Original Article
Effects of anesthesia induction using dexmedetomidine in thoracoscopic pulmonary segmentectomy on the safety and protection of lung function

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Abstract: Objective: This study aimed to evaluate the effects of anesthesia induction using dexmedetomidine in thoracoscopic pulmonary segmentectomy in terms of safety and protection of lung function. Methods: A total of 76 patients were randomized into the control group (n = 38) and the observation group (n = 38) Anesthesia was induced in the observation group using dexmedetomidine. The intraoperative and postoperative data as well as complications were compared between the two groups. At the time of tracheal intubation (T0), 1 h after incubation (T1), and 30 min after extubation (T2) venous blood samples were extracted to determine the levels of cortisol (Cor) and angiotensin-II (A-II) using enzyme-linked immunosorbent assay. Moreover, the mean arterial pressure (MAP) and heart rate (HR) at T0, T1, and T2 were compared. On the 5th d after surgery, the visual analog scale (VAS) was used to evaluate pain in the two groups; lung function was also assessed and compared between the groups. Results: MAP and HR at T0 were different ($P < 0.05$) between the two groups. At T1 and T2, the observation group had lower Cor and A-II ($P < 0.05$) levels than the control group. Neither group showed a significant difference in postoperative VAS scores ($P > 0.05$) or forced vital capacity and forced expiratory volume in 1 second before treatment ($P > 0.05$). However, the lung function progressively deteriorated after the surgery ($P < 0.05$). The degradation was less severe in the observation group than in the control group ($P < 0.05$). Conclusions: The use of dexmedetomidine for inducing anesthesia in thoracoscopic pulmonary segmentectomy provides more safety and greater protection of lung function.

Keywords: Thoracoscopic pulmonary segmentectomy, dexmedetomidine, anesthesia induction, lung protection

Introduction

Lung cancer is an important public health concern worldwide [1]; it is the most common cancer in men, and the second most common cancer in women in China, with an approximate mortality of 45.80 per 100,000 individuals [2]. Surgery remains an important treatment approach for early-stage lung tumors [3], and pulmonary segmentectomy is commonly performed because of its advantages of rapid recovery, less trauma, and effective preservation of lung functions [4, 5]. However, surgical stress response is always expected during pulmonary segmentectomy and anesthesia administration [6], and tracheal intubation increases the risk associated with anesthesia. A study has found that difficulty in or failure of trachea intubation is one of the main causes of anesthesia-related mortality and incidence [7]. Long-term exposure to stress response damages the organs and increases the case fatality rate in critical patients [8]. Therefore, properly designed anesthesia administration has the potential to relieve patients from surgical stress response and increase the safety of surgical treatment [9].

Dexmedetomidine is a highly selective α-adrenergic agonist owing to its ability to provide sedation and nerve protection [10]. Clinically, the drug is mainly used for sedation, analgesia, or auxiliary sedation in anesthesia [11]. Zhang et al. [12] have suggested that the combination of dexmedetomidine and propofol in laparoscopic surgery can effectively inhibit intraoper-

ative stress, relieve postoperative pain and dysphoria, and improve the quality of postoperative recovery. However, Li et al. [13] have demonstrated that when total intravenous anesthesia is administered with dexmedetomidine, surgical stress response decreases to a level expected only in epidural anesthesia and general anesthesia without affecting the hemodynamic stability and with minimum intraoperative adverse reactions. Yang et al. [14] have reported that the administration of dexmedetomidine in the perioperative period has the potential to reduce the incidence of postoperative cognitive dysfunction and inflammation in patients who receive general anesthesia. Taken together, these findings support the role of dexmedetomidine in reducing the stress response. However, only few studies have reported on the effects of anesthesia induction using dexmedetomidine in thoracoscopic pulmonary segmentectomy in terms of safety and protection of lung function.

Thus, we designed this study to observe the effects of dexmedetomidine on anesthesia induction for thoracoscopic pulmonary segmentectomy, so as to provide important information that would be useful in the clinical setting.

Materials and methods

Clinical data of the patients

A total of 76 patients who underwent thoracoscopic pulmonary segmentectomy at the Department of Thoracic Surgery in our hospital from May 2014 to September 2017 were selected and included as the study subjects for this randomized controlled double-blinded study. The patients were numbered according to the order of admission. Patients with odd number of the admission order were administered dexmedetomidin-induced anesthesia as the observation group, whereas those with even number were not administered dexmedetomidin-induced anesthesia as the control group. This study was approved by the Ethics Committee of Hainan Western Central Hospital, and all the patients voluntarily signed the written informed consent forms. Our study adheres to the CONSORT guidelines.

Inclusion and exclusion criteria

Inclusion criteria: Patients who were indicated for thoracoscopic pulmonary segmentectomy

for the treatment of early-stage lung cancer; who were aged > 18 years; who physically qualified for surgery; whose complete clinical data were available; and who consented to follow-up were included.

Exclusion criteria: Patients who were allergic to the drugs used; who had cognitive impairment or deliration; who had concurrent infections or tumors; who had serious inflammation and immunological deficiency; who had congenital functional deficits of the liver, kidney, and heart before surgery; and who had received antihypertensive drugs, antibiotics or other surgeries within 3 months before surgery were excluded.

Test kits and drugs

Enzyme-linked immunosorbent assay (ELISA) test kits for cortisol (Cor) (UNSCNK, CEAO-67Ge-1), angiotensin-II (A-II) (Shanghai J&L Biological Co., Ltd., JL 10881), dexmedetomidine (Jiangsu Hengrui Medicine Co., Ltd., GYZ Zi H20090248), midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., GYZ Zi H10980025), sulfentanyl (Yichang Humanwell Pharmaceutical Co., Ltd., GYZ Zi H20054172), atracurium (SinoBiopharma[Jiangsu]Co.,Ltd.,GYZZiH2012-3332), etomidate (Jiangsu Nhwa Pharmaceutical Co., Ltd., GYZ Zi H32022999), and propofol (Hebei Yipin Pharmaceutical Co., Ltd., GYZ Zi H20093542) were used.

Anesthesia schedule

The anesthesia schedule was initiated with a 10-min pump injection of dexmedetomidine at a dose of 0.6 μg/kg for anesthesia induction along with an intravenous injection of midazolam at a dose of 0.03 mg/kg, sulfentanyl at a dose of 0.5 μg/kg, atracurium at a dose of 0.8 mg/kg, and etomidate at a dose of 0.5 mg/kg in the observation group; the control group received a pump injection of normal saline of equivalent amount for anesthesia induction, and intravenous injections of the same drugs at the same doses. After about 4-5 min, tracheal intubation was initiated, followed by connection of the anesthesia machine for nasal-continuous positive airway pressure treatment at a breathing rate of 8-12 times/min, a tidal volume of 8-12 mL/kg, and a respiratory ratio of 1:2. Both groups were intravenously transfused with midazolam at a dose of 0.05 mg/kg, sulfentanyl at a dose of 0.3 μg/(kg·min) and propofol at a dose of 5 mg/(kg·h) to maintain anesthesia. During the surgery, atracurium was

administered to maintain muscular relaxation. During tracheal extubation, the patients were provided with an oxygen mask against hyoxemia, atropine was administered via venous transfusion against bradycardia, ephedrine was administered via venous transfusion against low blood pressure, and urapidil was administered against high blood pressure.

Test method

8 mL of blood was collected from the cubital vein at the non-I.V.T. side at the time of tracheal intubation (T0), 1 h after intubation (T1), and 30 min after extubation (T2) and centrifuged for 10 min at 3000 rpm. The liquid supernatant was recollected to determine the Cor and A-II levels with ELISA in strict accordance with the manufacturer's instruction.

Observation indicators

The surgical indicators and postoperative recovery between the two groups were monitored and compared, and the adverse reactions (abnormal reactions after surgery that are not conducive to recovery), mean arterial pressure (MAP), heart rate (HR), Cor, and A-II levels were compared in the two groups at T0, T1, and T2. On the 5 d after surgery, the visual analog scale (VAS) scale was used to evaluate the pain in both groups [17]; the lung functions before and 5 d after surgery in both groups were also compared.

Statistical analysis

The collected data were statistically analyzed using the SPSS20.0 (SPSS Co., Ltd. in Chicago, the United States), a medical statistical analysis software, and plotted with GraphPad Prism 7 (Graphpad Software Co., Ltd. in San Diego, the United States). Nominal data are expressed as %, subjected to chi-square test, and designated as X^2; the measurement data are expressed as mean ± standard deviation (mean ± SD). One-factor ANOVA was applied for comparisons among the groups, and t-test was used for comparisons between two groups. $P <$ 0.05 indicated statistical significance.

Results

Clinical data of the subjects show no significantly difference between the two groups

The clinical data of the subjects such as sex, age, disease type, body mass index (BMI), his-

tory of smoking and excessive alcohol consumption, domicile, systolic blood pressure (SBP), diastolic blood pressure (DBP), hemoglobin, and blood sugar levels had no significantly difference between the two groups (P > 0.05), which was comparable (**Table 1**).

The propofol consumption in the observation group was lower than the control group

The patients in both the studyand the controlgroups were compared in terms of total operation time, anesthesia time, bleeding amount, and transfusion volume, and propofol consumption. Among them, the observation group exhibited no significant difference in total operation time, anesthesia time, bleeding amount, and transfusion volume than the control group (P > 0.05). However, the propofol consumption in the observation group was (623.71 ± 95.21) mg, which was lower than (745.34 ± 83.69) mg in the control group, showing statistical difference (P < 0.05) (**Table 2**).

The postoperative wake-up time of the observation group was significantly shorter than the control group

The patients in both the study and the control groups were compared in terms of surgery-related parameters such as tracheal extubation time, indwelling time of the intrathoracic drain, postoperative length of stay (LOS), and postoperative wake-up time. Among them, the observation group showed no significant difference in tracheal extubation time, indwelling time of the intrathoracic drain, postoperative LOS than the control group (*P* > 0.05). However, the postoperative wake-up time of the observation group was (4.89 ± 1.34) min, which was significantly shorter than (5.58 ± 1.57) min of the control group, indicating statistical difference (*P* < 0.05) (**Table 3**).

The incidence of complications showed no statistically significant difference between the two groups

In the observation group, the reported surgery-related complications included atelectasis (n = 1), nausea and vomiting (n = 1), sinus irregularity (n = 1), and low blood pressure (n = 2), the incidence of adverse reactions was 13.16% in the observation group and 10.52% in the control group, which showed no statistically significance (*P* > 0.05) (**Table 4**).

Table 1. Comparison of the general demographic characteristics of the observation and control groups (mean ± SD) or [n (%)]

	Observation group (n = 38)	Control group (n = 38)	X^2/t	P
Sex			0.053	0.818
Male	21 (55.26)	20 (52.63)		
Female	17 (44.74)	18 (47.37)		
Disease type			0.021	0.721
Small-cell lung cancer (SCLC)	2	3		
Non-small cell lung cancer (NSCLC)	36	35		
Age (years)	55.93 ± 11.14	55.64 ± 10.81	0.115	0.9086
BMI (kg/m^2)	23.21 ± 4.56	24.02 ± 4.78	0.755	0.452
History of smoking			0.216	0.642
Yes	23 (60.53)	21 (55.26)		
No	15 (39.47)	17 (44.74)		
History of alcohol consumption			0.474	0.491
Yes	17 (44.74)	20 (52.63)		
No	21 (55.26)	18 (47.37)		
Domicile			0.057	0.810
Urban	25 (65.79)	24 (63.16)		
Rural	13 (34.21)	14 (36.84)		
SBP (mmHg)	137.55 ± 22.12	140.65 ± 18.57	0.662	0.510
DBP (mmHg)	85.74 ± 15.35	86.58 ± 16.21	0.198	0.843
Hemoglobin (g/L)	119.11 ± 19.81	122.58 ± 21.07	0.739	0.462
Blood sugar (mmol/L)	5.83 ± 2.97	5.85 ± 2.54	0.031	0.974

Table 2. Comparison of the surgical parameters of the patients

Intraoperative indicator	Observation group (n = 38)	Control group (n = 38)	t	P
Total operation time (min)	141.55 ± 23.85	143.79 ± 22.07	0.424	0.672
Anesthesia time (min)	172.46 ± 25.61	170.19 ± 22.19	0.412	0.680
Amount of bleeding (mL)	194.36 ± 32.95	197.18 ± 34.86	0.362	0.718
Transfusion volume (mL)	1247.48 ± 24.42	1239.25 ± 29.15	1.334	0.186
Propofol consumption (mg)	623.71 ± 95.21	745.34 ± 83.69	5.915	< 0.05

Table 3. Comparison of postoperative recovery between the observation and control groups

| Intraoperative indicator	Observation group (n = 38)	Control group (n = 38)	t	P
Postoperative wake-up time (min)	4.89 ± 1.34	5.58 ± 1.57	2.061	0.042
Tracheal extubation time (min)	7.33 ± 1.38	7.71 ± 1.21	1.276	0.205
Indwelling time of intrathoracic drain (d)	4.58 ± 1.32	4.49 ± 1.39	0.289	0.773
Postoperative LOS (d)	9.95 ± 2.38	10.28 ± 2.65	0.571	0.569

Comparison of the MAP and HR was lower in the observation group than the control group

Both groups exhibited changes in MAP and HR. At T0, no significant difference was observed (P > 0.05). At T1, MAP was (98.18 ± 12.74) mmHg and HR was (84.48 ± 10.43) beats/min in the observation group, whereas these values were (104.18 ± 11.32) mmHg and (91.52 ± 9.48) beats/min, respectively, in the control group, which were increased compared with those at T0 (P < 0.05), but MAP and HR in the observation group were lower than those in the control group (P < 0.05). At T2, MAP was (94.35 ± 10.63) mmHg and HR was (81.67 ± 9.74) beats/min in the observation group, whereas these values were (99.91 ± 11.24) mmHg and (86.43.52 ± 8.66) beats/min, respectively, in

Table 4. Comparison of the incidence of complications between the observation and control groups

Complication	Observation group (n = 38)	Control group (n = 38)	t	P
Atelectasis	1	0		
Pulmonary infection	0	1		
Nausea and vomiting	1	1		
Low blood pressure	2	1		
Sinus irregularity	1	1		
Total incidence	5 (13.16)	4 (10.52)	0.126	0.722
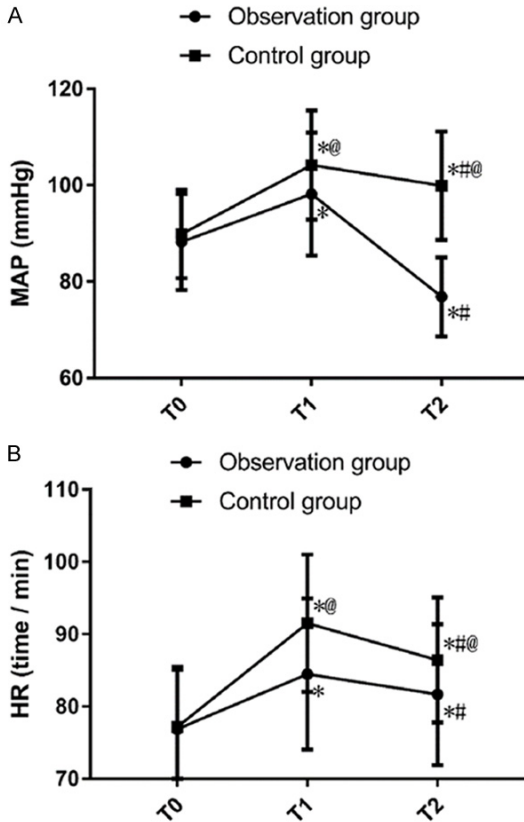
Figure 1. Comparison of MAP and HR between the observation and control groups. * indicates that compared with T0 in the same group, P < 0.05; # indicates that compared with T1 in the same group, P < 0.05; @ indicates that compared with the observation group at the same time, P < 0.05.

the control group, which were decreased compared with T1 ($P < 0.05$); MAP and HR in the observation group were lower than those in the control group ($P < 0.05$) (**Figure 1**).

The Cor and A-II levels in the observation group were lower than the control group

The patients' Cor and A-II levels were compared in the two groups. At T0, no statistical differ-

ence was observed ($P > 0.05$). At T1, Cor and A-11 levels were increased compared with those at T0 in both groups ($P < 0.05$), and Cor and A-II levels in the observation group were lower than those in the control group ($P < 0.05$). At T2, Cor and A-II levels were decreased compared with those at T1 in both groups (P < 0.05), and Cor and A-II levels in the observation group were lower than those in the control group ($P < 0.05$) (**Table 5**).

The severity of pain showed no statistically significant difference between the two groups

The postoperative VAS score was (1.87 ± 0.59) in the observation group and (1.82 ± 0.45) in the control group, indicating no statistical difference ($P > 0.05$) (**Figure 2**).

The FVC and FEV1 in the observation group were higher than those in the control group

There was no significant difference in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) between the two groups before treatment ($P > 0.05$). On the 5 d after surgery, FVC and FEV1 were decreased in both groups compared with those before surgery (P < 0.05), whereas FVC and FEV1 in the observation group were higher than those in the control group ($P < 0.05$) (**Table 6**).

Discussion

Surgical stress response is often expected in surgery [15], causing hemodynamics and neuroendocrine changes as well as inflammation and immune reactions [16]. As an adrenergic receptor agonist, dexmedetomidine inhibits the activity of the autonomic nerves and reduces hemodynamic response [17]. Shen et al. [18] have reported that dexmedetomidine hydrochloride can effectively block the oxidative stress and inflammatory response of Kupffer

Table 5. Changes in the Cor and A-II levels between the observation and control groups

Group	Cor (nmol/L)			A-II (ng/dL)		
	T0	T1	T2	T0	T1	T2
Observation group (n = 38)	219.75 ± 48.15	268.54 ± 78.14*	255.68 ± 75.58*,#	41.35 ± 10.05	58.44 ± 11.73*	48.51 ± 16.27*,#
Control group (n = 38)	228.71 ± 53.98	352.61 ± 96.45*,A	314.12 ± 86.47*,#,A	42.06 ± 11.32	65.38 ± 15.40*,A	59.29 ± 11.97*,#,A
t	0.763	4.175	33.137	0.289	2.210	3.291
P	0.447	< 0.05	< 0.05	0.772	< 0.05	< 0.05

Note: * indicates difference as compared with T0, # with T1, and A with the observation group at the same time point.
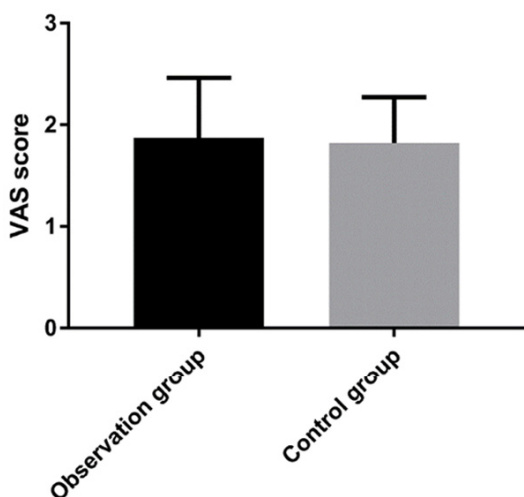
Figure 2. Comparison in the severity of pain between the observation and control groups. No significant difference (P > 0.05) was identified in postoperative VAS scores between the two groups.

cells by activating α (2)-adrenergic receptor. In this study, dexmedetomidine was administered for anesthesia induction to patients undergoing thoracoscopic pulmonary segmentectomy to evaluate its safety and protective effect on lung function, so as to provide a clinical reference.

First, a comparison of the surgical parameters between the two groups showed significant differences in propofol consumption and postoperative wake-up time ($P < 0.05$) after the administration of anesthesia, which is consistent with the findings previously reported by Georgia et al. [19] who used dexmedetomidine to treat patients and observed a significant reduction in propofol and morphine effects of opioids. A comparison of MAR and HR at T0, T1, and T2 showed no significant difference between the two groups at T1, but a significant increase at T1 and T2, with the observation group exhibiting lower values than the control group ($P < 0.05$). This could be attributed to the effect of dexmedetomidine in reducing the stress response of patients during surgery. Prosad et

al. [20] have compared the effects of dexmedetomidine and esmolol on perioperative hemodynamics in patients underwent laparoscopic cholecystectomy and found that dexmedetomidine has the potential to effectively reduce the increasing MAP and HR during and after pneumoperitoneum and provide hemodynamic stability during laparoscopic surgery, which is consistent with our findings.

Changes in Cor and A-II levels indicate stress response during the surgery [21-23]. In this study, a comparison of the changes in Cor and A-II levels between the two groups showed no significant difference before intubation, but a significant increase during the surgery, with the observation group exhibiting lower values than the control group. This could be attributed to the role of dexmedetomidine in reducing the Cor and A-II levels that were elevated due to surgical stress response. It is assumed that dexmedetomidine is capable of regulating the stress response [24] during surgery by reducing the arterenol released via stimulation of the α-2-adrenergic receptor on the presynaptic membrane. Here, the two groups were compared for adverse reactions and the postoperative VAS scores; no significant difference was found in the incidence of adverse reactions or postoperative VAS scores. However, adverse reactions of low blood pressure were reported in two patients in the observation group during the treatment, which is consistent with the findings reported by Wang [25] and Okello et al. [26] regarding the I.V. of dexmedetomidine. Finally, lung function that was deteriorated in both groups was compared and the deterioration in the observation group was found to be less serious than that in the control group ($P < 0.05$), indicating a protective role of dexmedetomidine in lung function when used for anesthesia induction in thoracoscopic pulmonary segmentectomy. This is consistent with the findings reported by Guo et al. wherein 124 patients with lung cancer underwent radical

Table 6. Comparison of lung functions before and after treatment between the observation and control groups

Group	FVC%				FEVI%			
	Before surgery	5 d after surgery	t	P	Before surgery	5 d after surgery	t	P
Observation group (n = 38)	98.28 ± 11.34	87.23 ± 10.38	4.431	< 0.001	95.39 ± 10.37	86.37 ± 9.48	3.957	< 0.001
Control group (n = 38)	97.48 ± 12.49	81.47 ± 9.18	6.367	< 0.001	94.47 ± 11.63	79.41 ± 9.92	6.073	< 0.001
t	0.292	2.562			0.364	3.127		
P	0.770	0.012			0.716	0.002		

surgery [27] under anesthesia induced using dexmedetomidine and Gao [28] and Gu et al. [29] who reported the role of dexmedetomidine in reducing lung injury. Jiang et al. [30] found that the protective role of dexmedetomidine in lung function is associated with the TLR4/My D88/MAPK signal channel.

The present study had certain limitations. All the patients were Asian, and the sample size was relatively small; these limitations may lead to biased results. When comparing the incidence of adverse reactions between the two groups, the fact that the experimental results may be caused by the randomness of the sample size was not ruled out. More large-scale studies are warranted to explore the efficacy of the drug in patients from different geographical regions and ethnicities. Further, more correlated tests are required to confirm the safety and protection of lung function with the use of dexmedetomidine for inducing anesthesia in thoracoscopic pulmonary segmentectomy.

In conclusion, our study showed that dexmedetomidine is beneficial in terms of enhancing the safety and protection of lung function to a certain degree when used for inducing anesthesia in thoracoscopic pulmonary segmentectomy

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Disclosure of conflict of interest

None.

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