Original Article

Role of Video-Assisted Thoracic Surgery for the Diagnosis of Indeterminate Pulmonary Nodule

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Purpose: A study was undertaken to evaluate the validity and efficacy of video-assisted thoracic surgery (VATS) for the diagnosis of indeterminate pulmonary nodules.
Materials and Methods: Between April 2001 and November 2004, 57 adult patients (31 males, 26 females) with a clinical diagnosis of pulmonary nodules by preoperative chest computed tomographic (CT) scanning were included in this study.
Results: A definitive tissue diagnosis was obtained in all 57 patients. The mean age of the patients was 66±9.8 yrs. The mean size of the tumor was 1.76±0.67 cm. 38 patients (67%) had malignant disease. Twenty eight patients (49%) had primary lung cancer and 10 patients (18%) had metastatic lung cancer from an extrathoracic primary neoplasm. The rate of malignancy was 65% in the tumor sizes equal to or less than 2 cm. Among primary lung cancer, most patients had primary adenocarcinoma (24 cases)(86%). Pathologic staging showed T1N0 (stage IA) in 18 cases (69%), T2N0 (stage IB) in 4 cases (15%), T2N1 (stage IIB) in 1 case (4%), and T1N2 (stage IIIA) in 3 cases (12%). In 10 patients (18%) who required preoperative placement of a localization hookwire with a string near the nodule, the rate of malignancy was 70%. In 7 patients with positive positron emission tomography (PET) imaging with F-18 fluorodeoxyglucose (FDG), the rate of malignancy was 57% and proved to be falsely positive in 3 cases (43%). There was no operative mortality and no significant morbidity in all cases.
Conclusion: We proposed that VATS, which is safe and offers virtually 100% sensitivity and specificity, should be performed for most small (<3 cm in diameter) and all indeterminate pulmonary lesions on the basis of these results. (Ann Thorac Cardiovasc Surg 2006; 12: 388–92)

Key words: video-assisted thoracic surgery, indeterminate pulmonary nodule

Introduction

Small indeterminate pulmonary nodules, which cannot be detected by conventional radiography, are often detected using helical computed tomographic (CT) screening. This type of lesion is difficult to diagnose by conventional methods such as bronchoscopy or transthoracic needle aspiration biopsy.[1,2] It has been reported that video-assisted thoracic surgery (VATS) was useful for the dignosis of indeterminate pulmonary nodules.[1–4] We undertook this study to investigate the relation between tumor size, the motive of consultation, indication for VATS, pathological findings, and preoperative CT scan findings in patients undergoing VATS lung biopsy. We then evaluated the validity and efficacy of VATS.

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Materials and Methods

Between April 2001 and November 2004, 57 adult patients (31 males, 26 females) with indeterminate pul-

Table 1. Patients' characteristics

Number of cases	57	
Sex (male:female)	31:26	
Mean age (range)	66±9.8 yrs (33–86 yrs)	
Tumor size (range)	1.76±0.67 cm (0.5–3.2 cm)	
Consultation motive	Medical checkup	22 (39%)
	Follow up for other diseases	25 (44%)
	Admission with respiratory complaints	10 (17%)
	(cough 4, bloody sputum 3, chest pain 2, dyspnea 1)	

yrs, years.

monary solitary nodules, detected by preoperative chest CT scanning were included in this study. The definition of an indeterminate solitary pulmonary nodule is a single nodule. VATS was performed under general anesthesia using single lung ventilation via a double-lumen endotracheal tube. This was placed in a lateral decubitus position in patients without low pulmonary function, for whom preoperative transbronchial biopsy and/or transthoracic needle biopsy is difficult or has failed (e.g., inadequate tissue sample or non specific inflammation in the histrogic examination). Usually, 3 intercostal incisions were required to introduce 3 trocars 11.5-mm in diameter (Autosuture Thoracoport; United States Surgical Corp., Norwark, CA) into the thoracic cavity and these were placed on an imaginary standard thoracotomy incision in the 5th intercostal space, in case a thoracotomy was required. After a flexible 10.5-mm video thoracoscope (LFT TYPE V2, Olympus Corp., Lake Success, NY) was inserted for the nodule detection, the adjacent lung was grasped with a lung clamp, and a wedge resection was performed using an endoscopic stapler (Autosuture Endo GIA stapler; United States Surgical Corp., Norwark, CA). If the nodule was immediately subpleural at more than 1 cm in depth, and/or less than 1 cm in size, a preoperative marking, using a hookwire with a string (Guiding-Marker System; Hakko Co., Ltd., Tokyo, Japan) near the nodule under CT scan control was performed. If for technical reasons this was not possible, the needle was placed adjacent to the nodule. All specimens were sent for immediate histologic examination. In primary malignant cases, we converted to a thoracotomy and performed a formal lobectomy with lymph node dissection according to the pulmonary function. When it was benign, with metastatic or poor pulmonary function, the procedure was terminated.

Results

A definitive tissue diagnosis was obtained in all 57 patients. Nine patients (16%) were converted to mini-thoracotomy under thoracoscopy, because it was difficult to proceed with thoracoscopic resection due to problems such as adhesion. The mean age of the patients was 66±9.8 yrs, with an age range of 33–86 yrs. The mean size of the tumor was 1.76±0.67 cm, with a size range of 0.5–3.2 cm. The motive of consultation was medical checkup in 22 patients (39%), follow up for other diseases in 25 patients (44%), admission with respiratory complaints such as a cough in 4 cases, bloody sputum in 3 cases, chest pain in 2 cases, and dyspnea in 1 case (17%)(Table 1). Indications for VATS were malignant findings on chest CT scanning in 23 patients (40%), the ruling out of malignancy in 15 patients without malignant findings on chest CT scanning (26%), nodule enlargement in 13 patients (23%), and screening for metastases in 6 patients with a known extrathoracic cancer (11%). Among the malignancy findings, 19 cases (83%) were malignant. Among the cases where malignancy was ruled out, 4 cases (27%) were actually malignant. For nodule enlargement, 9 cases (69%) were malignant. Among screening for metastases, 6 cases (100%) were malignant (Table 2). Thirty eight patients (67%) had malignant diseases. Among these, 28 patients (49%) had primary lung cancer and 10 patients (18%) had metastatic lung cancer from an extrathoracic primary neoplasm. Twenty four primary lung cancer patients had primary adenocarcinoma (86%). The other 19 patients (33%) had benign diseases (Table 3). The relationship between the rate of malignancy and size of pulmonary nodules is shown in Table 4. With a tumor size equal to or less than 2 cm, 26 cases were malignant (65%) and 14 (35%) were not. Even with a size equal to or less than 1 cm, the rate

Table 2. The relationship between the reasons for VATS lung biopsy and rate of malignancy

Indication for VATS	Number of cases	Malignancy
Malignant findings on chest CT scanning	23 (40%)	19 (83%)
Ruling out of malignancy	15 (26%)	4 (27%)
Enlargement of the nodule	13 (23%)	9 (69%)
Screening for metastases with a known extrathoracic cancer	6 (11%)	6 (100%)

VATS, video-assisted thoracic surgery; CT scanning, computed tomographic scanning.

Table 3. Histopathologic description of pulmonary nodules resected at VATS

Malignant	38 (67%)
Primary lung cancer	28 (49%)
Adenocarcinoma	24
Well differentiated	13
Moderately differentiated	9
Poorly differentiated	2
Squamous cell carcinoma	1
Adenosquamous cell carcinoma	1
Large cell carcinoma	1
Atypical carcinoid	1
Metastatic lung cancer	10 (18%)
Colon	3
Rectum	3
Renal	2
Liver	1
Cervix uteri	1
Benign	19 (33%)
Granuloma	5
Organized pneumonia	4
Inflammatory pseudotumor	2
Hamartoma	2
Cryptococcosis	1
Aspergillosis	1
Tuberculoma	1
Atypical adenomatous hyperplasia	1
Sclerosing hemangioma	1
Fibroelastic nodule	1

VATS, video-assisted thoracic surgery.

Table 4. The relationship between the tumor size and rate of malignancy

Tumor size (cm)	Benign	Malignancy	Rate of malignancy
≦1.0	7	6	46%
1.1–1.5	4	8	67%
1.6–2.0	3	12	80%
2.1–2.5	2	8	80%
2.6–3.0	2	2	50%
3.1–3.2	1	2	67%

Table 5. The relationship between staging and tumor size in primary lung cancer cases

Stage	Number of cases	Tumor size (cm)
IA	18 (69%)	1.69±0.52
IB	4 (15%)	2.00±0.68
IIA	–	–
IIB	1 (4%)	1.50
IIIA	3 (12%)	1.60±0.53
IIIB	–	–
IV	–	–

of malignancy was 46%. The relationship between the staging of the primary lung cancer and the size of pulmonary nodules is shown in Table 5. Pathologic staging of 26 cases showed T1N0 (stage IA) in 18 cases (69%), T2N0 (stage IB) in 4 cases (15%), T2N1 (stage IIB) in one case (4%), and T1N2 (stage IIIA) in 3 cases (12%). Among these cases, the mean size ranged from 1.50 cm to 2.00 cm.

Ten patients (18%) required preoperative placement of a localization hookwire with a string near the nodule. The nodules ranged in size from 0.4 cm to 1.5 cm, with an average diameter of 0.96±0.36 cm. The histologic diagnosis was primary adenocarcinoma in 7 cases (70%). The success rate was 100%, but a nonsymptomatic pneumothorax was obseved in one case and minor intrapulmonary hemorrhage in 2 cases.

Seven patients with positive positron emission tomography (PET) imaging with F-18 fluorodeoxyglucose (FDG) were evaluated by VATS preoperatively. The nodules ranged in size from 1.8 cm to 3.5 cm, with an average diameter of 2.17±0.64 cm. The histologic diagnosis

was benign tumor in 3 cases (tuberculosis, organized pneumonia, and granuloma) and primary adenocarcinoma in 4 cases (57%). The PET result proved to be falsely positive in 3 cases (43%). There was no operative mortality and no significant morbidity in all cases.

Discussion

Recently, screening for lung tumor with helical CT has become available. Many indeterminate small pulmonary nodules, which could not be detected by conventional radiography, are often detected using helical CT screening. Several options are available in the diagnosis and treatment of indeterminate solitary nodule: observation of growth, biopsy, and resection. The appropriateness of each option depends largely on the assessment of a number of factors: the radiologic characteristics, tumor size, patient's history, and physical examination. A lobed contour, as well as an irregular or spiculated margin with distortion of adjacent vessels are typically associated with malignancy. The growth rate is also of paramount importance in evaluating solitary nodules, and a 2–3 year stability is traditionally considered an indicator of benignity.

However, it has been reported that approximately 40–50% of solitary nodules are malignant, either bronchogenic carcinoma or metastatic from an extrathoracic site.[5] Also, in our studies, the rate of malignancy was 67%, and even among cases where malignacy was ruled out, the rate of malignancy was 27%. Futhermore, in lesions equal to or less than 2 cm in diameter, a positive diagnosis in the presence of malignancy was 63%; these findings are similar to the results of the study by Berquist et al.[6] Among patients who required preoperative placement of a localization hookwire with an average diameter of 0.96±0.36 cm, the rate of malignancy was 70%. Three nodules not exceeding 2.00 cm with an average diameter of 1.60±0.53 cm presented stage IIIA of primary lung cancer. On the basis of the results obtained in this study, we thought that observation of growth based on the radiologic characteristics or tumor size was limited to the diagnosis of pulmonary nodules and this might also cause difficulty in detecting the early stages of lung cancer. Therefore, a precise method must be employed to discover malignant lesions at an earlier stage in order to improve the prognosis of indeterminate pulmonary nodule.

In general, traditional methods such as bronchoscopy or transthoracic needle aspiration biopsy with or without CT guidance are not useful for the diagnosis of such small lung nodules. The diagnostic yield of bronchoscopy ranges from 20% to 80%.[7,8] Transthoracic needle aspiration biopsy in the diagnosis of malignancy has a sensitivity ranging from 64% to 97%.[9,10] After all, patients who still present indeterminate lesions after these methods usually need pulmonary wedge resection by an operative method.

Developments in video camera technology along with advances in percutaneous endoscopic instruments have expanded the role of diagnotic VATS for such small lung nodules. The advantages of VATS include excellent visualization of the entire lung surface, chest wall, and mediastinum, small incisions without the need for rib retractors, less postoperative pain, an earlier return to normal pulmonary funcion, and it is safer than traditional thoracotomy. Futhermore, it has been reported that VATS lung biopsy offered virtually 100% sensitivity and specificity[1–3] similarly to our results, and avoided thoracotomy for benign disease. When it is difficult to detect subpleural nodules which are too small or too far from the pleural surface (the diameter is less than 10 mm and/or the distance from the pleural surface is more than 10 mm), we recommend placing the preoperative CT-guided marking using a hookwire with a string, which can be done conveniently and promptly, nearby in target indeterminate lesions for VATS lung biopsy. We belive that it was a very useful method because of our high success rate, similar to the results of the study by Dendo et al.[11] However, we thought that VATS lung biopsy after marking should be done as soon as possible, if complications such as pneumothorax or intrapulmonary hemorrhage are to be avoided.

Recently, it has also been reported that PET with FDG provides useful information on malignant lesions. However, the specificity of FDG PET in a recent study was found to be low (52%), like our study,[12] because FDG uptake can be observed at sites of active, acute inflammation. Although PET provides significant staging and prognostic information on lung cancer patients considered operable by standard criteria, it can not offer the virtually 100% sensitivity and specificity offered by VATS. Therefore, VATS seems to be a useful procedure for the diagnosis of indeterminate pulmonary nodules and we believe it will play a larger role in thoracic surgery in the future on the basis of our results of; the relation between tumor size, the rate of malignancy, the staging of primary lung cancer, and preoperative CT scan findings.

In conclusion, as VATS lung biopsy is a safer and more

effective procedure for the accurate diagnosis of patients with indeterminate pulmonary nodules, being 100% sensitive and specific, with no associated mortality or significant morbidity depending on the surgeon's experience. We propose that it should be performed for most small (<3 cm in diameter) and all indeterminate pulmonary lesions, by-passing the need for radiographic observation, traditional nonoperative methods or thoracotomy.

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