 19.16	483.78 ± 31.90*	494.49 ± 37.76*	446.78 ± 33.00*†‡
	T_4	212.19 ± 27.58	224.29 ± 29.81*	209.73 ± 27.43*	212.87 ± 21.97*†‡

* $p < 0.05$ compared with Group A; † $p < 0.05$ compared with Group B; ‡ $p < 0.05$ compared with Group C.
All time points (T_1-T_4) showed statistically significant differences compared to baseline (T_0) in all groups ($p < 0.05$).

monary fluid balance via aquaporin-1 expression; and (3) activation of α_2-receptors on vascular smooth muscle, improving ventilation/perfusion ratios [22,23]. These mechanisms collectively contribute to reduced intrapulmonary shunting and improved oxygenation during OLV. Additionally, while our findings confirm that DEX can moderately reduce intrapulmonary shunting and improve oxygenation during OLV, several factors—including surgical manipulation, OLV itself, enhanced inflammatory responses, and HPV suppression—may limit the extent of this improvement, necessitating exploration of additional therapeutic strategies.

Secondly, for group C, our results demonstrate that at timepoints T_2 and T_3, Group C exhibited higher PaO_2 and OI with lower $A\text{-}aDO_2$, Q_s/Q_t, and RI compared to Group A ($p < 0.05$). This aligns with previous studies showing that TAES improves ventilation/perfusion balance, reduces intrapulmonary shunting, enhances oxygenation, and may decrease inflammatory markers during OLV [24]. Many studies support the individual benefits of the acupoints selected in our study: Feishu (Bladder Meridian) for regulating pulmonary function and ventilating the lungs [25,26], however, there is generally limited clinical evidence on the effects of combining all four of these acupoints. Our findings confirm that the acupoint combination of Feishu, Kongzui, Zusanli, and Hegu can improve ventilation/perfusion balance and oxygenation capacity during OLV, likely due to the complementary relationships between these meridians and their connections to pulmonary function. Regarding the physiological mechanisms underlying TAES (Group C), while the precise pathways remain unclear, two potential mechanisms have been identified: First, TAES may regulate the balance between endothelium-derived vasoconstrictors and vasodilators, which helps improve intrapulmonary shunting [19,27]. Second, TAES appears to enhance pulmonary function through activation of Aα and Aβ nerve fibers, providing protection against hypoxia-induced lung injury [24].

Thirdly, our study demonstrated that Group D (combined DEX abd TAES) demonstrated significantly better improvements in all measured parameters compared to both single-intervention groups, indicating a synergistic effect of the combined therapy. Additionally, although, Groups B

(DEX) and C (TAES) showed improvements compared to the control group, there were no significant differences between these two intervention groups. The physiological mechanisms underlying the superior efficacy of Group D (combined DEX abd TAES) may result from TAES enhancing DEX's effects by stimulating acupoints to increase endothelium-derived vasoconstrictor secretion, constricting collapsed-side pulmonary vessels, reducing blood flow to collapsed lung tissue, and further improving ventilation/perfusion imbalances [11,28].

Finally, regarding hemodynamic parameters, all four groups showed decreased HR, SBP, DBP, and MAP at timepoints T1-T4 compared to T0, but no significant differences were observed between groups at any timepoint. This lack of difference may be attributed to several factors: First, although DEX typically produces biphasic effects (initial hypertension with reflex bradycardia followed by stabilization below baseline [28]), we administered ephedrine and atropine to counteract DEX's sympatholytic effects that could cause intraoperative hypotension and bradycardia. Second, while TAES has been shown to bidirectionally regulate heart rate and reduce stress responses during lobectomy and endotracheal intubation, our use of vasoactive drugs likely masked these effects. Third, the combined therapy group showed no statistical differences compared to either the DEX or TAES groups, likely also due to vasoactive drug administration.

Our study has several important limitations to consider. First, our design included multiple groups with relatively small sample sizes, which, combined with numerous potential confounding factors, may have affected the reliability of our results. Second, we did not analyze patterns of vasoactive drug usage during anesthesia, which could have provided insights into whether TAES and DEX differently influenced hemodynamic parameters. Third, although our TAES protocol using Feishu, Kongzui, Hegu, and Zusanli acupoints showed benefits for intrapulmonary shunting during OLV, we still need additional research to identify the most effective acupoint combinations. Fourth, we did not measure changes in inflammatory mediators, which limited our understanding of how inflammation affects HPV in this context. Finally, the synergistic effects of combined DEX and TAES on intrapulmonary shunting and oxygenation during OLV under general anesthesia require further comprehensive investigation.

Conclusions

In conclusion, our study demonstrates that both dexmedetomidine and transcutaneous acupoint electrical stimulation individually improve intrapulmonary shunting and oxygenation during one-lung ventilation in thoracoscopic surgery, as evidenced by reduced Q_s/Q_t, increased OI, and decreased RI and A-aDO_2. Importantly, the combination therapy exhibits synergistic effects, providing superior improvement in these parameters compared to either intervention alone. This combined approach may represent an effective strategy for optimizing pulmonary function during OLV, potentially through enhanced HPV, reduced inflammation, and improved ventilation/perfusion matching.

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Abbreviations

The following abbreviations are used in this manuscript:

OLV	One-lung ventilation
TLV	Two-lung ventilation
TAES	Transcutaneous acupoint electrical stimulation
DEX	Dexmedetomidine
HPV	Hypoxic pulmonary vasoconstriction
PaO_2	Arterial oxygen partial pressure
OI	Oxygenation index
RI	Respiratory index
Q_s/Q_t	Intrapulmonary shunt fraction
A-aDO_2	Alveolar-arterial oxygen difference
ASA	American Society of Anesthesiologists
BMI	Body mass index
BIS	Bispectral index
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
MAP	Mean arterial pressure
HR	Heart rate
PCIA	Patient-controlled intravenous analgesia
FEV1	Forced expiratory volume in one second
FVC	Forced vital capacity

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