Am J Transl Res 2022;14(8):5915-5922
www.ajtr.org /ISSN:1943-8141/AJTR0136446

Original Article

Dexmedetomidine improved respiratory dynamics and arterial blood gas indices in patients with esophageal cancer after induction of anesthesia

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Received June 17, 2021; Accepted July 18, 2022; Epub August 15, 2022; Published August 30, 2022

Abstract: Objective: To retrospectively analyze the effects of dexmedetomidine after induction of anesthesia on intraoperative indices in patients with esophageal cancer. Methods: The clinical data of 93 patients with esophageal cancer that admitted to our hospital from January 2019 to December 2020 were retrospectively analyzed. The patients were divided into control group (n=31), case group A (n=31, continuous intravenous infusion of 0.3 μg/(kg·h) dexmedetomidine hydrochloride) and case group B (n=31, continuous intravenous infusion of 0.5 μg/(kg·h) dexmedetomidine hydrochloride) according to the application condition of dexmedetomidine hydrochloride. Heart rate, blood pressure, arterial blood gas indicators (all measured by blood gas analyzer), respiratory mechanics index (measured by mechanical ventilation), ephedrine and atropine utilization rate of the three groups were compared. Results: The plateau pressure, peak pressure and airway resistance at the end of one-lung ventilation and at chest closure in case groups A and B were lower than those in the control group, and the pulmonary compliance in case group B was higher than that in the control group ($P < 0.05$). PaO2, $P_{(A-a)}$O2, and RI before the start of OLV, at the end of OLV, and at chest closure in the three groups were significantly increased compared with those before induction of anesthesia ($P < 0.05$). Compared with the control group, PaO2 significantly increased, while $P_{(A-a)}$O2 and RI significantly decreased at the end of OLV and at chest closure in the case group B. Conclusion: Dexmedetomidine can improve respiratory dynamics and arterial blood gas indices after anesthesia induction of esophageal cancer, showing high safety and clinical feasibility.

Keywords: Esophageal cancer, dexmedetomidine, induction of anesthesia, dose, surgery, perioperative period

Introduction

Esophageal cancer mainly affects the elderly, most of whom have metabolic dysfunction, malnutrition, circulatory and respiratory comorbidities prior to surgical treatment. Coupled with the decline in the function of some organs and tissues, their tolerance of surgery and preoperative anesthesia will be reduced [1, 2]. Clinically, thoracotomy is used for the treatment of esophageal cancer. However, due to the severe trauma and complex procedures, the insertion of double-lumen tube can cause significant stimulation, pathological and physiological disorders. Meanwhile, patients maintain in lateral position, which affects the circulatory and respiratory system, significantly reducing the compliance and ventilation function of both lungs, easily leading to hypoxia, pneumonia, atelectasis, carbon dioxide accumulation, etc. In severe cases, systemic inflammatory response syndrome may occur, causing acute lung injury or respiratory distress syndrome, threatening the life safety of patients [3, 4]. In order to mitigate the adverse effects of one lung ventilation (OLV), for patients with esophageal cancer suitable for surgical indications, radical treatment is recommended, in which dexmedetomidine is commonly used as anesthesia induction [5, 6]. The severe fluctuation of hemodynamics during anesthesia induction can aggravate the imbalance of myocardial oxygen supply and demand in patients with coronary heart disease and significantly increase the risk of perioperative acute myocardial ischemia or myocardial infarction. Hypotension caused by circulatory inhibition of anesthetics reduces myocardial blood and oxygen supply, while hypertension and tachycardia caused by endotracheal intubation can significantly increase myocardial oxygen consumption. Previous studies have shown that intravenous dexmedetomidine prior to induction of anesthesia helps stabilize hemodynamics in patients undergoing coronary artery bypass grafting during induction of anesthesia. Other studies have shown that intravenous infusion of 0.25 μg/kg of dexmedetomidine prior to anesthesia induction is insufficient to resist the stress response induced by endotracheal intubation, while infusion of 1.0 μg/kg of dexmedetomidine can lead to a transient elevation of blood pressure, followed by an increased incidence of hypotension and bradycardia. Therefore, preoperative anesthesia is required, which is very necessary to improve the safety of anesthesia. Dexmedetomidine hydrochloride is a highly selective α2-adrenoceptor agonist that inhibits sympathetic activity and maintains hemodynamic stability, exerting sedative and analgesic effects. Multiple studies have shown that high concentrations of dexmedetomidine can cause high blood pressure and low heart rate. Both 0.3 μg/(kg·h) and 0.5 μg/(kg·h) are common clinical doses of dexmedetomidine, so the patients provided with these two concentrations were selected for this retrospective study [7, 8].

Dexmedetomidine hydrochloride is commonly used for postoperative sedation in patients with esophageal cancer [9, 10], and there are few clinical studies focusing on its application value in induction of anesthesia. Previous *in vitro* experimental studies have confirmed that intravenous infusion of dexmedetomidine hydrochloride before induction of anesthesia can improve perioperative blood gas status, but there are insufficient clinical studies to confirm this finding [11]. Based on this, this study specifically analyzed the effects of different doses of dexmedetomidine hydrochloride after the induction of anesthesia in 93 esophageal cancer patients underwent surgery, to understand the application value of dexmedetomidine hydrochloride before surgery and to provide clinical evidence for the application of dexmedetomidine hydrochloride after the induction of anesthesia.

Materials and methods

Case group

All patients diagnosed with esophageal cancer in Hainan Western Central Hospital from January 2019 to December 2020 and meeting the admission criteria were included. This study was conducted after being approved by the Ethics Committee of Hainan Western Central Hospital.

Inclusion criteria: 1). Patients who were continuously pumped intravenously with 0.3 μg/(kg·h) or 0.5 μg/(kg·h) dexmedetomidine hydrochloride after induction of anesthesia; 2). Patients with an age between 18 and 75 years; 3). Patients who were treated in our hospital and pathologically diagnosed as esophageal cancer after surgical resection.

Exclusion criteria: 1). Patients who received previous gastrointestinal surgery or esophagectomy; 2). Patients who received preoperative radiotherapy, chemotherapy or immunotherapy; 3). Patients with a previous history of malignant tumor; 4). Patients with a previous diagnosis of chronic hepatitis, alcoholic hepatitis, non-alcoholic fatty liver disease, drug hepatitis, autoimmune hepatitis, fatty liver, primary biliary cirrhosis (PBC), secondary sclerosing cholangitis, primary sclerosing cholangitis (PSC), or igG4-related sclerosing cholangitis (IgG4-SC); 5). Patients with inflammatory bowel disease; 6). Patients with incomplete clinical information.

Control group

Normal non-tumor esophageal patients hospitalized at the same time in Hainan Western Central Hospital were selected.

Inclusion criteria: 1). Patients who received no dexmedetomidine hydrochloride; 2). Patients with an age between 18 and 75 years; 3). Patients with concurrent diagnosis of non-esophageal cancer.

The exclusion criteria were the same as the case group.

Outcomes

The patient's general information, including medical history, serological indicators, tumor site, pathological stage, were collected.

(1) Baseline data: gender, age, BMI, intraoperative blood volume, operative time, duration of OLV, pathological type, tumor location, and TMN staging were recorded in the three groups.

(2) Medical history: Family history: first-degree relatives' history of esophageal cancer; Previous surgical history: history of biliary tract diseases (including cholecystectomy, gallbladder polyps, and gallstones), and appendectomy; History of chronic diseases: diabetes, hypertension, coronary heart disease, and thyroid disease (hypothyroidism, hyperthyroidism); Medication history: history of hypoglycemic drugs, history of antihypertensive drugs, history of aspirin, history of clopidogrel, and history of statins were recorded.

(3) Heart rate and blood pressure: 1 mL of radial artery blood was obtained before induction of anesthesia, before the start of OLV, at the end of OLV, at chest closure, and at 24 h after surgery, respectively. The systolic blood pressure, diastolic blood pressure, and heart rate were measured using a blood gas analyzer.

(4) Respiratory mechanics: plateau pressure, peak pressure, airway resistance, and lung compliance were measured by mechanical ventilation before the start of OLV, at the end of OLV, and at chest closure, respectively. Pulmonary compliance = VT/(PAWpeam-PEEP).

(5) Arterial blood gas indicators: partial pressure of oxygen (PaO2), alveolar-arterial oxygen gradient ($P_{(A-a)}O2$), and respiratory index (RI) before induction of anesthesia, before the start of OLV, at the end of OLV, at chest closure, and at 24 h after surgery were measured using blood gas analyzers in the three groups.

(6) Intraoperative drug consumption rate: the intraoperative consumption rate of ephedrine and atropine was compared among the three groups. Vasoactive drugs were used according to the following criteria: 1. The administration of intravascular vasoactive drugs should be started with small doses and concentrations, and vital signs such as blood pressure should be closely monitored. Invasive blood pressure monitoring can be used when necessary, and blood pressure can be dynamically and continuously monitored. 2. Extravasation of liquid medicine should be strictly prevented, and central venous infusion should be used when necessary. If there is local swelling and pain, the blood transfusion vessel should be replaced in time, and local procaine block should be given to prevent local necrosis if necessary. 3. Drug withdrawal should be achieved by slowing down the speed of drug infusion gradually to prevent adverse reactions. 4. Concentration and speed should be paid attention to when using vasoactive drugs. For the sake of safety, it is best to pump in with a micro pump, which is safer and more accurate. 5. It can be used in patients with systolic blood pressure > 110 mmHg. The treatment method was tested several times and the average result was taken.

Statistical methods

All data were analyzed using SPSS 23.0. Count data [n (%)] were tested by X^2. Measurement data were indicated by mean ± standard deviation (mean ± SD) with independent samples *t* test for comparison between groups, and paired t test for comparison before and after treatment. Multipoint comparisons were analyzed with ANVOA. Repeated measure ANOVA with LSD *post hoc* test were performed on repeated measurement data. Graphs were plotted with GraphPad Prism 8. $P < 0.05$ indicated significant difference.

Results

General information

There was no significant difference in gender, mean age, mean BMI, mean intraoperative blood volume, mean operative time, mean duration of OLV, ASA classification, pathological type, tumor location, and TMN staging among the three groups (all $P > 0.05$) (**Table 1**).

Heart rate and blood pressure

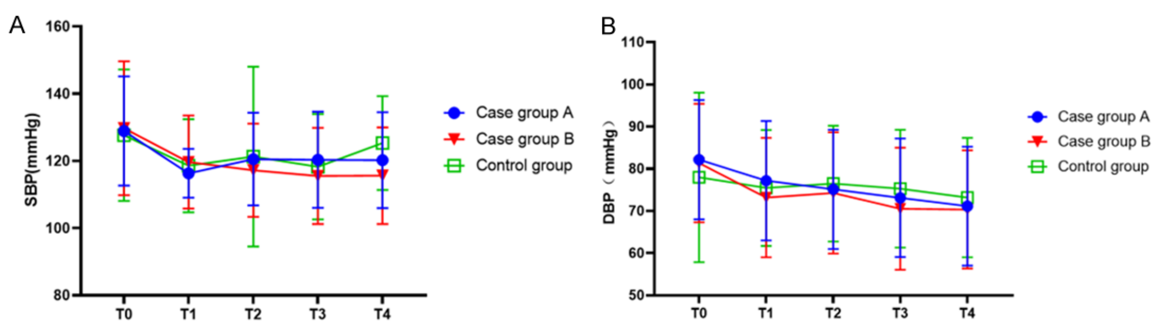
The systolic blood pressure, diastolic blood pressure, and heart rate did not change significantly before induction of anesthesia, before the start of OLV, at the end of OLV, at chest closure, and at 24 h after surgery within the same group (all $P > 0.05$), and no significant difference was found between groups at multiple time points (all $P > 0.05$) (**Figure 1**).

Respiratory mechanics

Intra-group comparison showed that there was no statistical significance in plateau pressure and airway resistance before the start of OLV,

Table 1. Comparison of baseline data (mean ± SD)/[n (%)]

Data		Case group A (n=31)	Case group B (n=31)	Control group (n=31)	*F*/X^2	*P*
Gender	Male	19 (61.29)	17 (54.84)	18 (58.06)	0.265	0.876
	Female	12 (38.71)	14 (45.16)	13 (41.94)		
Age (years)		64.12±13.18	65.83±14.75	64.53±14.12	0.125	0.883
BMI (kg/m^2)		22.13±1.67	22.09±1.72	22.16±1.59	0.014	0.986
Intraoperative bleeding (mL)		318.45±82.13	323.62±80.52	329.76±80.57	0.151	0.860
Operative time (min)		165.53±28.94	160.38±30.44	162.73±31.18	0.226	0.798
One-lung ventilation (min)		140.18±30.23	142.82±32.69	141.82±32.46	0.054	0.947
ASA Classification	Grade I	18 (58.06)	20 (64.52)	17 (54.84)	0.623	0.732
	Class II	13 (41.94)	11 (35.48)	14 (45.16)		
Pathological type	Squamous carcinoma	27 (87.10)	26 (83.87)	26 (83.87)	1.082	0.622
	Adenocarcinoma	2 (6.45)	3 (9.68)	2 (6.45)		
	Small cell carcinoma	2 (6.45)	1 (3.23)	2 (6.45)		
	Undifferentiated carcinoma	0 (0.00)	1 (3.23)	1 (3.23)		
Tumor location	Middle esophagus	25 (80.65)	23 (74.19)	24 (77.42)	1.234	0.527
	Lower esophagus	6 (19.35)	8 (25.81)	7 (22.58)		
TMN staging	T	10 (32.26)	12 (38.71)	11 (35.48)	0.189	0.116
	M	13 (41.94)	10 (32.26)	9 (29.03)		
	N	8 (25.81)	9 (29.03)	11 (35.49)		



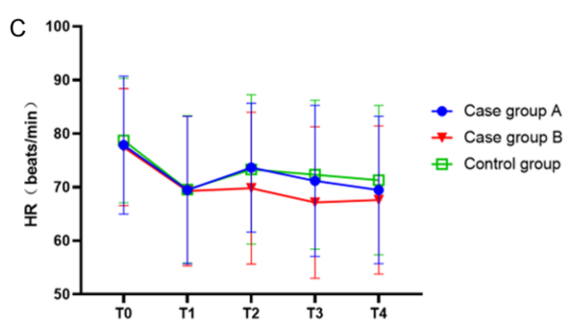


Figure 1. Comparison of blood pressure and heart rate among the three groups. No statistically significant differences were found in systolic blood pressure (A), diastolic blood pressure (B), and heart rate (C) levels before induction of anesthesia, before the start of one-lung ventilation, at the end of one-lung ventilation, at chest closure, and at 24 h after surgery among the case group A, case group B, and the control group ($P > 0.05$).

at the end of OLV, and at chest closure among the three groups ($P > 0.05$). There was no significant difference in peak pressure between case group A and control group ($P > 0.05$), while peak pressure in case group B was gradually decreased from the start of OLV, at the end of OLV, and at chest closure ($P < 0.05$). The lung compliance of case group A and control group was gradually decreased from the start of OLV, at the end of OLV, and at chest closure ($P < 0.05$), while that of case group B had no significance differences at these three time points ($P > 0.05$). Plateau pressure, peak pressure, and airway resistance at the end of OLV and at

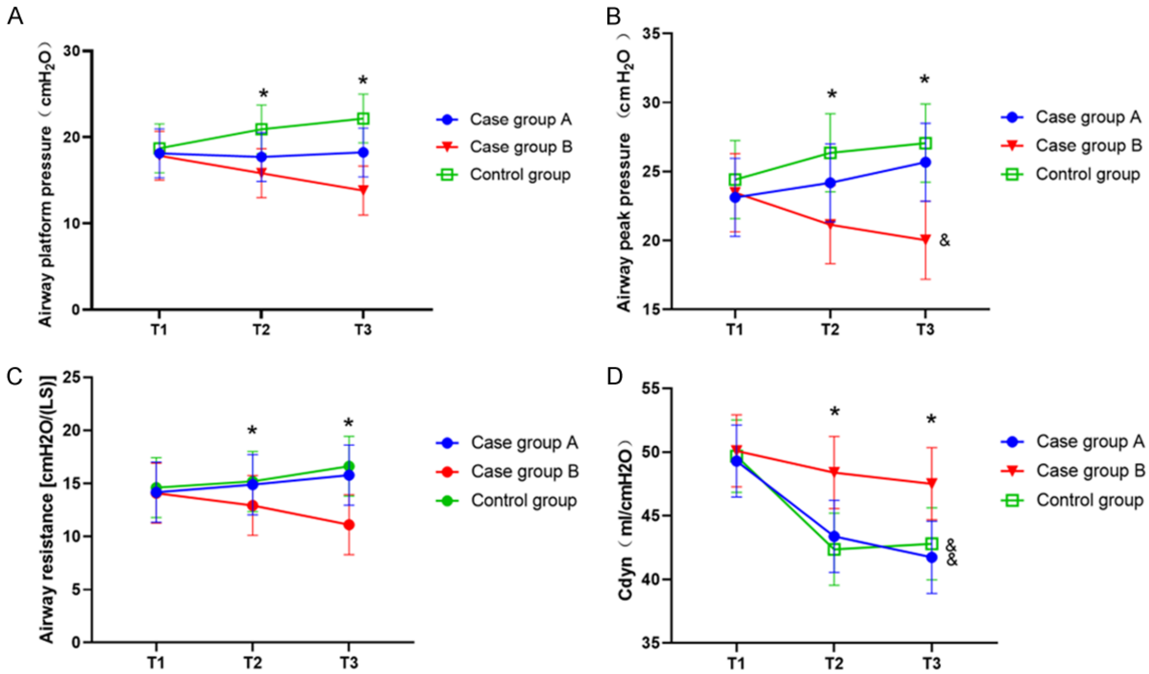


Figure 2. Comparison of respiratory mechanics. There was no significant difference in plateau pressure (A) and airway resistance (C) before the start of one-lung ventilation, at the end of one-lung ventilation, and at chest closure among the three groups ($P > 0.05$). There was no significant difference in peak pressure (B) between case group A and control group ($P > 0.05$), while peak pressure in case group B was gradually decreased from the start of OLV, at the end of OLV, and at chest closure ($P < 0.05$). The lung compliance (D) of case group A and control group before the start of OLV, at the end of OLV, and at chest closure was gradually decreased ($P < 0.05$), while that of case group B had no statistical significance at these three time points ($P > 0.05$). There was significant difference in plateau pressure, peak pressure, airway resistance, and pulmonary compliance among the three groups at the end of one-lung ventilation and at chest closure ($P < 0.05$). *$P < 0.05$ for comparison between groups; &$P < 0.05$ for intra-group comparison.

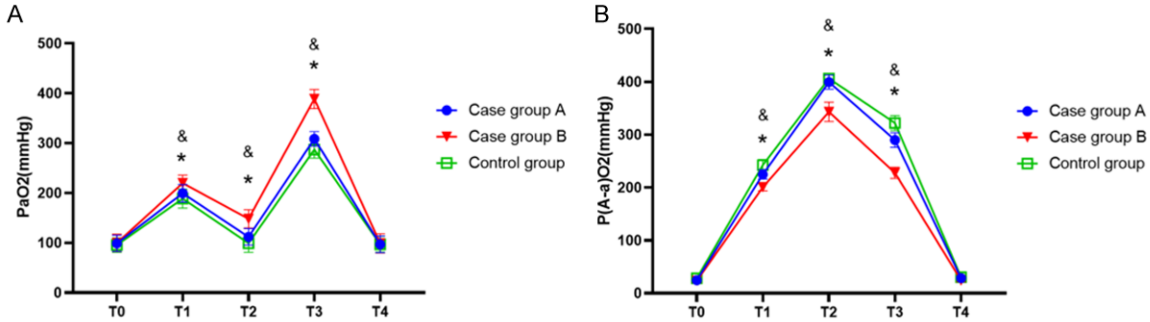
chest closure in the case groups A and B were lower than those in the control group, and lung compliance in the case group B was higher than that in the control group ($P < 0.05$). Plateau pressure, peak pressure, and airway resistance at the end of OLV and at chest closure were higher, whereas lung compliance was lower in the case group A than those in the case group B ($P < 0.05$) (**Figure 2**).

Arterial blood gas indicators

The difference in PaO2, $P_{(A-a)}$O2, and RI among the three groups before induction of anesthesia and at 24 h after surgery was not statistically significant ($P > 0.05$). Intragroup comparisons showed that PaO2, $P_{(A-a)}$O2, and RI before the start of OLV, at the end of OLV, and at chest closure in the three groups were significantly increased compared with those before induction of anesthesia ($P < 0.05$), and no statistically significant difference in PaO2, $P_{(A-a)}$O2, and RI at 24 h after surgery compared with those before induction of anesthesia ($P > 0.05$). The case group A and the control group showed no significant difference in PaO2, $P_{(A-a)}$O2, and RI at the end of OLV and at chest closure ($P > 0.05$), while compared with the control group, PaO2 significantly increased, and $P_{(A-a)}$O2 and RI significantly decreased at the end of OLV and at chest closure in the case group B ($P < 0.05$) (**Figure 3**).

Intraoperative drug consumption rate

There were 2 cases of intraoperative ephedrine consumption and 1 case of atropine consumption in the case group A, 3 cases of intraoperative ephedrine consumption and 4 cases of atropine consumption in the case group B, and 2 cases of intraoperative ephedrine consumption and 2 cases of atropine consumption in the control group ($P > 0.05$), exhibiting no significant difference in intraoperative drug consumption rate among the three groups (**Table 2**).



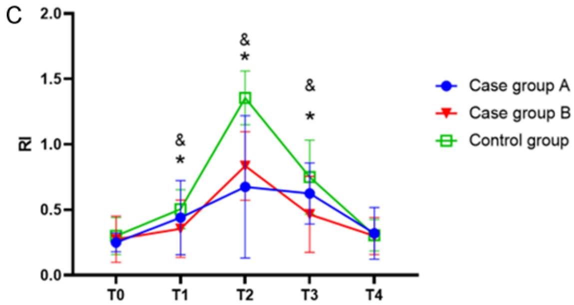


Figure 3. Comparison of arterial blood gas indices among the three groups. There was no significant difference in PaO2 (A), $P_{(A-a)}O2$ (B), and RI (C) before induction of anesthesia and at 24 h after surgery among the case group A, the case group B, and the control group ($P > 0.05$). PaO2, $P_{(A-a)}O2$, and RI were statistically different among the three groups before the start of one-lung ventilation, at the end of one-lung ventilation, and at chest closure ($P < 0.05$). *$P < 0.05$ for comparison between groups; &$P < 0.05$ for intra-group comparison.

Table 2. Comparison of intraoperative ephedrine and atropine consumption [n (%)]

Subgroup	Number of cases	Ephedrine consumption rate	Atropine consumption rate
Case group A	31	2 (6.45)	1 (3.23)
Case group B	31	3 (9.68)	2 (6.45)
Control group	31	2 (6.45)	4 (12.90)
X^2		0.309	2.163
P		0.857	0.339

Discussion

Dexmedetomidine hydrochloride is a highly selective α2A-adrenoceptor agonist, exerting sedative and hypnotic effects via the nucleus locus ceruleus [12]. The specific mechanism may be explained as follows. First, adenylate cyclase is inhibited through three effects mediated by G proteins, resulting in the reduction of intracellular cAMP aggregation and accelerating potassium ion efflux by activating potassium ion channels, thus achieving a membrane hyperpolarization shifts and generating postsynaptic inhibition [13, 14]. Second, dexmedetomidine hydrochloride can exert analgesic effects through the spinal cord because the drug acts on α2 adrenergic receptors on the presynaptic membrane of primary neurons and postsynaptic membrane of secondary neurons in the posterior horn of the spinal cord, activates the intracellular second messenger, opens the potassium channels, promotes cell membrane hyperpolarization, inhibits the elevation of intracellular calcium ions, and reduces substance P in primary neurons, making it difficult to generate action potentials in secondary neurons, and thus cutting off transmission of injurious information at synaptic sites [15-17]. It was found in clinical studies that dexmedetomidine hydrochloride significantly reduced the incidence of acute lung injury caused by hemorrhagic shock [18]. Clinical studies have reported that dexmedetomidine hydrochloride can significantly reduce the release of inflammatory factors in surgical patients [19]. Animal evidence showed that dexmedetomidine hydrochloride administration reduced lung permeability and improved hemodynamic stability in rats [20].

$P_{(A-a)}O2$ and RI are all indicators of pulmonary diffusion, which can predict lung damage more accurately, and intraoperative test showed that higher $P_{(A-a)}O2$ and RI indicated more severe lung injury [21]. Lung compliance is an indicator of lung tissue elasticity, and it has been found in clinical studies that influencing factors of lung compliance include loss of surface-active substances in the lungs, inactivation, pulmonary atelectasis, obstruction by secretions, bronchospasm, and pulmonary edema etc. [22] In patients with esophageal cancer undergoing thoracotomy, perioperative monitoring of pulmonary compliance is crucial for determining the patient's condition. The results of this study showed that PaO2, $P_{(A-a)}O2$ and RI levels increased and lung compliance decreased in the three groups during OLV. The control group had the largest fluctuation in each index, and the case group B had less fluctuation in each index compared with the case group A, and the fluctuations in the case groups A and B were smaller than those in the control group, indicating that the degree of lung function impairment after dexmedetomidine administration was improved while oxygen diffusion was less affected, decreasing the elasticity of lung tissue. Previous studies have also shown that the application of dexmedetomidine in anesthesia can significantly reduce the fluctuation range of arterial blood gas indicators compared with the patients without the application of dexmedetomidine [23], which is consistent with the finding of this study. This may be due to the anti-inflammatory effect of dexmedetomidine, which reduces the edema of lung tissue and the activity of lung surfactants, thus reducing lung compliance.

In this study, the difference in the levels of respiratory mechanics among the three groups at admission was not significant. After surgery, OLV and intensity of stimulation were increased, and the respiratory mechanics of patients gradually fluctuated due to the longer duration of surgery, indicating that all the three groups experienced oxygenation changes and stress reactions during the perioperative period, and the stress reactions became more pronounced as the surgery progressed. In this study, changes in plateau pressure, peak pressure, and airway resistance were observed in all the three groups before the start of OLV, at the end of OLV, and at chest closure. Plateau pressure, peak pressure, and airway resistance gradually increased in the control group and the case group A, but decreased in the case group B. At chest closure, plateau pressure, peak pressure, and airway resistance showed significant differences between the case group B and the other two groups, indicating that 0.5 μg/(kg·h) of dexmedetomidine stabilized the intraoperative respiratory mechanics more significantly. Other studies also indicated that there was no significant difference in plateau pressure at different time points of surgery in patients receiving dexmedetomidine hydrochloride during anesthesia induction, confirming that dexmedetomidine has no significant effect on the respiratory status of patients undergoing surgery [24]. This may be due to the fact that dexmedetomidine can reduce the activity of central sympathetic nervous system, inhibit the release of hormones such as norepinephrine, reduce the excitability of post-synaptic membrane, and reduce the stress of surgery, thereby reducing the influence on respiratory status.

In summary, dexmedetomidine hydrochloride can improve respiratory dynamics and arterial blood gas indices after induction of anesthesia in patients with esophageal cancer, with high safety and clinical feasibility. However, few indicators were analyzed in this study, and only two doses were compared, resulting in the lack of comprehensive and representative results. In addition, the research on the mechanism of action is not deep enough. For future research, indicators can be supplemented including total postoperative analgesic requirements, postoperative pain, perioperative inflammation, blood cell count, incidence of adverse events, and incidence of chronic pain, so as to further enrich the research content.

Disclosure of conflict of interest

None.

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