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Original Article

A retrospective study of risk and prognostic factors in relation to lower respiratory tract infection in elderly lung cancer patients

Dan Qiao[1*], Zhiyu Wang[1*], Yaohong Lu[2], Xiaoting Wen[1], Hongtao Li[1], Hui Zhao[1]

[1]Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai 200233, China; [2]Department of Clinical Skill Laboratory, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai 200233, China. [*]Equal contributors.

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Abstract: Lung cancer (LCa) is one of the most common and deadly malignancies in elderly patients. During the course of the disease, these patients frequently present with lower respiratory tract infection. Therefore, this study aims to investigate the clinical features of lower respiratory tract infection in elderly LCa patients and evaluate the impact on overall survival rate. Clinical and laboratory data were analyzed retrospectively for a total of 1936 patients that were over 60-years-old. Patients were classified into three groups based on pulmonary diseases: Group 1, lung cancer (LCa); Group 2, chronic obstructive pulmonary disease (COPD); and Group 3, other medical diseases without pulmonary problems (OMD). Univariate and multivariate analysis were used to evaluate related risk factors of infections and prognostic factors. The infection rate of the LCa group (46.25%) was significantly higher than the COPD (31.40%) and OMD (23.33%) groups. Polymicrobial infections were most prevalent in the LCa group (28.75%), which far exceeded the prevalence in COPD (11.05%) and OMD (4.44%) groups. In LCa patients, the most frequent pathogens were Gram-negative bacteria (44.87%), followed by fungi (34.62%) and Gram-positive bacteria (20.51%), the major pattern of polymicrobial infections was mixed Gram-negative bacteria and fungi (43.48%). Multivariate analysis revealed that COPD, pleural effusion, anatomical type, low cellular immune function, and length of hospital stay were related risk factors of lower respiratory tract infection in elderly LCa patients. A multivariate Cox proportional hazards regression model revealed that age, stage of TNM, surgical resection, antitumor therapy, lower respiratory tract infection, COPD, and pleural effusion were independent prognostic factors for cancer-related death. Patients who received effective antimicrobial treatment had a better outcome than those who did not respond to antimicrobial drugs (HR = 0.458, $P < 0.05$). Understanding lower respiratory tract infection in elderly LCa patients is vital if we are to set up corresponding measures and to target effective antimicrobial treatment.

Keywords: Lung cancer, infection, risk factors, prognosis

Introduction

Lung cancer (LCa) is the leading cause of cancer-related mortality worldwide [1]. The incidence in the elderly has been increasing rapidly in the last few years [2], with over half of 500,000 patients diagnosed annually with LCa worldwide being over the age of 70 [3, 4]. Despite the rising incidence of LCa with age, a substantial number of elderly LCa patients have distant tumor spread at diagnosis because of atypical presentation, which results in lower histological confirmation rates [5, 6], less accurate staging [7], and fewer opportunities of surgical resection. Therefore, chemotherapy and radiation are the anticancer treatments of choice. Individuals suffering from LCa can expect a high symptom burden, particularly from fatigue and breathlessness [8, 9], together with the highest rates of co-morbidities found among all tumors [10, 11], including cardiovascular disease (23%), chronic obstructive airways disease (COPD) (22%), and other malignancies (15%) [11]. Indeed, with advancing age the likelihood that at least one significant medical illness will co-exist increases substantially; the risk of developing respiratory infections and pneumonia further rises when various conditions are present such as malnutrition, obstructive lung disease, congestive heart failure, dia-

betes mellitus, renal disease, or immunosuppressive therapy [12-14]. Numerous factors can predispose elderly LCa patients to develop lower respiratory tract infection, and damage to anatomical barriers that offer the opportunity for pathogen is common after chemotherapy, radiation therapy, inflammation, or invasive procedures (e.g., bronchoscopy and tracheal intubation).

LCa patients suffer frequent infections that not only thwart the effect of oncological treatment but also affect overall survival [15-18]. Fever, as the most constant and often the only indicator of infection, is hard to distinguish from other causes, including malignant disease, drugs, allergic reactions, or thromboembolic events [19]. With subtle or absent respiratory symptoms, diagnosis of infection can often be delayed, which can readily lead to increased morbidity and mortality for elderly individuals. Specific microbiological diagnosis is necessarily established for respiratory tract infection. However, few studies have specifically documented microbiological infections in elderly LCa patients. Therefore, the aim of this study is to more precisely delineate the microbiological characteristics of lower respiratory tract infection and associated risk factors in elderly LCa patients and to evaluate the infection and antimicrobial treatment contributing to survival rate.

Materials and methods

Study participants

The medical records of a total of 1936 patients over 60-years-old who hospitalized in the Shanghai Sixth People's Hospital between January 2011 and January 2014 were retrospectively reviewed. All the patients were classified into the following three groups: Group 1, patients with LCa confirmed by clinical symptoms and radiological or cytological laboratory findings (few had pathological evidence taken from bronchoscopy or by CT-guided fine needle biopsy); Group 2, patients with COPD as identified by physical examination, chest radiograph, and the demonstration of airflow obstruction by spirometry (the spirometric finding of a post-bronchodilator forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) ratio of less than 0.70 is accepted as being diagnostic of significant airflow obstruction) [20, 21]; Group 3, patients with other medical diseases (OMD), including diabetes mellitus, cardiovascular disease, cerebrovascular disease, digestive disease, or other medical diseases (no incidence of hematologic malignancy, solid tumor malignancy, history of pulmonary disease including bronchitis, COPD and tuberculosis).

Infection diagnosis standard

A case definition for typical infection includes the following findings: (i) the clinical manifestations of respiratory infection, and/or (ii) a positive test result for the presence of bacteria isolated from sputum samples obtained from lower respiratory tract. Infections occurring in other locations, such as generalized septicemia or urinary tract infection, were not included in the present study.

The success of antimicrobial therapy was defined according to Kern's criteria: no fever for three successive days, the absence of clinical signs, or the eradication of an identified pathogen. The data collected by the physician in charge of all the patients was based on results provided by the microbiology laboratory and the infectious disease consultant [22].

Samples collection

Samples were obtained from patients suspected to have infection. Sputum sample collection was performed according to standard procedures. Sputum was sampled early in the morning, before the patient had anything to eat or drink. First, patient's mouth was rinsed with water to decrease mouth bacteria and dilute saliva. Then, through a deep cough, the patient coughed up sputum from within the chest. Taking deep breaths and lowering the head was observed to help bring up the sputum. The sputum sample must not be held in the mouth but immediately spat into a sterile container.

Covariates used in the analyses

Demographic information (age, gender), anatomical type, stage of TNM, surgical resection, antitumor therapy including chemotherapy and radiation, cellular immune function measured by T lymphocyte subpopulation (normal CD4: 25.8~41.6% and normal CD8: 18.1~29.6%) and natural killer (NK) cell (normal: 8.1~25.6%), invasive procedures, co-morbidities, length of hospital stay and duration of illness (time from

Table 1. Characteristics of the study group

Item	LCa	COPD	OMD
Number of patients	160	516	1260
Gender (Male/Female)	108/52	291/225	658/602
Median age (y)	75.0	70.2	73.6
Comorbidity			
COPD*	75	516	0
Cardiovascular disease	49	117	329
Diabetes mellitus	41	81	486
Pleural effusion	58	79	43
Low cellular immune function (CD4 < 25.8%, CD8 < 18.1%, NK < 8.1%)	104	156	252
Invasive procedures	58	77	168
Length of hospital stay of > 14 days	65	102	241

*COPD: chronic obstructive pulmonary disease.

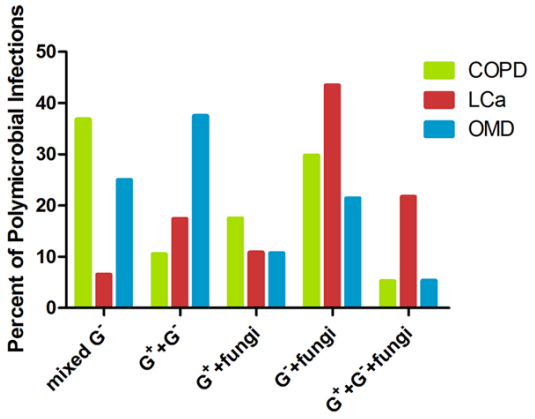

Figure 1. The principal patterns of polymicrobial infections among 3 groups: LCa, COPD and OMD. *G^+, Gram-positive bacteria; G^-, Gram-negative bacteria.

diagnosis to death) were used as covariates in analyzing related risk factors of infections and prognostic factors.

Statistical methods

Statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS) software, version 16 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 5.1 (GraphPad, San Diego, CA, USA). Binary variables were compared by the Pearson's chi-squared test. Multivariate analyses using logistic regression were performed to evaluate the risk factors for lower respiratory tract infection. The prognostic influence of variables on survival was analyzed using the log-rank test for univariate analysis and the Cox proportional hazards model for multivariate analysis. An alpha level of $P < 0.05$ was considered as statistically significant.

Results

Patient characteristics

Over a period of three years, 160 LCa patients over 60-years-old were hospitalized in the Department of Oncology at the Shanghai No. 6 People's Hospital (8.26% of the total of 1,936 elderly patients during that period). Patient characteristics are reported in **Table 1**. Of 160 LCa patients, 76 presented with central type pulmonary carcinoma, while 84 patients had peripheral carcinoma. The patients tended to present with more advanced stages of cancer (stage I, n = 16; stage II, n = 23; stage III, n = 55; and stage IV, n = 66). The following comorbidities and/or potentially predisposing conditions were found when diagnosing the infectious episode [22]: surgical resection (n = 39), antitumor therapy (n = 65), low cellular immune function (n = 104), invasive procedures (n = 58), length of hospital stay of > 14 days (n = 65).

Infection pattern

We found lower respiratory tract infection presented more frequently in the LCa group than the COPD group (46.25% vs 31.40%; $x^2 = 7.721$; $P < 0.05$) and the OMD group (46.25% vs 23.33%; $x^2 = 7.721$; $p < 0.05$). The data showed that the LCa group (46/160, 28.75%) was associated with higher rates of polymicrobial infections than the COPD group (57/516, 11.05%) and the OMD group (56/1260, 4.44%). There

Table 2. Documented pathogens based on the site of lower respiratory tract infection

	LCa		COPD		OMD	
Pathogens	No.	%	No.	%	No.	%
Staphylococcus aureus	17	10.90	16	6.35	46	12.89
Acinetobacter baumannii	10	6.41	9	3.57	28	7.84
Streptococcus pneumoniae	3	1.92	5	1.98	14	3.92
Other Gram-positive bacilli	2	1.28	3	1.19	17	4.76
Klebsiella pneumoniae	20	12.82	30	11.90	39	10.92
Pseudomonas aeruginosa	18	11.54	33	13.10	60	16.81
Acinetobacter baumannii	12	7.69	24	9.52	41	11.48
Escherichia coli	6	3.85	17	6.75	22	6.16
Enterobacter cloacae	3	1.92	10	3.97	9	2.52
Stenotrophomonas maltophilia	4	2.56	9	3.57	7	1.96
Other Gram-negative bacilli	7	4.49	6	2.38	25	7.00
Candida albicans	31	19.87	42	16.67	33	9.24
Other Fungi	23	14.74	48	19.04	16	4.48
Total	156	100	252	100	357	100

were 159 documented polymicrobial infections; the distribution of all groups is shown in **Figure 1**. The patterns of polymicrobial infections in the LCa group were as follows: mixed Gram-negative bacteria and fungi (20/46, 43.48%), mixed bacteria and fungi (10/46, 21.74%), mixed Gram-negative and Gram-positive species (8/46, 17.39%), mixed Gram-positive bacteria and fungi (5/46, 10.87%), and mixed different Gram-negative species (3/46, 6.52%). In the COPD group, mixed different Gram-negative bacteria (21/57, 36.84%) and mixed Gram-negative bacteria and fungi (17/57, 29.82%) occurred more often. The majority pattern of polymicrobial infections in OMD group was mixed Gram-negative and Gram-positive species (21/56, 37.50%).

Pathogens

Bacterial infection accounted for 74.77% of infectious episodes with a total of 765 microorganisms. The most frequent pathogens were Gram-negative bacteria (402/765, 52.55%) followed by fungi (193/765, 25.23%) and Gram-positive bacteria (170/765, 22.22%). The documented pathogens based on the lower respiratory tract infection are reported in **Table 2**.

In the LCa group, the most frequent pathogens were *Candida albicans, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus*. Major isolated pathogens in the COPD group were similar to the LCa group and included *Candida albicans, Pseudomonas aeruginosa,* and *Klebsiella pneumoniae*. However, there were more *Staphylococcus aureus* observed in the OMD group, and the percentage of *Candida albicans* (9.24%) was significantly less than in the LCa group (19.87%) and the COPD group (16.67%).

Risk factors of infection

We compared clinical data between LCa patients with infection (Infection (+)) and those without infection (Infection (-)). In univariate analysis, the baseline characteristics were similar between the two groups. Patients with central type pulmonary carcinoma were more likely to catch infections than those with peripheral carcinoma (P = 0.002). LCa patients with COPD had a significantly higher infection rate than those patients without a comorbidity (P < 0.001). In contrast, those associated with cardiovascular disease and/or diabetes mellitus did not differ significantly between Infection (+) and Infection (-). Pleural effusion and lower cellular immune function were statistically different between the two groups (P = 0.001 and P = 0.022). Invasive procedures and length of hospital stay > 14 days had a significant impact on the Infection (+) group (both P < 0.001). Age, stage of TNM, surgical resection, and antitumor therapy including chemotherapy and radiation did not differ significantly between the two groups (**Table 3**).

Multivariate analysis showed that COPD, pleural effusion, anatomical type, cellular immune function, and length of hospital stay other than invasive procedures were independent risk factors of infection in elderly LCa patients (**Table 4**).

Survival analysis

The median follow-up time of elderly LCa patients was 19.0 months (range, 2-71 months). A total of 105 of 160 elderly LCa patients (65.63%) died during the follow-up period; the median survival time (MST) of the group was 13.0 months (range, 3-52 months). The 1-, 2-

Table 3. Risk factors of LCa patients with lower respiratory tract infection

Variables	Infection (+)	Infection (-)	*P* value
Age			
60-69	26	27	
70-79	25	29	0.843
≥ 80	23	30	
COPD	47	28	< 0.001
Cardiovascular disease	22	27	0.820
Diabetes mellitus	21	20	0.459
Tumor stage			
I, II	18	21	0.989
III, IV	56	65	
Anatomical type			
Peripheral carcinoma	29	55	0.002
Central type pulmonary carcinoma	45	31	
Treatment			
Surgical resection	21	18	0.274
Antitumor therapy	36	29	0.055
Invasive procedures	39	19	< 0.001
Pleural effusion	37	21	0.001
Low cellular immune function	55	49	0.022
Length of hospital stay of > 14 days	43	22	<0.001

Table 4. Logistic model of risk factors of LCa patients with lower respiratory tract infection

Variables	OR	95% CI	*P* value
COPD	5.807	2.458-13.719	< 0.001
Pleural effusion	2.401	1.053-5.476	0.037
Central type pulmonary carcinoma	0.439	0.198-0.973	0.043
Invasive procedures	1.034	0.438-2.442	0.939
Low cellular immune function	4.676	1.974-11.079	< 0.001
Length of hospital stay of > 14 days	4.844	2.089-11.231	< 0.001

and 3-year overall survival (OS) rates for all the LCa patients were 57.0%, 24.6%, and 17.0%, respectively. However, for Infection (+) patients, the 1-, 2- and 3-year OS rates were 40.1%, 11.6%, and 7.7%, respectively. The MST was in excess of 9.0 months. It is noteworthy that the MST in patients with polymicrobial infections was significantly shorter than patients with simple infection (8.0 vs 15.0 months, P = 0.003) and patients without infection (8.0 vs 16.0 months, P < 0.001) (**Figure 2A**).

To better understand the risk factors associated with improved outcomes, univariate and multivariate analyses were performed using relevant clinical parameters. Univariate analyses revealed that age, COPD, pleural effusion, stage of TNM, anatomical type, surgical resection, antitumor therapy, cellular immune function, and infection were prognostic factors (**Table 5**). In the Cox regression analysis, infection was the most important prognostic factor with an HR of 3.284 (P < 0.001). From multivariate analysis, age (HR = 1.789; P < 0.001), COPD (HR = 1.576; P = 0.049), pleural effusion (HR = 1.998; P = 0.002), stage (HR = 2.566; P = 0.001), surgical resection (HR = 0.468; P = 0.006), and antitumor therapy (HR = 0.375; P < 0.001) were found to be independent predictors of overall survival (**Table 6**).

In Infection (+) patients, antimicrobial treatment was a significant predictor of improved outcomes. Patients who received effective antimicrobial treatment (44/74) presented MST 13.0 months, which was statistically significantly longer than the MST of 6.0 months in patients who did not respond to antimicrobial drugs (30/74) (P < 0.001). The survival difference at two years between the two groups was 28.3% (54.6% vs 26.3%) (**Figure 2B**).

Discussion

In our cohort of 1936 hospitalized patients over 60-years-old, 530 episodes of lower respiratory tract infection were documented. The most prominent group of infection was LCa group. In our study, 46.25% of LCa patients experienced infections, and 28.75% of these patients were associated with polymicrobial infections. Meanwhile, we found that Gram-negative bacteria accounted for the majority of documented pathogens in LCa patients, and

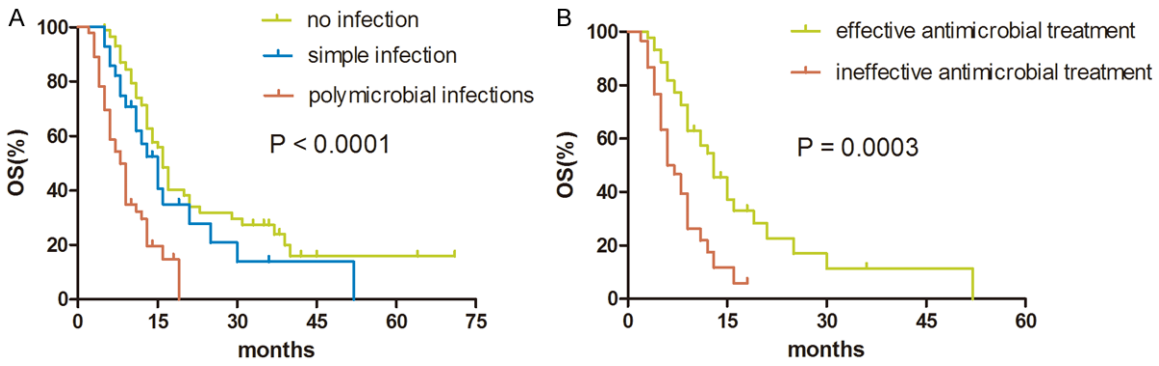

Figure 2. A. Survival difference among 3 groups: patients without infection, patients with simple infection and polymicrobial infections; B. Survival difference between infection (+) patients with effective and ineffective antimicrobial treatment.

Table 5. Univariate analyses of factors in relation to LCa survival

Variables	No. of patients	MST	*P* value
Age			
60-69	53	17.0	< 0.001
70-79	54	14.0	
≥ 80	53	9.0	
Gender			
Male	108	13.0	0.868
Female	52	13.0	
COPD			
Yes	75	11.0	0.001
No	85	16.0	
Cardiovascular disease			
Yes	49	13.0	0.436
No	111	14.0	
Diabetes mellitus			
Yes	41	13.0	0.448
No	118	13.0	
Pleural effusion			
Yes	58	9.0	< 0.001
No	102	15.0	
Tumor stage			
I, II	39	30.0	< 0.001
III, IV	121	11.0	
Anatomical type			
Peripheral carcinoma	84	15.0	0.206
Central type pulmonary carcinoma	76	12.0	
Surgical resection			
Yes	39	21.0	0.001
No	121	13.0	
Antitumor therapy			
Yes	65	16.0	< 0.001
No	95	11.0	
Low cellular immune function			
Yes	104	13.0	0.006
No	56	16.0	
Infection			
Yes	74	9.0	< 0.001
No	86	16.0	

the major pattern of polymicrobial infections was mixed Gram-negative bacteria and fungi. This pattern was very different as compared to the COPD and OMD groups. The most predominant pathogen in our LCa patients were *Candida albicans*, followed by *Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Staphylococcus aureus,* which each accounted for approximately 10% of the documented microorganisms. However, in the literature, *Haemophilus influenzae, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and *Enterobacter cloacae* have been documented in lung infections in up to 68% of cases, and *Staphylococcus aureus* has also been frequently found [15, 23, 24].

The present study revealed that COPD, pleural effusion, central type pulmonary carcinoma, length of hospital stay > 14 days, and low cellular immune function were independent risk factors of lower respiratory tract infection in elderly LCa patients. These patients often represent an invariable population with COPD, and in these individuals, mucociliary clearance is significantly impaired, while bacterial colonization with *Streptococcus pneumoniae* or *Hemophilus influenzae* is common [19]. As a result, acute tracheobronchi-

Table 6. Multivariate analyses of factors in relation to LCa survival

Variables	HR	95% CI	*P* value
Infection	3.284	2.002-5.387	< 0.001
Age	1.789	1.359-2.354	<0.001
COPD	1.576	1.002-2.477	0.049
Pleural effusion	1.998	1.285-3.106	0.002
Stage	2.566	1.440-4.570	0.001
Surgical resection	0.468	0.271-0.807	0.006
Antitumor therapy	0.375	0.232-0.606	< 0.001

tis preceding acute exacerbations of COPD is more common and serious in LCa patients than in patients without pulmonary diseases. Malignant pleural effusion is a common concomitant phenomenon of LCa; invasive procedures include thoracentesis, tunneled indwelling pleural catheters, and tube thoracostomy are considered appropriate options for pleural effusion, which are also considered a risk factor of infection. Central type pulmonary carcinoma is more easily complicated with obstructive pneumonia and bronchial obstruction, which can further result in atelectasis and lung collapse. Subsequently, microorganism colonization can lead to infection.

Lower respiratory tract defenses against infection include mechanical defenses such as cough, the barrier function of mucus and epithelium, and mucociliary clearance which, in concert with innate immune responses, help clear aspirated or inhaled substances including infectious agents [25]. However, both non-immune and immune defenses tend to decline with advancing age; naive T lymphocyte subpopulation and NK cell gradually decline. The underlying malignancy itself or antitumor therapy, including chemotherapy, radiation therapy and corticosteroids, can lead to immune defects. It was worth noting that in our results lower cellular immune function was a significant predictor in univariate analysis but was rejected by multivariate analysis. This inconsistent finding may be the result of selection bias because most LCa patients have suppressed cellular immunity but few take immunotherapy. In addition, elderly residents of long-term care facilities have a high incidence of infection with case fatality rates that range up to 40% [26, 27]. Regular lengthy in-hospital stays lead to changes and colonization of endogenous microflora, which, in combination with obstruction of natural passages by neoplasm, facilitate microorganism proliferation and result in increased morbidity and mortality [28, 29].

In our analysis of 160 elderly LCa patients, multiple factors were associated with overall survival rate. Older age, COPD, pleural effusion, and advanced stage (stage III, IV) indicated very poor prognosis, while early stage (stage I, II), surgical resection and antitumor therapy had favorable impact on survival. Most of these variables are consistent with prior studies and provided additional evidence to support the benefit of current therapy. However, lower respiratory tract infection and antimicrobial treatment were found to be independent predictors of survival.

Increased patient age and advanced stage are frequently associated with significantly worse outcomes in our study; this is consistent with previous reports [30-33]. Although earlier studies have identified gender as an important prognostic factor [30, 32, 33], being male was not associated significantly with a better outcome than being female. The reasons for discrepancies between our findings and those of other studies may reflect different sample sizes and study designs. In one study of 100 patients of who died of LCa in America [31], the most common immediate cause of death was attributed to respiratory failure in 38% of cases, probably because most patients had lung diseases besides cancer. Therefore, the impairment of lung function caused by the malignancy was aggravated by other lung diseases. In our study, 82.5% of patients had comorbidities, including COPD and pleural effusion, which placed the patients at a high risk of respiratory infection, dyspnea, and reduced physical capability. Respiratory failure is a function of not only a single lung disease, but rather a set of them. The frequency and contribution of surgery is evident in the outcomes and survival of elderly LCa patients. A retrospective review of elderly patients showed a non-significant difference in operative mortality for patients aged < 69 years, 70-79 years, and > 80 years of 1.6%, 4.2% and 2.8%, respectively. However, pneumonectomy was significantly associated with mortality in the elderly [34]. In Osaki et al. Study [35] of 851 LCa patients (mean age = 65.4 years) in Japan, there has been an increase in the mean age of patients undergoing surgery over the last two decades in combination with

an increase in 5 year survival and lower operative mortality. A subset of patients in this study received radiotherapy to the chest, bone, or brain in addition to chemotherapy. We also found that active antitumor therapy (chemotherapy and radiotherapy) was associated with improved survival, which is consistent with previous studies [36-38].

Among the long-term survivors, many elderly LCa patients experienced lower respiratory tract infection. The clinical manifestations of most patients with polymicrobial infections will eventually progress (after an initial response to antimicrobial treatment), and the patients will succumb to severe pneumonia accompanied by respiratory failure. In our study, 65.63% of elderly LCa patients died during the follow-up period, and the MST of all the patients was 13.0 months. In Cox regression analysis, infection was the most important prognostic factor with an HR of 3.284 ($P < 0.001$). On comparing 1-, 2- and 3-year OS rates of Infection (+) patients with all the LCa patients cases, significantly worse OS rates were observed in the former group. It is noteworthy that the MST in patients with polymicrobial infections was significantly shorter than patients with simple infection (8.0 vs 15.0 months) and in patients without infection (8.0 vs 16.0 months, $P < 0.001$). Polymicrobial infections severely affect the quality of life and lead to significant morbidity; this phenomenon results from refractory polymicrobial infections because of increasing multi-resistant pathogens and many kinds of bacterial toxins. In addition, we found that patients with infection that received effective antimicrobial treatment would indeed benefit from the management of antibiotics.

The choice of empiric antimicrobial therapy is crucial when presenting with fever and cough with a suspicion of lower respiratory tract infection because these infections are associated with potentially life-threatening complications, particularly in LCa patients with a co-morbidity of COPD. Empiric antimicrobial therapy must adequately cover Gram-negative bacteria as the most common documented pathogens in lower respiratory tract infection. In our study, the majority of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were susceptible to a combination of amikacin and cefoperazone-sulbactam. However, suspicion of *Staphylococcus* infection should not be forgotten in febrile patients with LCa because these infections are occasionally rapidly fatal. We detected that half of *Staphylococcus* were resistant to penicillin and erythromycin, but 100%, 88.2%, and 82.3% of the strains were susceptible to vancomycin, linezolid, and rifampicin, respectively. If polymicrobial infections are suspected, empiric antibiotic therapy must be frequently administered. Fungi have been documented in polymicrobial infections in up to 76.1% of cases, and the majority was *Candida albicans,* which were susceptible to fluconazole, ketoconazole, and 5-fluorocytosine. We considered that the frequent occurrence of fungi might be associated with catheter use and excessive use of antibiotics during previous infections. As discussed above, a combination of broad-spectrum amikacin with antifungal drug could be used successfully for lower respiratory tract infection in LCa patients.

Antibiotic prophylaxis is not recommended because side effects, susceptibility to enteric infections, and emergence of resistant endogenous organisms are of concern [39]. Nevertheless, the reduction in mortality and infection rates outweighs the detriments associated with antibiotic administration [40], prompt initiation of empiric treatment is recommended in all LCa patients, and antibiotics should be rationally used in clinical application based on the results of susceptibility test. In order to define the precise association between infection and LCa, further studies with a larger number of cases are necessary.

This study had some limitations. First, it was a retrospective study with a small sample size. Second, pathologic diagnosis could not be confirmed in all LCa patients. Finally, variable antibiotics were used because LCa patients repeatedly suffered lower respiratory tract infections; there was a lack of consistency in antimicrobial therapy of polymicrobial infections.

In conclusion, our study demonstrated that elderly LCa patients had higher infection rate and that polymicrobial infections were more common than COPD and OMD. Gram-negative bacteria accounted for the majority of documented pathogens in elderly LCa patients; the principal pathogens were *Candida albicans*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Infection was the most important prognostic factor for

elderly LCa patients. Thus, effective antimicrobial treatment is critical to prolonging the survival time.

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Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hui Zhao, Department of Oncology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai 200233, China. Tel: +86 021-24058430; Fax: +86 021-64179712; E-mail: zhao-hui@sjtu.edu.cn

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