

Treatment outcomes of tuberculosis in patients with lung cancer: a retrospective analysis

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Abstract

Background Lung tuberculosis (TB) and cancer have a complex relationship. Data concerning TB treatment in lung cancer patients are still incomplete. The aim of this study was to investigate the clinical characteristics and treatment responses of lung tuberculosis in lung cancer patients. **Methods** In a retrospective cohort study, lung cancer patients with tuberculosis were identified between January 2013 and December 2016. These patients were divided into a TB treatment group and a TB nontreatment group. Age- and sex-matched lung cancer patients without tuberculosis were selected as control subjects. The clinical courses and responses of patients with and without tuberculosis were examined and compared. **Results** A total of 98 consecutive lung cancer patients were diagnosed with lung tuberculosis (47 patients in the TB treatment group and 51 patients in the TB nontreatment group). Fifty-one lung cancer patients without TB were enrolled as control subjects. Most patients in the three groups were elderly, had advanced non-small cell lung cancer and had tumor burdens. Compared with patients in the TB nontreatment group, the patients in the TB treatment group had more active TB (66% vs. 5.9%, $p < 0.001$) and were newly diagnosed (55.3% vs. 23.5%, $p < 0.001$). The anti-cancer chemotherapy response rate in the TB nontreatment group was not different from that in the TB treatment group (58.8% vs. 76.6%, $p = 0.061$), but it was significantly lower than that in the lung cancer group (58.8% vs. 88.2%, $p < 0.001$). The median survival times of patients in the TB treatment group, TB nontreatment group and cancer patients (control group) were not different (56, 55 and 58 weeks, respectively). No significant differences in serious side effects of chemotherapy were observed among the three groups. **Conclusion** Both anticancer and antituberculosis treatments can be safely and effectively administered in lung cancer patients with tuberculosis. Attention should be paid to the risk of tuberculosis in lung cancer patients in tuberculosis high-burden countries.

Background

Lung cancer and tuberculosis (TB) represent major public health problems worldwide, especially in developing countries. In China, the annual numbers of new cases of lung cancer and tuberculosis were estimated to be nearly 3,804,000 cases in 2014 [1] and 889,000 cases in 2017 [2], respectively.

The possible relationship between lung cancer and TB has attracted attention for several decades. An increasing number of studies have demonstrated that TB is associated with an increased risk and mortality of lung cancer and vice versa [3-6]. However, data concerning tuberculosis treatment in lung cancer patients are still incomplete, except for studies involving a small number of patients and showing inconsistent results [7, 8].

To investigate the treatment responses of TB in lung cancer patients, we performed a retrospective case-control study in a cohort of patients.

Methods

Setting

The study was performed at Anhui Provincial Chest Hospital, a tertiary referral hospital for TB in Anhui Province that has an intermediate incidence of active TB cases (58.4/100,000) [9].

Design

The study was approved by the ethics committee of our hospital. Using the electronic patient data system, patients with lung cancer and lung TB were screened from January 2013 until December 2016. According to TB treatment status, patients were divided into the TB treatment group or the TB nontreatment group. Age-, sex- and cancer stage-matched control subjects were randomly selected from lung cancer patients without TB during the same period at Anhui Provincial Chest Hospital. The diagnosis of tuberculosis was made on the basis of bacteriologic, pathologic, or clinical findings [10]. The diagnosis of cancer was confirmed by histopathological examination [11]. We excluded multidrug-resistant tuberculosis in the analysis to avoid bias caused by the cases.

The treatment of lung cancer and TB was in accordance with national guidelines [10, 11]. In brief, antituberculosis chemotherapy was initially administered with three drugs: rifampicin, isoniazid, and ethambutol for at least 6 months. Anticancer chemotherapy was administered with third-generation platinum-based regimens for non-small cell lung cancer or cisplatin plus etoposide for small cell lung cancer. No molecular targeted therapy or radiotherapy for lung cancer was given to any patient during the study period.

The responses to anticancer treatment were defined according to the response evaluation criteria in solid tumors (RECIST) [12]. The outcome of antituberculosis treatment was defined according to the national guideline [11]. The side effects of chemotherapy were graded using the National Cancer Institute Common Terminology Criteria for adverse events, version 4.0.

Statistical Analysis

Continuous variables were expressed as the median (interquartile range), and differences between groups were analyzed using the Mann-Whitney test. Categorical variables were expressed as absolute values and percentages and were analyzed using the chi-square or Fisher's exact tests. $P < 0.05$ was considered to be statistically significant. A statistical software package was used for the analyses (SPSS 16.0, SPSS, Chicago, USA).

Results

During the study period, 98 consecutive lung cancer patients were diagnosed with lung tuberculosis. Among them, antituberculosis treatment was administered in 47 patients (TB treatment group). The other 51 patients did not receive tuberculosis treatment (TB nontreatment group). The lung cancer control group included 51 age-, sex- and cancer stage-matched patients without TB.

The clinical characteristics of the patients in the three groups (Table 1)

Table 1 Comparison of clinical, laboratory and cancer characteristics among three groups

variable	With TB		<i>P</i> value	Without TB	
	TB treatment	TB nontreatment		Lung cancer	<i>P</i> value
Demographic					
Age, years	64.0(55.0-70.0)	67.5(64.0-75.0)	0.006	65.4(60.0-70.0)	0.997
Male, n (%)	45(95.7)	43(84.3)	0.062	43(84.3)	1.000
BMI (kg/m ²)	20.8(19.8-21.5)	21.0(20.3-21.3)	0.710	21.9(20.5-23.0)	0.022
Smoker, n (%)	32(68.1)	31(60.8)	0.451	28(54.9)	0.547
Laboratory					
Hypoalbuminemia, n (%)	19(40.4)	13(25.5)	0.350	12(23.5)	0.818
Anemia, n (%)	13(27.7)	12(23.5)	0.639	17(33.3)	0.272
Liver dysfunction, n (%)	5(10.6)	5(9.8)	0.892	8(15.7)	0.373
Renal dysfunction, n (%)	11(23.4)	10(19.6)	0.647	12(23.5)	0.630
ESR elevation, n (%)	17(43.6)	9(21.4)	0.033	13(32.5)	0.258
Cancer					
Tumor burden, n (%)	44(93.6)	43(84.3)	0.230	42(82.4)	0.790
Type					
Non-small cell, n (%)	41(87.1)	43(84.3)	0.705	37(72.6)	0.531
Small cell, n (%)	6(12.8)	8(15.7)		14(27.5)	
Stage					
I, n (%)	0(0)	2(3.9)	0.663	2(3.9)	1.000
II, n (%)	3(6.4)	3(5.9)		3(5.9)	
III, n (%)	13(27.7)	15(29.4)		15(29.4)	
IV, n (%)	24(51.1)	26(51.0)		26(51.0)	

Hypoalbuminemia was defined as a serum albumin concentration < 35 g/L. Anemia was defined as a hemoglobin level < 120 g/L in women and < 130 g/L in men. Liver dysfunction was defined as the total bilirubin levels ≥50 μmol/L and/or prothrombin time index <50%. Renal dysfunction was defined as serum creatinine ≥ 1.5 mg/dL. ESR (erythrocyte sedimentation rate) elevation was defined as ESR ≥ 100 mm/h

The median ages in the three groups were approximately 65 years. The age of patients in the TB nontreatment group was older than that of the patients in the TB treatment group. Male patients comprised 84%-95% of each group. Compared to the TB nontreatment group, the lung cancer patients had a higher body mass index (BMI).

The laboratory findings, including hypoalbuminemia, anemia, liver and renal dysfunction, were nearly similar among the three groups. However, the erythrocyte sedimentation rate (ESR) in the TB treatment group was higher than that in the TB nontreatment group.

The cancer type and stage were similar among the three groups. Most patients had advanced non-small cell lung cancer and had tumor burdens.

Clinical course and response to anticancer treatments (Table 2, Figure-1)

Table 2 Comparison of anticancer therapies among three groups

variable	With TB		P value	Without TB	
	TB treatment	TB nontreatment		Lung cancer, n (%)	P value
	n (%)	n (%)			
chemotherapy regimen					
single agent	6(12.8)	10(19.6)	0.360	10(19.6)	1.000
two agents	41(87.2)	41(80.4)		41(80.4)	
treatment completion rate					
completion	27(57.4)	29(56.9)	0.306	40(78.4)	0.057
delayed completion	7(14.9)	4(7.8)		4(7.8)	
early termination	6(12.8)	12(23.5)		3(5.9)	
reduction in dose	5(10.6)	6(11.8)		3(5.9)	
active withdrawal	2(4.3)	0(0)		1(2.0)	
response					
complete response	0(0)	0(0)	0.061	1(2.0)	0.001
partial response	5(10.6)	5(9.8)		4(7.8)	
stable disease	31(66.0)	25(49.0)		40(78.4)	
progressive disease	11(23.4)	21(41.2)		6(11.8)	
median survival(weeks)	56(26-61)	52(32-60)		57(20-64)	
KPS change					
increase	6(12.8)	14(27.5)	0.388	10(19.6)	0.645
decrease	3(6.4)	1(2.0)		1(2.0)	
no change	38(80.9)	36(70.6)		40(78.4)	

The anticancer chemotherapy regimens and treatment completion rates were similar among the three groups. The response rates were similar between the TB treatment and TB nontreatment groups, although more patients in the TB treatment group were in stable disease. However, the response rate was significantly higher in the lung cancer group compared to the TB nontreatment group. The median survival time and KPS changes were similar among the three groups.

Clinical course and response to antituberculosis treatments (Table 3)

Table 3 Comparison of TB characteristics and therapies

Variable	TB treatment n (%)	TB nontreatment n (%)	<i>P</i> value
Type			
Active	31(66.0)	3(5.9)	0.000
Inactive	16(34.0)	48(94.1)	
Time of diagnosis			
Before cancer diagnosis	21(44.7)	39(76.5)	0.000
At the same time	19(40.4)	12(23.5)	
During anticancer therapy	2(4.3)	0(0)	
After anticancer therapy	5(10.6)	0(0)	
Diagnosis of TB			
Culture proven	18	1	
Diagnosed clinically			
Antituberculosis regime			
Single agent	2(4.3)	-	
Two agents	10(21.3)	-	
Three agents	35(74.4)	-	
Treatment completion rate			
Completion	39(83.0)	-	
Delayed completion	1(2.1)	-	
Early termination	6(12.8)	-	
Reduction in dose	1(2.1)	-	
Tuberculosis treatment outcome			
Cure	0(0)	0	0.001
Improvement	27(57.4)	0	
Stabilization	14(29.8)	44(86.3)	
Deterioration	6(12.8)	7(13.7)	

Most patients in the TB treatment group (66%) had active TB, with a significantly higher percentage than that in the TB nontreatment group (5.9%). TB was diagnosed at different time points. Most patients in the TB nontreatment group (76.5%) were diagnosed with TB before cancer diagnosis. However, 55.3% of patients in the TB treatment group were newly diagnosed with TB. Most patients in the TB treatment group received multidrug combination therapy (74.4%), completed the TB treatment (83%), and had improved outcomes (57.4%).

Side effects of treatments (Table 4)

Table 4 Comparison of side effects of therapies among three groups

variable	With TB			Without TB	
	TB treatment	TB nontreatment	<i>P</i>	Lung cancer	<i>P</i>
	n (%)	n (%)	value	n (%)	value
leukocyte deficiency					
grade 3	2(4.3)	2(3.9)	0.460	4(7.8)	0.488
grade 4	2(4.3)	1(2.0)		0(0)	
thrombocytopenia					
grade 3	1(2.1)	1(2.0)	0.642	5(9.8)	0.769
grade 4	0(0)	1(2.0)		2(3.9)	
renal toxic effects					
grade 3	0(0)	0(0)	0.072	0(0)	0.843
grade 4	0(0)	0(0)		0(0)	
neutropenic toxicity					
grade 3	3(8.1)	2(3.9)	0.255	0(0)	0.377
grade 4	0(0)	1(2.0)		0(0)	
gastrointestinal toxicity					
grade 3	0(0)	1(2.0)	0.218	1(2.0)	0.412
grade 4	0(0)	0(0)		0(0)	
diarrheal toxic effects	8(17.0)	6(11.8)	0.458	7(13.7)	0.767
uropathy	0(0)	1(2.0)		0(0)	

Severe toxic complications in the three groups were similar. Patients in the TB treatment group did not have more severe toxic complications.

Discussion

The main finding of the current study is that patients with coexisting lung cancer and active tuberculosis could safely receive both anticancer and antituberculosis treatments. This information will help physicians make clinical management decisions for patients with coexisting lung cancer and active tuberculosis.

Lung cancer and tuberculosis are two major public health problems in China. It was demonstrated that there were 28.49 lung cancer-related deaths per 100,000 population in 2014 [1] and 2.6 tuberculosis-related deaths per 100,000 population in 2017 in China [2]. Meanwhile, lung cancer and tuberculosis have a complicated relationship, which means that they are risk factors for each other. As a tuberculosis high-burden country, the incidence of tuberculosis in lung cancer patients was as high as 12.72% in our past research [13]. In the current study, the features of patients were elderly with advanced non-small cell lung cancer. In addition, most patients in the TB treatment group were newly diagnosed and had active tuberculosis. Hence, caution should be paid to the risk of tuberculosis in lung cancer patients.

Tuberculosis treatment in cancer patients is still not conclusive, especially for advanced non-small cell lung cancer patients with synchronous antituberculosis and anticancer treatments. Kim *et al.* showed that in cancer patients (including 8% with lung cancer), anticancer chemotherapy is not an obstacle to treating tuberculosis [7]. Hirashima *et al.* demonstrated that in patients with metastatic colorectal cancer,

both cancer chemotherapy and tuberculosis treatment could be concurrently administered safely and efficiently[8]. In our study, comparing patients in the TB nontreatment group to lung cancer patients, tuberculosis significantly affected the response rate of anticancer treatment in the TB nontreatment patients. On the other hand, comparing patients in the TB treatment group to patients in the TB nontreatment group, synchronous antituberculosis and anticancer treatments did not lower the response rate of the anticancer treatment and did not increase the severe side effects. Therefore, our findings suggest that both anticancer and antituberculosis treatments could be safely and effectively administered in advanced lung cancer patients with tuberculosis.

Limitations

First, this was a retrospective study with inevitable selection bias. Second, the sample size was a small cohort of patients, limiting the power of the statistical analysis. Third, patients receiving molecular targeted therapy were excluded because there were too few cases for analysis.

Conclusion

Our results indicate that both anticancer and antituberculosis treatments can be safely and effectively administered in lung cancer patients with tuberculosis, and attention should be paid to the risk of tuberculosis in lung cancer patients in a tuberculosis high-burden country.

List Of Abbreviations

TB: tuberculosis; BMI: body mass index, ESR: erythrocyte sedimentation rate

Declarations

Authors' contributions

CM performed research and analyzed data; CM and SQM Design the research. All authors read and approved the final manuscript.

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None.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

none

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Anhui Chest Hospital.

Competing interests

The authors declare that they have no competing interests.

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Figures

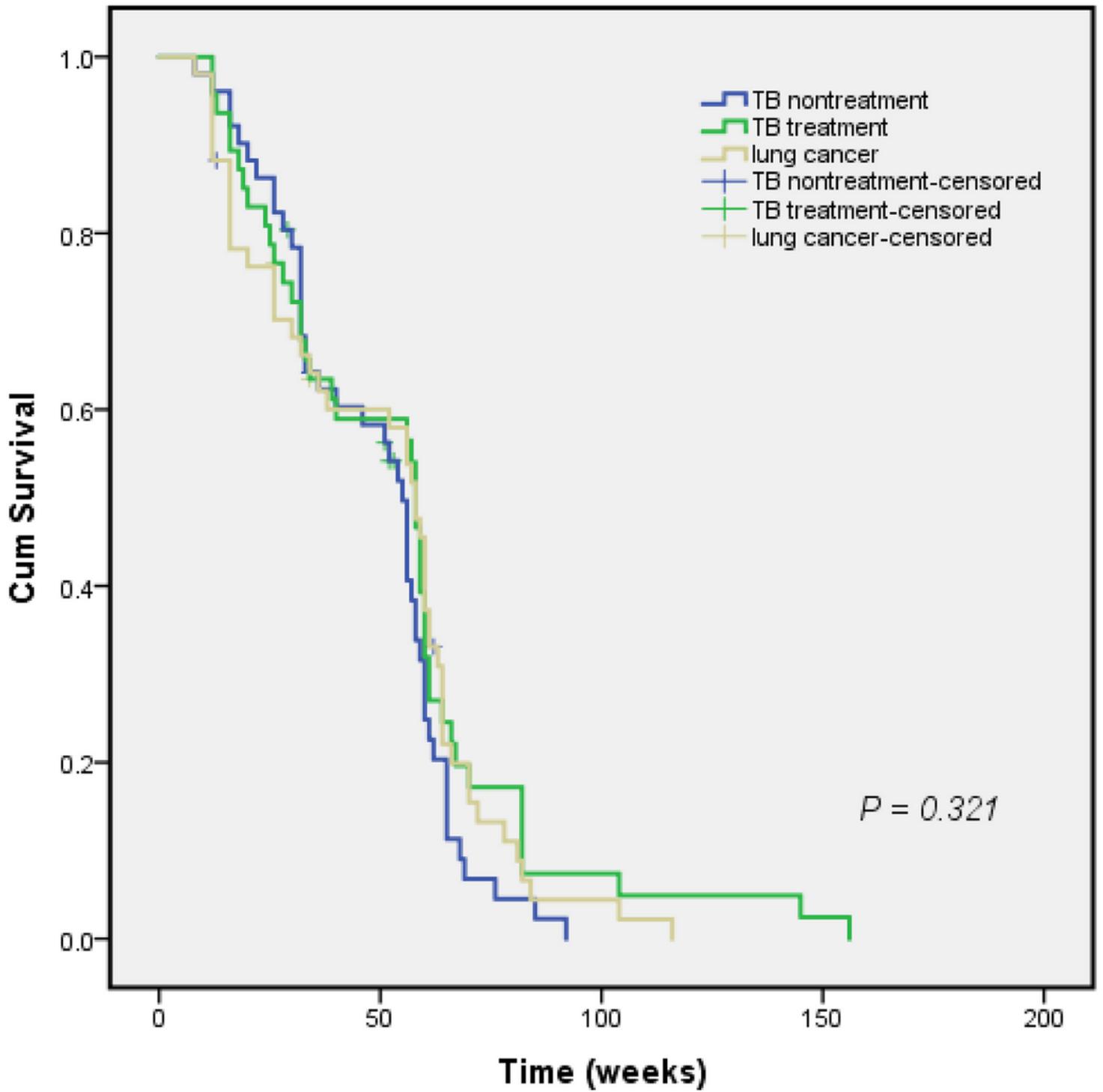


Figure 1

Comparison of Kaplan-Meier curves of survival of three groups