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Original Article

Analysis of respiratory failure after lung cancer operation and efficacy of ventilator-assisted ventilation

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Abstract: Background: Surgery remains the main way to treat lung cancer. However, failure after lung cancer operation impedes the prognosis. This study aims to explore the clinical value of ventilator-assisted respiration. Methods: A total of 58 patients diagnosed with lung cancer, complicated with respiratory failure after operation in Ningbo Medical Center Lihuili Eastern Hospital from August 2015 to August 2016 were enrolled as observation group, and they were randomly divided into a conventional group (n=29) and a ventilator group (n=29) according to whether a ventilator was applied. The patients in the observation group were all treated with routine treatment, while patients in the ventilator group were additionally treated with ventilator-assisted respiration. Another 90 patients without respiratory failure after lung cancer operation during the same period were enrolled as the control group. The general data were collected and the risk factors for respiratory failure were analyzed via multivariate analysis. Moreover, the blood gas, oxygen metabolism and pulmonary function indexes were analyzed and compared between groups at different time points before and after treatment. Results: The comparison of general data between the observation and control groups showed an increases in age, smoking rate, COPD, preoperative pulmonary function, Lobectomy, colloid infusion amount, intraoperative bleeding amount and postoperative complications were significantly implicated to the occurrence and development of lung cancer and function as risk factors for respiratory failure after lung cancer operation ($P<0.05$). The levels of PaO_2, BE, $ScvO_2$, PvO_2, $CERO_2$, MVV, MMF and PEmax were significantly elevated in the ventilator group compared to that in the conventional group, along with statisitical reduction of $PaCO_2$, at 48 h post treatment ($P<0.05$). Conclusion: Our data demonstrate that timely ventilator-assisted respiration has a positive effect in improving the patient's respiratory status, highlighting its necessity to enhance perioperative management and avoid postoperative complications.

Keywords: Lung cancer, respiratory failure, ventilator-assisted respiration, multivariate analysis

Introduction

According to an epidemiological survey, the 5-year (2006-2011) prevalence rate of lung cancer in China was 130.2 (1/100,000), and both morbidity and mortality rates show increasing trends throughout the world. In particular, lung cancer imposes increasingly greater burden in developing countries [1-3]. Currently, the main clinical method to cure lung cancer is still operative treatment [4]. It has been demonstrated that the incidence rate of respiratory failure, the most common severe perioperative complication [7], fluctuates between 4.7% and 7.9% after lung cancer operation [5, 6], and it is characterized by intractable treatment and has a high fatality rate. The clinical efficacy of ventilator-assisted respiration has been recognized in the treatment of respiratory failure after lung cancer operation [8]. In this paper, we evaluated the clinical value of ventilator-assisted respiration in after lung cancer after operation by analyzing the risk factors for respiratory failure as well as functional indexes.

Patients and methods

Clinical data

A total of 58 patients diagnosed with lung cancer complicated with respiratory failure after operation in Ningbo Medical Center Lihuili Eastern Hospital from August 2015 to August

2016 were enrolled as an observation group, and they were randomly divided into a conventional group (n=29) and a ventilator group (n=29) according to the application of a ventilator. The patients in the conventional group were only treated with routine treatment, while those in the ventilator group were further treated with ventilator-assisted respiration assistance in addition to the routine treatment. Another 90 patients without respiratory failure after lung cancer operation in the same hospital during the same period were enrolled as control group. The diagnostic criteria for lung cancer and respiratory failure in all patients were in line with the *Standards for the Diagnosis and Treatment of Primary Lung Cancer (2015 version) in China* [4]. The inclusion criteria were patients who had pneumonectomy, malignant tumor surgery for the lung (thoracotomy), or thoracoscopic surgery. The exclusion criteria included death from lung cancer before the surgery, a lung transplantation, suspected diagnosis, and pneumonia within 3 months before being diagnosed with lung cancer. Respiratory disease was defined as pneumonia. Exclusion criteria: Age younger than 18 years, pneumonectomy, sleeve lobectomy, chest wall or diaphragm resection, or bilateral procedures. This study was ethically reviewed by Ningbo Medical Center Lihuili Eastern Hospital, and the patients were informed and signed a consent form.

Collection of general clinical data of patients

The following data were recorded: gender, age, smoking status, previous history of chronic obstructive pulmonary disease (COPD), tumor site (left and right sides), degree of preoperative pulmonary dysfunction [normal and mild dysfunction: forced expiratory volume in 1 s (FEV1)=60-69%, moderate dysfunction: FEV1 =40-59%, and severe dysfunction: FEV1<40%] [9], operation time, lesion size, operation method (total pneumonectomy and partial lobectomy), colloid infusion amount (>1000 mL and ≤1000 mL), intraoperative bleeding amount (>800 mL and ≤800 mL) and severe postoperative complications.

Treatment methods

The patients in the conventional group were treated with routine treatment, including oxygen inhalation, sputum suction, anti-infection, spasmolysis and relief of asthma. The patients in the ventilator group, were additionally treated with ventilator-assisted respiration, and the non-invasive positive pressure-assisted ventilation via face mask was performed (oxygen flow rate: 8-10 L/min, tidal volume: 8-12 mL/kg, inspiratory pressure: 8-16 cm H_2O and expiratory pressure: 4-8 cm H_2O, 1 cm H_2O=0.098 kPa).

Observation indexes

Blood was drawn from the 58 patients in the observation group before treatment and at 48 h after treatment, and then the following items were detected: blood gas indexes, including arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$) and base excess (BE), oxygen metabolism indexes, including central venous oxygen saturation ($ScvO_2$), mixed partial venous oxygen pressure (PvO_2) and cerebral oxygen extraction rate ($CERO_2$), and pulmonary function indexes, including maximal voluntary ventilation (MVV), maximal mid-expiratory flow velocity (MMF) and maximal expiratory pressure (PEmax). PaO_2, $PaCO_2$, BE, $ScvO_2$, PvO_2 and $CERO_2$ were detected using a full-automatic blood gas analyzer, and MVV, MMF and PEmax were detected using a pulmonary function tester.

Statistical methods

SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical processing. Enumeration data were expressed as ($\bar{x}$ ± s), and *t* test and chi-square test were adopted for statistical analysis. The risk factors and independent risk factors for respiratory failure after lung cancer operation were analyzed via univariate and multivariate Logistic regression analysis. P<0.05 suggested that the results had statistical differences.

Results

Comparisons of general data between the observation group and control group

In a comparison between the observation and control groups, significant differences in an increase of age, smoking rate, COPD, preoperative pulmonary function, operation time,

Table 1. Comparisons of general data between the observation group and control group ($\overline{x}$ ± s, n, %)

General data	Observation group (n=59)	Control group (n=90)	χ^2/*t*	*p*
Gender				
Male/female	49/10	76/14	2.835	0.076
Age (years old)	65.12 ± 10.23	59.14 ± 11.35	3.158	0.002
Smoking (n)			15.146	0.000
Yes	41	56		
No	19	34		
COPD (n)			7.102	0.008
Yes	17	11		
No	42	79		
Tumor site (n)			0.342	0.528
Left	21	26		
Right	38	64		
Preoperative pulmonary dysfunction (n)			7.592	0.040
Normal	24	49		
Mild dysfunction	20	19		
Moderate dysfunction	11	9		
Severe dysfunction	4	13		
Operation time (min)	188.42 ± 72.25	170.74 ± 38.92	2.046	0.039
Lesion size (cm)	5.28 ± 2.50	4.87 ± 1.96	1.178	0.093
Operation method (n)			25.47	0.000
Total pneumonectomy	25	71		
Lobectomy	34	19		
Colloid infusion amount			6.214	0.026
>1000	26	31		
≤1000	33	59		
Intraoperative bleeding amount			5.910	0.031
>800	28	29		
≤800	31	61		
Postoperative complications			17.436	0.000
Yes	21	22		
No	38	68		

Lobectomy, colloid infusion amount, intraoperative bleeding amount and postoperative complications led to the occurrence and development of lung cancer (P<0.05). There were no statistically significant differences in gender, tumor sites, and lesion sites between the two groups (P>0.05) (**Table 1**).

Univariate analysis of respiratory failure after lung cancer operation

According to the univariate analysis, the age, smoking, previous history of COPD, degree of preoperative pulmonary dysfunction, operation method, colloid infusion amount >2500 mL and severe postoperative complications were found as significant risk factors for respiratory failure after lung cancer operation (P<0.05). Besides, the gender, tumor site, operation time, lesion size and intraoperative bleeding amount had no significant differences (P>0.05) (**Table 2**).

Multivariate analysis of respiratory failure after lung cancer operation

The Logistic regression analysis was performed with the statistically different indexes in the univariate analysis as independent variables and the respiratory failure after lung cancer operation as the outcome variable. It was found that the age, degree of preoperative pulmonary

Table 2. Univariate analysis of respiratory failure after lung cancer operation

Independent variable		χ^2/t	P
Gender	Male	0.815	0.367
	Female		
Age (years old)	>65	10.510	0.003
	≤65		
Smoking (n)	Yes	5.642	0.021
	No		
Concurrent COPD (n)	Yes	6.471	0.015
	No		
Tumor site (n)	Left	1.023	0.324
	Right		
Preoperative pulmonary dysfunction (n)	Normal	5.127	0.026
	Mild dysfunction		
	Moderate dysfunction		
	Severe dysfunction		
Operation time (min)	>180	1.810	0.195
	≤180		
Lesion size (cm)	>5	1.589	0.268
	≤5		
Operation method (n)	Total pneumonectomy	6.718	0.012
	Lobectomy		
Colloid infusion amount	>1000	4.624	0.029
	≤1000		
Intraoperative bleeding amount	>800	1.762	0.212
	≤800		
Postoperative complications	Yes	7.438	0.009
	No		

dysfunction, colloid infusion amount >2500 mL, total pneumonectomy and severe postoperative complications were high-risk factors for respiratory failure after lung cancer operation (**Table 3**).

Comparisons of blood gas indexes between conventional group and ventilator group at different time points before and after treatment

There were no statistically significant differences in PaO_2, $PaCO_2$ and BE between conventional group and ventilator group before treatment [(92.38 ± 0.102) vs. (92.21 ± 0.98) mmHg, (41.96 ± 1.12) vs. (42.03 ± 1.13) mmHg, (-1.01 ± 0.07) vs. (-0.99 ± 0.08) mmol/L] ($P>0.05$). At 48 h after treatment, the above indexes were obviously improved in both groups compared with those before treatment, and the improvement was significantly greater in the ventilator group compared to that in the conventional group [(95.07 ± 0.97) vs. (98.53 ± 0.104) mmHg, (39.41 ± 0.85) vs. (37.28 ± 0.82) mmHg, (0.13 ± 0.04) vs. (0.60 ± 0.05) mmol/L] (P<0.05) (**Figure 1**).

Comparisons of oxygen metabolism indexes between the conventional group and ventilator group at different time points before and after treatment

There were no statistically significant differences in $ScvO_2$, PvO_2 and $CERO_2$ between the conventional group and ventilator group before treatment [(60.01 ± 3.38) vs. (59.98 ± 3.40)%, (4.06 ± 0.29) vs. (4.05 ± 0.30) kPa, (31.12 ± 2.76) vs. (31.15 ± 2.74)%] ($P>0.05$). However, at 48 h after treatment, the above indexes were clearly improved in both groups compared with those before treatment, and the additional treatment of the ventilation significantly improved oxygen metabolism indexes (P<0.05) (**Figure 2**).

Table 3. Multivariate analysis of respiratory failure after lung cancer operation

Variable	Regression coefficient	Standard error	Wald	p	OR	95% CI
Age	1.843	0.512	14.074	0.000	6.310	2.102-18.915
Smoking	0.526	0.531	0.934	0.317	1.581	0.687-5.013
Previous history of COPD	1.425	0.827	3.058	0.085	4.162	0.824-20.376
Preoperative pulmonary dysfunction	2.105	0.756	10.259	0.008	9.125	1.826-85.134
Total pneumonectomy	2.114	0.637	10.125	0.002	7.759	2.704-24.536
Colloid infusion amount >2500 mL	1.803	0.579	8.765	0.004	5.746	1.358-15.627
Severe postoperative complications	2.118	0.601	13.146	0.000	7.163	2.354-22.346

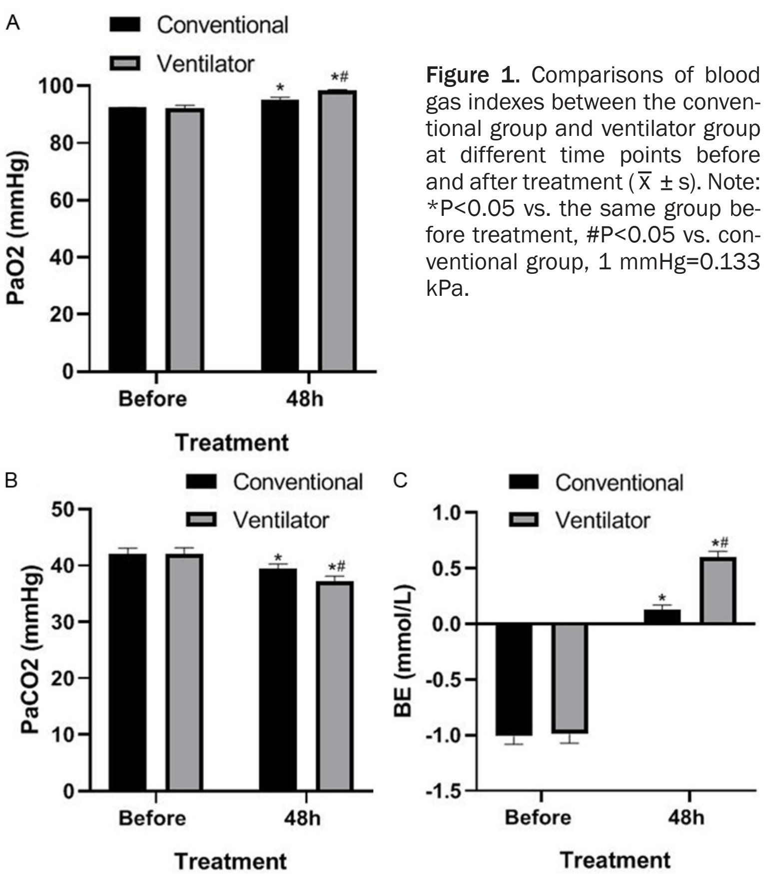

Figure 1. Comparisons of blood gas indexes between the conventional group and ventilator group at different time points before and after treatment ($\overline{x}$ ± s). Note: *P<0.05 vs. the same group before treatment, #P<0.05 vs. conventional group, 1 mmHg=0.133 kPa.

Comparisons of pulmonary function indexes between the conventional group and ventilator group at different time points before and after treatment

MVV, MMF and PEmax had no statistically significant differences between the conventional group and ventilator group before treatment [(42.15 ± 3.68) vs. (42.13 ± 3.71) L/min, (0.76 ± 0.07) vs. (0.78 ± 0.05) L/s, (31.34 ± 2.21) vs. (31.30 ± 2.20) %] (P>0.05). At 48 h after treatment, the above indexes were statistically increased in both groups compared with those before treatment (P<0.05). Moreover, the values of MVV, MMF and PEmax were significantly better in the ventilator group compared to those in conventional group [(52.97 ± 4.16) vs. (61.04 ± 4.27) L/min, (1.33 ± 0.11) vs. (1.71 ± 0.16) L/s, (43.09 ± 3.15) vs. (48.67 ± 3.43)%] (P<0.05) (**Table 4**).

Discussion

Respiratory failure is the most common severe complication after lung cancer operation; which is characterized by intractable treatment and a high fatality rate, seriously threatening the health of patients and bringing great economic burden. In the present study, the age, degree of preoperative pulmonary dysfunction, colloid infusion amount >2500 mL, total pnemonectomy and severe postoperative complications were high-risk factors of respiratory failure after lung cancer operation. Respiratory failure after lung cancer operation is associated with the combined action of multiple factors. The results also confirmed that increased smoking rate, concurrent COPD, operation time, intraoperative bleeding amount in the observation group were greater compared to those in control group. The surgical risk of lung cancer patients with low pulmonary function is far higher than that of patients with normal pulmonary function, and the incidence

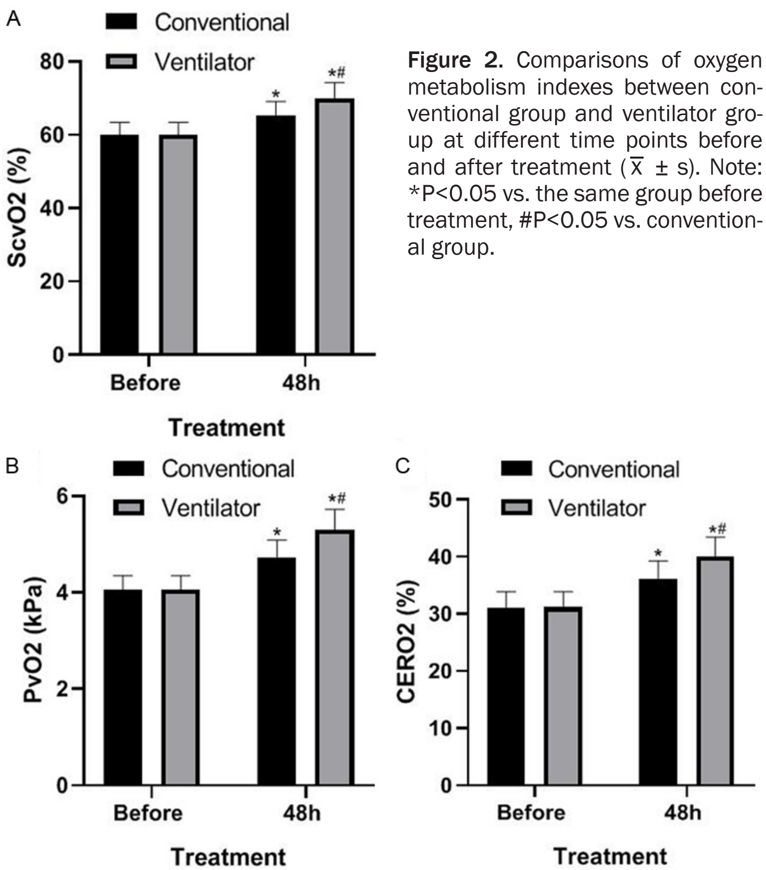

Figure 2. Comparisons of oxygen metabolism indexes between conventional group and ventilator group at different time points before and after treatment ($\overline{x} \pm s$). Note: *P<0.05 vs. the same group before treatment, #P<0.05 vs. conventional group.

rate of postoperative respiratory failure is dramatically increased [10]. With the improvement in medical technology, the postoperative survival rate of elderly patients with lung cancer has been greatly increased, and operative treatment can be actively performed for eligible patients. With the increase of age, however, the surgical risk is also relatively increased. Elderly patients who are long-term smokers and have had COPD in the past, their airway secretion retention occurs easily after operation, their organ function declines in varying degrees, and their oxygen exchange area is reduced, leading to pulmonary insufficiency and respiratory failure, more easily. The large-volume and rapid intravenous infusion during and after lung cancer operation aggravates the cardiopulmonary burden and easily results in respiratory decompensation. Previous study suggested that thoracotomy is not suitable if FEV1 is less than 60% and MVV is less than 35 L/min [11]. It has been proposed that FFV1 should be greater than 0.9 L, 1.2 L and 1.7 L in pulmonary wedge resection, lobectomy and total pneumonectomy, respectively [12]. Moreover, previous findings indicated that lobectomy is not suitable if MVV is less than 0 L/min or if FEV1 is less than 0.8 L [13]. For patients with poor cardiopulmonary function, total pneumonectomy should be cautiously adopted, and lobectomy should be performed in a simple way, rather than a complicated way.

The blood gas indexes, oxygen metabolism indexes and pulmonary function indexes are important factors for evaluation of therapeutic effect [14]. At present, the grading of pulmonary dysfunction is mainly analyzed based on FEV and FEV1. MVV mainly indicates the pulmonary ventilation function reserve, and reflects the elasticity of lung tissues and airway resistance [15]. In the present study, PaO_2, $PaCO_2$, BE, $ScvO_2$, PvO_2, $CERO_2$, MVV, MMF and PEmax were markedly elevated in the conventional group and ventilator group at 48 h after treatment compared with those before treatment, and the increased levels were significant and evident in the ventilator group (*P*<0.05), suggesting that patients with lung cancer have improved after application of ventilator-assisted respiration [16]. Early diagnosis and intervention with ventilator-assisted respiration are essential for patients with respiratory failure after lung cancer operation, which can avoid vital organ damage caused by long-term severe hypoxia and carbon dioxide retention. The traditional positive pressure ventilation with large tidal volume and low respiratory rate easily induces ventilator-associated lung injury. It has been demonstrated that the high alveolar transmural pressure and excessive alveolar volume are the direct determinants of lung injury [17]. According to another study, lung injury can also be aggravated by hyperpnea (>25-30/min) [18]. In recent years, the ventilation strategy of correcting the high airway pressure and large tidal volume limits the high alveolar transmural pressure and large alveolar volume that can not only ensure effective ventilation but

Table 4. Comparisons of pulmonary function indexes between the conventional group and ventilator group at different time points before and after treatment ($\bar{x} \pm s$)

Group	MVV (L/min)	MMF (L/s)	PEmax (%)
Conventional group (n=29)			
Before treatment	42.15 ± 3.68	0.76 ± 0.07	31.34 ± 2.21
48 h after treatment	52.97 ± 4.16*	1.33 ± 0.11*	43.09 ± 3.15*
Ventilator group (n=29)			
Before treatment	42.13 ± 3.71	0.78 ± 0.05	31.30 ± 2.20
48 h after treatment	61.04 ± 4.27*,#	1.71 ± 0.16*,#	48.67 ± 3.43*,#

Note: *P<0.05 vs. the same group before treatment, #P<0.05 vs. conventional group.

also reduce or even avoid lung injury [19]. In this study, the oxygen flow rate was set at 8-10 L/min, tidal volume at 8-12 mL/kg, inspiratory pressure at 8-16 cm H_2O and expiratory pressure at 4-8 cm H_2O. It is believed that the non-invasive ventilation does not affect the progression of disease before the deterioration of disease, but is significant in alleviating clinical symptoms. The indications for non-invasive ventilation need to be paid attention to [20]. The limitation in the study exists that the clinical efficacy of Ventilator-Assisted respiration on the long-term prognosis still requires further validation with a larger amont of patients with lung cancer.

Conclusion

In conclusion, our data demonstrate the promising effect of timely ventilator-assisted respiration improving the respiratory status of patients with lung cancer by evaluating serial functional indexes, which provides new insights for the perioperative management and strategies against postoperative complications.

Disclosure of conflict of interest

None.

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