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Original Article

Efficacy of video-assisted thoracoscopic surgery for radical resection of non-small cell lung cancer in elderly patients

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Abstract: Objective: To explore the efficacy of video-assisted thoracoscopic surgery (VATS) versus thoracotomy for radical resection of non-small cell lung cancer (NSCLC) in elderly patients. Methods: One hundred elderly patients with NSCLC who were admitted to our hospital between January 2013 and June 2015 were recruited in this study and randomly divided into the observation group and the control group, with 50 cases in each group. Patients in the observation group were treated with radical resection of NSCLC by VATS, while those in the control group underwent radical resection of NSCLC by conventional thoracotomy. Patients in the two groups were compared in the perioperative indicators (operative time, the amount of intraoperative blood loss, the number of mediastinal lymph nodes dissected, the time to chest tube removal and the time to ambulation) and the rates of cardiopulmonary complications. The serum levels of C-reactive protein (CRP), interleukin-6 (IL-6), and interleukin-10 (IL-10), and the percentages of CD^4+T cells and CD^8+T immune cells were also compared between the two groups before and 3 days after treatment, respectively. Results: No significant difference was noted in the number of mediastinal lymph nodes dissected between the two groups (P>0.05). When compared with the control group, the observation group had significantly shorter operative time, reduced intraoperative bleeding, shorter time to chest tube removal and shorter time to ambulation (all P<0.05), as well as significantly lower rates of cardiopulmonary complications (P<0.001). Before treatment, insignificant differences were seen between the two groups in pulmonary function, the levels of inflammatory cytokines, and the percentages of CD^4+T cells and CD^8+T cells (all P>0.05); forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and maximum voluntary ventilation (MVV) of the observation group were significantly higher than those of the control group (all P<0.05). Three days after treatment, the CRP, IL-6 and IL-10 levels in the observation group were significantly lower than those in the control group, but the percentages of CD^4+T cells and CD^8+T cells were significantly higher than those in the control group (all P<0.05). Conclusion: For elderly patients with NSCLC, radical resection of NSCLC by VATS can significantly reduce the rates of cardiopulmonary complications and the expression levels of inflammatory cytokines, and improve recovery of pulmonary and immune functions; hence, it is worthy of clinical generalization.

Keywords: Non-small cell lung cancer, elderly patient, radical resection for lung cancer by video-assisted thoracoscopic surgery, conventional thoracotomy, efficacy

Lung cancer (LC) is one of the most frequently-occurred malignant tumors in clinical practice, and it seriously threatens physical and mental health of patients. The morbidity and mortality of LC are on the increase in recent years, especially in elderly patients. Approximately 80% of patients with LC have non-small cell lung cancer (NSCLC) [1, 2]. Thoracotomy is currently considered to be the most commonly used technique for elderly patients with NSCLC [3]. However, thoracotomy is inclined to cause trauma, cardiopulmonary complications, aggravate the release of inflammatory cytokines and inhibit the immune function of elderly patients, leading to a decline in the success rate of surgery, poorer postoperative recovery, prolonged operative time and great pain in such population [4, 5]. Therefore, under the premise of guaranteeing the efficacy of surgeries for elderly patients with NSCLC, to minimize the degree

of trauma has become the goal of thoracic surgeons when they are seeking for new surgical techniques.

With the popularization of minimally invasive concepts and the development of minimally invasive techniques, video-assisted thoracoscopic surgery (VATS) plays an increasingly important role in the treatment of NSCLC. Its effectiveness, safety and minimal-invasiveness have been confirmed by many studies of evidence-based medicine [6, 7]. VATS is advantageous over thoracotomy in less postoperative pain, smaller trauma and faster recovery. Studies have demonstrated that the rates of lymph nodes dissected and 5-year survival of patients undergoing VATS are basically close to those of patients undergoing thoracotomy, but the rates of local recurrence and distant metastasis in patients undergoing VATS are significantly higher [8, 9]. Current studies have proved that VATS is more minimally invasive than conventional thoracotomy in terms of the clinical data primarily including the size of the incisions, the amount of intraoperative blood loss and the rates of postoperative complications [10-12]. However, there are few reports on the microscopic differences in the indicators of cardiopulmonary functions and inflammation between the two surgical techniques in the special population of elderly patients with NSCLC. Therefore, this study was designed to compare the efficacy of video-assisted thoracoscopic surgery (VATS) and thoracotomy for radical resection of NSCLC in elderly patients, expecting to provide experimental basis for the choice of surgical strategy for elderly patients with NSCLC.

Materials and methods

General information

From January 2013 to June 2015, 100 elderly patients with NSCLC were recruited and randomly assigned to the observation group (n=50) and the control group (n=50). Patients in the observation group received radical resection for NSCLC by VATS, whereas those in the control group underwent radical resection for NSCLC by conventional thoracotomy. Elderly patients older than 60 years of age were eligible if they had stage I or II NSCLC confirmed by imaging and pathological examination; no involvement of mediastinal and hilar lymph nodes, no lymph node metastasis nor distant metastasis. Elderly patients were ineligible if they had surgical contraindications such as coagulation dysfunction, severe renal and hepatic insufficiency, had received chemotherapy, radiotherapy and other targeted therapy before treatment, a history of thoracotomy; immune system disease, did not actively cooperate in this study or had incomplete clinical data. This study got approval from the Ethics Committee of the hospital, and all the patients submitted written informed consent.

Surgical procedures

After general anesthesia and double-lumen endotracheal intubation, each patient was placed in the contralateral decubitus position and ventilated in the contralateral lung. Patients in the observation group underwent radical resection of NSCLC by VATS. A 4-cm incision was made as an operating port at the third or fourth intercostal space (ICS) in the anterior axillary line; a 2-cm incision was made as an auxiliary operating port at the 7th ICS in the subscapular line; a 1.5-cm incision was made as an observation port at the 7th or 8th ICS) in the middle axillary line. A thoracoscope was placed into the thoracic cavity; a coagulation hook, non-invasive grasping forceps, surgical staplers and other instruments were placed into the operating port. Rubber trocars were used to protect the incisions. After the location of the tumor was determined under thoracoscopy, lobectomy was performed, followed by lymphadenectomy.

Patients in the control group underwent conventional thoracotomy. An incision was made at the posterolateral thorax where the skin was cut layer by layer to separate the subcutaneous tissues, the latissimus dorsi and serratus anterior muscles. A posterolateral thoracotomy in the fourth intercostal space was performed to open the ribs. The ribs at the inferior border of the incision were cut off if necessary. The pulmonary arteries, pulmonary veins and bronchi in the lobes with the tumor lesions were separated under direct vision. The tumor lobes were removed and routine lymphadenectomy was performed simultaneously.

The bronchia and blood vessels of the two groups were sutured by direct ligation or surgical staplers. The incisions were washed with normal saline; drainage tubes were placed; the thorax cavity was closed layer by layer after hemostasis; routine lung dilation and ventila-

Table 1. Basic data of patients in the two groups

Variable	CG (n=50)	OG (n=50)	t/χ^2	*P* value
Age (year)	64.6±5.7	65.3±6.1	0.593	0.555
Male/female (n)	31/19	34/16	0.396	0.529
PT (adenocarcinoma/SCC)	27/23	29/21	0.162	0.687
TD (cm)	2.9±0.8	3.1±1.0	1.104	0.272
PS (I/II)	33/17	30/20	0.386	0.534
LT (peripheral/central)	37/13	41/9	0.932	0.334
Smoking history (n)	29	32	0.378	0.539
Hypertension (n)	27	24	0.360	0.548
Diabetes mellitus (n)	25	28	0.160	0.689

Note: CG, denotes control group; OG, observation group; PT, pathological type; SCC, squamous cell carcinoma; TD, tumor diameter; PS, pathological stage; LT, lesion type.

Table 2. Perioperative indicators of patients

Variable	CG	OG	t/χ^2	*P* value
Case (n)	50	50		
OT (min)	134.8±55.7	109.5±42.3	2.558	0.012
IBL (mL)	292.3±65.2	145.7±49.1	12.700	<0.001
MLND (n)	11.4±6.2	10.7±6.8	0.538	0.592
TCTR (d)	5.3±0.8	3.4±0.6	13.440	<0.001
TA (d)	3.2±0.9	1.4±0.5	12.360	<0.001

Note: CG, denotes control group; OG, observation group; OT, operative time; IBL, intraoperative blood loss; MLND, mediastinal lymph nodes dissected; TCTR, time to chest tube removal; TA time to ambulation.

Table 3. Rates of cardiopulmonary complications of the two groups (n)

Variable	CG	OG	χ^2	*P* value
Case (n)	50	50		
Tachycardia	4	1	1.895	0.169
AF	3	2	0.211	0.646
PC	3	1	1.042	0.307
Atelectasis	6	2	2.174	0.140
Hypoxemia	8	1	5.983	0.014
IC	5	1	2.837	0.092
OCC	29 (58%)	8 (16%)	18.920	<0.001

Note: CG, denotes control group; OG, observation group; AF, atrial fibrillation; PC, premature contractions; IC, involuntary cough; OCC, overall cardiopulmonary complications.

tion was asked to perform before thorax closure, and routine anti-infection treatment was given after treatment. Postoperative outpatient appointments and telephone follow-up were carried out. The patients were followed up once a month; imaging examination including the chest CT plain scans and enhancement were performed periodically every six months.

Outcome measures

The two groups were compared in the operation-related indicators (operative time, the amount of intraoperative blood loss, the number of mediastinal lymph nodes dissected, the time to chest tube removal and the time to ambulation).

The rates of cardiopulmonary complications were compared between the two groups within one month after treatment. Cardiac complications included tachycardia, atrial fibrillation and premature contractions; pulmonary complications included atelectasis, hypoxemia and involuntary cough.

The lung function indicators, which included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and maximum voluntary ventilation (MVV), were compared between the two groups at 6 months after treatment.

The serum levels of interleukin-6 (IL-6), interleukin-10 (IL-10) and C-reactive protein (CRP) were also compared between the two groups. Elbow venous blood (5 ml) was collected from each patient in the fasting state before and 3 days after treatment, placed in an anticoagulant tube, and centrifuged for 15 minutes at 3000 r/min; the serum was isolated and stored at -20°C. The serum levels of CRP, IL-6 and IL-10 were detected by the enzyme-linked immunosorbent assay (ELISA). The CRP, IL-6 and IL-10 kits were all purchased from R&D Science Company, USA, and the experiments were performed strictly in accordance with the instructions.

Moreover, the percentages of CD^4+T cells and CD^8+T cells were also compared between the two groups. The percentages of CD^4+T cells and CD^8+T cells were measured by a Beckmann Quanta SC flow cytometer (Beckmann

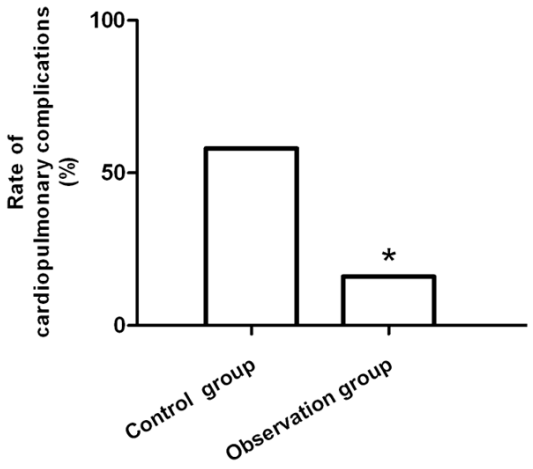

Figure 1. Comparison of the rates of cardiopulmonary complications between the two groups. Compared with the control group, *P<0.001.

Coulter, USA) before and 3 days after treatment. Antithrombin (100 μL) was drawn from each patient, added with directly fluorescence-conjugated mouse anti-human CD^4-FITC and CD^8-PE monoclonal antibodies, and mixed thoroughly. The mixture was cultured away from light in the room temperature for 15 min, added with 500 μL of erythrocyte lysis buffer (Beckmann Coulter, USA), and mixed thoroughly. The mixture was cultured away from light in room temperature for 20 min, and then centrifuged for 5 min at 3,000 r/min. After centrifugation, the supernatant was removed, added with 500 μL of PBS buffer, and mixed thoroughly. Subsequently, the percentages of CD^4+T cells and CD^8+T cells were measured by flow cytometry.

Statistical analysis

The experimental data were processed with the use of SPSS software, version 21.0. Measurement data are presented as mean ± sd, and the independent sample t test was used for between-group comparison; the paired t test was applied for comparison before and after treatment. Count data were described as percentage, and the chi-square test was employed for between-group comparison. P< 0.05 was deemed to be significantly different.

Results

Basic data of patients

The two groups were basically similar in age, sex, pathological type, tumor diameter, pathological stage, lesion type and smoking history (all P>0.05), so they were comparable (**Table 1**).

Perioperative indicators

The patients in the two groups differed insignificantly in the number of mediastinal lymph nodes dissected. Compared with the control group, the observation group had significantly reduced operative time, intraoperative blood loss, the time to chest tube removal and time to ambulation (all P<0.05; **Table 2**).

Cardiopulmonary complications

The rate of cardiopulmonary complications was 16% (8/50) in the observation group and 58% (29/50) in the control group, insignificantly different between the two groups (χ^2=18.920, P<0.001), as shown in **Table 3** and **Figure 1**.

Pulmonary functions

There were no significant differences in the preoperative indicators of FVC, FEV1 and MVV between the two groups (all P>0.05). At 6 months after treatment, the indicators of FVC, FEV1 and MVV in the observation group were significantly higher than those of the control group (all P<0.05; **Table 4**).

CRP, IL-6 and IL-10

No significant differences were observed in the expression levels of CRP, IL-6 and IL-10 between the two groups before treatment (all P>0.05); at 3 days after treatment, significantly lower levels of CRP, IL-6 and IL-10 were seen in the observation group were than those in the control group (all P<0.001; **Table 5**).

CD^4+T cells and CD^8+T cells

The percentages of CD^4+T cells and CD^8+T cells were insignificantly different between the two groups before treatment (all P>0.05). However, the rates of CD^4+T cells and CD^8+T cells were significantly higher in the observation group than in the control group 3 days after treatment (all P<0.05; **Figure 2**).

Tumor-free survival

After treatment, the 1-year, 2-year and 3-year survival rates were respective 78%, 58% and 34% in the control group, and 82%, 60% and 40% in the observation group, so there were no

Table 4. FVC, FEV1 and MVV indicators of the two groups

Variable	Case	FVC (L)		FEV1 (L)		MVV (L)	
		BT	AT	BT	AT	BT	AT
CG	50	3.1±0.7	2.0±0.5	2.6±0.5	1.4±0.3	78.7±19.6	59.8±15.7
OG	50	3.0±0.6	2.6±0.9	2.5±0.4	1.9±0.5	80.1±21.3	68.1±17.4
t/χ^2		0.767	4.121	1.104	6.063	0.342	2.504
P value		0.445	<0.001	0.272	<0.001	0.733	0.014

Note: CG denotes control group; OG observation group; FVC forced vital capacity; BT before treatment; AT after treatment; FEV1 forced expiratory volume in one second; MVV maximum voluntary ventilation.

Table 5. Inflammatory cytokines expression of the two groups

Variable		CG	OG	t	*P* value
Case (n)		50	50		
IL-6 (ng/L)	BT	15.1±1.7	15.3±1.8	0.571	0.569
	AT	39.2±6.7	25.8±5.9	10.610	<0.001
t		18.742	26.421		
P		<0.001	<0.001		
IL-10 (ng/L)	BT	42.7±7.5	43.5±7.7	0.526	0.600
	AT	38.5±6.3	24.6±4.6	12.600	<0.001
t		19.528	25.906		
P		<0.001	<0.001		
CRP (g/L)	BT	12.7±1.3	13.0±1.5	1.069	0.288
	AT	94.8±15.8	58.2±10.5	13.640	<0.001
t		53.509	32.677		
P		<0.001	<0.001		

Note: CG, denotes control group; OG, observation group; IL-6, interleukin-6; BT, before treatment; AT, after treatment; IL-10, interleukin-10; CRP, C-reactive protein.

significant differences between the two groups (all P>0.05; **Table 6**).

Discussion

For elderly patients with NSCLC who are characteristic of old age, decreased immunity and slow recovery, undergoing conventional thoracotomy tend to result in more cardiopulmonary complications, further damages to the immune function and greater pain. Over the years, the advance of VATS has provided advantages for the surgical treatment of elderly patients with NSCLC. VATS is advantageous over conventional thoracotomy in smaller incisions, milder pain, less influence on cardiopulmonary functions, and quicker postoperative recovery. It is increasingly widely used in clinical practice [13]. It has been reported that VATS can significantly improve respiratory muscle strength compared with conventional thoracotomy [14]. However, it is still controversial regarding the effects of radical resection of NSCLC by VATS versus conventional thoracotomy on cardiopulmonary complications, pulmonary function indicators, inflammatory cytokines and immune function in elderly patients with NSCLC [15]. In this study, the two groups differed insignificantly in basic data such as age, sex, pathological type, tumor diameter, pathological stage, pathological type and smoking history. Therefore, this study could better objectively evaluate the efficacy of VATS for radical resection of NSCLC in elderly patients.

The results of this study showed no significant difference in the rates of tumor-free survival between the two groups within 3 years after treatment. Besides, the two groups also differed insignificantly in the number of mediastinal lymph nodes dissected, suggesting that VATS for radical resection of NSCLC allowed a good exposure of visual fields and thorough dissection of lymph nodes. The operative time, intraoperative blood loss, the time to chest tube removal and the time to ambulation in the observation group significantly reduced compared with those in the control group, and the differences were statistically significant. Operative time and amount of perioperative intraoperative blood loss are indicators reflecting surgical trauma of patients, whereas the time to chest tube removal and the time to ambulation are important indicators reflecting recovery of patients from the operation. It is thus clear that VATS for radical resection of lung cancer in elderly patients is associated with less trauma and blood loss, and quicker recovery. This may be due to the facts that the ribs were not required to open during VATS for radical resection of lung cancer, which resulted in small damages to muscle and

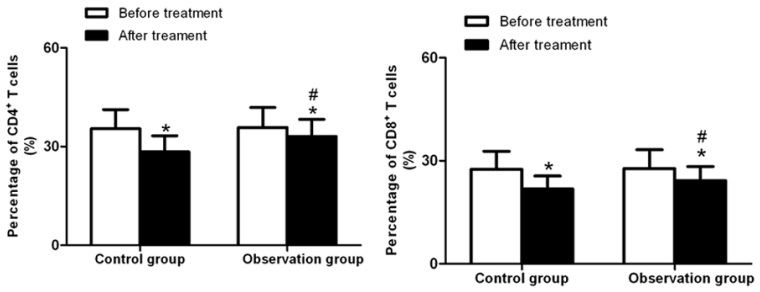

Figure 2. Comparison of the percentages of CD^4+T cells and CD^8+T cells between the two groups. Compared within the same groups before and after treatment, *P<0.05; compared with the control group, *P<0.05.

Table 6. Tumor-free survival of the two groups during 3 years of follow-up (n, %)

Variable	Case	1 year	2 year	3 year
CG	50	39 (78%)	29 (58%)	17 (34%)
OG	50	41 (82%)	30 (60%)	20 (40%)
χ^2		0.250	0.041	0.386
P		0.617	0.839	0.534

Note: CG, denotes control group; OG, observation group.

other tissues; additionally, small incisions could alleviate the patients' fears, so that the patients could ambulate earlier; the magnification function of thoracoscopes enabled precise anatomy, complete hemostasis, and reduced intraoperative blood loss [16]. VATS for radical resection of NSCLC is more favorable than conventional thoracotomy in elderly patients. These are consistent with the findings reported by Song et al. and Hwang et al. [17, 18].

In this study, we also discussed the value of VATS for radical resection of NSCLC in elderly patients from the aspects of cardiopulmonary complications and recovery of pulmonary functions. The occurrence of cardiopulmonary complications may lead to lower success rates of surgery and poor postoperative recovery. The results of this study demonstrated that the rate of cardiopulmonary complications in the observation group was significantly lower than that in the control group, but the levels of FVC, FEV1 and MVV indicators in the observation group were significantly higher than those in the control group at 6 months after treatment. This might be attributed to minimally invasion, small damages to tissues and mild postoperative pain brought about by VATS for radical resection of NSCLC, which help patients to make deep breathing, expectoration of sputum by means of coughs. Early ambulation also helps them recover pulmonary function. These results are generally consistent with those reported by Yan et al. and Whitson et al. [19, 20].

Surgical trauma is closely related to inhibition of the immune function in elderly patients [21]. Surgical trauma can result in production and response of cytokines, with the main manifestations of dramatically elevated levels of inflammatory cytokines and cytokines inhibiting cellular immunity. The impacts of surgical trauma on cytokines are different; the greater the surgical trauma is, the higher the levels of cytokines are [22]. The results of this study revealed that the levels of CRP, IL-6 and IL-10 were higher in the two groups 3 days after treatment than those before treatment, with lower mean levels in the observation group than in the control group; the percentages of CD^4+T cells and CD^8+T cells in the two groups 3 days after treatment were lower than those before treatment, with higher percentages in the observation group than in the control group. All this above indicates that elderly patients undergoing VATS for radical resection of NSCLC had fewer inflammatory reactions, fewer impacts on the immune function and faster recovery of immune functions, which are basically in line with the results of studies conducted by Bobocea et al. and by Ng et al. [23, 24].

In conclusion, radical resection of NSCLC by VATS in elderly patients is more significantly favorable than by conventional thoracotomy in perioperative indicators, cardiopulmonary complications, lung function and immune function. However, there are still some limitations in this study, such as small sample size, single-center study, no results of long-term follow-ups, etc. Prospective randomized controlled trials with larger sample size and long-term follow-up are required in the future research to further validate the advantages of VATS for radical resection of NSCLC in elderly patients.

Disclosure of conflict of interest

None.

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References

[1] Roach MC, Bradley JD and Robinson CG. Optimizing radiation dose and fractionation for the definitive treatment of locally advanced non-small cell lung cancer. J Thorac Dis 2018; 10: S2465-S2473.

[2] VanderLaan PA. Updates in lung cancer cytopathology. Surg Pathol Clin 2018; 11: 515-522.

[3] Rodgers-Fischl PM, Martin JT and Saha SP. Video-Assisted Thoracoscopic versus open lobectomy: costs and outcomes. South Med J 2017; 110: 229-233.

[4] Xue Y, Wang YY, Zhang K, Cong W, He B and Zeng FC. A study of complete video-assisted thoracoscopic surgery lobectomy in treatment of elderly patients with non-small cell lung cancer: curative effect and Impact on clinical prognosis. Cell Biochem Biophys 2015; 73: 399-404.

[5] Pages PB, Delpy JP, Orsini B, Gossot D, Baste JM, Thomas P, Dahan M and Bernard A. Propensity score analysis comparing videothoracoscopic lobectomy with thoracotomy: a french nationwide study. Ann Thorac Surg 2016; 101: 1370-1378.

[6] Vannucci F and Gonzalez-Rivas D. Is VATS lobectomy standard of care for operable non-small cell lung cancer? Lung Cancer 2016; 100: 114-119.

[7] Bendixen M, Jorgensen OD, Kronborg C, Andersen C and Licht PB. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: a randomised controlled trial. Lancet Oncol 2016; 17: 836-844.

[8] Wang S, Sun T, Sun H, Li X, Li J, Zheng X, Mallampati S, Sun H, Zhou X, Zhou C, Zhang H, Cheng Z and Ma H. Survival improvement in patients with non-small cell lung cancer between 1983 and 2012: analysis of the surveillance, epidemiology, and end results database. Tumour Biol 2017; 39: 101042831 7691677.

[9] Qiang G, Liang C, Guo Y, Shi B, Tian Y, Song Z and Liu D. Video-assisted thoracoscopic lobectomy for elderly nonsmall cell lung cancer: short-term and long-term outcomes. J Cancer Res Ther 2015; 11: 793-797.

[10] Oh DS, Reddy RM, Gorrepati ML, Mehendale S and Reed MF. Robotic-assisted, video-assisted thoracoscopic and open lobectomy: propensity-matched analysis of recent premier data. Ann Thorac Surg 2017; 104: 1733-1740.

[11] Wood DE. Re: propensity score-matching analysis of hybrid video-assisted thoracoscopic surgery and thoracoscopic lobectomy for clinical stage I lung cancer. Eur J Cardiothorac Surg 2016; 49: 1068-1069.

[12] Whitson BA, Groth SS, Duval SJ, Swanson SJ and Maddaus MA. Surgery for early-stage non-small cell lung cancer: a systematic review of the video-assisted thoracoscopic surgery versus thoracotomy approaches to lobectomy. Ann Thorac Surg 2008; 86: 2008-2016; discussion 2016-2008.

[13] Kim SW, Hong JM and Kim D. What is difficult about doing video-assisted thoracic surgery (VATS)? A retrospective study comparing VATS anatomical resection and conversion to thoracotomy for lung cancer in a university-based hospital. J Thorac Dis 2017; 9: 3825-3831.

[14] Saito H, Nakagawa T, Ito M, Imai K, Ono T and Minamiya Y. Pulmonary function after lobectomy versus segmentectomy in patients with stage I non-small cell lung cancer. World J Surg 2014; 38: 2025-2031.

[15] Al-Ameri M, Bergman P, Franco-Cereceda A and Sartipy U. Video-assisted thoracoscopic versus open thoracotomy lobectomy: a Swedish nationwide cohort study. J Thorac Dis 2018; 10: 3499-3506.

[16] Upham TC and Onaitis MW. Video-assisted thoracoscopic surgery versus robot-assisted thoracoscopic surgery versus thoracotomy for early-stage lung cancer. J Thorac Cardiovasc Surg 2018; 156: 365-368.

[17] Song CY, Sakai T, Kimura D, Tsushima T and Fukuda I. Comparison of perioperative and oncological outcomes between video-assisted segmentectomy and lobectomy for patients with clinical stage IA non-small cell lung cancer: a propensity score matching study. J Thorac Dis 2018; 10: 4891-4901.

[18] Hwang Y, Kang CH, Kim HS, Jeon JH, Park IK and Kim YT. Comparison of thoracoscopic segmentectomy and thoracoscopic lobectomy on the patients with non-small cell lung cancer: a propensity score matching study. Eur J Cardiothorac Surg 2015; 48: 273-278.

[19] Yan TD, Black D, Bannon PG and McCaughan BC. Systematic review and meta-analysis of randomized and nonrandomized trials on safety and efficacy of video-assisted thoracic surgery lobectomy for early-stage non-small-cell lung cancer. J Clin Oncol 2009; 27: 2553-2562.

[20] Whitson BA, Andrade RS, Boettcher A, Bardales R, Kratzke RA, Dahlberg PS and Maddaus MA. Video-assisted thoracoscopic surgery is more favorable than thoracotomy for

resection of clinical stage I non-small cell lung cancer. Ann Thorac Surg 2007; 83: 1965-1970.
[21] Ng CS and Lau KK. Surgical trauma and immune functional changes following major lung resection. Indian J Surg 2015; 77: 49-54.
[22] Albertsmeier M, Quaiser D, von Dossow-Hanfstingl V, Winter H, Faist E and Angele MK. Major surgical trauma differentially affects T-cells and APC. Innate Immun 2015; 21: 55-64.
[23] Bobocea AC, Trandafir B, Bolca C and Cordos I. Minimally invasive surgery in cancer. Immunological response. Chirurgia (Bucur) 2012; 107: 154-157.
[24] Ng CS, Lee TW, Wan S, Wan IY, Sihoe AD, Arifi AA and Yim AP. Thoracotomy is associated with significantly more profound suppression in lymphocytes and natural killer cells than video-assisted thoracic surgery following major lung resections for cancer. J Invest Surg 2005; 18: 81-88.