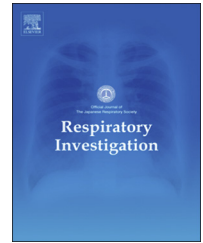




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### Original article

# Cumulative incidence of tuberculosis in lung cancer patients in Japan: A 6-year observational study



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#### ABSTRACT

**Background:** Tuberculosis (TB) remains a health-related problem worldwide, and certain malignancies are known to be associated with an increased risk of TB. Lung cancer is the leading cause of cancer-related death, and the number of patients with lung cancer has been reportedly increasing. As the prognosis of lung cancer remains poor, aggressive comprehensive therapies have been used. The immunosuppression caused by cancer itself and treatment-associated immune modulation may increase the risk of TB. The present study was conducted to investigate the cumulative incidence of TB in lung cancer patients. **Methods:** This observational study included 904 consecutive patients diagnosed with histologically confirmed lung cancer from March 2007 to March 2013 and followed until March 2015 (mean 25.2 months). The cumulative incidence of TB was estimated using the Kaplan–Meier method.

**Results:** Nine lung cancer patients (1.00%) developed TB during the observation period. In all cases, TB occurred within 2 years of the diagnosis of lung cancer. The cumulative incidence of TB at 6 months, 1 year, and 2 years was 0.65%, 1.15%, and 1.38%, respectively. **Conclusions:** The cumulative incidence of TB in lung cancer patients was 1.38% in Japan.

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## 1. Introduction

Understanding the epidemiology of tuberculosis (TB) caused by *Mycobacterium tuberculosis* is critical for its prevention and control. Although the prevalence of TB is currently beyond

the peak stage and appears to be gradually declining, an estimated 9 million people developed TB, and 1.5 million people died as a result of this disease in 2013 [1]. The relative risk factors of TB can be categorized as environmental factors and factors related to impaired immune status of the host,

Abbreviations: TB, tuberculosis; HIV, human immunodeficiency virus

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including age, sex, nutrition status, substance abuse, and systemic diseases such as malignancy, diabetes, renal diseases, and human immunodeficiency virus (HIV) infection [2].

Among the malignancies associated with increased risk of TB, lung cancer has been considered to have a relatively lower risk of TB compared with hematological malignancies or head and neck cancer [3]. However, the association between lung cancer and TB has been reported previously [4–10]. Several studies have indicated that shared immune escape mechanisms are involved in the development and pathogenesis of both diseases [11–14]. In practice, aggressive comprehensive treatments have been administered to lung cancer patients, particularly to patients with advanced disease. Moreover, the occurrence of lung cancer has markedly increased annually, and hence, it is currently the most common cause of cancer-related death [15]. Thus, an increased number of lung cancer patients may be at a high risk of TB as a result of the immunosuppressive effects of cancer treatment and the malignancy itself. Hence, the estimation of the risk of TB is crucial and will enable the creation of an appropriate strategy for the prevention of TB in lung cancer patients. In the present study, we aimed to estimate the recent cumulative incidence of TB in patients with lung cancer.

## 2. Patients and methods

### 2.1. Patients

The study protocol was approved by the Ethical Committee of Iwata City Hospital on April 13, 2015 (approval number 26-38). The need for patient approval and/or informed consent was waived because the study involved a review of patient records, images, and pathologies.

We reviewed the records of 963 consecutive patients with thoracic malignancies including lung cancer, malignant mesothelioma, thymic cancer, and sarcoma from March 2007 to March 2013. Among the 963 patients, 39 patients diagnosed clinically, eight patients diagnosed with malignant mesothelioma, eight patients diagnosed with sarcoma, and four patients diagnosed with thymic cancer were excluded. Accordingly, 904 patients with histologically confirmed lung cancer (684 men and 220 women; mean age, 69.9 years) were enrolled in the present study. The disease was staged in all patients according to the 7th edition of the International Association for the Study of Lung Cancer criteria [16]. The histological types were classified according to the World Health Organization criteria [17].

### 2.2. Diagnosis of TB

Pulmonary TB was diagnosed based on the isolation of *M. tuberculosis* and evidence of new radiographic pulmonary infiltration. *M. tuberculosis* from patient samples was cultured using the BACTEC™ MGIT™ (Mycobacteria Growth Indicator Tube) 960 system (BD, Sparks, MD, USA) for 6 weeks. Sputum smears were graded as negative (culture-positive), scanty (1–9 bacilli/100 fields), ++ (1–9/field), or +++ (≥ 10/field).

### 2.3. Data collection

Clinical data were obtained from the patients' medical records.

### 2.4. Statistical analysis

Discrete variables are expressed as number (percentage), whereas continuous variables are presented as mean (range), unless otherwise specified. The Mann–Whitney *U*-tests were used for continuous variables. Categorical data were compared between the groups using the  $\chi^2$  test for independence. The cumulative incidence of TB patients was estimated using the Kaplan–Meier method. PASW was used for statistical analysis (SPSS, Chicago, IL, USA). A *p* value <0.05 was considered significant.

## 3. Results

The clinical characteristics of 904 patients with lung cancer are summarized in Table 1. Among the 904 patients, 535 patients (59.2%) had adenocarcinoma, 199 patients (22.0%) had squamous cell carcinoma, and 93 patients (10.3%) had small cell carcinoma. In total, 327 patients (36.2%) had stage I disease, 214 patients (23.7) had stage III disease, and 303 patients (33.5%) had stage IV disease. None of the patients were infected with HIV. The mean observation period was 25.2 months.

During the observation period, nine patients (1.0%, eight men and one woman; mean age, 76.2 years) developed TB,

**Table 1 – Characteristics of 904 patients with lung cancer.**

	Patients with lung cancer	Patients with lung cancer and TB	<i>p</i> Value
No. of patients	904	9	
Sex, M/F	684/220	8/1	NS
Age (years)	69.9 (23–96)	76.2 (58–89)	NS
Adenocarcinoma	535 (59.2%)	5 (55.6%)	
Squamous cell carcinoma	199 (22.0%)	2 (22.2%)	
Small cell carcinoma	93 (10.3%)	1 (11.1%)	
Undifferentiated	44 (4.9%)	1 (11.1%)	
Adenosquamous carcinoma	13 (1.4%)	0 (0%)	
Pleomorphic carcinoma	10 (1.1%)	0 (0%)	
Large cell carcinoma	6 (0.7%)	0 (0%)	
LCNEC	4 (0.4%)	0 (0%)	
Lung cancer stage			
I	327 (36.2%)	2 (22.2%)	NS
II	60 (6.6%)	1 (11.1%)	
III	214 (23.7%)	3 (33.3%)	
IV	303 (33.5%)	3 (33.3%)	
Observation period (months)	25.2 (0.03–100.0)		

Data are expressed as *n* (%) or mean (range). F, female; LCNEC, large cell neuroendocrine carcinoma; M, male; NS, not significant; TB, tuberculosis.

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