

Futile lobectomies following video-thoracoscopic exploration for indeterminate pulmonary nodules: a retrospective study

Gabrielle Drevet¹[^], Yaniss Belaroussi¹, Michael Duruisseaux², Lara Chalabreysse³, Renaud Grima¹, Jean-Michel Maury^{1,4}, François Tronc¹

¹Department of Thoracic Surgery, Lung and Heart-Lung Transplantation, Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; ²Respiratory Medicine Department, Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; ³Department of Pathology, Louis Pradel Hospital, Hospices Civils de Lyon, Lyon, France; ⁴UMR 754, Claude Bernard Lyon 1 University, Lyon, France

Contributions: (I) Conception and design: F Tronc; (II) Administrative support: MDuruisseaux, L Chalabreysse; (III) Provision of study materials or patients: G Drevet, R Grima, JM Maury, F Tronc; (IV) Collection and assembly of data: G Drevet; (V) Data analysis and interpretation: Y Belaroussi; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Gabrielle Drevet. Service de Chirurgie Thoracique, Hôpital Louis Pradel, F-69677, Lyon, France. Email: gabrielle.drevet@chu-lyon.fr.

Background: Lung cancer screening is correlated with an increase in detection of small indeterminate pulmonary nodules and these nodules often require operative resection to obtain the diagnosis. In suspected early-stage lung cancer, video-assisted thoracoscopic surgery (VATS) has become the preferred option. In this context of minimally invasive surgery, diagnostic wedge resection is sometimes difficult to perform for small deep impalpable nodules. So, our purpose was to determine whether performing VATS for indeterminate pulmonary nodule increases the risk of lobectomy for benign lesions.

Methods: A retrospective analysis was carried out in our center from January 2013 to January 2019 on patients who underwent resection for a solitary pulmonary nodule suspicious for cancer. Resection method, frozen section analysis, post-operative outcomes, operative and pathology reports were reviewed.

Results: Six hundred fifty-one patients underwent surgical exploration for a solitary pulmonary nodule. Thirty hundred and forty-five patients underwent VATS and 306 patients underwent thoracotomy. Patients in the VATS group underwent significantly more wedge resections (P=0.012) and diagnosis of lung cancer was significantly more frequent in the thoracotomy group (P<0.001). One hundred and thirty-two patients (38.3%) in the VATS group and 60 patients (19.6%) in the thoracotomy group underwent lobectomy without frozen section analysis of the pulmonary nodule. There was no significant difference in terms of lobectomy performed for a benign lesion between the two groups.

Conclusions: VATS was associated with a higher rate of benign lesion resection but was not associated with a higher rate of lobectomies for benign lesion in our study.

Keywords: Solitary pulmonary nodule; video-assisted thoracoscopic surgery; lung cancer

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Introduction

Lung cancer screening has been of much interest since the end of the 1990's. The Early Lung Cancer Action Project evaluated lung cancer screening by low-dose CT scan in patients at high risk of malignancy. An increase in small pulmonary nodules detection and possibly an increase of the detection of lung cancers at an early and curable stage

^ ORCID: 0000-0003-1174-7655.

have been reported (1). When a solitary pulmonary nodule is detected, the prevalence of malignancy ranges from 1.1% to 12% (2). Non-surgical biopsies can be helpful to make a diagnosis such as percutaneous CT-guided fine needle aspiration, transbronchial needle aspiration or endobronchial ultrasound guided transbronchial needle aspiration (3). Unfortunately, these techniques have an imperfect sensitivity and limited negative predictive value. Diagnostic yield of these techniques ranges from 48.5% to 93% depending on the lesion size and the technique itself (4-7). Thus, a negative biopsy cannot exclude the possibility of malignancy, and surgical resection remains a reliable option for a definitive diagnosis. The use of surgical minimally invasive techniques is recommended whenever possible along with wedge resection and frozen section analysis (4). If lung cancer is confirmed, oncologic resection with lobectomy and lymph node dissection are performed. Over the past few years, video-assisted thoracoscopic surgery (VATS) has been increasingly preferred in this indication allowing similar overall, cancer specific and disease-free survival for patients undergoing thoracoscopic lobectomy compared to open lobectomy for lung cancer (8-10). The admitted advantages of VATS are its lower incidence of post-operative complications, shorter hospital length of stay and faster recovery time compared with thoracotomy (11). VATS has now become a standard and common way lung cancer resections are performed, even if, sometimes, wedge resection is difficult even impossible due to a small or deep pulmonary nodule. The negative effect is that the thoracic surgeon could be tempted to perform a larger lung resection in order to avoid thoracotomy inconvenience. The aim of this study was to assess if VATS development increased the risk of lobectomy for benign lesions. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd. amegroups.com/article/view/10.21037/jtd-21-1789/rc).

Methods

Patient population

Retrospective analysis of medical charts was conducted for all patients who underwent pulmonary resection whether by video-assisted thoracoscopic surgery or thoracotomy, at Louis Pradel Hospital (Lyon, France), from January 2013 to January 2019, for a solitary pulmonary nodule or a mass suspicious for cancer. Patients who had a preoperative diagnosis of malignancy or benign lesion were excluded from the study. All patients benefited from complete preoperative and functional evaluation including computed tomography (CT) scan of the chest, positron emission tomography scan, CT scan of the brain and pulmonary function test. For each patient, surgical management of solitary pulmonary nodule or mass suspicious for cancer was validated by a multidisciplinary team. VATS consisted of a standard three-port procedure with a four-centimeter access port, and thoracotomy consisted of a postero-lateral one, placed in the fifth intercostal space. When non-small cell lung cancer was confirmed intra-operatively by frozen section analysis, lobectomy with systematic lymph node dissection was performed. The choice of thoracotomy or VATS approach was at the discretion of the operating surgeon. However, in our institution, we usually perform VATS for clinical N0 patients with a lesion of less than 7 cm. The following data were extracted: age, smoking history, type of surgery, frozen section analysis, conversion rate and causes for video-assisted thoracoscopic surgery, definitive pathologic diagnosis, post-operative classification of lung cancer, 90-day post-operative complications, Clavien classification of surgical complications (12) and hospital length of stay. Data were collected until October 2019. There was no missing data and no patient was lost to follow up. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and informed consent was taken from all the patients. In accordance with French legislation, submission to an ethics committee was not required owing to the observational nature of the study.

Statistical analysis

Qualitative data were described in terms of counts and percentages. Continuous variables were described with mean and standard deviation. Quantitative variables were compared with parametric *t*-test. Qualitative variables were compared with either the Chi-2 test (with or without Yates correction) or Fisher Test. A threshold of α =0.05 was considered for statistical significance. Statistical analysis was performed using R software version 3.5.2 and following packages were used: tidyr, epiDisplay, survival, epiR and base (13).

Results

Patient characteristics

A total of 1,524 patients were scheduled for indeterminate pulmonary nodules surgical exploration at our institution.

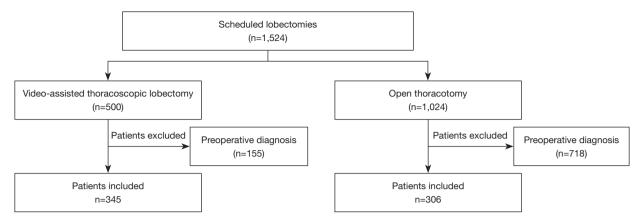


Figure 1 Patient selection criteria.

873 patients had a preoperative diagnosis and were excluded from the study. 651 patients (42.7%) needed per-operative exploration of a solitary pulmonary nodule or mass with frozen section examination and were included in final analysis (Figure 1). 345 patients underwent VATS and 306 patients underwent thoracotomy. There were no significant differences in terms of age and smoking history between the two groups (Table 1). Patients in the VATS group underwent significantly more wedge resection (n=50 (14.5%) in the VATS group vs. n=25 (8.2%) in the thoracotomy group) and less lobectomy (n=295 (85.5%) in the VATS group vs. n=281 (91.8%) in the thoracotomy group) (P=0.012). Diagnosis of lung cancer was significantly more frequent in the thoracotomy group [n=270 (88.2%) in the thoracotomy group vs. n=280 (81.2%) in the VATS group, P<0.001].

Surgical resection

In the video-assisted thoracoscopic surgery group (n=345), 47 patients (13.6%) required conversion to thoracotomy: 5 patients (10.6%) required conversion for a nodule that could not be found, 18 patients (38.3%) required conversion for a vascular accident, 12 patients (25.5%) for dissection difficulties, 8 patients (17%) for multiple adhesions and 4 patients (8.5%) for one-lung ventilation difficulties. Among the VATS group, 213 patients (61.7%) benefited from intra-operative diagnosis by frozen section analysis. 163 patients (47.2%) had a diagnosis of nonsmall cell lung cancer, 6 patients (1,7%) had a diagnosis of metastasis and 44 patients (12.7%) had a diagnosis of benign lesion (*Table 2*). For the latter 44 patients, surgery consisted of wedge resection only. 132 patients (38.3%) underwent lobectomy without prior diagnosis.

Thoracotomy was performed in 306 patients. Intraoperative diagnosis by frozen section analysis was performed for 246 patients (80.4%). 218 patients (71.2%) had an intraoperative diagnosis of non-small cell lung cancer, 3 patients (1%) had a diagnosis of metastasis and 25 patients (8.2%) had a diagnosis of benign lesion. For the latter 25 patients, surgery consisted of wedge resection only. Sixty patients (19.6%) underwent lobectomy without prior diagnosis. There were significantly more lobectomies performed without prior diagnosis in the VATS group compared with the thoracotomy group (P<0.001).

In total, 83 patients (12.7%) had a final pathology of a benign lesion. Regarding patients whose frozen section examination revealed a benign lesion, 5 patients (11.4%) in the VATS group and 2 patients (8%) in the thoracotomy group had a final pathologic assessment of cancer (*Table 3*).

Among patients who underwent lobectomy without prior diagnosis, the proportion of benign lesions was equivalent in both groups (3.8% in the VATS group *vs.* 2.6% in the thoracotomy group, P=0.16).

Post-operative outcomes

90-day post-operative complications occurred in 117 patients (33.9%) of the VATS group and in 114 patients (37.3%) of the thoracotomy group. There were no significant differences in terms of overall post-operative complications between the two groups (P=0.3738), but pneumonias were significantly more frequent in the thoracotomy group (P=0.0039) compared to the VATS group (*Table 4*). Atrial fibrillation (29 patients (8.4%) in the VATS group, 28 patients (8.1%) in the thoracotomy group) and prolonged

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Table	1	Patients	characteristics
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Characteristics	VATS group (n=345), n (%) or mean (standard deviation)	Thoracotomy group (n=306), n (%) or mean (standard deviation)	P value
Age, years	63.8 (10.3)	63.0 (9.8)	0.293
Gender			0.005
Male	205 (59.4)	215 (70.3)	
Female	140 (40.6)	91 (29.7)	
History of smoking			0.781
Current smoker	101 (29.3)	95 (31.0)	
Former smoker	180 (52.2)	160 (52.3)	
Never smoker	64 (18.6)	51 (16.7)	
Number of packs/year	37.2 (17.6)	40.0 (19.1)	
Surgical resection			0.012
Lobectomy	295 (85.5)	281 (91.8)	
Wedge resection	50 (14.5)	25 (8.2)	
Lung cancer	280 (81.2)	270 (88.2)	<0.001
Stage I	218 (63.2)	154 (50.3)	
Stage II	40 (11.6)	57 (18.6)	
Stage III	22 (6.4)	59 (19.3)	
Stage IV	0	0	
NA	2	3	
Histology			<0.001
Final pathology			
Adenocarcinoma	206 (59.7)	160 (52.3)	
Squamous cell carcinoma	41 (11.9)	63 (19.6)	
Large cell carcinoma	7 (2.0)	16 (5.2)	
Carcinoid tumors	14 (4.1)	15 (4.9)	
Others	12 (3.5)	16 (5.2)	
Benign lesion	52 (15.1)	31 (10.1)	
Hamartochondroma	13 (3.8)	5 (1.6)	
Fibro-inflammatory lésions	7 (2.0)	3 (1.0)	
Tuberculosis	6 (1.7)	5 (1.6)	
Organizing pneumonia	4 (1.2)	5 (1.6)	
Others	22 (6.4)	13 (4.2)	

VATS, video-assisted thoracoscopic surgery; NA, not available.

air leak (32 patients (9.3%) in the VATS group, 19 patients (6.2%) in the thoracotomy group) were also observed. Most of post-operative complications were grade II of Clavien

classification of surgical complications (12) (19.4% in the VATS group *vs.* 22.2% in the thoracotomy group). The mean hospital length of stay was significantly higher in the

	VATS group	o, n=345	Thoracotomy g	roup, n=306
Final pathology	Patients evaluated with frozen section analysis, n=213	Patients with no frozen assessment, n=132	Patients evaluated with frozen section analysis, n=246	Patients with no frozen assessment, n=60
Lung cancer	163 (76.5%)	112 (84.8%)	218 (88.6%)	52 (86.7%)
Metastasis	6 (2.8%)	7 (5.3%)	3 (1.2%)	0
Benign lesion	44 (20.7%)	13 (9.9%)	25 (10.2%)	8 (13.3%)

Table 2 Final pathologic assessment according to surgical approach

VATS, video-assisted thoracoscopic surgery.

Table 3 Concordance between frozen section analysis and final pathology according to surgical approach

			Frozen section	n examination		
Final pathology		VATS group, n=213	3	Tho	racotomy group, n	=246
	Lung cancer	Metastasis	Benign lesion	Lung cancer	Metastasis	Benign lesion
Lung cancer	162	1	5	216	0	2
Metastasis	1	5	0	2	3	0
Benign lesion	0	0	39	0	0	23

VATS, video-assisted thoracoscopic surgery.

thoracotomy group (P<0.0001). Mean hospital stay was 8.5 days for the thoracotomy group while it was 6.6 days in the VATS group. 90-day post-operative mortality was 0.6% in the VATS group vs. 0.3% in the thoracotomy group.

Among patients who had a final diagnosis of benign lesion, there were no significant differences in terms of number, type and grade of post-operative complications between patients who had lobectomy compared with patients who underwent wedge resection only (P=0.589), independently of the surgical approach (*Table 4*). Most of the post-operative complications in these patients were pneumonias and grade I and II of Clavien classification of surgical complications (12). However, mean hospital stay in patients who underwent lobectomy without prior diagnosis seems to be longer than that of patients who underwent wedge resection only.

Discussion

Although the benefit of lung cancer screening and diagnosing early stage lung cancer has largely been demonstrated (14), some authors consider the risk of over-diagnosis. Some indolent tumors would not impact the patients' life if left untreated (15) and some authors focus on additional cost, anxiety and morbidity associated with cancer diagnosis and treatment. 4.2% of patients, in whom a pulmonary nodule has been detected, underwent surgery (16). We demonstrate in this investigation that 12.7% of surgeries for indeterminate pulmonary nodules were performed for benign lesions. Our aim was to find out whether the development of VATS generated more lobectomies for benign lesions compared to thoracotomy. In our study, there was a trend toward more surgeries for benign lesions in the VATS group but the proportion of lobectomies performed for a benign lesion was equivalent in both groups.

One of the solutions to avoid surgery for benign lesions is to make a preoperative diagnosis. Non-surgical biopsy is suggested for solid nodules measuring >8 mm when probability of malignancy is low to moderate (4). Many techniques are available to obtain the diagnosis of an indeterminate pulmonary nodule, but their diagnostic yield is not 100% (4-7). Therefore, many patients undergo surgery without prior diagnosis. We report 42.7% of patients who underwent surgery without preoperative diagnosis. Our rate is at the lower limit of what has already been published the literature (17,18). Operating on patients without prior diagnosis leads inevitably to perform surgery

				VATS for b	VATS for benian lesion (n=52)		Thoracotomv f	Thoracotomy for benian lesion (n=30)	1=30)
Characteristics	VATS group (n=345), N (%*)	Thoracotomy group P value (n=306), N (%*)	IP value	Lobecton prior di	Wedge resection with frozen section P value	-	bectomy without prior diagnosis	Lobectomy without Wedge resection prior diagnosis with frozen section	n P value
Post-operative complications	117 (33.9)	114 (37.3)	0.3738	2 (15.4)		0.589	0	3 (13.6)	0.545
Prolonged air leak	32 (9.3)	19 (6.2)	0.1462	0	1 (2.6)		0	0	
Atrial fibrillation	29 (9.5)	28 (8.1)	0.5397	0	0		0	1 (4.5)	
Pneumonia	35 (10.1)	55 (18.0)	0.0039	2 (15.4)	1 (2.6)		0	1 (4.5)	
Pleural effusion	8 (2.3)	1 (0.3)	0.0663	0	0		0	0	
Recurrent paralysis	5 (1.4)	3 (1.0)	0.8528	0	0		0	0	
Other	13 (3.8)	17 (5.6)	0.2776	0	1 (2.6)		0	1 (4.5)	
Clavien classification			0.2230		0.1	0.115			-
0	229 (66.4)	119 (62.7)		11 (84.6)	37 (94.9)		8 (100.0)	19 (86.4)	
_	23 (6.7)	24 (7.8)		0	1 (2.6)		0	1 (4.5)	
=	67 (19.4)	68 (22.2)		2 (15.4)	0		0	2 (9.1)	
Illa	16 (4.6)	12 (3.9)		0	0		0	0	
qIII	8 (2.3)	4 (1.3)		0	0		0	0	
IVa	0 (0.0)	5 (1.6)		0	0		0	0	
dVI	0 (0.0)	0 (0.0)		0	0		0	0	
>	2 (0.6)	1 (0.3)		0	0		0	0	
Mean hospital length of stay, mean (SD)	6.6 (5.7)	8.5 (6.3)	<0.0001	5.2 (2.2)	4.3 (2.5) 0.0	0.0411	6.0 (2.2)	5.8 (1.9)	0.8050

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for benign lesions and sometimes to perform avoidable surgeries. 12.7% of patients underwent surgery for a benign lesion in our study. This observation is compatible with data in the literature where benign lesion resection ranges from 9 to 35.6% (17,19,20) and this is a particular issue for patients enrolled in lung cancer screening trial (21).

Over the past two decades, video-assisted thoracoscopic surgery has been increasingly used worldwide (22) and, as other centers, we registered a distinct increase of VATS in our institution. Like other teams (23), we observed more resections for benign lesions in the VATS group compared to the thoracotomy group (15.1% versus 10.1%), with significantly more wedge resections in the VATS group. In our study, despite a significantly higher proportion of lobectomies without prior diagnosis in the VATS group, the number of lobectomies performed for benign lesions was equivalent in both groups, as also reported by Kuo et al. (23). Multidisciplinary decision for surgical exploration associated with the per-operative clinical judgment of the operating surgeon led to a reasonable number of benign lesion resection. In addition, benign lesion resection was not correlated with an excessive morbidity rate and did not cause any death in our study. Resecting a benign lesion, preferably by wedge, is not necessarily futile and allows for a new diagnosis or a change in treatment in 85% of cases (24).

In our study, benign lesion resection was relatively safe, with a non-significant difference in terms of postoperative complications between patients who underwent lobectomy versus those who underwent wedge resection for a benign lesion. Still, improvements in techniques are needed to detect indeterminate pulmonary nodules intra-operatively to prevent futile lobectomy or conversion to thoracotomy in these patients. Several methods have already been reported such as preoperative and per operative percutaneous hookwire localization or color dye labeling injection of the nodule under CT scan guidance (25-28). Other teams described electromagnetic navigational bronchoscopic injection of autofluorescent or methylene blue dye (29,30). In these series, about 98% of nodules were successfully localized and no conversion to thoracotomy for lung palpation was reported. So, in case of indeterminate pulmonary nodule difficult to localize, these techniques may help avoid the need for conversion to thoracotomy or for larger resections.

Our study is not without some limitations. It is a retrospective, nonrandomized study, which creates possible biases. Maybe this was circumvented in part by having a multidisciplinary decision for indeterminate pulmonary nodule exploration on each patient in the study. Although 12.7% of our patients had a definitive diagnosis of benign lesion, and reaching 15.1% in the VATS group, the risk of malignancy was felt to be sufficiently high to warrant surgical exploration. However, surgery for a benign lesion is not useless in most cases, as it resulted in a new diagnosis or a treatment change.

Conclusions

With its lower morbidity and its similar oncologic benefit compared to thoracotomy, VATS has become the surgical approach of choice for small, solitary, indeterminate pulmonary nodules. One disadvantage of VATS is the absence of lung palpation, making it sometimes difficult to find small and deep pulmonary nodules. Despite this, VATS was not associated with an increase in lobectomies for benign lesion in our study. Although benign lesion resection was relatively safe, attention must be paid to perform diagnostic lobectomy infrequently and to make benign lesion resections as uncommon as possible without compromising early lung cancer diagnosis and treatment.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd. amegroups.com/article/view/10.21037/jtd-21-1789/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups. com/article/view/10.21037/jtd-21-1789/coif). GD reports personal fees from ASTRA ZENECA, outside the submitted work. MD reports personal fees from ROCHE, PFIZER, MSD, Boerhinger Ingelheim, NOvartis,

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ABBVIE, TAKEDA, BMS and ASTRA ZENECA, outside the submitted work. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and informed consent was taken from all the patients. In accordance with French legislation, submission to an ethics committee was not required owing to the observational nature of the study.

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