



Main bronchus location is a predictor for metastasis and prognosis in lung adenocarcinoma: A large cohort analysis

Lin Yang^{a,b}, Shidan Wang^b, David E. Gerber^{c,d}, Yunyun Zhou^{b,e}, Feng Xu^f, Jiewei Liu^f, Hao Liang^f, Guanghua Xiao^{b,d,g}, Qinghua Zhou^f, Adi Gazdar^{d,h,i}, Yang Xie^{b,d,g,*}

^a Department of Pathology, National Cancer Center, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, 100021, China

^b Quantitative Biomedical Research Center, Department of Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

^c Division of Hematology Oncology, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

^d Harold C. Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, 75390, USA

^e Department of Data Science, University of Mississippi Medical Center, MS, 39216, USA

^f Lung Cancer Center/Lung Cancer Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, 610041, China

^g Department of Bioinformatics, UT Southwestern Medical Center, Dallas, TX, 75390, USA

^h Department of Pathology, UT Southwestern Medical Center, Dallas, TX, 75390, USA

ⁱ Hamon Center for Therapeutic Oncology Research, UT Southwestern Medical Center, TX, 75390, USA

ARTICLE INFO

Keywords:

Lung adenocarcinoma
Tumor location
Main bronchus
Surgery
Patient prognosis
The National Cancer Database

ABSTRACT

Objectives: In the literature, inconsistent associations between the primary locations of lung adenocarcinomas (ADCs) with patient prognosis have been reported, due to varying definitions for central and peripheral locations. In this study, we investigated the clinical characteristics and prognoses of ADCs located in the main bronchus.

Methods: A total of 397,189 lung ADCs registered from 2004 to 2013 in the National Cancer Database (NCDB) were extracted and divided into main bronchus-located ADCs (2.5%, N = 10,111) and non-main bronchus ADCs (97.5%, N = 387,078). The ADCs located in the main bronchus and those not in the main bronchus were compared in terms of patient prognosis, lymph node involvement, distant metastases and other clinical features, including rate of curative-intent resection, histologic grade, and stage.

Results: ADCs located in the main bronchus had significantly worse patient survival than those in the non-main bronchus, both for all patients (HR = 1.82, 95% CI 1.78–1.86) and for those undergoing curative-intent resection (HR = 2.49, 95% CI 2.23–2.78). Furthermore, ADCs located in the main bronchus had a significantly higher rate of lymph node involvement and distant metastasis than those not in the main bronchus, when stratified by tumor size (trend test, $p < e^{-16}$). Multivariate analysis of overall survival showed that main bronchus location is a prognostic factor (HR = 1.15, 95% CI 1.08–1.23) independent of other clinical factors.

Conclusions: Main bronchus location is an independent predictor for metastasis and worse outcomes irrespective of stage and treatment. Tumor primary location might be considered in prognostication and treatment planning.

1. Introduction

Lung adenocarcinoma (ADC) incidence has been gradually increasing over the past few years, and currently accounts for more than 50% of non-small cell lung cancer (NSCLC) cases [1]. ADCs generally occur in peripheral lung tissues, but centrally located primary ADCs have not been uncommon in recent years [1,2]. Tumor location (central vs. peripheral) has been reported to be associated with prognosis of ADC patients. However, the results among different studies are inconsistent or conflicted, mainly due to different definitions of tumor locations, small sample sizes, and non-comprehensive statistical analysis.

For example, to define the tumor location, Onn et al. used the distance [3]; Ito et al. used computed tomography (CT) imaging on the basis of hilar structures [4]; Ketchedjian et al. used whether a tumor can be visualized within the inner third of the lung field or on bronchoscopy [5]. Furthermore, the main bronchus has not been analyzed as a separate location in terms of the above definitions. Recently, therapeutic interventions by endoscopy or laser therapy are making great advancements in treating tumors in the main bronchus, especially small ones [6–8]. These findings greatly increase the importance of studying tumors arising from the main bronchus location. In contrast to ADC, previous studies in lung squamous cell carcinoma (SqCC), the second

* Corresponding author at: Quantitative Biomedical Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, 75390, USA.
E-mail address: yang.xie@utsouthwestern.edu (Y. Xie).

major subtype accounting for 30% of NSCLC cases [9], found no significant differences in patient prognosis between central and peripheral locations [10,11]. Consequently, this study focuses only on lung ADCs.

Anatomically, the main bronchi are the two main air passages that branch from the trachea, about 2 centimeters (cm) in length on the right and 5 cm on the left. The main bronchi are closer to vital organs, such as the great vessels and the heart, than the lobular bronchi (secondary) and segmental (tertiary) bronchi. Because the main bronchi are physically close to critical anatomic structures, lung cancer located in the main bronchi could have a high risk of involving surrounding organs and a comparatively lower rate of curative-intent resection. We hypothesized that ADCs located in the main bronchus have worse prognosis and significantly different clinical-pathological characteristics compared with those in other locations, such as the lobes or segmental bronchi.

In this study, we extracted 397,189 cases from the National Cancer Database (NCDB) diagnosed between 2004 and 2013 in the United States, and compared the ADCs located in the main bronchus and those not in the main bronchus in terms of patient survival outcomes and clinical features, including rate of curative-intent resection, histologic grade, and stage. Furthermore, lymph node involvement and distant metastases were compared between main bronchus and non-main bronchus ADCs, stratified by tumor size. To our best knowledge, there is no similar study on lung ADCs located in the main bronchus.

2. Patients and methods

2.1. Database and study sample

To test our hypothesis, a large cohort from the NCDB was used. NCDB is maintained jointly by the American Cancer Society and the American College of Surgeons. Information submitted by tumor registries throughout the United States represents an estimated 70% of newly diagnosed cancer cases [12]. NCDB is a valuable database for cancer research; more than 10,000 papers have been published based on NCDB, including about 1000 papers on lung cancer. Furthermore, information from such a large database can increase statistical stability and reduce the biases associated with institutional studies.

NCDB data from 2004 to 2013 on lung cancer patients were included in this study, which in total included 1,163,465 NSCLC cases from 1287 facilities in the United States. The cases were independent and recorded by annual reports from all the CoC-accredited programs. Only patients with a single malignant primary tumor were included in this study, while those who developed a subsequent malignant invasive or in situ primary tumor were excluded from analysis. The ADC locations were determined by the International Classification of Diseases for Oncology (ICD-O)-3 topographic codes of C34.0 (main bronchus location), C34.1 (upper lobe), C34.2 (middle lobe), and C34.3 (lower lobe), and C33.9 (tracheal location). However, there is no data under the category of C33.9 for tracheal tumors. Thus, only C34.0, C34.1, C34.2, and C34.3 categories were included in the analysis, and tracheal tumors were completely excluded. Patients with diagnoses other than ADC were further excluded from the analysis; the remaining 397,189 patients were included in this analysis.

The database provided diagnostic, demographic, and treatment information for each patient, and the clinical stage information was determined using the new 8th edition AJCC/UICC staging system [13,14]. Patients containing any missing information on resection, histologic grade, or clinical stage were excluded in the following analysis. Patients without survival data were further excluded from survival analysis. Univariate analysis showed that ADCs arising in different lobes had similar prognoses, and thus the primary locations, including upper, middle, and lower lobes, were combined together under non-main bronchus location in the following analyses (Supplemental Fig. 1).

Table 1

Comparison of demographic and clinical characteristics between main bronchus and non-main bronchus located adenocarcinomas.

		Main bronchus (N = 10,111, 2.5%)	Non-main bronchus (N = 387,078, 97.5%)	p value
Age (years)	< 65	4984 (49.3)	157,754 (40.8)	< 2e ⁻¹⁶
	≥ 65	5127 (50.7)	229,324 (59.2)	
Gender	Male	5077 (50.2)	185,914 (48)	< 2e ⁻¹⁶
	Female	5034 (49.8)	201,164 (52)	
Race	White	8397 (83)	324,342 (83.8)	< 2e ⁻¹⁶
	Black	1276 (12.6)	44,394 (11.5)	
	Other	438 (4.3)	18,342 (4.7)	
Surgery	Yes	512 (5.2)	116,152 (30.6)	< 2e ⁻¹⁶
	No	9392 (94.8)	262,851 (69.4)	
	Unknown ^a	207	8075	
Histologic grade	Well differentiated	180 (1.8)	34,563 (8.9)	< 2e ⁻¹⁶
	Moderately differentiated	934 (9.2)	82,395 (21.3)	
	Poorly differentiated	3200 (31.6)	101,312 (26.2)	
	Undifferentiated	61 (0.6)	2052 (0.5)	
	Unknown ^a	5736 (56.7)	166,756 (43.1)	
Clinical stage	Stage I	141 (4.3)	17,165 (16.1)	< 2e ⁻¹⁶
	Stage II	200 (6.1)	8103 (7.6)	
	Stage III	1343 (40.7)	35,060 (32.9)	
	Stage IV	1616 (49.0)	46,344 (43.4)	
	Unknown ^a	6811	280,406	

^a Patients containing unknown information were excluded for comparison analysis between two groups.

2.2. Statistical analyses

Overall survival (OS) was calculated from the date of diagnosis until death or the last follow-up contact date, and presented using Kaplan-Meier (KM) curves. Univariate and multivariate survival analyses were performed with the Cox proportional hazard model. Chi-square analysis was performed to identify whether the main bronchus group and non-main bronchus group had different rates of lymph node involvement and distant metastases stratified by tumor size. The odds ratio of resection was calculated using multivariate logistic regression. All statistical analyses were performed using statistical program R, version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria). R package “survival” (version 2.41-3) was used. All results were considered statistically significant if two-sided p value < 0.05.

3. Results

Of the 397,189 lung ADC patients from the NCDB database, the main bronchus locations accounted for 2.5% and non-main bronchus locations accounted for the remaining 97.5% (Table 1). Compared with non-main bronchus locations, patients with ADCs located in the main bronchus were more likely to be elderly (age ≥ 65 years), male, and black, less likely to receive surgery, and tended to have more severe histologic grade and more advanced clinical stage once diagnosed (Table 1).

Consistent with the unfavorable clinical features of main bronchus locations shown in Table 1, ADCs arising in the main bronchus had worse survival than those in non-main bronchus locations (upper, middle, and lower lobes) for all patients (median survival time [MST] 5.8 vs. 13.6 months, HR = 1.82 [1.78–1.86], Fig. 1A). To test if the worse survival of main bronchus ADCs resulted from a lower resection rate (Table 1), survival outcomes of the patients who had undergone curative-intent surgery were compared between main and non-main bronchus locations. However, for the resected patients, main bronchus ADCs still showed significantly worse survival than non-main bronchus located ones (MST 21.9 vs. 70.9 months, HR = 2.49 [2.23–2.78],

Download English Version:

<https://daneshyari.com/en/article/8453803>

Download Persian Version:

<https://daneshyari.com/article/8453803>

[Daneshyari.com](https://daneshyari.com)