

Diagnostic Yield of Fluoroscopy-Guided Transbronchial Lung Biopsy in Non-Endobronchial Lung Lesion

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Background: Parenchymatous lung lesions often present as peripheral non-endobronchial lesions, which are not visible through conventional flexible fiberoptic bronchoscopy. Tissue diagnosis from these lesions is usually obtained by transbronchial lung biopsy (TBLB). The lesion location is estimated by chest radiograph (CXR) or computerized tomography (CT) of the chest. The diagnostic yield of TBLB is limited and variable, ranging from 16-80%. Fluoroscopy is used simultaneously with FOB during TBLB for better localization of parenchymatous lesions. Nevertheless, fluoroscopy-guided transbronchial biopsy (Flu-TBLB) is not widely used at present. The advantages and safety of Flu-TBLB have not yet been verified.

Objective: To compare the diagnostic yields and complications of TBLB with and without fluoroscopy guidance for non-endobronchial lung lesion.

Study design: Descriptive study with subgroup analysis

Material and Method: Medical and bronchoscopic data records of patients who underwent TBLB at Siriraj Hospital from January 2001 to June 2005 were reviewed. The patients were divided into two groups according to the use of fluoroscopy during TBLB. Patient demographic data, underlying diseases, CXR findings, diagnoses, complications and yields of TBLB of the two groups were compared.

Statistical analysis: Student t-test and chi-square test

Results: Six hundred and fifty patients were included in the present study. Three hundred and thirty-one patients were in Flu-TBLB group, 319 patients were in non fluoroscopy-guided transbronchial biopsy (NFlu-TBLB) group. The overall diagnostic yield of Flu-TBLB group was statistically significantly higher than NFlu-TBLB group (43.8% vs. 32.9%; $p = 0.003$). When comparing the diagnostic yields of the 2 groups by CXR findings, the yields of Flu-TBLB group were statistically significantly higher than NFlu-TBLB group for lung masses (41.4% vs. 29.5%; $p = 0.036$) and focal infiltrative lesions (46.2% vs. 29.4%; $p = 0.008$), respectively. The yield of Flu-TBLB group was slightly higher than NFlu-TBLB group for diffuse infiltrative lesion (45.1% vs. 40%; $p = 0.289$). No significant difference in the rate of pneumothorax discovery between the two groups (1.2% in Flu-TBLB group and 0.6% in NFlu-TBLB group) was observed.

Conclusion: Flu-TBLB significantly increases the diagnostic yields of non-endobronchial lung masses and focal infiltrates compared to NFlu-TBLB. There is no clinical significant difference in the rate of pneumothorax discovery between the two groups. Flu-TBLB is also more cost-saving.

Keywords: Fluoroscopy, Transbronchial, Biopsy.

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Fiberoptic bronchoscopy (FOB) is widely used to diagnose various lung diseases, especially endobronchial lung lesions. It gives diagnostic yields

as high as 70-90%^(1,2). In contrast, peripheral non-endobronchial lung lesions have been and continue to be a challenge to clinicians. Without accurate localization, the diagnostic yield of transbronchial lung biopsy (TBLB) is limited and variable, ranging from 16-80%⁽²⁻⁹⁾. Fluoroscopy has been introduced and used together with TBLB since 1974. However, this procedure

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has not been accepted to use as a standard procedure despite the fact that it seems to improve the diagnostic yield in localized lung parenchymal disease as well as reducing the rate of pneumothorax.

The primary objective of the present study was to compare the diagnostic yields and complications of TBLB with and without fluoroscopic guidance in non-endobronchial lung lesion. The secondary objective was to determine whether the fluoroscopy-guided transbronchial biopsy (Flu-TBLB) has an economic benefit.

Material and Method

The data of all adult patients with non-endobronchial lung lesions who underwent FOB and TBLB at the Pulmonary Procedure Unit (PPU), Division of Respiratory Diseases and Tuberculosis, Department of Medicine, Siriraj Hospital, Thailand between January 2001 and June 2005 were reviewed. Since the fluoroscopy method was first introduced in the authors' Pulmonary Procedure Unit in July 2002, patients who had FOB with TBLB done from January 2001 to June 2002 were included in the non fluoroscopy-guided transbronchial biopsy (NFlu-TBLB) group and those who had FOB with TBLB done under fluoroscopy guidance from January 2003 to June 2005 were included in the Flu-TBLB group. Medical and bronchoscopic data, including patient demographics, underlying diseases, CXR findings, diagnoses, complications and diagnostic yields of TBLB of all the patients recruited in the present study were recorded. Three CXR patterns were also recorded separately as a mass (or nodule) lesion, a focal infiltrative lesion and a diffuse infiltrative lesion.

Statistic analysis

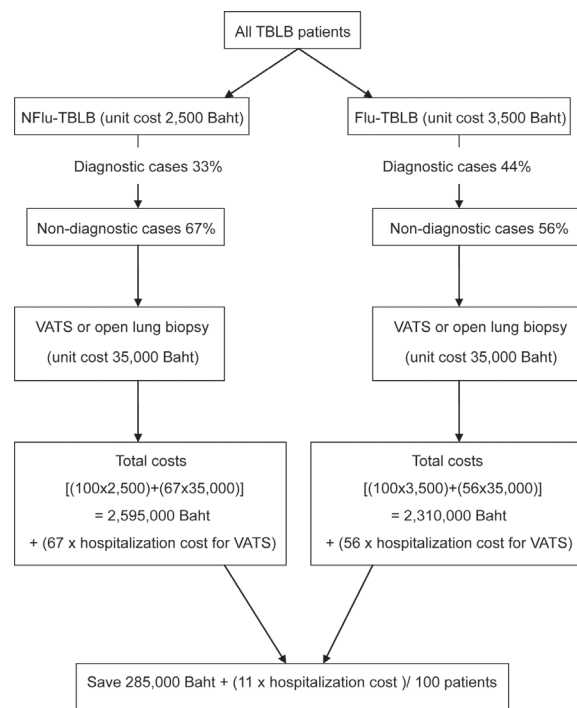
Descriptive statistics were used to describe the study population. All continuous data (such as diagnostic yields, frequency of each underlying disease, frequency of each radiographic pattern, final diagnoses of Flu-TBLB and NFlu-TBLB group, pneumothorax rate) were compared between the two groups. A 2-sample (unpaired) t-test was used to compare mean of quantitative variable (e.g. age) between two groups, whereas a Pearson's chi-square test was for comparison of qualitative variable (e.g. underlying disease, final diagnosis) between groups. All statistical analyses were performed using statistical software (SPSS for Windows, Version 10.0, Chicago, IL).

Results

Six hundred and fifty patients were enrolled

in the present study. Three hundred and thirty-one patients were in Flu-TBLB and 319 patients in NFlu-TBLB group. Between the two groups, there were no statistically significant differences in mean age, sex and the rate of underlying diseases (such as hematologic disease, steroid use, systemic lupus erythematosus (SLE) or post transplantation) except for human immunodeficiency viral infection (HIV) that the rate was higher in NFlu-TBLB group than Flu-TBLB group. The data are summarized in Table 1.

The overall diagnostic yield of Flu-TBLB group was statistically significantly higher than NFlu-TBLB group (43.8% vs. 32.9%; $p = 0.003$). Comparing the diagnostic yields of the two groups by using different CXR patterns, the yields of Flu-TBLB group were statistically significantly higher than NFlu-TBLB group for lung masses (41.4% vs. 29.5%; $p = 0.036$) and focal infiltrative lesions (46.2% vs. 29.4%; $p = 0.008$). However, the yield of the Flu-TBLB group was not different from the NFlu-TBLB group for diffuse infiltrative lesion (45.1% vs. 40%; $p = 0.289$).



VATS = video-assisted thoracoscopic surgery

Fig. 1 Algorithm showed estimated cost saving by using Flu-TBLB, assumed that all non-diagnostic patients would proceed for VATS or open lung biopsy

Table 1. Demographic data and underlying diseases of the patients

Total (n = 650)	Number (%) or Mean $\pm$ SD		p-value
	Flu-TBLB (n = 331)	NFlu-TBLB (n = 319)	
Age (years)	54 $\pm$ 8.9	55 $\pm$ 8.2	0.579
Sex :			
male	186 (56.2)	198 (62.1)	0.128
Female	145 (43.8)	121 (37.9)	
Underlying diseases			
- None	277 (83.7)	247 (77.4)	0.160
- HIV	15 (4.5)	29 (9.1)	
- Steroid use	19 (5.7)	18 (5.6)	
- Hematologic disease	10 (3.0)	15 (4.7)	
- SLE	8 (2.4)	6 (1.9)	
- Post transplantation	2 (0.6)	4 (1.3)	

n = number, HIV = human immunodeficiency viral infection, SLE = systemic lupus erythematosus

Table 2. Frequency of the different radiographic patterns and final diagnoses in Flu-TBLB and NFlu-TBLB groups

	Number (%)		p-value
	Flu-TBLB (n = 331)	NFlu-TBLB (n = 319)	
Radiographic finding			
Mass or nodule	145 (43.8)	105 (32.9)	0.010
Focal infiltrative lesion	104 (31.4)	109 (34.2)	
Diffuse infiltrative lesion	82 (24.8)	105 (32.9)	
Final diagnosis			
Granuloma	58 (17.5)	58 (18.2)	0.140
Malignancy	70 (21.1)	43 (13.5)	
Pneumocystis pneumonia	9 (2.7)	13 (4.1)	
Interstitial pneumonitis	12 (3.6)	8 (2.5)	
Fungal infection	6 (1.8)	4 (1.3)	
Others	5 (1.5)	3 (0.9)	
Non diagnostic	171 (51.7)	190 (59.6)	

Among the three different patterns of radiographic abnormality, the authors found mass or nodular lung lesions the most common, followed by focal infiltrative lesions and then by diffuse infiltrative lesions in Flu-TBLB group. These three radiographic abnormalities were distributed almost equally in the NFlu-TBLB group. More patients had masses or nodular lesions in Flu-TBLB than NFlu-TLB, as shown in Table 2.

Patients' final diagnoses from TBLB are shown in Table 2. Malignancy and granuloma were

found most frequently, ranking first and second among other diagnoses in both Flu-TBLB and NFlu-TBLB groups. The rest of the diagnoses were pneumocystis pneumonia, interstitial pneumonitis, fungal infection, alveolar proteinosis, pulmonary alveolar capillaritis, and nocardia infection. The rate of malignancy diagnosis was significantly higher in the Flu-TBLB group compared to the NFlu-TBLB group (21.1% vs. 13.5%; $p < 0.05$).

In the present study, among 650 patients, pneumothorax occurred only in six patients (four had

Table 3. Diagnostic yields of TBLB among different studies

Studies	n	Mass(%)		Focal lesion (%)		Diffuse lesion(%)	
		Flu	NFlu	Flu	NFlu	Flu	NFlu
Popp W, 1990	99		36				
Chechani V, 1996	49	57					
Cortese D, 1979	48	46					
Yang MC, 2004	96	39		61			
De Fenoyl O, 1989	174						87
Ailani R.K, 1993	30						76
Anders GT, 1988	112	73	26			72	77
Our study	650	42	30	46	29	45	40

diffuse infiltrative lesion and two had focal infiltrative lesion). There was no clinical significant difference between the two groups (two patients (0.6%) in the NFlu-TBLB group and four patients (1.2%) in the Flu-TBLB group). Among these six patients, only two patients required intercostal chest tube drainage, two patients underwent transthoracic needle aspiration. They were all discharged after 72 hours of hospitalization. The other two patients were asymptomatic and no intervention was required. There was no mortality reported.

Discussion

The use of fluoroscopy during TBLB has been debated for several years. It is uncertain whether fluoroscopy may aid the diagnosis of non-endobronchial lung lesions and/or reduce the rate of complications from the procedures. In addition, the fluoroscopy itself is not available in many institutions. There were a few case reports regarding the diagnostic yields of fluoroscopy-guided TBLB, most of these were done in a small number of patients with lung masses or nodules. A few reports, however, compared the yields of Flu-TBLB and NFlu-TBLB in the same studies. The additional yields from fluoroscopy use during TBLB were conflicting. The diagnostic yields of TBLB with fluoroscopy guidance varied from 39-73%^(2-4,7-10) as shown in Table 3.

In 1988, Anders GT et al reported a higher diagnostic yield of TBLB with fluoroscopy than without fluoroscopy for the mass lesion, but had similar yields for diffuse infiltrative lesion in 112 patients⁽³⁾. In the present study, the authors demonstrated overall significantly higher diagnostic yields of Flu-TBLB in much larger group of patients (650 patients). The

authors also demonstrated that not only is the diagnostic yield of lung masses improved by fluoroscopy guided-TBLB, but also the yields of focal infiltrative lesions. While in the diffuse disease, the yield was not different, it seemed to be higher in the fluoroscopy-use group. The authors believe that fluoroscopy did enhance the yield in distinct radiographic patterns of non-endobronchial lung lesion.

The number of patients with final diagnosis of malignancy in Flu-TBLB group was significantly higher than the NFlu-TBLB group. This might be from the higher number of patients with lung masses or nodules included in Flu-TBLB group. Since these types of lesions had a high likelihood of being malignant lesions in general, this might indirectly increase the diagnostic yields of malignancy in Flu-TBLB group.

TBLB does increase the risk of procedure-related pneumothorax. Reported risks of TBLB-related pneumothorax were ranged from 0.3 to 3%⁽¹¹⁻¹³⁾ but the risk could increase in diffuse infiltrative lesion ranging from 0.5 to 14%^(9,12,13).

A few studies reported that the pneumothorax rate in TBLB might decrease with fluoroscopy⁽⁹⁾. In the present study, pneumothorax occurred very minimally, only about 1% in both the Flu-TBLB and NFlu-TBLB groups. The majority of cases with pneumothorax occurred in diffuse infiltrative lesion, the same as in other reports. Nevertheless, the rate of pneumothorax in the presented NFlu-TBLB group might be underestimated because post-bronchoscopic CXR was performed only in suspected cases, while in the Flu-TBLB group all the patients underwent fluoroscopic screening for pneumothorax immediately after the procedure.

The authors also used their hospital unit price (calculated by considering the price of equipments,

labor cost, maintenance cost, average number of patients using the equipment over 10 years) to approximate the cost of fluoroscopy use and the cost of other additional procedures such as open lung biopsy or video-assisted thoracoscopic surgery (VATS) that might be needed once the TBLB results were non-diagnostic.

Under the assumption that all the patients with non-endobronchial lung lesion who underwent TBLB with non-diagnostic result would be sent for open lung biopsy or VATS, the authors estimated the total cost needed to obtain final diagnosis. In the Flu-TBLB group, with the diagnostic yield of 44%, the estimated total cost for obtaining final diagnoses in a hundred cases was 2,310,000 Thai Baht plus hospitalization cost for VATS or open lung biopsy of 56 cases. In the NFlu-TBLB group, with the diagnostic yield of 33%, estimated total cost for obtaining final diagnoses in a hundred cases was 2,595,000 Thai Baht plus hospitalization cost for VATS of 67 cases. In this scenario, Flu-TBLB might save at least 285,000 Thai Baht plus hospitalization cost for VATS or open lung biopsy of 11 cases per a hundred cases, shown in Fig. 1.

Conclusion

Flu-TBLB significantly increases the diagnostic yields of non-endobronchial lung masses and focal infiltrates compared to NFlu-TBLB. No clinically significant difference in the rate of pneumothorax between the two groups was observed. Flu-TBLB is also more cost-saving.

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การวินิจฉัยพยาธิสภาพในเนื้องอกโดยการใส่ฟลูออโรสโคปนำในการตัดชิ้นเนื้องอกผ่านทางกล้องส่องหลอดลม

วรางคณา ฤทธิรักษ์, สุรีย์ สมประติกุล

ภูมิหลัง: การตัดชิ้นเนื้อผ่านทางกล้องส่องหลอดลมเพื่อวินิจฉัยพยาธิสภาพในเนื้องอกนั้น มักต้องอาศัยการคาดเดาตำแหน่งจากภาพรังสีทรวงอก หรือเอกซเรย์คอมพิวเตอร์ โดยทั่วไปโอกาสตรวจพบพยาธิสภาพดังกล่าวคือร้อยละ 16-80 การใช้ฟลูออโรสโคปร่วมในการตัดชิ้นเนื้องอกผ่านทางกล้องส่องหลอดลมจะช่วยเพิ่มความแม่นยำในการกำหนดตำแหน่งของปอดส่วนที่มีพยาธิสภาพ

วัตถุประสงค์: เปรียบเทียบผลการวินิจฉัยพยาธิสภาพในเนื้องอก ผลข้างเคียงและค่าใช้จ่ายของการตัดชิ้นเนื้อผ่านทางกล้องส่องหลอดลมเมื่อใช้หรือไม่ใช้ฟลูออโรสโคปร่วม

วัสดุและวิธีการ: เก็บข้อมูลลักษณะทางคลินิกรวมทั้งลักษณะภาพรังสีทรวงอก ผลการวินิจฉัยพยาธิสภาพในเนื้องอกโดยการตัดชิ้นเนื้อผ่านทางกล้องส่องหลอดลม และผลข้างเคียงจากการส่องหลอดลมของผู้ป่วยที่ได้รับการตรวจตัดชิ้นเนื้อผ่านทางกล้องส่องหลอดลมระหว่าง กรกฎาคม 2001 ถึงมิถุนายน 2005 ณ สาขาวิชาโรคระบบการหายใจ โรงพยาบาลศิริราช วิเคราะห์ข้อมูลโดยแบ่งผู้ป่วยเป็นสองกลุ่ม คือกลุ่มที่ใช้ฟลูออโรสโคปร่วมด้วยและกลุ่มที่ไม่ใช้ การวิเคราะห์ทางสถิติ student t-test และ chi-square test

ผลการศึกษา: ผู้ป่วย 331 รายอยู่ในกลุ่มที่ใช้ฟลูออโรสโคปร่วม และผู้ป่วย 319 รายไม่ได้ใช้ฟลูออโรสโคปร่วม กลุ่มที่ใช้ฟลูออโรสโคปร่วมได้ผลการวินิจฉัยรวมมากกว่าอย่างมีนัยสำคัญทางสถิติคือ ร้อยละ 43.8 เทียบกับร้อยละ 32.9 ในกลุ่มที่ไม่ได้ใช้; $p=0.003$ ในผู้ป่วยที่มีภาพรังสีทรวงอกเป็นลักษณะก้อนหรือฝ้าขาวเป็นหย่อมเฉพาะที่นั้นกลุ่มที่ใช้ฟลูออโรสโคปร่วมได้ผลการวินิจฉัยมากกว่าอย่างมีนัยสำคัญทางสถิติ ส่วนในผู้ป่วยที่มีภาพรังสีทรวงอกเป็นฝ้าขาวกระจายทั่วไป กลุ่มที่ใช้ฟลูออโรสโคปร่วมได้ผลการวินิจฉัยมากกว่าเล็กน้อย อัตราการเกิดปอดรั่วของทั้งสองกลุ่มไม่แตกต่างกัน การคำนวณค่าใช้จ่ายรวมพบว่า กลุ่มที่ใช้ฟลูออโรสโคปร่วมประหยัดค่าใช้จ่ายรวมกว่ากลุ่มที่ไม่ใช้

สรุป: การใช้ฟลูออโรสโคปร่วมในการตัดชิ้นเนื้องอกผ่านทางกล้องส่องหลอดลมจะช่วยเพิ่มโอกาสวินิจฉัยโรคในผู้ป่วยที่มีพยาธิสภาพของเนื้องอกแบบก้อนหรือฝ้าขาวเป็นหย่อมเฉพาะที่ โดยมีอัตราเสี่ยงการเกิดปอดรั่วไม่แตกต่างกัน และประหยัดค่าใช้จ่ายในการวินิจฉัยโดยรวมกว่า
