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Original Article

A study on video-assisted mini-thoracotomy for treatment of lung cancer

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Abstract: Objective: This study aims to explore the application value of video-assisted mini-thoracotomy (VAMT) for the treatment of lung cancer. Methods: Sixty patients with lung cancer were randomized into a control group which received open pulmonary lobectomy and an observation group which received VAMT. The two groups of patients were compared in terms of thoracotomy time, time of sternal closure, operative time, intraoperative blood loss, postoperative hospitalization time, drainage tube indwelling time, the number and scope of lymph node dissection, complications, recurrence and metastasis, as well as changes of endocrine hormones and inflammatory markers before and after operation. The patients' quality of life was evaluated according to the Functional Assessment of Cancer Therapy-Lung (FACT-L) at 6 months after operation. Results: Compared with the control group, patients in the observation group had significantly shorter thoracotomy time, time of sternal closure, operative time, drainage tube indwelling time, postoperative hospitalization time and less intraoperative blood loss ($P < 0.05$), but there was no significant difference in the number and scope of lymph node dissection between the two groups ($P > 0.05$). On the 7th day after operation, the levels of cortisol (Cor), adrenocorticotropic hormone (ACTH), prostaglandin E2 (PGE2), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) in the observation group were significantly lower than those in the control group ($P < 0.05$). At 6 months after operation, the scores of physical, emotional, functional, social/family and additional conditions and the total scores of FACT-L in the observation group were significantly higher than those in the control group ($P < 0.05$). Postoperative follow-up for 5-36 months showed no recurrence or metastasis in patients. The incidence of complications in the observation group was significantly lower than that in the control group ($P < 0.05$). Conclusion: VAMT for the treatment of lung cancer and lymph node dissection has high safety and efficacy, with small trauma, little blood loss, small stress and fast postoperative recovery.

Keywords: Lung cancer, pulmonary lobectomy, thoracoscope, small incision, efficacy

Introduction

According to the statistics of the International Agency for Research on Cancer in 2012, China had about 653,000 new cases and about 597,000 deaths of lung cancer, which has become one of the diseases with the highest mortality in the country [1]. Lung cancer is currently treated by surgery, radiotherapy, chemotherapy, targeted therapy and immunotherapy. However, radiotherapy and chemotherapy have over 30% incidence of complications, so the patients treated by these therapies are seriously injured [2]. Targeted therapy frequently needs changes due to gene mutations in tumor cells. Immunotherapy is rarely used due to its uncertain short- and long-term efficacy. Moreover, targeted therapy and immunotherapy are expensive and difficult for patients to afford. Therefore, surgery assisted by radiotherapy and chemotherapy is mainly used for the treatment of lung cancer, and curability and functional protection should be considered in the principle of surgical treatment [3, 4]. In terms of curability, open pulmonary lobectomy has been recognized as the standard surgery for the treatment of lung cancer, but the patients undergoing it have large surgical injury, slow postoperative recovery and many complications [5].

With the development of minimally invasive thoracic surgery and thoracoscopic surgery, video-assisted thoracoscopic surgery (VATS) has be-

en gradually applied to the treatment of lung bulla [6], rib fracture [7] and traumatic hemopneumothorax [8]. Patients undergoing VATS have small surgical trauma, slight pain, small lung injury and fast postoperative recovery. Video-assisted mini-thoracotomy (VAMT) has been gradually applied to the clinical treatment of lung cancer in recent years [9, 10], but its safety and thoroughness for the treatment of malignant tumors remain controversial [11, 12]. Therefore, the application value of VAMT for the treatment of lung cancer was explored in this study, to provide references for application.

Materials and methods

General information

Sixty patients with lung cancer treated in The Second People Hospital of Dezhou from May 2015 to March 2018 were randomized into the control and observation groups (n = 30 for each group) according to random number table. Inclusion criteria: (1) Patients confirmed with primary lung cancer by chest CT, abdominal ultrasound and postoperative pathological examination; (2) patients with a tumor diameter < 5 cm and TNM staging of below IIb [13]; (3) patients with good general condition, those who had indications for pulmonary lobectomy; (4) patients who had signed an informed consent form. Exclusion criteria: (1) Patients complicated with cardiopulmonary insufficiency, coagulation disorders, immune dysfunction and infections, those who were intolerable to surgery and anesthesia; (2) patients with peripheral infiltration or distant metastasis, those who could not undergo radical operation; (3) patients who had received radiotherapy and chemotherapy before operation; (4) patients with poor compliance and mental disorders, which affected efficacy evaluation. This study was reviewed and approved by the Medical Ethics Committee of The Second People Hospital of Dezhou.

Therapeutic methods

The patients were treated with combined intravenous anesthesia and a double-lumen tube for one-lung ventilation, under a position on the unaffected side, a dorsal elevated position and a Jackknife's position. Patients in the control group were treated with open pulmonary lobectomy. A 15-20 cm incision was made at the 4th and 5th intercostal space in the midaxillary line of the posterior-lateral affected chest, with muscle groups such as latissimus dorsi and serratus anterior cut off. After the scalpel entered the chest from the intercostal space to open the lungs, pulmonary lobectomy and lymph node dissection were carried out. Patients in the observation group were treated with VAMT. An incision of about 1.5 cm was made at the 7th or 8th intercostal space in the midaxillary line and used as an observation hole. An Olympus-us thoracoscope (Olympus Optical Co., Ltd., Japan) was inserted through Trocar (Covidien Ilc, USA) to probe the thoracic cavity. The specific location of the major operating hole was determined after the determination of lesion location, mainly the 4th and 5th intercostal space for upper lobectomy or the 5th and 6th intercostal space for lower lobectomy. A 6-10 cm major incision for operation was made down along the selected intercostal space from the outer margin of latissimus dorsi. After separation of adhesion, the lesion position was probed through direct view combined with the monitor. For undiagnosed cases, the lesion was completely removed first, and then pulmonary lobectomy was performed after the cases were confirmed by rapid pathological examination using frozen sections. Pulmonary veins and arteries were treated in turn before the incision was ligated with silk thread and then sutured. Lymph nodes were systematically cleaned based on the scope of thoracotomy, and a TLS-B endoluminal stapler (Zhejiang Tiansong Medical Instrument Co., Ltd.) was used to close the bronchial stump. After the resected lobe was taken out from the major operating hole, hemorrhage was arrested, the thoracic cavity was washed, and then the catheter was inserted. Finally, the thoracic cavity was closed.

The patients were admitted to ICU after operation and transferred to general wards after their vital signs became stable and their ability of expectoration was restored. The thoracic catheter was withdrawn after the thoracic drainage volume was less than 100 mL.

Outcome measures

(1). The thoracotomy time, time of sternal closure, operative time, intraoperative blood loss, postoperative hospitalization time, drainage tube indwelling time and the number of lymph node dissection of patients in the two groups

Table 1. Comparison of baseline information ($\bar{x}$ ± sd)

General information	Control group (n = 30)	Observation group (n = 30)	t/χ^2	*P* value
Gender composition			0.278	0.598
Male	17	19		
Female	13	11		
Average age (year)	57.27 ± 8.72	57.34 ± 8.91	0.031	0.976
BMI (kg/m^2)	26.35 ± 2.48	26.49 ± 2.60	0.231	0.832
Tumor size (cm)	3.17 ± 1.23	3.22 ± 1.19	0.160	0.873
Lesion location			0.393	0.983
Left upper	12	11		
Left lower	2	3		
Right upper	8	9		
Right middle	2	2		
Right lower	6	5		
TNM staging			1.221	0.748
Ia	4	6		
Ib	14	12		
IIa	7	5		
IIb	5	7		

Note: BMI, body mass index.

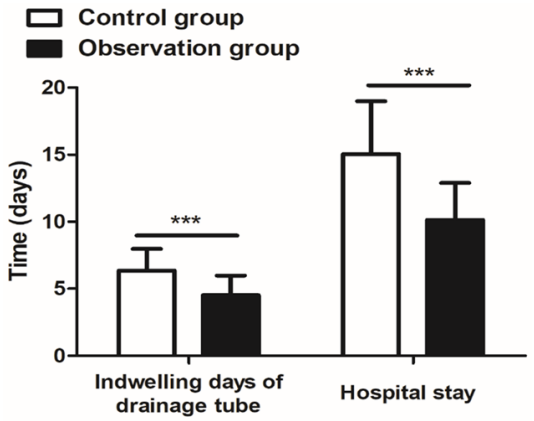

Figure 1. Comparison of surgical conditions. Comparison between control group and observation group, ***P < 0.001.

were observed and recorded. (2). Peripheral venous blood was extracted from the patients before and 7 days after operation to centrifuge and separate serum. After that, chemiluminescent immunoassay (CLIA) was used to detect endocrine hormones such as cortisol (Cor), adrenocorticotropic hormone (ACTH) and prostaglandin E2 (PGE2), as well as inflammatory markers such as C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6). The detection kits were purchased from Shenzhen New Industries Biomedical Engineering Co., Ltd. (3). The patients' quality of life was evaluated according to the Chinese version of the Functional Assessment of Cancer Therapy-Lung (FACT-L) [14] at 6 months after operation. The scale included physical, emotional, functional, social/family and additional conditions. The former 4 aspects each included 5 items, while the last one aspect included 6 items, with each item having 0-4 points. The FACT-L score was the sum of the item scores included. The higher the FACT-L score was, the better the patients' quality of life was. (4). During the follow-up for 5-36 months, complications and recurrence and metastasis were counted.

Statistical methods

SPSS 21.0 was used for data analysis. Independent t test was used for the comparison of measurement data such as thoracotomy time, time of sternal closure and intraoperative blood loss, paired t test for the comparison of Cor, ACTH and PGE2 in the same group before and after treatment, χ^2 test for the comparison of count data such as gender ratio and recurrence rate. $P < 0.05$ indicates a statistically significant difference.

Results

Comparison of baseline information

There was no significant difference between the observation and control groups in gender composition, age, tumor size, lesion location and TNM staging ($P > 0.05$). More details are shown in **Table 1**.

Comparison of surgical conditions

Compared with the control group, patients in the observation group had significantly shorter thoracotomy time, time of sternal closure, operative time, drainage tube indwelling time, postoperative hospitalization time and less intraoperative blood loss ($P < 0.05$), but there was no significant difference in the number of lymph node dissection between the two groups ($P > 0.05$). More details are shown in **Figure 1** and **Table 2**.

Table 2. Comparison of surgical conditions ($\bar{x}$ ± sd)

Index of observations	Control group (n = 30)	Observation group (n = 30)	t value	*P* value
Thoracotomy time (min)	21.38 ± 6.62	10.57 ± 4.89	7.194	0.000
Time of sternal closure (min)	36.95 ± 7.30	21.16 ± 6.54	8.824	0.000
Operative time (min)	173.84 ± 36.31	154.05 ± 27.98	2.365	0.021
Intraoperative blood loss (mL)	272.36 ± 41.45	209.78 ± 56.71	4.880	0.000
Drainage tube indwelling time	6.36 ± 1.62	4.53 ± 1.46	4.596	0.000
Postoperative hospitalization time (d)	15.05 ± 3.94	10.14 ± 2.75	5.597	0.000
Number of lymph node dissection				
Left thorax	4.35 ± 1.05	4.41 ± 1.12	0.214	0.831
Right thorax	6.60 ± 1.22	6.74 ± 1.18	0.452	0.653

Table 3. Comparison of endocrine hormones ($\bar{x}$ ± sd)

Index	Time	Control group (n = 30)	Observation group (n = 30)	t value	*P* value
Cor (ng/mL)	Before operation	62.55 ± 19.48	62.43 ± 19.27	0.024	> 0.05
	7 d after operation	107.55 ± 23.48***	91.49 ± 16.51***	3.065	< 0.05
ACTH (ng/mL)	Before operation	3.21 ± 1.79	3.13 ± 1.52	0.186	> 0.05
	7 d after operation	4.92 ± 1.25***	4.15 ± 1.06**	2.573	< 0.05
PGE2 (pg/mL)	Before operation	89.37 ± 11.07	89.31 ± 10.22	0.022	> 0.05
	7 d after operation	213.92 ± 26.74***	132.71 ± 18.80***	13.608	< 0.05

Note: Compared with the group before operation, **P < 0.01, ***P < 0.001. Cor, cortisol; ACTH, adrenocorticotropic hormone; PGE2, prostaglandin E2.

Table 4. Comparison of inflammatory markers ($\bar{x}$ ± sd)

Index	Time	Control group (n = 30)	Observation group (n = 30)	t value	*P* value
CRP (mg/L)	Before operation	7.60 ± 1.93	7.54 ± 1.85	0.123	> 0.05
	7 d after operation	16.45 ± 2.62***	12.38 ± 2.24***	6.467	< 0.05
TNF-α (ng/L)	Before operation	32.16 ± 2.09	32.58 ± 2.17	0.763	> 0.05
	7 d after operation	55.08 ± 4.73***	43.36 ± 3.94***	10.428	< 0.05
IL-6 (ng/L)	Before operation	29.83 ± 7.86	30.04 ± 8.05	0.102	> 0.05
	7 d after operation	61.48 ± 11.37***	41.29 ± 9.34***	7.515	< 0.05

Note: Compared with the group before operation, ***P < 0.001. CRP, C-reactive protein; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6.

Comparison of endocrine hormones

On the 7th day after operation, the levels of Cor, ACTH and PGE2 in the observation and control groups were significantly higher than those before operation (P < 0.05), but the levels in the observation group were significantly lower than those in the control group (P < 0.05). More details are shown in **Table 3**.

Comparison of inflammatory markers

On the 7th day after operation, the levels of CRP, TNF-α and IL-6 in the observation and control groups were significantly higher than those before operation (P < 0.05), but the levels in the observation group were significantly lower than those in the control group (P < 0.05). More details are shown in **Table 4**.

Comparison of quality of life

At 6 months after operation, the scores of physical, emotional, functional, social/family and additional conditions and the FACT-L score in the observation group were significantly higher than those in the control group (P < 0.05). More details are shown in **Table 5**.

Table 5. Comparison of quality of life ($\bar{x}$ ± sd)

Group	Physical condition	Emotional condition	Functional condition	Social/family condition	Additional condition	Total scores
Control group (n = 30)	15.53 ± 1.56	13.12 ± 1.68	14.36 ± 2.51	14.38 ± 1.58	15.67 ± 1.29	73.06 ± 4.29
Observation group (n = 30)	18.79 ± 1.23	17.58 ± 1.14	18.39 ± 2.18	16.32 ± 1.51	20.35 ± 2.14	91.43 ± 3.71
t value	8.988	12.032	6.639	4.862	10.258	17.740
P value	0.000	0.000	0.000	0.000	0.000	0.000

Table 6. Comparison of complications (n, %)

Group	Pneumonia	Air leakage	Incision infection	Total incidence (%)
Control group (n = 30)	3 (10.00)	2 (6.67)	3 (10.00)	26.67
Observation group (n = 30)	1 (3.33)	0 (0.00)	1 (3.33)	6.67
χ^2 value	0.268	2.069	0.268	4.320
P value	0.605	0.150	0.605	0.038

Follow-up and complications

Postoperative follow-up for 5-36 months showed no recurrence or metastasis in patients. The incidence of complications in the observation group was significantly lower than that in the control group (P < 0.05). More details are shown in **Table 6**.

Discussion

One of the cancers with the highest incidence and mortality in China is lung cancer, which is mainly treated by pulmonary lobectomy at present [15, 16]. During open pulmonary lobectomy, a 15-20 cm incision is usually made to cut off chest wall muscles, and ribs are opened and even broken to fully expose the lobe to be excised. This causes large trauma, much intraoperative blood loss and intense postoperative pain, as well as many complications [17, 18]. With the progress of minimally invasive surgery, markedly effective VAMT has been widely used in the treatment of lung cancer [19, 20]. It has many advantages compared with thoracotomy [21, 22]. (1) A major incision of only 6-10 cm is needed for operation, and the patients' chest wall muscles are unnecessary to be cut off during the operation with the significantly reduced intraoperative blood loss. (2) There is no need to cut off ribs, so the patients have slight postoperative pain and short hospitalization time. (3) TV images are used to directly see the thoracic cavity and cold light source is used for intrathoracic illumination, so the operation is quicker, safer and more convenient. The results of this study showed that compared with the control group, patients in the observation group had significantly shorter thoracotomy time, time of sternal closure, operative time, drainage tube indwelling time, postoperative hospitalization time and less intraoperative blood loss, but there was no significant difference in the number and scope of lymph node dissection between the two groups, which is consistent with the results of Luo Guojun et al. [23] and Li Jianrong [24]. This suggests that the efficacy of VAMT is the same as that of open pulmonary lobectomy, but patients undergoing VAMT have significantly shorter operative time and smaller trauma.

Stress indexes are important references for evaluating surgical trauma, and large surgical trauma leads to acute stress reaction of the body. The larger the trauma is, the stronger the stress reaction is [25, 26]. The hypothalamus-pituitary-adrenal cortex axis, a main regulatory pathway to cope with stress, is activated after stress occurs. The pituitary releases a large amount of ACTH, Cor and PGE2, the levels of which significantly increase, thereby regulating the immune function of the body [27, 28]. The higher the levels of ACTH, Cor and PGE2 are, the larger the trauma to the body is [29]. The results of this study showed that on the 7th day after operation, the levels of Cor, ACTH, PGE2, CRP, TNF-α and IL-6 in the observation group were significantly lower than those in the control group (P < 0.05). In a study on lung cancer by Wang Huibin et al., the levels of ACTH, Cor, IL-6 and CRP after VAMT were significantly lower than those after open surgery [30], indicating that VAMT causes smaller trauma. In addition, postoperative pain is difficult to solve in thoracotomy. Surgical trauma stress can lead to inflammation of surrounding tissues and peripheral nerve injury, activate peripheral nociceptors and phosphorylate neurotransmitters, as well as increase the body's sensitivity

to nociceptive stimulus. As a result, neurons are abnormally excited and then peripheral pain sensation is enhanced [31, 32]. PGE2 is a commonly used marker for evaluating stress pain. The more intense the pain is, the higher the PGE2 level is [33]. The results of this study suggest that the patients' pain is reduced after VATS.

Postoperative follow-up for 5-36 months showed no recurrence or metastasis in patients. According to the comparison of quality of life, at 6 months after operation, the scores of physical, emotional, functional, social/family and additional conditions and the FACT-L score in the observation group were significantly higher than those in the control group, which shows that postoperative rehabilitation in the observation group is superior to that in the control group. The incidence of complications in the observation group was significantly lower than that in the control group, indicating the safety of VAMT in the treatment of lung cancer.

Due to the small sample size and the short follow-up time in this study, the long-term efficacy and recurrence rate of VAMT in the treatment of patients with lung cancer were not explored, which need further discussion. VAMT for the treatment of lung cancer and lymph node dissection has high safety and exact efficacy, with small trauma, little blood loss, small stress and fast postoperative recovery.

Disclosure of conflict of interest

None.

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