Occult Intrathoracic Lymph Node Metastasis in Clinical N0 Non-Small Cell Lung Cancer Patients on Preoperative Chest CT: Prevalence and Risk Factors

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Objective: *To evaluate the prevalence and risk factors of occult intrathoracic lymph node metastasis on preoperative chest computed tomography (CT) in clinical N0 non-small cell lung cancer (NSCLC) patients.*

Material and Method: *We retrospectively reviewed 490 definitely diagnosed NSCLC cases. Eighty-three individuals who met the criteria for clinical N0 NSCLC were enrolled. CT findings of these patients were reviewed for tumor side, tumor location, lobar involvement, tumor size, and histology. Prevalence and risk factors of occult intrathoracic lymph node metastasis were analyzed by univariate and multivariate analysis.*

Results: *Eighty-three patients with confirmed clinical N0 NSCLC were evaluated, including 44 men and 39 women, ages ranging from 38 to 86 years (mean 65.27±11.27). Prevalence of occult N1-2 (intrathoracic) and N2 (mediastinal) lymph node involvement were 15.7% (13/83) and 8.4% (7/83), respectively. According to univariate analysis, risk factors for occult N1-2 disease were left-sided tumor ($p = 0.038$), left lower lobe (LLL) tumor ($p = 0.045$), and clinical T2 tumor ($p = 0.028$). By multivariate analysis, risk factors for occult N1-2 disease included LLL tumor ($p = 0.031$) and clinical T2 tumor ($p = 0.036$). Clinical T2 tumor was identified as a significant risk factor for predicting occult N2 disease ($p = 0.033$).*

Conclusion: *Prevalence of occult intrathoracic and mediastinal lymph node involvement in clinical N0 NSCLC patients were 15.7% and 8.4%, respectively. As such, preoperative cervical mediastinoscopy is recommended in N0 NSCLC patients with clinical T2 to rule out mediastinal lymph node involvement.*

Keywords: *Clinical N0 non-small cell lung cancer (NSCLC), Occult intrathoracic lymph node metastasis, Skip metastasis*

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Between 2007 and 2009 in Thailand, lung cancer was the second most common cancer in men and the fourth most common cancer in women[1]. Lung cancer is classified into two broad classifications, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). In most cases, NSCLC has a better prognosis than SCLC. Treatment of NSCLC is dependent on clinical staging. Treatment guidelines for patients with NSCLC at our institution (Siriraj Hospital, Bangkok, Thailand) are shown in Fig. 1.

Mediastinal lymph node involvement is the most important prognostic factor in the absence of distant metastasis[2] and a guide for the further management of NSCLC. Survival is improved in patients with stage IIIA who receive preoperative chemoradiotherapy followed by surgery, as compared to those receiving surgery alone[3-5].

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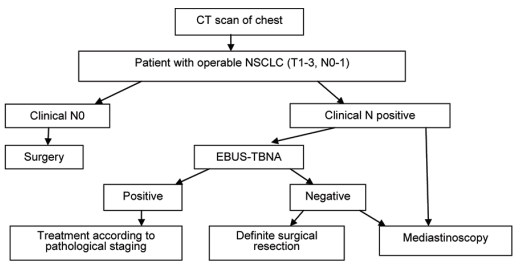
Positron emission tomography (PET) remains the most accurate non-invasive tool for nodal staging due to its high sensitivity and specificity in detecting nodal metastasis[6]. However, PET is not widely used in Thailand due to its high cost. As a diagnostic alternative, clinicians in Thailand routinely use computed tomography of the chest (chest CT) in staging NSCLC. However, chest CT has been shown to have a relatively low sensitivity and specificity in



NSCLC, non-small cell lung cancer; EBUS, endobronchial ultrasound; TBNA, transbronchial needle aspiration

Fig. 1 Treatment guideline flow chart for patients with operable N0 non-small cell lung cancer at Siriraj Hospital.

the staging of mediastinal lymph nodes. Because size is used to determine the presence or absence of nodal metastasis, lymph nodes greater than 1 cm in short axis diameter are generally considered to be metastatic. However, just as micrometastases can develop in normal-sized nodes, nodal enlargement can also result from benign diseases, such as granulomatous infection[7]. Many previous studies have reported high false-negative rates in detecting mediastinal lymph node metastasis[7-12]. As a result, patients with clinical N0 NSCLC on preoperative chest CT who had occult mediastinal lymph node metastasis underwent surgery without receiving neoadjuvant therapy prior to surgery; a course of treatment that could adversely affect patient outcome.

Accordingly, accurate staging before treatment decision is an important factor in optimizing treatment result and clinical outcome. The objective of the present study was to evaluate the prevalence of and risk factors for occult intrathoracic lymph node metastasis on preoperative chest CT in NSCLC patients with intrathoracic lymph node smaller than 1 cm in short axis diameter.

Material and Method

Patients

The protocol for the present retrospective study was approved by the Siriraj Institutional Review Board (SIRB), with informed consent being waived. Four hundred ninety definitely diagnosed NSCLC patients that underwent lung resection with mediastinal lymph node dissection between January 2005 and July 2011 were evaluated. Four hundred seven patients were excluded from the study for one or more of the following reasons: 1) patient had no record of preoperative chest CT on the Siriraj Hospital Picture Archiving and Communication System (PACs), 2) patient received neoadjuvant treatment, and/or 3) patient had intrathoracic lymph node of 1 cm or larger in short axis diameter. Eighty-three patients identified as having clinical N0 NSCLC (intrathoracic lymph node smaller than 1 cm in short axis diameter) according to preoperative chest CT were included in the present study.

CT scan protocol

Two different brands of 64 slice multiple detector computed tomography (MDCT) machine were used to evaluate patients in the present study (GE Lightspeed VCT 64 Slice CT, GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom; and Somatom Definition AS, Siemens Healthcare Global, Erlangen, Germany). Chest CT was performed in both pre-contrast phase and post-contrast enhancement phase with patient in the supine position. Non-ionic iodinated contrast material (≈ 80 cc) was administered intravenously at an injection rate of 3 ml/second with 40 seconds scan delay after contrast administration. CT images were obtained from the supraclavicular region to the upper abdomen (end of lower aspect of diaphragm). The Siemens scanner was set using the following scan parameters: collimation 64x0.6 mm, table feed/rotation 0.5 mm, slice width 1.25 mm, volume pitch 16, 120 kVp, and 250 to 300 mAs. The GE scanner was set, as follow: collimation 64x0.625 mm, table feed/rotation 0.5 mm, slice width 1.25 mm, volume pitch 16, 120 kVp, and 250 mAs. Standard mediastinal window images (window width 400 HU and window level 60 HU) were used for displaying and reviewing images on the PACs workstation. Both axial CT images and multiplanar reformation (MPR) were evaluated. Duration between preoperative chest CT and operation was recorded.

Image analysis

Two experienced thoracic radiologists retrospectively reviewed CT images of patients who underwent lung resection with mediastinal lymph node dissection and were confirmed as having NSCLC. Patients who had intrathoracic lymph node smaller than 1 cm in short axis diameter were selected. Imaging was used to determine tumor side (right or left lung), tumor location (central or peripheral area), lobar involvement (right upper lobe [RUL], right middle lobe [RML], right lower lobe [RLL], left upper lobe [LUL], or left lower lobe [LLL]), and tumor size. Reported findings represented the consensus decision between the two reviewed thoracic radiologists.

Surgical technique

Patients underwent lung resection (lobectomy or wedge resection) with systematic mediastinal lymph node dissection. Intrathoracic lymph nodes were identified according to the International Association for the Study of Lung Cancer (IASLC) lymph node map.

Pathologic analysis

Pathologic data, including tumor cell type and differentiation, presence of nodal metastasis, and pathologic nodal staging were recorded and analyzed.

Statistical analysis

All statistical analysis was performed using SPSS Statistics version 18.0 (SPSS Inc., Chicago, IL, USA). Unpaired t-test, Chi-square test, or Fisher's exact test and odds ratio (95% confidence interval [CI]) were used for univariate analysis. Multivariate analysis was conducted using multiple logistic regression (forward stepwise) method. A *p*-value less than 0.05 was considered statistically significant.

Results

Eighty-three patients with confirmed clinical N0 NSCLC who had lung resection and mediastinal lymph node dissection were evaluated. They comprised of 44 men and 39 women, ages ranging from 38 to 86 years (mean 65.27±11.27). Patient demographic data, clinical data, CT findings, and pathologic findings were listed in Table 1.

Prevalence of occult N1-2 (intrathoracic) lymph node involvement and occult N2 (mediastinal) lymph node involvement in clinical N0 NSCLC patients from preoperative chest CT was 15.7% (13/83 patients) and 8.4% (7/83 patients), respectively.

From univariate analysis, significant risk factors for predicting occult N1-2 disease were left-sided tumor ($p = 0.038$), LLL tumor ($p = 0.045$), and clinical T2 tumor (tumor size 3 to 7 cm) ($p = 0.028$) (Table 2). Significant risk factors according to multivariate analysis were LLL tumor (adjusted OR 5.7 (95% CI 1.2, 27.1), $p = 0.031$) and clinical T2 tumor (adjusted OR 3.9 (95% CI 1.1, 14.2), $p = 0.036$) (Table 3). The only significant risk factor for predicting occult N2 disease was clinical T2 tumor ($p = 0.033$) (data not shown).

From 13 patients with occult N1-2 lymph node involvement, occult pathological N1 presented in 6/13 patients (Fig. 2, 3) and occult pathological N2 was found in 7/13 patients, as described according to lymph node station (Table 4). Subaortic node metastases were found in three patients with LUL tumor (Fig. 4). Right paratracheal node metastases were found in two patients with RUL tumor (Fig. 5). Subcarinal node metastases were found in one patient with LLL tumor and one patient with RLL tumor (Fig. 6). Skip metastasis was found in 3/7 patients (43%), with LUL tumor with drainage to subaortic lymph nodes in two patients and LLL tumor with drainage to subcarinal lymph nodes in one patient.

Discussion

Effective treatment of bronchogenic carcinoma is dependent upon clinical staging. In patients with stage I or II disease, surgery is the first-line therapy with good prognosis. Patients with mediastinal lymph node involvement (stage IIIA) should receive preoperative neoadjuvant therapy to improve prognosis. As such, careful and accurate mediastinal node staging is crucial. Chest CT and cervical mediastinoscopy remain the gold standard for mediastinal lymph node staging in NSCLC[13].

Table 1. Demographic data, clinical data, CT findings, and pathologic findings from 83 clinical N0 NSCLC patients

Characteristics/findings	Results
Gender	
Male	44 (53.0)
Female	39 (47.0)
Age (years)	
Mean ± SD	65.27±11.27
Range	38 to 86
Duration between CT scan and operation (days)	
Mean ± SD	51±33
Range	2 to 137
Side	
Right	53 (63.9)
Left	30 (36.1)
Location	
Central	14 (16.9)
Peripheral	69 (83.1)
Distribution	
Right upper lobe (RUL)	28 (33.7)
Right middle lobe (RML)	6 (7.2)
Right lower lobe (RLL)	18 (21.7)
Left upper lobe (LUL)	22 (26.5)
Left lower lobe (LLL)	9 (10.8)
T staging	
T1 (tumor size <3 cm)	55 (66.3)
T2a (tumor size >3 cm but <5 cm)	25 (30.1)
T2b (tumor size >5 cm but <7 cm)	3 (3.6)
C staging	
IA (T1N0)	55 (66.3)
IB (T2aN0)	25 (30.1)
IIA (T2bN0)	3 (3.6)
Cell type	
Adenocarcinoma	75 (90.4)
Squamous cell carcinoma	6 (7.2)
Large cell carcinoma	2 (2.4)
Differentiation	
Well differentiation	8 (9.6)
Moderate differentiation	53 (63.9)
Poor differentiation	18 (21.7)
Pathologic lymph nodes	
pN0	70 (84.3)
pN1 + pN2	13 (15.7)
pN2	7 (8.4)

CT = computed tomography; NSCLC = non-small cell lung cancer
Data presented as number and percentage, unless specified otherwise

Table 2. Univariate analysis of risk factors associated with occult N1-2 disease in NSCLC patients with intrathoracic lymph node <1 cm in short axis diameter on preoperative chest CT

Risk factors	pN1 + pN2 (n = 13)	pN0 (n = 70)	Crude OR (95% CI)	*p*-value
Gender				0.948
Male	7 (53.8)	37 (52.9)	1	
Female	6 (46.2)	33 (47.1)	0.96 (0.29, 3.15)	
Age (years), mean ± SD	67.2±11.5	64.9±11.3	-	0.514
Duration between preoperative chest CT and operation (days), mean ± SD	46±25	52±34	-	0.564
Side				0.038
Right	5 (38.5)	48 (68.6)	1	
Left	8 (61.5)	22 (31.4)	3.49 (1.02, 11.90)	
Location				0.219
Central	4 (30.8)	10 (14.3)	1	
Peripheral	9 (69.2)	60 (85.7)	0.38 (0.10, 1.45)	
Lobar involvement				0.045
RUL	3 (23.1)	25 (35.7)	1	
RML	0 (0.0)	6 (8.6)	-	
RLL	1 (7.7)	17 (24.3)	0.49 (0.05, 5.12)	
LUL	5 (38.5)	17 (24.3)	2.45 (0.52, 11.64)	
LLL	4 (30.8)	5 (7.1)	6.67 (1.13, 39.47)	
T staging				0.028
T1	5 (38.5)	50 (71.4)	1	
T2a + T2b	8 (61.5)	20 (28.6)	4.00 (1.17, 13.71)	
C staging				0.063
IA + IB	11 (84.6)	69 (98.6)	1	
IIA	2 (15.4)	1 (1.4)	12.55 (1.05, 150.31)	
Cell type				0.605
Adenocarcinoma	11 (84.6)	64 (91.4)	1	
Non-adenocarcinoma	2 (15.4)	6 (8.6)	1.94 (0.35, 10.87)	
Differentiation				0.357
Well differentiation	0 (0.0)	8 (11.9)	-	
Moderate differentiation	8 (66.7)	45 (67.2)	1	
Poor differentiation	4 (33.3)	14 (20.9)	1.61 (0.42, 6.15)	

OR = odds ratio; CI = confidence interval
Data presented as number and percentage, unless specified otherwise
p-value <0.05 are considered statistically significant

Table 3. Multivariate analysis of predictors of occult N1-2 disease in NSCLC patients with intrathoracic lymph node <1 cm in short axis diameter on preoperative chest CT

Risk factors	Adjusted OR (95% CI)	*p*-value
T staging	3.9 (1.1, 14.2)	0.036
Distribution	5.7 (1.2, 27.1)	0.031

OR = odds ratio; CI = confidence interval

Meyers et al[14] reported that occult mediastinal lymph node metastasis was found in only 5.6% of patients with clinical stage I lung cancer, as screened by CT and PET, and suggested that the routine use of mediastinoscopy in these patients is not cost effective. Cerfolio et al[15] found that after both integrated PET/CT and CT, only 2.9% of clinical N0 patients had positive mediastinoscopic results and only 3.7% had positive endoscopic ultrasound-guided fine needle aspiration biopsy (EUS-FNA) results. Thus, they recommended against routine mediastinoscopy or EUS-FNA in clinical N0 patients.

At our medical center, we use cervical mediastinoscopy or endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) in clinical N-positive patients. Patients with clinical N0 went directly to surgery, without cervical mediastinoscopy or EBUS-TBNA. Accordingly, knowledge of prevalence and risk factors relating to occult mediastinal lymph node metastasis would be very useful information for identifying candidates for cervical mediastinoscopy or EBUS-TBNA in clinical N0 patients.

Prevalence of occult N1-2 lymph node metastasis in the present study was 15.7%. Prevalence of occult N2 lymph node metastasis was 8.4%, which

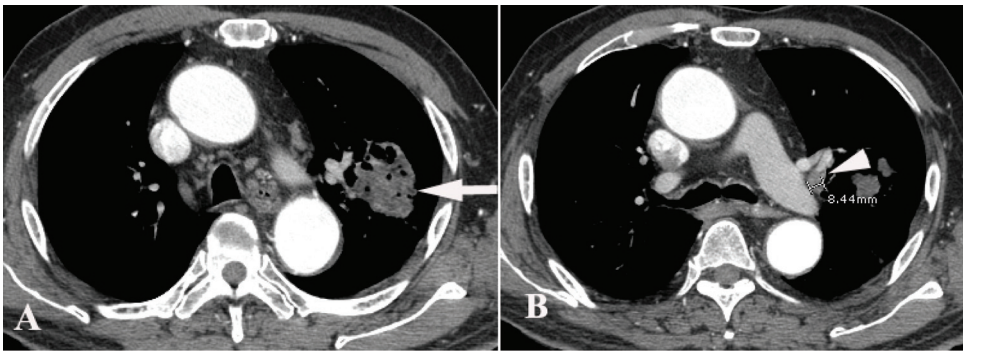


Fig. 2 Axial preoperative chest CT of a 77-year-old man with confirmed squamous cell carcinoma: A) primary tumor at left upper lobe (arrow), measuring approximately 3.3x3.9 cm (T2a); B) subcentimeter lymph node at left peribronchial area (arrowhead), measuring approximately 0.84 cm in short axis diameter (pN1 at left peribronchial lymph node).

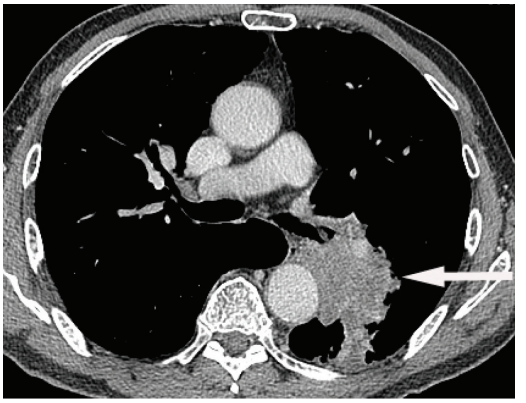


Fig. 3 Axial preoperative chest CT of a 74-year-old woman with confirmed squamous cell carcinoma at left lower lobe (arrow), measuring approximately 6.2x4.0 cm (T2b), with involved peribronchial area (pN1 at left peribronchial area).

was lower than many previous studies. Gomez-Caro et al[2], Al Sarraf et al[6], and Kanzaki et al[13] reported incidence of occult N2 disease of 14.4%, 16%, and 11%, respectively. Risk factors for occult N2 disease reported in previous studies included adenocarcinoma cell type[2,13,15,16], RUL tumor[6,13-15], RML tumor[13], large tumor size[13,16], central location[6,16], high PET maximum standardized uptake value (SUVmax) of primary tumor[13,15,16], positive N1 nodes on PET[6], and female gender[2]. In the present study, prevalence of occult N1-2 metastases increased significantly in the presence of LLL tumor and clinical T2 tumor (tumor size 3 to 7 cm). Prevalence of occult N2 metastases increased significantly in the presence of clinical T2 tumor. In the present study, large tumor size was a significant risk factor for occult N2 disease, similar to many previous studies[13,16]. Primary tumor cell type

Table 4. Pattern of pN1-2 involvement in patients with negative intrathoracic lymph node on preoperative chest CT (n = 13)

No.	Distribution	T staging	Duration between preoperative chest CT and operation	pN1	pN2
1	LLL	T2a	1 month 4 days	Positive	Negative
2	RUL	T1	21 days	Positive	Negative
3	LLL	T2b	1 month 21 days	Positive	Negative
4	LUL	T2a	1 month 11 days	Positive	Negative
5	LLL	T1	2 month 1 day	Positive	Negative
6	LUL	T1	3 months 10 days	Positive	Negative
7	RUL	T1	11 days	Positive	Right paratracheal
8	LUL	T2b	1 month 19 days	Positive	Subaortic
9	LUL	T2a	9 days	Negative	Subaortic
10	LLL	T2a	1 month 8 days	Negative	Subcarina
11	RLL	T2a	2 months 13 days	Positive	Subcarina
12	RUL	T2a	2 months 6 days	Positive	Right paratracheal
13	LUL	T1	1 month 18 days	Negative	Subaortic

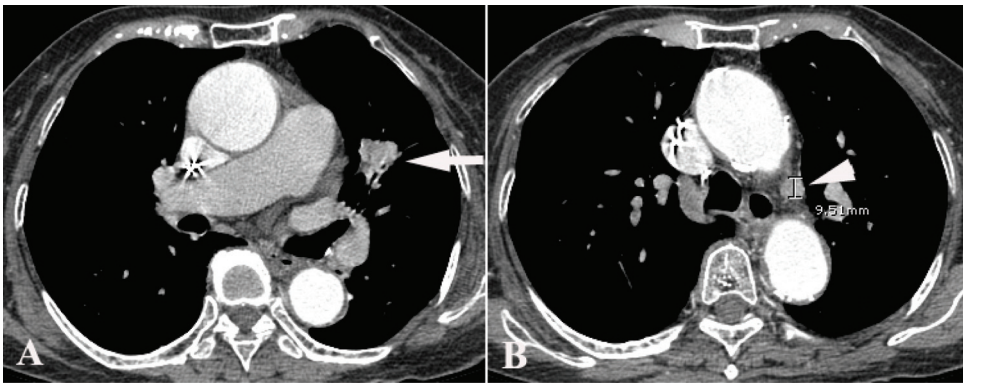


Fig. 4 Axial preoperative chest CT of an 85-year-old woman with adenocarcinoma: A) primary tumor at left upper lobe (arrow), measuring approximately 1.6x1.5 cm (T1); B) subcentimeter lymph node at subaortic region (arrowhead), measuring approximately 0.95 cm in short axis diameter (pN2 at subaortic region).

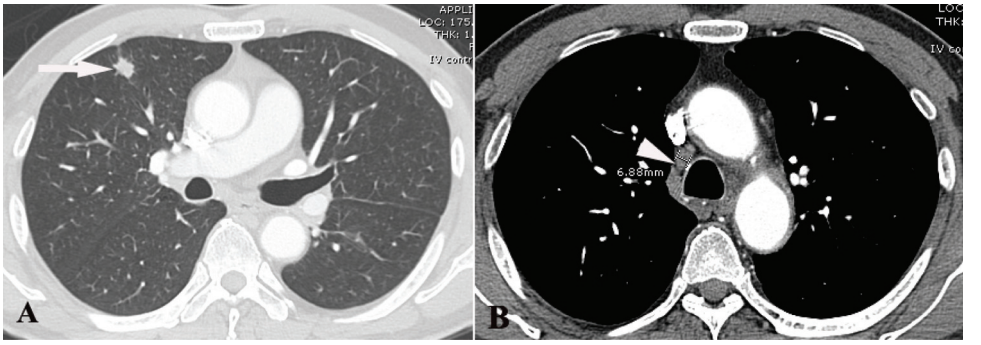


Fig. 5 Axial preoperative chest CT of a 58-year-old man with confirmed adenocarcinoma: A) primary tumor at right upper lobe (arrow), measuring approximately 0.6x0.9 cm in size (T1); B) subcentimeter lymph node at right lower paratracheal area (arrowhead), measuring approximately 0.69 cm in short axis diameter (arrowhead) (pN2 at right paratracheal area).

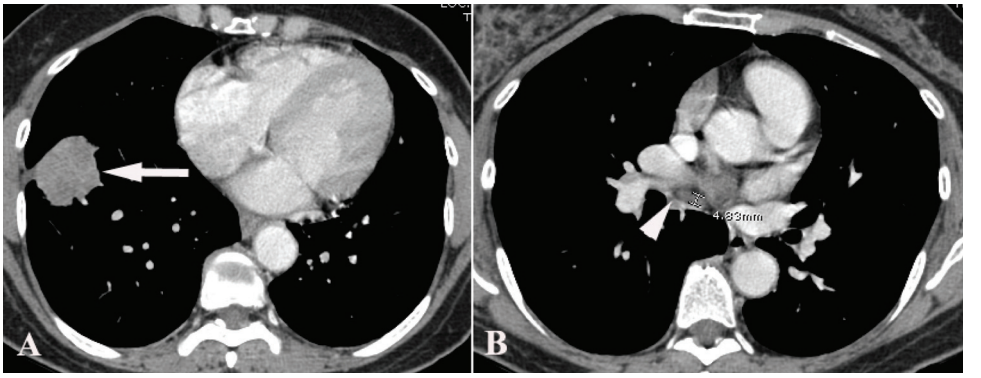


Fig. 6 Axial preoperative chest CT of a 54-year-old woman with confirmed adenocarcinoma: A) primary tumor at right lower lobe (arrow), measuring approximately 3.3x2.9 cm in size (T2a); B) subcentimeter lymph node at subcarina, measuring approximately 0.48 cm in short axis diameter (arrowhead) (pN2 positive at subcarina).

did not affect the prevalence of occult N2 metastases, which agreed with the reported findings of Al Sarraf et al[6]. Other risk factors, such as RUL tumor, RML tumor, and central location, which was shown to be a significant risk factor for occult N2 disease in previous studies, were not significant risk factors in the present study. This may be due to a small sample size in the occult N2 patient group.

The present study found occult N1 in 6/13 patients. We endeavored to retrospectively investigate

the cause of false-negative results for intrathoracic lymph node staging in these patients. In some cases, we found that the tumor had blended with these occult N1 lymph nodes, so lymph node involvement in these instances could not be identified.

In our study, patterns of mediastinal lymph node involvement varied according to lobar involvement of the primary tumor, as follows: right upper lobe tumor drained into the right paratracheal node, left upper lobe tumor drained into the subaortic node, and left and right lower lobe tumors drain into the subcarinal node. These observed patterns were identical to the patterns reported in a previous study[17].

Mediastinal node metastasis may develop via direct lymphatic drainage that bypasses the hilar nodes; a condition most commonly seen in the upper lobes[17]. Our study found skip metastasis in 3/7 patients (43%), as follows: LUL tumor with drainage to subaortic lymph nodes in two patients and LLL tumor with drainage to subcarinal lymph nodes in one patient, which was similar to results reported by Kanzaki et al[13]. The most common tumor location was the upper lobe.

Although our study found a wide variation in duration between preoperative chest CT and operation (2 to 137 days), there was no significant difference between non-occult intrathoracic lymph node metastasis patients and occult intrathoracic lymph node metastasis patients ($p = 0.564$).

Limitations of the present study include its retrospective design and the small sample size of clinical N0 NSCLC.

Conclusion

From preoperative chest CT in clinical N0 NSCLC patients, prevalence of occult N1-2 involvement and occult N2 involvement was 15.7% and 8.4%, respectively. Risk factors for occult intrathoracic lymph node metastasis were LLL tumor and clinical T2 tumor. Clinical T2 tumor was identified as a risk factor for occult mediastinal lymph node metastasis. These findings suggest that clinical N0 NSCLC patients with clinical T2 tumor (tumor size 3 to 7 cm) should undergo preoperative cervical mediastinoscopy to rule out mediastinal lymph node involvement.

What is already known on this topic?

Treatment of bronchogenic carcinoma depend mainly on TNM staging and one of the most important factor is mediastinal node staging. The previous studies report many risk factors for occult nodal metastasis including adenocarcinoma cell type, RUL tumor, RML tumor, large tumor size, central location, high PET SUVmax of primary tumor, positive N1 nodes on PET, and female gender.

What this study adds?

The present study focusses on risk factors for occult nodal metastasis. The result shows that LLL tumor, which has not been mention in previous publications, is one of the main factor for occult nodal metastasis.

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Potential conflicts of interest

None.

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อัตราการเกิดและปัจจัยเสี่ยงของการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 เซนติเมตร จากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดในผู้ป่วยที่เป็นมะเร็งปอดระยะต้น

กันยารัตน์ โตธนะรุ่งโรจน์, พัชรา วัชรินทร์ยานนท์, นิศา เมืองแมน

วัตถุประสงค์: *ศึกษาถึงอัตราการเกิดและปัจจัยเสี่ยงของการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 ซม. จากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดในผู้ป่วยที่เป็นมะเร็งปอดระยะต้น*

วัสดุและวิธีการ: *ศึกษาภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดในผู้ป่วยที่เป็นมะเร็งปอดระยะต้นที่มารับการผ่าตัดปอดร่วมกับการเลาะต่อมน้ำเหลืองในเมดิแอสตินัม ระหว่างเดือนมกราคม พ.ศ. 2548 ถึง กรกฎาคม พ.ศ. 2554 โดยจะนำเฉพาะภาพเอกซเรย์คอมพิวเตอร์ทรวงอกที่พบต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 ซม. มาศึกษาลักษณะทางเอกซเรย์คอมพิวเตอร์ที่อาจเป็นปัจจัยเสี่ยงของการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 ซม. ได้แก่ ตำแหน่ง ขนาด ลักษณะทางพยาธิวิทยาของก้อนเนื้องอก แล้วนำมาเปรียบเทียบกับผลทางพยาธิวิทยา*

ผลการศึกษา: *ผู้ป่วย 83 ราย ที่ภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดพบต่อมน้ำเหลืองในช่องอกมีขนาดน้อยกว่า 1 ซม. เป็นชาย 44 ราย หญิง 39 ราย มีอายุระหว่าง 38-86 ปี (ค่าเฉลี่ย 65.27±11.27 ปี) พบอัตราการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกทั้งบริเวณขั้วปอดหรือในเมดิแอสตินัม คิดเป็นร้อยละ 15.7 (13/83 ราย) ส่วนอัตราการเกิดการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในเมดิแอสตินัม คิดเป็นร้อยละ 8.4 (7/83 ราย) ร้อยละ 43 ของผู้ป่วยพบว่ามีการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในเมดิแอสตินัมโดยที่ไม่พบการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในบริเวณขั้วปอด ปัจจัยเสี่ยงของการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 ซม. จากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดโดยใช้ univariate analysis ได้แก่ ก้อนเนื้องอกที่อยู่ปอดซ้าย (p = 0.038) กลีบล่างของปอดซ้าย (p = 0.045) และก้อนเนื้องอกระยะ T2 (p = 0.028) ถ้าใช้ multivariate analysis จะพบว่าปัจจัยเสี่ยงของการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกที่มีขนาดน้อยกว่า 1 ซม. จากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัด ได้แก่ ก้อนเนื้องอกที่อยู่กลีบล่างของปอดซ้าย (adjusted OR 5.7 (95% CI 1.2, 27.1), p = 0.031) และก้อนเนื้องอกระยะ T2 (adjusted OR 3.9 (95% CI 1.1, 14.2), p = 0.036) ถ้าศึกษาเฉพาะการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในเมดิแอสตินัมเท่านั้นจะพบว่าปัจจัยเสี่ยงคือ ก้อนเนื้องอกระยะ T2*

สรุป: *อัตราการเกิดการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในช่องอกทั้งบริเวณขั้วปอดและในเมดิแอสตินัมที่มีขนาดน้อยกว่า 1 ซม. จากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัดในผู้ป่วยที่เป็นมะเร็งปอดระยะต้น คิดเป็นร้อยละ 15.7 ปัจจัยเสี่ยงของการแพร่กระจาย ได้แก่ ก้อนเนื้องอกที่อยู่กลีบล่างของปอดซ้าย และ ก้อนเนื้องอกระยะ T2 ส่วนอัตราการเกิดการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในเมดิแอสตินัม คิดเป็นร้อยละ 8.4 และปัจจัยเสี่ยงของการแพร่กระจาย ได้แก่ ก้อนเนื้องอกระยะ T2 ดังนั้นผู้ป่วยระยะ T2 (ขนาดก้อนเนื้องอก 3-7 ซม.) ควรได้รับการทำ cervical mediastinoscopy ก่อนผ่าตัดทุกรายเพื่อดูว่ามีการแพร่กระจายของมะเร็งปอดไปยังต่อมน้ำเหลืองในเมดิแอสตินัมหรือไม่ ถึงแม้ว่าจะไม่พบต่อมน้ำเหลืองโตจากภาพเอกซเรย์คอมพิวเตอร์ทรวงอกก่อนผ่าตัด*