Am J Transl Res 2022;14(4):2393-2401
www.ajtr.org /ISSN:1943-8141/AJTR0141815

Original Article

Analysis of perioperative complications and related risk factors of thoracotomy and complete video-assisted thoracoscopic surgery lobectomy

Hongwei Su[1*], Guorong Yan[1*], Zijian Li[1], Lin Fu[2], Lingdi Li[2]

[1]Thoracic Department II, [2]Department of Orthopedics, Hebei Chest Hospital, Shijiazhuang, Hebei, China. [*]Equal contributors.

Received January 17, 2022; Accepted March 7, 2022; Epub April 15, 2022; Published April 30, 2022

Abstract: Objective: To evaluate the perioperative complications and related risk factors of thoracotomy and complete video-assisted thoracoscopic surgery (c-VATS) lobectomy. Methods: A total of 93 patients with early lung cancer (LC) treated in our hospital from Mar. 2017 to Mar. 2021 were retrospectively enrolled. Among them, 45 patients underwent conventional thoracotomy lobectomy was classified as the control group (Con group, n=45) and other 48 patients underwent c-VATS lobectomy was classified as the observation group (Obs group, n=48). Surgical indicators of the two groups were compared, and the changes of Visual Analog Scale (VAS) score, plasma levels of vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6), and pulmonary function indexes were compared before and after operation. Additionally, postoperative complications were compared between the two groups. Multivariate logistic regression was carried out to analyse the independent risk factors for postoperative complications. Results: The Obs group showed significantly less intraoperative blood loss than the Con group and experienced significantly shorter operation time than the Con group (both P<0.001). The Obs group had significantly lower VAS scores than the Con group at 1 day and 7 days after surgery (P<0.05), and showed significantly lower levels of plasma IL-6 and VEGF than the Con group (both P<0.001). In addition, higher forced vital capacity (FVC) and maximum ventilation per minute (MVV) were found in the Obs group than in the Con group (P<0.001), and the Obs group showed a significantly lower incidence of postoperative complications than the Con group (P<0.05). Multivariate logistic regression analysis revealed that age, body mass index (BMI) and operation mode were independent risk factors for postoperative complications. Conclusion: Compared with conventional thoracotomy, c-VATS lobectomy brings a lower incidence of postoperative complications, and age, BMI and operation mode were independent risk factors for postoperative complications.

Keywords: Thoracotomy lobectomy, complete video-assisted thoracoscopic surgery lobectomy, complications, risk factors

Introduction

Lung cancer (LC) is a leading cause of cancer-related death worldwide [1], and its morbidity and mortality also rank the top ones of malignant tumours in China [2]. The global prevalence of tobacco gives rise to a rapid increase in the number of new LC cases and the resultant deaths out of LC [3]. Second-hand tobacco smoke is also a crucial cause of LC [4]. The terribly high incidence and mortality of LC has become a heavy economic and health burden to the whole world. Despite the great progress in diagnosis and treatment of LC, its 5-year overall survival rate is still only appropriate 15% [5]. The outcome of patients with LC is unfavourable, so the early diagnosis, therapy and prognosis of LC are still the hot issues of great concern worldwide.

According to an American statistic, early lung cancer screening can lower the mortality of high-risk groups by 20%, so early detection and early therapy can substantially improve the outcome of patients with LC [6]. At the current stage, LC is primarily treated by chemotherapy, radiotherapy and radical resection for LC [7]. The traditional radical operation for LC is lobec-

tomy and lymph node dissection through posterolateral incision of chest, which has the disadvantages of large incision, much bleeding and great pain [8]. As video-assisted thoracoscopic surgery (VATS) advances, complete VATS (c-VATS) lobectomy, a new technology of minimally invasive surgery, has been extensively adopted to treat various lung diseases including LC, and may become the gold standard for early LC treatment in the future [9, 10]. Many scholars at home and abroad have compared it with thoracotomy, and found its advantages of minimally invasive property, less inflammatory reaction, less pain, short hospital stay and quick recovery [11]. However, radical resection for LC is accompanied by a high incidence of complications, which compromises the prognosis of patients [12]. The related risk factors for complications after conventional thoracotomy lobectomy and c-VATS are rarely studied.

Accordingly, this study investigated the postoperative complications and related risk factors for thoracotomy and c-VATS to provide reference for clinical therapy and prognosis of patients with LC.

Clinical data and methods

Clinical data

A total of 93 patients with early LC treated in our hospital from Mar. 2017 to Mar. 2021 were enrolled, and retrospectively analysed. Among them, 45 patients underwent conventional thoracotomy lobectomy were assigned into the control group (Con group, n=45) and 48 patients underwent c-VATS lobectomy were assigned into the observation group (Obs group, n=48).

The inclusion criteria: Patients with confirmed LC by biopsy before operation [13]; patients with detailed clinical data; patients with the maximum diameter of tumour <5 cm; patients without mediastinal lymph nodes as indicated in preoperative imaging examination; patients who had not received radiotherapy and chemotherapy before surgery; patients who met the indications of thoracotomy lobectomy; and those whose preoperative clinical stage of LC was T1-2 N0-1 M0. The exclusion criteria: Patients with severe liver or kidney dysfunction; patients with severe blood diseases or other primary tumours; and those with autoimmune disease.

Ethics statement

This study was carried out with permission from the Medical Ethics Committee of Hebei Chest Hospital with the approved no. of 2017-LC-221.

Surgical regimen

Each patient was given general anesthesia administered by the intravenous or inhalation route, double lumen endotracheal catheter intubation, and one-lung ventilation under a lateral position.

The Obs group: Three holes of 2 cm, 2 cm and 3-5 cm were cut in the 7th intercostal of the midline axillary, 4th intercostal of the front axillary line and 7th intercostal of the rear axillary line, respectively, and lobectomy and mediastinal lymph node dissection were performed under VATS. During the operation, pulmonary veins, arteries and bronchi were treated with disposable linear suture device, ultrasonic knife amputation after double ligation of silk thread, hemlock clamping and so on. The treatment sequence of pulmonary artery, pulmonary vein and bronchus was determined according to the development of interlobar fissure, the safety of operation and the operative habits of the operator. The dissected lymph nodes included intrapulmonary, hilar and mediastinal lymph nodes. The left LC was dissected in groups 3, 4-9 and 10-14, and the right LC was dissected in groups 2, 3, 4, 7, 8, 9 and 10-14.

The Con group: lung lobectomy with standard posterolateral incision and mediastinal lymph node dissection were routinely carried out.

Collection and detection of samples

The serum levels of VEGF and IL-6 was determined by Elisa. Fasting peripheral venous blood (5 mL) was extracted from each patient at admission and one day after surgery, and stored in anticoagulant tubes for concentration determination. The VEGF (cat no. PV963) and IL-6 (cat no. PI330) Elisa kits were provided by Beyotime Biotechnology Co., Ltd (Shanghai, China).

Outcome measures

Primary outcome measures: The intraoperative blood loss and operation time of the two

Table 1. General clinical data of the two groups

Factors	The control group (n=45)	The observation group (n=48)	t/χ^2	P
Age (years)				
<65	31 (68.89)	37 (77.08)	0.794	0.373
≥65	14 (31.11)	11 (22.92)		
Gender				
Male	27 (58.70)	33 (48.53)	0.438	0.508
Female	19 (41.30)	35 (51.47)		
BMI (kg/m^2)	22.18±1.75	22.35±1.88	0.451	0.653
Pathological type				
Adenocarcinoma	22 (48.89)	30 (62.50)	2.261	0.323
Squamous carcinoma	17 (37.78)	15 (31.25)		
Large cell carcinoma	6 (13.33)	3 (6.25)		
Differentiation				
Low	35 (77.78)	41 (85.42)	0.907	0.341
Moderate	10 (22.22)	7 (14.58)		
TNM staging				
Stage I	37 (82.22)	43 (89.58)	1.047	0.306
Stage II	8 (17.78)	5 (10.42)		
Smoking index				
≥400 PCs/year	6 (13.33)	11 (22.92)	1.428	0.232
<400 PCs/year	39 (86.67)	37 (77.08)		
History of hypertension				
Yes	13 (28.89)	19 (39.58)	1.177	0.278
No	32 (71.11)	29 (60.42)		
History of diabetes mellitus				
Yes	12 (26.67)	7 (14.58)	2.086	0.149
No	33 (73.33)	41 (85.42)		
History of alcoholism				
Yes	36 (80.00)	35 (72.92)	0.645	0.422
No	9 (20.00)	13 (27.08)		
Place of residence				
Urban	28 (62.22)	22 (45.83)	2.510	0.113
Rural	17 (37.78)	26 (54.17)		

groups were recorded, and the occurrence of postoperative complications in two groups were evaluated. Multivariate logistic regression was conducted to analyze the independent risk factors for postoperative complications.

Secondary outcome measures: With a total score of 10 points, the Visual Analog Scale (VAS) was adopted for pain analysis: 0 point indicates no pain, and a higher VAS score implies more severe pain. Plasma VEGF and IL-6 in the patients were determined before and after operation, and the changes of forced vital capacity (FVC) and maximum ventilation per minute (MVV) were observed before and after operation.

Statistical analyses

SPSS23.0 software (SPSS Co., Ltd., Chicago, the States) was used for statistical analyses of all collected data, and GraphPad Prism 8 (graphpad Software Co., Ltd., San Diego, the States) for figure rendering. Counting data (%) were analysed using the chi-square test, and presented by χ^2, and measurement data (Mean ± SD) were compared using the independent-samples T test between groups, and presented by t. Analysis of multi-time-point detection was carried out using the repeated measures analysis of variance, and represented by F. Bonferroni was adopted of post-hoc test. $P<0.05$ implies a significant difference.

Results

Comparison of clinical data

According to analysis of general clinical data of the two groups, there were no statistical differences in age, gender, body mass index (BMI), pathological type, differentiation, TNM staging, history of hypertension, history of diabetes mellitus, history of alcoholism, and place of residence between the two groups (all $P>0.05$), indicating comparability (**Table 1**).

Comparison of surgical indicators

According to statistics, the intraoperative blood loss and thoracic drainage on the first day in the Obs group were significantly less than those

Table 2. Comparison of surgical indicators

Group	Intraoperative blood loss (ml)	Operation time (min)	Thoracic drainage on the first day (ml)	The number of dissected lymph nodes	Extubation time (d)
The control group (n=45)	273.61±31.27	161.58±28.63	365.55±48.93	13.28±5.29	3.56±1.30
The observation group (n=48)	193.45±28.75	132.43±25.46	219.46±29.45	14.39±4.59	3.66±0.91
t	12.88	5.196	17.604	1.708	0.479
P	<0.001	<0.001	<0.001	0.283	0.633

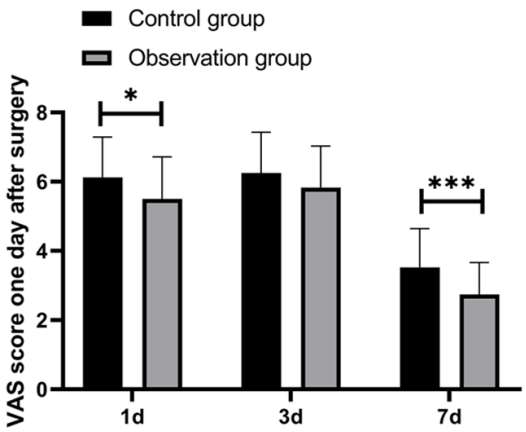

Figure 1. VAS score. Comparison of VAS score changes at different time points in each group. *P<0.05; ***P<0.001.

in the Con group, and the operation time was significantly shorter than that in the Con group (all P<0.001, **Table 2**). However, there was no significant difference in the number of dissected lymph nodes and extubation time between the two groups (all P>0.05, **Table 2**).

VAS score

According to the pain evaluation results by VAS, the Obs group got notably lower VAS score than the Con group one day after surgery (P<0.05); the VAS scores of the two groups at Day 3 after surgery were not significantly different (P>0.05); the Obs group got notably lower VAS score than the Con group at Day 7 after therapy (P<0.001, **Figure 1**).

Plasma VEGF and IL-6 levels

According to ELISA results, before surgery, plasma IL-6 and VEGF levels in the two groups were not significantly different (P>0.05), but at Day 1 after surgery, the levels in both groups increased significantly (P<0.001), with greatly lower levels of them in the Obs group than in the Con group (P<0.001, **Figure 2**).

Pulmonary function index

The pulmonary function indexes of the two groups were determined. Before surgery, the two groups were similar in FVC and MVV (both P>0.05), but 3 months after surgery, FVC and MVV of both groups decreased (P<0.001), with higher FVC and MVV levels in the Obs group than in the Con group (P<0.001, **Figure 3**).

Incidence of postoperative complications

Statistics of postoperative complications in the two groups revealed a significantly lower incidence of postoperative complications in the Obs group than in the Con group (P<0.05, **Table 3**).

Univariate analysis of postoperative complications

The general clinical data and surgical indicators of patients with and without complications were collected. According to the analysis, the two groups were greatly different in age, BMI, history of diabetes mellitus, operation mode, and operation time, all of which were the risk factors for postoperative complications (**Table 4**).

Multivariate analysis of postoperative complications

Indicators with differences in univariate analysis were subjected to multivariate logistic regression analysis by the Forward: LR. The results showed that age, BMI and operation mode were all independent risk factors for postoperative complications (**Table 5**).

Discussion

Early diagnosis and treatment can increase the 5-year survival rate of patients with stage IA LC to 80% [14]. With the spread use of low-dose spiral CT screening, a growing number of

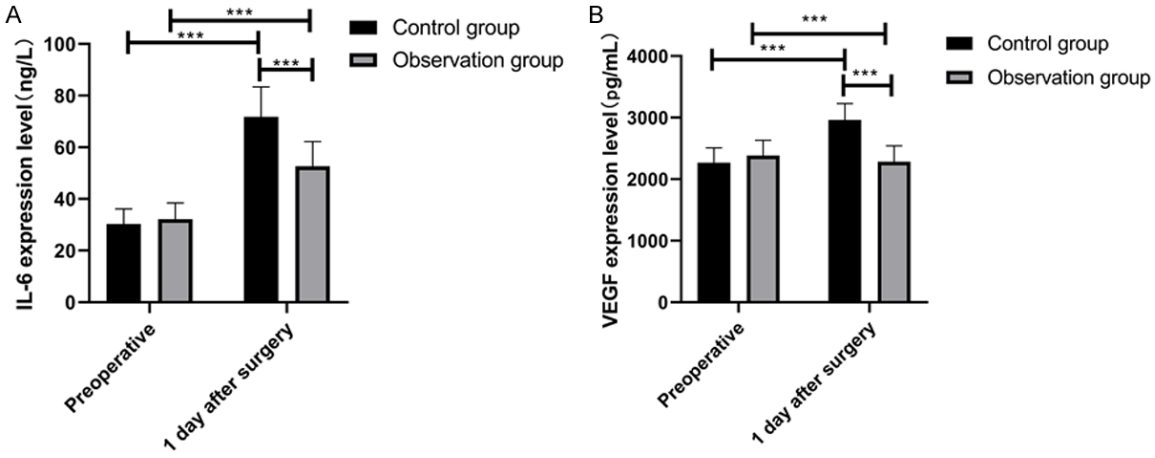

Figure 2. Plasma VEGF and IL-6 levels. (A) indicated the results of VEGF and (B) indicated the results of IL-6. Before surgery, plasma IL-6 and VEGF levels in the two groups were not greatly different, but at 1 day after surgery, the levels of them in both groups increased notably, with notably lower levels of them in the observation group than in the control group [7, 8]. ***P<0.001.

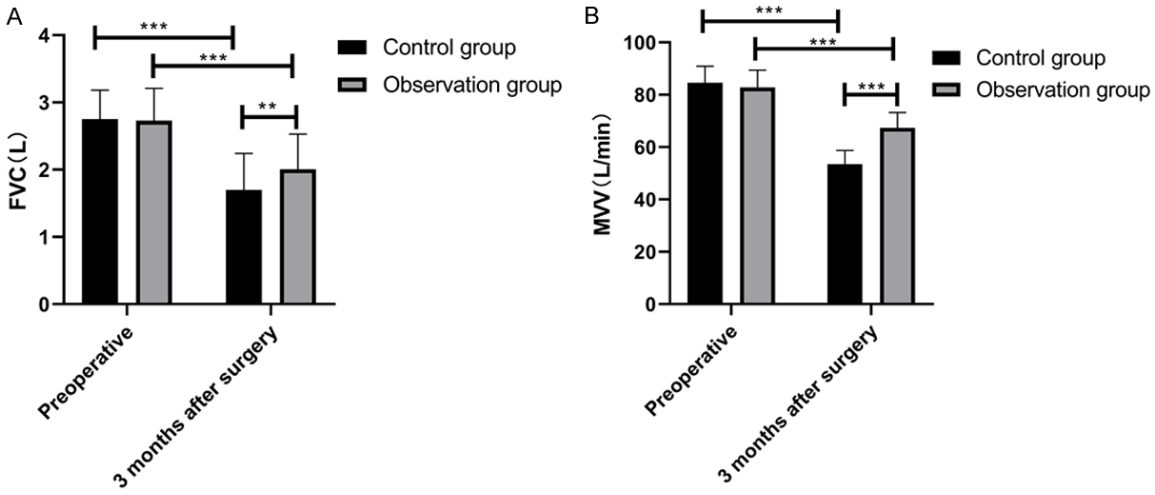

Figure 3. Comparison of FVC and MVV. (A) indicated the results of FVC and (B) indicated the results of MVV. Before surgery, the two groups were similar in FVC and MVV, but at 3 months after surgery, FVC and MVV of both groups decreased (P<0.001), with higher FVC and MVV levels in the observation group than in the control group [9, 10]. ***P<0.001.

Table 3. Incidence of postoperative complications

Group	Pulmonary infection	Arrhythmia	Pulmonary atelectasis	Hypoxemia	Pneumothorax	Total
The control group (n=45)	2 (4.44)	3 (6.67)	3 (6.67)	4 (8.89)	2 (4.44)	14 (31.11)
The observation group (n=48)	1 (2.08)	1 (2.08)	1 (2.08)	2 (4.17)	0 (0.00)	5 (10.42)
χ^2						6.119
P						0.013

patients with early LC can diagnosed in time [15, 16]. For these patients with early LC, surgical treatment is still the optimal choice [17], and many patients with early LC can now be treated with VATS [18]. Different from conventional thoracotomy, minimally invasive lung sur-

Table 4. Univariate analysis of postoperative complications

Factors	Complication group (n=19)	Non-complication group (n=74)	t/χ^2	P
Age (years)				
<65	6 (31.58)	62 (83.79)	20.96	<0.001
≥65	13 (68.42)	12 (16.22)		
Gender				
Male	13 (68.42)	47 (63.51)	0.159	0.690
Female	6 (31.58)	27 (6.49)		
BMI (kg/m^2)				
≤24	12 (63.16)	71 (95.95)	16.94	<0.001
524	7 (36.84)	3 (4.05)		
Pathological type				
Adenocarcinoma	11 (57.89)	41 (55.41)	1.393	0.498
Squamous carcinoma	5 (26.32)	27 (36.49)		
Large cell carcinoma	3 (15.79)	6 (8.11)		
Differentiation				
Low	13 (68.42)	63 (85.14)	2.827	0.093
Moderate	6 (31.58)	11 (14.86)		
TNM staging				
Stage I	14 (73.68)	66 (89.19)	3.023	0.082
Stage II	5 (26.32)	8 (10.81)		
History of hypertension				
Yes	7 (36.84)	25 (33.78)	0.063	0.802
No	12 (63.16)	49 (66.22)		
History of diabetes mellitus				
Yes	9 (47.37)	10 (13.51)	10.66	0.001
No	10 (52.63)	64 (86.49)		
History of alcoholism				
Yes	14 (73.68)	57 (77.03)	0.094	0.760
No	5 (26.32)	17 (22.97)		
Place of residence				
Urban	8 (42.11)	42 (56.76)	1.306	0.253
Rural	11 (57.89)	32 (43.24)		
Operation mode				
Conventional thoracotomy	14 (73.68)	31 (41.89)	6.119	0.013
Complete video-assisted thoracoscopic surgery lobectomy	5 (26.32)	43 (58.11)		
Intraoperative blood loss (ml)	192.52±30.45	181.42±29.51	1.375	0.174
Operation time (min)				
<180	7 (36.84)	4 (5.41)	14.33	<0.001
≥180	12 (63.16)	70 (94.59)		

gery causes milder injury to the chest wall of patients by reducing the incision, and reduces the hospital stay and the treatment cost of patients, but does not reduce the 5-year disease-free survival rate [19, 20].

In our study, the Obs group showed significantly less intraoperative blood loss and experienced significantly shorter operation time than the Con group. The reasons were as follows: VATS caused a smaller incision, so that the operating mirror didn't need to go in and out of the operation hole repeatedly during the operation, and the intraoperative blood loss was less accordingly. However, conventional thoracotomy lobectomy requires a wider operation field

Table 5. Multivariate logistic regression analysis

Factors	B	S.E.	Wals	Sig.	Exp (B)	95% C.I. of EXP (B)	
						Lower limit	Upper limit
Age	-2.862	0.933	9.420	0.002	0.057	0.009	0.355
BMI	-5.184	1.562	11.012	0.001	0.006	0.000	0.120
History of diabetes mellitus	1.665	0.932	3.193	0.074	5.284	0.851	32.805
Operation mode	2.662	1.188	5.015	0.025	14.319	1.394	147.077
Operation time	2.178	1.164	3.501	0.061	8.829	0.902	86.452

to thoroughly clean the lymph nodes, and the incision is often larger, which might lead to more intraoperative blood loss and serious body injury, and the complicated surgery prolonged the operation time [21]. The Obs group had significantly lower VAS score than the Con group at Day 1 and 7 after surgery. In the early postoperative period, the observation group had less surgical trauma and faster postoperative recovery, so the VAS score was lower at Day 1 and 7 after therapy. As the effects of anesthesia weaned off, the VAS would increase slightly, so the VAS scores of the two groups 3 days after surgery were not significantly different. The results imply that the pain caused by VATS is less than that caused by thoracotomy, and VATS is conducive to accelerating the postoperative recovery of patients. The levels of circulating cytokines like IL-6 and VEGF are directly bound up with surgical trauma, inflammatory reaction and immune status in the acute stage after operation [22]. IL-6 is a pleiotropic cytokine secreted by T cells, mononuclear macrophages or fibroblasts, which is able to stimulate the release of other cytokines and thus trigger inflammatory reaction [23]. It has been reported that IL-6 up-regulated TIM-4 in non-small cell LC cells via NF-κB signalling pathway, and both TIM-4 and IL-6 intensified the invasion, migration, and epithelial-mesenchymal transformation of non-small cell lung cancer (NSCLC) cells [24]. VEGF can specifically act on vascular endothelial cells, accelerate division and proliferation of blood vessels and the formation of new blood vessels, and increase the permeability of tumour blood vessels, so that cancer cells are more likely to spread into the blood and metastasize [25]. It has also been shown that significantly high level of VEGF was detected in the blood of patients with LC compared with patients with benign lung masses [26]. The quantification results of ELISA showed that at postoperative Day 1, the levels of plasma IL-6 and VEGF in both groups increased significantly, with significantly lower levels of them in the Obs group than in the Con group. According to the results, surgery will up-regulate IL-6 and VEGF, but VATS causes less trauma to the patient's body and significantly milder inflammatory reaction and immunosuppression due to the trauma than the open operation. So, VATS is more conducive to the recovery of patients and reduces the occurrence of complications. After lobectomy, the increase level of VEGF caused by the healing process may promote the proliferation of tumour blood vessels and the spread of cancer cells, thus increasing the possibility of tumour recurrence and metastasis. VATS causes smaller incision and less trauma and thus brings a lower risk.

At the current stage, the main clinical treatment for LC is surgery, in which patients' lung lobes are resectioned and their pulmonary function is protected to the greatest extent [27]. The pulmonary function indexes of the two groups were determined. Before surgery, the two groups were similar in FVC and MVV, but 3 months after surgery, FVC and MVV of both groups decreased, with higher FVC and MVV levels in the Obs group than in the Con group. The results imply milder pulmonary function injury in patients given VATS than in patients underwent thoracotomy, which can be explained by the fact that VATS lobectomy can keep the integrity of the patient's chest contour to the maximum extent, and has less detrimental to the patient's cardiopulmonary function.

Pneumonia and atelectasis are common pulmonary complications after thoracic surgery in clinical scenarios, which greatly increase the mortality in hospital and prolong ICU transition time and postoperative hospitalization time [28]. In addition, a significantly lower incidence of postoperative complications was found in the Obs group than in the Con group in

our study. The general clinical data and surgical indicators of patients with complications and those without complications were collected. According to analysis of them, the two groups were greatly different in age, BMI, history of diabetes mellitus, operation mode, and operation time, all of which were the risk factors for postoperative complications. Multivariate logistic regression analysis showed that age, BMI, and operation mode were independent risk factors for postoperative complications. Reportedly, BMI≥24 kg/m^2 [29], complications [30], total pneumonectomy and long operation time [31] were independent risk factors for complications after lobectomy.

The current study still has some limitations. Due to the retrospective nature, the sample size and the data that can be collected are few. We hope to conduct a randomized controlled study in the future to further confirm our research conclusions. Secondly, in this study, we didn't explore the life quality of patients after surgery and was not clear whether the two schemes have any influence on patients' postoperative survival. Therefore, we will follow up patients in the future to observe the influence of the two schemes on patients' survival.

To sum up, VATS can reduce the incidence of inflammation and pulmonary complications after lobectomy compared with thoracotomy. Age, BMI, history of diabetes mellitus, operation mode and operation time are the risk factors for postoperative complications. Patients should be fully informed of the risks before operation and active preventive measures should be taken after operation.

Disclosure of conflict of interest

None.

Address correspondence to: Lingdi Li, Hebei Chest Hospital, No. 372 North Shengli Rd, Changan District, Shijiazhuang 050040, Hebei, China. Tel: +86-15633035980; E-mail: lilingdi1033@163.com

References

[1] Barta JA, Powell CA and Wisnivesky JP. Global epidemiology of lung cancer. Ann Glob Health 2019; 85: 8.

[2] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.

[3] Schabath MB and Cote ML. Cancer progress and priorities: lung cancer. Cancer Epidemiol Biomarkers Prev 2019; 28: 1563-1579.

[4] Carreras G, Lugo A, Gallus S, Cortini B, Fernandez E, Lopez MJ, Soriano JB, Lopez-Nicolas A, Semple S and Gorini G; TackSHS Project Investigators. Burden of disease attributable to second-hand smoke exposure: a systematic review. Prev Med 2019; 129: 105833.

[5] Molina JR, Yang P, Cassivi SD, Schild SE and Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. Mayo Clin Proc 2008; 83: 584-594.

[6] Duma N, Santana-Davila R and Molina JR. Non-Small Cell Lung cancer: epidemiology, screening, diagnosis, and treatment. Mayo Clin Proc 2019; 94: 1623-1640.

[7] Understanding Lung Cancer Treatment Advances. Oncology (Williston Park) 2019; 33: 688718.

[8] van der Ploeg APT, Ayez N, Akkersdijk GP, van Rossem CC and de Rooij PD. Postoperative pain after lobectomy: robot-assisted, video-assisted and open thoracic surgery. J Robot Surg 2020; 14: 131-136.

[9] Watanabe A, Miyajima M, Mishina T, Tsuruta K, Takahashi Y, Maki R and Tada M. Video-assisted thoracoscopic surgery node dissection for lung cancer treatment. Surg Today 2017; 47: 1419-1428.

[10] Sihoe ADL. Video-assisted thoracoscopic surgery as the gold standard for lung cancer surgery. Respirology 2020; 25 Suppl 2: 49-60.

[11] Mun M, Nakao M, Matsuura Y, Ichinose J, Nakagawa K and Okumura S. Video-assisted thoracoscopic surgery lobectomy for non-small cell lung cancer. Gen Thorac Cardiovasc Surg 2018; 66: 626-631.

[12] Suzuki K, Saji H, Aokage K, Watanabe SI, Okada M, Mizusawa J, Nakajima R, Tsuboi M, Nakamura S, Nakamura K, Mitsudomi T and Asamura H; West Japan Oncology Group; Japan Clinical Oncology Group. Comparison of pulmonary segmentectomy and lobectomy: safety results of a randomized trial. J Thorac Cardiovasc Surg 2019; 158: 895-907.

[13] Gould MK, Donington J, Lynch WR, Mazzone PJ, Midthun DE, Naidich DP and Wiener RS. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013; 143: e93S-e120S.

[14] Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, Nicholson AG, Groome P, Mitchell A and Bolejack V; Interna-

tional Association for the Study of Lung Cancer Staging and Prognostic Factors Committee, Advisory Boards, and Participating Institutions; International Association for the Study of Lung Cancer Staging and Prognostic Factors Committee Advisory Boards and Participating Institutions. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (Eighth) edition of the TNM classification for lung cancer. J Thorac Oncol 2016; 11: 39-51.

[15] Field JK, Oudkerk M, Pedersen JH and Duffy SW. Prospects for population screening and diagnosis of lung cancer. Lancet 2013; 382: 732-741.

[16] National Lung Screening Trial Research Team, Church TR, Black WC, Aberle DR, Berg CD, Clingan KL, Duan F, Fagerstrom RM, Gareen IF, Gierada DS, Jones GC, Mahon I, Marcus PM, Sicks JD, Jain A and Baum S. Results of initial low-dose computed tomographic screening for lung cancer. N Engl J Med 2013; 368: 1980-1991.

[17] Rossi D. What can we save for the first-line treatment of NSCLC in 2016? World J Oncol 2017; 8: 31-33.

[18] Jiao W and Qiu T. The minimally invasive thoracic surgery for lung cancer: a voice from China. Indian J Cancer 2015; 51 Suppl 2: e2.

[19] Kamel MK, Nasar A, Stiles BM, Altorki NK and Port JL. Video-assisted thoracoscopic lobectomy is the preferred approach following induction chemotherapy. J Laparoendosc Adv Surg Tech A 2017; 27: 495-500.

[20] Zhao J, Li W, Wang M, Liu L, Fu X, Li Y, Xu L, Liu Y, Zhao H, Hu J, Liu D, Shen J, Yang H and Li X. Video-assisted thoracoscopic surgery lobectomy might be a feasible alternative for surgically resectable pathological N2 non-small cell lung cancer patients. Thorac Cancer 2021; 12: 21-29.

[21] Findik G, Incekara F, Demiroz M, Sayilir E, Inan K, Hazer S, Aydogdu K and Kaya S. First experiences and complications in video-assisted thoracoscopic surgery lobectomy at a thoracic surgery center. Turk Gogus Kalp Damar Cerrahisi Derg 2018; 26: 116-122.

[22] Saribal D, Hocaoglu-Emre FS, Erdogan S, Bahtiyar N, Caglar Okur S and Mert M. Inflammatory cytokines IL-6 and TNF-alpha in patients with hip fracture. Osteoporos Int 2019; 30: 1025-1031.

[23] Hirano T. IL-6 in inflammation, autoimmunity and cancer. Int Immunol 2021; 33: 127-148.

[24] Liu W, Wang H, Bai F, Ding L, Huang Y, Lu C, Chen S, Li C, Yue X, Liang X, Ma C, Xu L and Gao L. IL-6 promotes metastasis of non-small-cell lung cancer by up-regulating TIM-4 via NF-kappaB. Cell Prolif 2020; 53: e12776.

[25] Wang X, Freire Valls A, Schermann G, Shen Y, Moya IM, Castro L, Urban S, Solecki GM, Winkler F, Riedemann L, Jain RK, Mazzone M, Schmidt T, Fischer T, Halder G and Ruiz de Almodovar C. YAP/TAZ orchestrate VEGF signaling during developmental angiogenesis. Dev Cell 2017; 42: 462-478, e467.

[26] Frezzetti D, Gallo M, Maiello MR, D'Alessio A, Esposito C, Chicchinelli N, Normanno N and De Luca A. VEGF as a potential target in lung cancer. Expert Opin Ther Targets 2017; 21: 959-966.

[27] Sui T, Liu A and Jiao W. Difference of Lung Function Retention after Segmentectomy and Lobectomy. Zhongguo Fei Ai Za Zhi 2019; 22: 178-182.

[28] Hoshikawa Y and Tochii D. Postoperative atelectasis and pneumonia after general thoracic surgery. Kyobu Geka 2017; 70: 649-655.

[29] Yang R, Wu Y, Yao L, Xu J, Zhang S, Du C and Chen F. Risk factors of postoperative pulmonary complications after minimally invasive anatomic resection for lung cancer. Ther Clin Risk Manag 2019; 15: 223-231.

[30] Okami J, Higashiyama M, Asamura H, Goya T, Koshiishi Y, Sohara Y, Eguchi K, Mori M, Nakanishi Y, Tsuchiya R and Miyaoka E; Japanese Joint Committee of Lung Cancer Registry. Pulmonary resection in patients aged 80 years or over with clinical stage I non-small cell lung cancer: prognostic factors for overall survival and risk factors for postoperative complications. J Thorac Oncol 2009; 4: 1247-1253.

[31] Pei G, Zhou S, Han Y, Liu Z and Xu S. Risk factors for postoperative complications after lung resection for non-small cell lung cancer in elderly patients at a single institution in China. J Thorac Dis 2014; 6: 1230-1238.