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ORIGINAL ARTICLE

Anatomic lung resections for benign pulmonary diseases by video-assisted thoracoscopic surgery (VATS)

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Abstract
Purpose Based on increasing evidence of its benefits regarding perioperative and oncologic outcome, video-assisted thoracoscopic surgery (VATS) has gained increasing acceptance in the surgical treatment of early stage non-small cell lung cancer (NSCLC). However, the evidence for a VATS approach in anatomic lung resection for benign pulmonary diseases is still limited.
Methods Between March 2011 and May 2014, data from 33 and 63 patients who received VATS anatomic lung resection for benign diseases (VATS-B) and early stage NSCLC (VATS-N), respectively, were analyzed retrospectively. For subgroup analyses, VATS-B was subdivided by operation time and underlying diseases. Subgroups were compared to VATS-N.
Results Three patients from VATS-B and four from VATS-N experienced conversion to open surgery. Causes of conversion in VATS-B were intraoperative complications, whereas conversions in VATS-N were elective for oncological concerns ($p < 0.05$). Operation time and duration of postoperative mechanical ventilation were longer by tendency; postoperative stay on intensive care unit and chest tube duration were significantly longer in VATS-B. Subgroup analyses showed a longer operation time as a predictor for worse perioperative outcome regarding postoperative mechanical ventilation, postoperative stay on intensive care unit, chest tube duration, and length of hospital stay. Patients with longer operation time suffered from more postoperative complications. Differences in perioperative outcome data were not significantly dependent on the underlying benign diseases compared to VATS-N.
Conclusions VATS is feasible and safe in anatomic lung resection for benign pulmonary diseases. Not the underlying disease, but a longer operation time is a factor for worse postoperative outcome.

Keywords Video-assisted thoracoscopic surgery · Anatomic lung resection · Lobectomy · Benign pulmonary diseases · NSCLC

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Introduction

Video-assisted thoracoscopic surgery (VATS) has undergone a continuous evolution since its beginning in the early 1990s [1], and today, VATS has become a standard approach in major pulmonary resections [2–4]. There is a strong evidence for benefits of VATS for anatomic lung resections, especially in lobectomies, for early stage non-small cell lung cancer (NSCLC) [2, 5–9]. VATS has been proven to provide good functional results, faster recovery, less morbidity as well as an improved quality of life, and some data even suggest better oncological outcome when compared to open surgery [2, 5–12]. Thus, VATS has been stated as the favorable approach for early stage NSCLC [2–9]. Even technically more advanced surgical procedures like sublobar or extended pulmonary resections were shown to be safely feasible [12–14].

However, in contrast to the broad experience with VATS in lung cancer patients, limited data is given on the feasibility of anatomic lung resections by VATS for benign pulmonary diseases.

Materials and methods

Between March 2011 and May 2014, 33 patients were scheduled for VATS anatomic lung resection for benign pulmonary diseases (VATS-B group) and 63 patients for pathologically confirmed stage I (UICC 7th edition) NSCLC (VATS-N group).

Each patient was treated by the institutional standard of care. Patient data were retrospectively analyzed from the prospectively maintained institutional database. The acquisition of data was approved by the local ethics committee.

Indications for surgery in the VATS-B group were failure of conservative/medical therapy with chronic inflammative and infectious status in the subgroup of aspergilloma patients ($n = 6$), recurrent hemoptysis or/and infections in patients with bronchiectasis ($n = 9$), volume reduction in COPD patients ($n = 4$), destroyed lung syndrome ($n = 11$), and others ($n = 3$). In the VATS-N group, indication was pre- or intraoperatively proven NSCLC in pathological stage I (Table 1). All patients underwent general anesthesia, and a double-lumen endotracheal tube was placed for selective lung ventilation during surgery. The surgical technique for anatomic lung resection was similar in both groups. Patients were placed in lateral decubitus position. An anterior three-incision VATS approach without rib-spreading was used, with one thoracentesis in the fourth (anterior axillary line) and two centeses in the eighth intercostal space (anterior and posterior axillary line, respectively). By hilar dissection, the pulmonary vessels and bronchi were individually controlled using endoscopic stapling devices [2]. Whenever present, complete adhesiolysis was performed as a first step and prior to lung resection. A systematic lymph node (LN) dissection was performed in all oncologic resections as recommended by the European Society of Thoracic Surgeons [15]. Surgery was performed by one experienced surgeon. In the majority of patients in both groups, one chest tube was placed via the anterior thoracentesis in the eighth intercostal space and negative pressure was applied until chest X-ray confirmed complete expansion of the remaining lobe(s). Chest tube was removed as soon as air leakage had stopped.

Statistical analysis was performed using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego, CA, USA, www.graphpad.com. Patients who underwent conversion to conventional open surgery (VATS-B: three patients and VATS-N: four patients) were excluded in order to focus on the effects of the VATS approach. In the first step, data of both groups VATS-B and VATS-N were analyzed using Fisher's exact or Pearson's X^2 test for categorical data in cross-tabulation, independent two-tailed Student's t test for two-group comparisons of parametric, and Man-Whitney U test for non-parametric data. Normally distribution of data was tested previously by Shapiro-Wilk test.

Following initial analysis, patients of the VATS-B group were subdivided based on the operation time with a cut-off level at 190 min (<190 min: VATS-B1 and >190 min: VATS-B2). Furthermore, patients of the VATS-B group were subdivided based on their underlying disease: aspergilloma (VATS-Ba), bronchiectasis (VATS-Bb), and destroyed lung (VATS-Bd). Patients who underwent anatomic lung resection for lung volume reduction in emphysema by VATS and other indications were excluded from the latter subgroup analysis because of small sample sizes. Perioperative outcome data of these subgroups were compared to those of VATS-N patients as the reference group (Table 4). Data in cross-tabulation were analyzed as described above. After Shapiro-Wilk test, statistical analyses were performed using One-way ANOVA for normally distributed or Kruskal Wallis test for non-parametric data and, when applicable, followed by Dunnett's Multiple Comparison or Mann-Whitney U as post hoc tests to compare means ± SEM or medians (range) of the subgroups with the VATS-N group.

Table 1 Indications for surgery

VATS-B		VATS-N	
n	33	*n*	63
Destroyed lobe	11 (33.3 %)	pT1N0M0	38 (60.3 %)
Bronchiectasis	9 (27.3 %)	pT2aN0M0	25 (39.7 %)
Aspergilloma	6 (18.2 %)	Histological subgroup[a]	
Volume reduction in COPD	4 (12.1 %)	Adenocarcinoma	31 (49.2 %)
Others	3 (9.1 %)	Squamous cell carcinoma	20 (31.7 %)
Chondrohamartoma Inflammatory pseudotumor Sarcoidosis		Large cell carcinoma	11 (17.5 %)

[a] Histopathologic sub-differentiation of NSCLC was retrospectively not available in one case

p values <0.05 were considered to indicate statistical significance. Normally distributed data are given in mean ± SEM, and not-normally distributed data as well as hemoglobin (Hb) and C-reactive protein (CRP) values are given in median (range).

Results

Patients characteristics

Patients from the VATS-B group were significantly younger and suffered from less risk factors and chronic diseases, leading to a better preoperative ASA-score (Table 2).

The types of pulmonary resection were similar in both groups regarding operation side and extent of the pulmonary resection. However, major adhesions necessitating complete adhesiolysis before pulmonary resection were observed in 76.7 % ($n=23$) of the VATS-B but only in 35.6 % ($n=21$) of the VATS-N group ($p < 0.05$). The lymph node dissection rate also differed significantly with 100 % in the NSCLC-patients versus only 23.3 % ($n = 7$) in the VATS-B group ($p < 0.0001$). Concerning intraoperative complications, in the VATS-N group one (laceration of a segmental bronchus, controlled minimally-invasive by suturing) and in the VATS-B group three (a lesion of the bronchus intermedius in a right upper lobectomy and an injury of the diaphragm during adhesiolysis, both managed minimally-invasively, and one intraoperative bleeding from a pulmonary artery branch leading to conversion to open thoracotomy) were observed. The four (6.3 %) conversions to open surgery in the VATS-N group were classified as "elective" (non-emergent) due to oncological concerns, whereas in the VATS-B group (9.1 %; Table 2) two were "elective" for technical problems and one emergent for pulmonary arterial bleeding.

Perioperative results

Operation time was longer in VATS-B compared to VATS-N ($p = 0.1245$, Table 2). Right at the end of the operating procedure, 66 % ($n=22$) of the patients in VATS-B and 82 % ($n=52$) of the patients in VATS-N group were extubated in the operating room. In patients requiring postoperative mechanical ventilation, the duration was longer by tendency ($p = 0.0634$) in those of the VATS-B group, with a consecutive longer postoperative stay at the intensive care unit (Table 2).

Overall duration of chest tubes was significantly longer in patients of VATS-B compared to VATS-N group, whereas no differences were observed between both groups regarding the frequency of prolonged (chest tube duration >7 days) or recurrent (pneumothorax and/or subcutaneous emphysema after initial chest tube removal) air leakage. Postoperative complication (14 and 19 patients from VATS-B and VATS-N experienced 29 and 26 complications, respectively) and mortality rate were similar in both groups as was the length of postoperative hospital stay (Tables 2 and 3).

Regarding the surgery related trauma, patients from VATS-B group had significantly lower hemoglobin levels immediately after surgery which remained lower by tendency at the time of discharge ($p = 0.0565$). Preoperative C-reactive protein (CRP) levels were equal in both groups, but postoperative levels were consistently higher in VATS-B group and also showed a higher increase compared to the preoperative levels immediately after the operation ($p < 0.0001$) as well as on postoperative day 1 ($p < 0.05$, Table 2).

Subgroup analysis based on operation time

Subgroup analysis for operation time with a cut-off level at 190 min (up to: VATS-B1, 13 patients; above: VATS-B2, 17 patients) revealed some differences in perioperative outcome data. Adhesiolysis was performed significantly more frequent in patients of the VATS-B2 group. Intraoperative blood loss was lower in VATS-B1 but higher in VATS-B2 compared to VATS-N group and consequently leads to a difference in postoperative Hb-values of VATS-B2. Similar results were found for perioperative CRP-values; while no differences between the groups were observed preoperatively, CRP-levels in patients of VATS-B2 but not of VATS-B1 were significantly higher immediately after surgery and on postoperative day 1, reflected by a higher increase from preoperative to postoperative levels in VATS-B2 when compared to VATS-N patients ($p < 0.0001$ and $p < 0.05$).

Prolonged mechanical ventilation time was significantly higher and resulted in a longer stay at intensive care unit in VATS-B2 compared to VATS-N patients. Chest tube duration as well as total and postoperative hospital stay were similar among VATS-B1 and VATS-N groups but significantly longer for VATS-B2.

Overall complication rate was similar in both VATS-B1 and VATS-B2 when compared to VATS-N. However, the six patients (46.2 %) in VATS-B1 experienced six complications, whereas the eight patients (47.1 %) in VATS-B2 had 23 complications (Table 4).

Subgroup analysis based on underlying diseases

VATS-B group was subdivided into patients with aspergilloma (VATS-Ba, five patients), bronchiectasis (VATS-Bb, nine patients), and destroyed pulmonary lobe (VATS-Bd, 10 patients). Patients in VATS-Bb and VATS-Bd but not in VATS-Ba group were younger and ASA-score of VATS-Bb patients was significantly lower compared to control group VATS-N. Adhesions were present in all of the

Table 2 Patient characteristics, procedures performed, and perioperative results

	VATS-B	VATS-N	*p* value
Gender			=1.0
Male	24	45	
Female	9	18	
Age (year)[a]	62 (13–76)	70 (48–87)	<0.0001
BMI (kg/m^2)	24.1 ± 0.9	27.2 ± 0.6	<0.05
ASA[a]	3 (2–4)	3 (2–4)	<0.05
1	0	0	
2	14	10	
3	17	50	
4	2	3	
5	0	0	
Chronic diseases (*n*)			
COPD	10	35	<0.05
Emphysema	8	7	ns
CAD	6	33	<0.05
DM	2	19	<0.05
Lung function[a,b]			
FEV1 (l)	1.8 (0.9–4.0)	1.94 (0.7–3.5)	ns
FEV1 (%)	60.5 (31.2–105.9)	64.5 (26.4–143.7)	ns
Operation side (including conversions) (*n*)			ns
Right	19 (21)	35 (37)	
Left	11 (12)	24 (24)	
Conversion (*n*)			
Surgical problems	3[c]	–	<0.05
Oncologic reasons (“elective”)	–	4	
Type of pulmonary resection (*n*)			ns
Right:			
UL	10	19	
ML	2	3	
LL	5	10	
Sublobar	1[m]	3[e]	
Pneumonectomy	1	0	
Left:			
UL	1	12	
LL	4	9	
Sublobar	6[d]	2[f]	
Pneumonectomy	0	1	
Extended resection (*n*)	3	3	ns
LN assessment (*n*)	7	59	<0.0001
Adhesiolysis (*n*)	23	21	<0.05
Previous thoracic operations (*n*)	6[h]	13[i]	ns
Intraoperative complications (*n*)[g]	3	1	ns
Operation time (min)[a]	203 (76–574)	168 (103–468)	=0.1245
Intraoperative blood loss (ml)[a,j]	250 (0–2100)	250 (0–1500)	ns
Intraoperative blood transfusion			=0.0562
Patients (*n*)	6	3	
Total transfusion (ml)	3600	3000	
Extubation in OR (*n*)	22	52	ns
Postoperative mechanical ventilation (min)[a]	0 (0–68428)	0 (0–887)	=0.0634
Postoperative length of stay on ICU (min)[a]	1601 (693–147928)	1341 (712–160863)	<0.05

Table 2 (continued)

	VATS-B	VATS-N	*p* value
Chest tube duration (day)[a,l]	4.5 (1–49)	3 (1–23)	<0.05
Length of hospital stay (day)[a]			
Total	10 (4–104)	9 (4–74)	ns
Postoperative	8.5 (3–66)	7 (2–46)	ns
Postoperative blood transfusion			ns
Patients (*n*)	6	5	
Total transfusion (ml)	5400	3900	
Hemoglobin (mg/dl)			
Preoperative[a]	128.5 (79–182)	138 (81–183)	ns
Postoperative	111 (75–164)	126 (85–155)	<0.05
At discharge	108 (72–166)	120 (78–148)	=0.0565
CRP (mg/dl)			
Preoperative[a]	5.1 (0.5–147.7)	4.5 (0.5–153.2)	ns
Postoperative[a,k]	11.3 (0.5–156.4)	4.9 (0.5–131.1)	<0.05
POD1[a]	87.3 (10.1–303.3)	65.5 (24.4–360.7)	<0.05
Maximal postoperative[a]	158.6 (26.6–331.5)	137.8 (30.1–488.6)	ns
At discharge[a]	59.2 (2.7–281.7)	49.1 (3.7–254.9)	ns

Normally distributed data are given in mean ± SEM. Laboratory data (Hb and CRP) are given in median (range).

BMI body mass index, *ASA* American society of anesthesiologists' classification of physical health (assessed preoperatively), *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *DM* diabetes mellitus, *FEV1* forced expiratory volume in 1 second, *RUL* right upper lobe, *ML* middle lobe, *RLL* right lower lobe, *LUL* left upper lobe, *LLL* left lower lobe, *LN* lymph node, *OR* operating room, *ICU* intensive care unit, *CRP* C-reactive protein, *POD1* postoperative day 1, *ns* not significant ($p > 0.05$)

[a] Non-parametric data, given in median (range). Laboratory data (Hb and CRP) are given in median (range).

[b] Not available retrospectively in four patients of each group

[c] One conversion from VATS to open surgery in each group of anatomic lung resection for destroyed lobe, aspergilloma, and volume reduction in COPD

[d] Anatomic lingula ($n = 4$), segment 6 ($n = 1$), segments 1–3 ($n = 1$) resection

[e] Anatomic segment 6 ($n = 2$), segment 2 ($n = 1$) resection

[f] Anatomic lingula ($n = 1$), segments 1–3 ($n = 1$) resection

[g] Intraoperative complications without those requiring conversion to open surgery

[h] Including lung transplantation ($n = 2$), pulmonary resection ($n = 3$), open heart surgery ($n = 1$)

[i] Including pulmonary resection ($n = 6$), open heart surgery ($n = 7$)

[j] Not available retrospectively in one patient of the VATS-B group

[k] Not assessed in five patients of the VATS-N group

[l] Duration of the primary (intraoperatively placed) chest tube. Chest tube re-insertion et cetera was classified as a complication.

[m] anatomic segments 2 and 6 resection

VATS-Ba and VATS-Bb patients ($p = 0.0001$) leading to a prolonged operation time, significantly in the VATS-Bb and by tendency in the VATS-Ba group ($p = 0.0717$) but not among VATS-Bd patients.

The rate of postoperative mechanical ventilation was higher in VATS-Bd group when compared to VATS-N. Although no significant differences were observed among the four groups, length of stay at intensive care unit, chest tube duration and total as well as postoperative hospital stays were not significantly higher in VATS-Bd when compared to VATS-N patients. No differences in complication rate were observed (Table 4).

Discussion

With increasing experience and ongoing technical progress, VATS has been applied to a broader range of patients and to technically more challenging procedures [12–14]. Among those, the most frequent and thus the one with the highest evidence level is pulmonary lobectomy in early stage NSCLC [6, 8]. Some few reports do exist on VATS anatomic lung resections for benign pulmonary diseases; however, evidence is based on retrospective, mostly non-controlled case series. Benign indications for anatomic pulmonary resections vary, with the most relevant being persistent aspergilloma,

Table 3 Perioperative complications

Complication	VATS-B	VATS-N	*p*
Patients (*n*)	14	19	ns
Respiratory			
Acute insufficiency	1	1	
Chronic insufficiency	3	2	
Pneumonia	3	1	
Empyema	1	0	
Prolonged air leak			
>7 days	6	7	
Chest tube re-insertion	6	7	
Chylothorax	0	2	
Chest tube re-insertion	0	1	
Re-VATS	5[a]	1[b]	
Cardiac			
Arrhythmia with hemodynamic decompensation	0	3	
Myocardial infarction	0	1	
Resuscitation	1	0	
Stroke	1	1	
Bleeding[c]	1	0	
Acute rejection after LTX	1	0	
In-hospital and 30d mortality	1	1	

LTX lung transplantation

[a] Re-VATS for empyema ($n = 1$), hemothorax ($n = 2$), air leak ($n = 1$), follow-up ($n = 1$)

[b] Re-VATS for air leak

[c] Requiring surgical intervention

tuberculosis, bronchiectasis, and destroyed lung [16, 17]. Destroyed lung usually results from an underlying chronic inflammatory disease like non-specific bronchiectasis or tuberculosis [18]. In benign diseases, the type of resection (anatomical versus atypical) is of less importance as long as all affected pulmonary tissue is removed [19, 20]. Anatomic instead of wedge resection is indicated, however, for technical reasons: stapling across the affected rigid lung tissue without respecting segmental or lobar border lines bears a high risk of immediate (bleeding) or secondary (persistent air leaks) failure.

One of the earliest reports on major pulmonary resections for benign indications compared 10 patients who underwent VATS-lobectomy for various benign diseases with patients who underwent minimally-invasive or open lobectomy for malignant diseases. No differences were observed regarding operation time, chest tube duration, and postoperative hospital stay [21]. Recently, Chen and colleagues discussed the role of VATS compared to open surgery for anatomic lung resection in pulmonary aspergilloma. The length of hospital stay and complication rate were worse after the open approach. Nevertheless, the authors highlighted the extensive difficulties with fibrotic changes to the lung hilum in the VATS approach [17]. Similar results were reported by Zhang et al. in patients who underwent major lung resection by VATS or thoracotomy for bronchiectasis [22]. Yen et al. reported a shorter length of hospital stay and fewer complications after both VATS wedge resection and lobectomy in selected patients with tuberculosis compared to thoracotomy. However, they concluded that conventional open surgery was preferable since performing a pneumonectomy or extended pulmonary resection by VATS was found to be technically extremely challenging in these patients [23]. Also, Weber and colleagues, who did not observe any differences in the outcome between VATS and open surgery for benign pulmonary diseases, stressed that VATS in benign diseases was technically much more sophisticated when compared to oncologic resections [24]. Adhesions, neovascularization, and LN-enlargement would outweigh the challenge of adequate tumor clearance [21, 24].

The results of this study confirm the great technical challenge of VATS anatomic lung resections in chronic inflammatory diseases. Although a delicate systematic LN-dissection was performed in all VATS-N patients, there was a tendency to longer operation times in the VATS-B group. This may reflect the limitations and difficulties of the VATS approach for these indications: the take-down of dense inflammatory adhesions of the lung to the diaphragm, mediastinum, and chest wall, the dissection of a lung hilum which is altered by fibrotic reactions and adjacent lymph nodes as well as the control of a rigid but nevertheless very vulnerable lung parenchyma [16, 18, 24, 25]. Lesions to the visceral pleura during adhesiolysis and hilar dissection are one main cause of prolonged postoperative air leakage and longer chest tube duration [17, 21]. Nevertheless, complete adhesiolysis is essential for a good hilum exposure which remains difficult even in a fully mobilized lung due to the extended weight, size, and stiffness of the inflammatory altered lung parenchyma. The intraoperative complications and conversions as well as the prolonged chest tube duration in VATS-B patients are interpreted as being directly related to the inflammatory changes: in the two cases of technically induced conversions to open surgery, adhesions were found as being too dense and dissection of hilar structures was classified as not being safely feasible by means of VATS. Yen et al. proposed several imaging characteristics, such as the degree of pleural thickening and peribronchial LN calcification, for preoperative assessment of the extent of fibrotic changes [25]. If these parameters were proven to be reliable, they might help to exclude patients with a high chance of excessive operation times and/or conversions to thoracotomy from a VATS approach.

The high impact of the operation time on perioperative outcome got evident after subgroup analysis in VATS-B with

Table 4 Results of subgroup analysis in terms of operation time (<190 min: VATS-B1 and >190 min: VATS-B2) and the underlying disease (aspergilloma: VATS-Ba, bronchiectasis: VATS-Bb, and destroyed lung: VATS-Bd)

	VATS-B1	VATS-B2	VATS-Ba	VATS-Bb	VATS-Bd	VATS-N
Gender						
Male	8	3	3	7	9	42
Female	5	14	2	2	1	17
Age (year)	60.2 ± 3.2*	60.1 ± 5.2**	63.0 ± 5.1	36.1 ± 6.2**	59.7 ± 4.3*	69.3 ± 1.1
BMI (kg/m^2)	23.2 ± 1.5	22.8 ± 1.2*	23.3 ± 1.0	23.7 ± 2.2	23.9 ± 1.8	27.5 ± 0.6
ASA	2 (2–3)*	3 (2–4)	3 (2–4)	2 (2–3)*	2.5 (2–4)	3 (2–4)
FEV1 (l)[a]	1.8 (0.9–4.0)	1.8 (1.3–3.0)	1.5 (1.3–2.0)	1.8 (1.5–3.0)	2.2 (1.5–4.0)	2 (0.9–3.5)
FEV1 (%)[a]	73.5 (31.2–105.9)	60.2 (34.6–99.2)	60.5 (53–76.6)	59.3 (45.0–74.0)	70.6 (48.6–105.9)	66.8 (26.4–143.7)
Operation side (*n*)[b]						
Right	8	11	3	4	10	35
Left	5	6	2	5	0	24
Type of pulmonary resection (*n*)						
Right:						
UL	2	8	2	2	4	19
ML	2	0	0	1	1	3
LL	3	2	1	1	3	10
Sublobar	1	0	0	0	1	3
Pneumonectomy	0	1	0	0	1	0
Left:						
UL	0	1	0	1	0	12
LL	2	2	1	2	0	9
Sublobar	3	3	1	2	0	2
Pneumonectomy	0	0	0	0	0	1
Extended resection (*n*)	1	2	0	2	1	3
LN assessment (*n*)[##]	4	3	0	1	4	59
Adhesiolysis (*n*)[#]	7	16	5	9	7	21
Previous thoracic operations (*n*)	2	4	1	2	3	13
Intraoperative complications (*n*)[c]	0	2	1	0	1	1
Operation time (min)[a]	<190	>190	215 (165–356)	247 (76–380)*	187 (101–574)	168 (103–468)
Intraoperative blood loss (m)[a,d]	150 (0–300)*	575 (100–2100)*	350 (150–1100)	250 (100–2100)	275 (0–1150)	250 (0–1500)
Extubation in OR (*n*)[#]	12	10	4	7	5	52
Postoperative mechanical ventilation (min)[a]	0 (0–19757)	0 (0–68428)*	0 (0–315)	0 (0–90)	0 (0–68428)*	0 (0–887)
Postoperative length of stay on ICU (min)[a]	1365 (693–40095)	2542 (1137–147928)*	2634 (1191–4199)	1371 (939–8265)	2568 (693–147965)	1341 (712–160863)
Chest tube duration (day)[a]	4 (1–7)	6 (2–49)*	4 (2–11)	4 (2–8)	5 (1–44)	3 (1–23)
Length of hospital stay (day)[a]						
Total	9 (4–80)	14 (6–104)*	14 (8–78)	10 (6–23)	18 (4–104)	9 (4–74)
Postoperative	7 (3–19)	9 (5–66)*	9 (6–66)	8 (5–20)	10 (3–60)	7 (2–46)
Hemoglobin (mg/dl)						
Preoperative[a]	140 (79–158)	120 (87–182)	130 (87–137)	133 (118–149)	109.5 (91–158)	138 (81–183)
Postoperative[a]	124 (87–151)	109 (87–164)*	104 (94–124)	125 (75–142)	109.5 (95–151)	126 (85–155)
At discharge	117 (81–152)	99 (72–166)*	108 (92–113)	99 (72–143)*	104 (72–152)	120 (78–148)
CRP (mg/dl)						
Preoperative[a]	2.9 (0.5–42.1)	6.4 (0.5–147.7)	6.8 (2.9–37.0)	5.2 (0.5–34.9)	5.4 (0.5–147.7)	4.5 (0.5–135.2)
Postoperative[a]	8.1 (0.5–153.5)	14.7 (1.5–156.4)*	62.5 (6.8–153.5)	11.8 (2.8–55.4)*	11.2 (0.5–156.4)*	4.9 (0.5–131.1)
POD1[a]	71.6 (10.1–186.4)	98.0 (55.4–303.3)*	111.2 (64.8–186.4)	78.7 (62.2–143.1)	87.3 (10.1–303.3)	65.5 (24.4–360.7)

Table 4 (continued)

	VATS-B1	VATS-B2	VATS-Ba	VATS-Bb	VATS-Bd	VATS-N
Maximal postoperative[a]	100.9 (26.6–209.8)	240.4 (66.0–331.5)*	186.2 (153.5–254.0)	140.1 (66.0–265.9)	225.1 (30.7–331.5)	137.8 (30.1–488.6)
At discharge[a]	34.2 (13.5–168.9)	66.6 (2.7–281.7)	93.6 (2.7–127.2)	57.3 (30.6–198.3)	80.1 (17.3–281.7)	49.1 (3.7–254.9)

BMI body mass index, *ASA* American society of anesthesiologists' classification of physical health (assessed preoperatively), *FEV1* forced expiratory volume in 1 second, *ICU* intensive care unit, *RUL* right upper lobe, *ML* middle lobe, *RLL* right lower lobe, *LUL* left upper lobe, *LLL* left lower lobe, *LN* lymph node, *OR* operating room, *CRP* C-reactive protein, *POD1* postoperative day 1, *ns* not significant ($p > 0.05$)

*$p < 0.05$ and **$p < 0.0001$ compared to VATS-N as the control group for post hoc testing

#$p < 0.05$ and ##$p < 0.0001$ in cross-tabulation (comparing (1.) VATS-B1 and VATS-B2 with VATS-N or (2.) VATS-Ba, VATS-Bb, and VATS-Bd with VATS-N)

[a] Non-parametrical data

[b] Not including conversions to open surgery

[c] Intraoperative complications without these, leading to conversion to open surgery

[d] Not available retrospectively in one patient of the VATS-B2/VATS-Ba group

a cut-off level at 190 min. In nearly all patients of VATS-B2, dense adhesions required a time consuming take-down and lead to a higher intraoperative blood loss. The extensively long operation time in patients of this subgroup resulted in a higher rate of prolonged mechanical ventilation and consecutively a prolonged stay on intensive care unit compared to VATS-N. Also, chest tube duration and overall length of hospital stay were longer in this subgroup of patients. Regarding subgroup analysis for underlying diseases, differences were seen in VATS-Bb patients compared to VATS-N. Since all VATS-Bb patients had dense inflammatory adhesions, the operation time within this subgroup was longer in comparison to the control group. The younger age of these patients and the shorter course of the diseases may explain why in this subgroup the longer operation time did not show a similar negative impact on the outcome. Overall, the small sample sizes of the subgroups stratified for underlying diseases are a relevant limitation of this study and do not allow a generalization of these specific results.

Conclusion

In this cohort of selected patients with various chronic inflammatory lung diseases, VATS anatomic pulmonary resection was found to be feasible and safe. It is, however, a technically extremely challenging and time-consuming procedure requesting an extensive experience in VATS. Subgroup analyses suggest that not the specific underlying disease but the operation time, which is primarily influenced by the extent of adhesions and fibrotic hilar alterations, determines the perioperative outcome. Whenever operation time tends to exceed, conversion to open surgery should be considered in order to prevent poor perioperative outcome.

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Study conception and design: Martin Reichert, Johannes Bodner.

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Compliance with ethical standards The data are collected and the manuscript is written and submitted in accordance to the COPE guidelines.

The study was approved by the local ethics committee. For this type of study, formal consent is not required. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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