Current Lung Cancer Screening Guidelines may Miss the High-risk Population in the Real-world Physical Examination Population: A Large Prospective Study

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Abstract

Background: Despite much research published on lung cancer screening, China has had no large-scale study on the missed diagnosis of lung cancer in physical examination population. We therefore did a real-world study using the current lung cancer screening guidelines to the physical examination population in China to determine the proportion of lung cancer cases that have been missed.

Methods: A real-world prospective cohort study of screening, with the use of low-dose computed tomography, was conducted among people who took yearly health checkup in health management center of West China Hospital between 2006 and 2017. We respectively used current guidelines including lung cancer screening guidelines of the U.S. Preventive Services Task Force (USPSTF) and expert consensus on low dose spiral CT lung cancer screening in China.

Results: In a total of 15996 participants with physical examination who completed the baseline screening, 6779 (42.4%) subjects had at least one positive finding, and 142 (2.1%) cases of lung cancer were screened positive. The false positive rate was 97.9%. Of 142 lung cancer cases detected in our study, only 9.2% met the lung cancer screening guidelines proposed by the USPSTF, and 24.4% met that of China. The rates of missed diagnosis were as high as 90.8% and 75.6% respectively. In addition, we did an in-depth analysis by gender. We found that among male lung cancer patients, the proportion of smokers was 75%, and the proportion of young people under 50 was 23.2%. Among female patients with lung cancer, the proportion of smokers was only 5.8%, and the proportion of young people under 50 was up to 33.3%.

Conclusions: The rate of missed diagnosis was as high as 90.8% applying the current lung cancer screening guidelines to the physical examination population in China. Further study to determine screening guidelines for targeted populations, is warranted.

Background

Lung cancer is the most frequent cancer and the leading cause of cancer death all over the world [1]. According to a status report produced by the International Agency for Research on Cancer, it is estimated that there will be 2.1 million new lung cancer cases (11.6% of the total new cancer cases) and 1.77 million deaths for lung cancer (18.4% of the total cancer deaths) in 2018 [1]. According to the latest data from the National Central Cancer Registry of China, there will be an estimated 733,300 new lung cancer cases and 610,200 lung cancer deaths in 2015 in China [2]. It is reported that the survival rate of lung cancer was negatively correlated with the clinical and pathological stages at the time of diagnosis [3]. The patient of carcinoma in situ sees almost 100% in 5-year survival rate [3]. However, the 5-year survival rate for stage IV patients can be as low as 2% [3]. Unfortunately, these early lung cancers are asymptomatic. When symptoms appear, the disease is usually advanced and incurable [4]. The study showed that low-dose computed tomography (LDCT) can detect some tumors at early stages [5]. Many

authoritative medical organizations in the United States and in the China have launched screening guidelines, which recommended lung cancer screening in high-risk groups with LDCT [6–8].

At present, due to different regions, there are differences in the definition of high-risk groups in domestic and foreign guidelines. Generally, age and smoking are the main criteria to define high-risk groups in domestic and foreign guidelines. Researches showed that except for smoking, the causes of lung cancer were also attributed to air pollution, environmental exposure, genetic factors [9,10]. Although most lung cancers are caused by smoking, a lot of lung cancer cases worldwide have been reported in nonsmokers[9]. In the U.S., there were approximately 17,000–26,000 never-smokers develop lung cancer annually [11]. Furthermore, global statistics estimate that 53% lung cancer in women are not attributable to smoking [12]. It was reported that more than 300,000 patients die of non-smoking lung cancer every year [9]. If lung cancer in never smoker was considered as a separate category, it would be the seventh most common cause of cancer death around the world [12].

To date, research has focused on cancer in children and the elderly people [13]. The cancer burden of young adults has rarely been explored in depth [13]. It was reported that 975 396 new cancer cases and 358 392 cancer-associated deaths occurred among young adults worldwide in 2012, which equated to an incidence of 43.3/100000 and mortality of 15.9/100 000 [13]. It was reported that of the 4114 cases of primary lung cancer in the study, 6.83% was under 45 years old [15]. The incidence of lung cancer also shows a trend of youth in recent years [13–15]. Furthermore, studies showed higher incidence rates of lung cancer among young women than among young men [16,17]. Thus it can be see young lung cancer patients have gradually become a disease group that can not be ignored [13–15].

For these reasons, the current lung cancer screening guidelines may miss some persons at high risk of lung-cancer especially young or non-smoking people [6–8]. Research showed about two-thirds of newly diagnosed lung cancer patients in the United States would not meet the current screening criteria of lung cancer recommended by the U.S. Preventive Services Task Force (USPSTF) [18–19]. According to the report, between 1984 and 2011, the proportion of lung cancer cases in Olmsted County meeting the USPSTF screening criteria decreased significantly, with only 50% of male and 37% of female patients eligible for screening in the most recent time interval [19]. It indicates that using the current screening guidelines of lung cancer, more and more lung cancer patients may be missed in screening [19]. However, China has had no large-scale study on the missed diagnosis of lung cancer in physical examination population. Therefore, in order to determine whether the current screening guidelines of lung cancer will lead to missed diagnosis of lung cancer cases in China, and to determine the fraction of lung cancer cases that would be missed, we did a real-world prospective study which applied these screening guidelines to the physical examination population in West China Hospital.

Methods

Trial Oversight

We applied the current guidelines to the physical examination population and compared them with the real world. This research, a prospective cohort study of screening with the use of LDCT, was conducted among the people taking yearly health checkup in health management center of West China Hospital.

Participants

Participants were enrolled and screened from June 30, 2006 through June 30, 2017. They were followed for events that occurred before December 31, 2017.

Eligible subjects did not have undergone chest imaging within 18 months before enrollment, and there were no new or aggravating cough, expectoration, hemoptysis, chest distress, dyspnea and other symptoms. Persons with any of the following conditions were excluded from this study: 1) previously received a diagnosis of unknown pulmonary nodules or malignant pulmonary nodules, masses, hilar enlargement, atelectasis; 2) a history of total or partial lobectomy; 3) history of lung cancer; 4) an unexplained weight loss of more than 5 kg in the past year. A total of 15,996 persons were enrolled. A written informed consent was obtained from every participant. Eligible participants completed a questionnaire that covered some topics, including demographic characteristics, smoking behavior, and medical history.

Guidelines

In this study, we respectively used two kinds of the current lung cancer screening guidelines including lung cancer screening guidelines of the U.S. Preventive Services Task Force (USPSTF) and expert consensus on low dose spiral CT lung cancer screening in China to the physical examination population in China to determine the proportion of lung cancer cases that have been missed. The USPSTF recommended annual screening for lung cancer with LDCT in adults aged 55 to 80 years, who currently smoke or have quit within the past 15 years, and who have an at least 30 pack-years of cigarette smoking history [6,7]. The consensus of Chinese experts suggest that annual LDCT lung-cancer screening for individuals aged 50 - 75 years, combining at least one of the following risk factors: 1) at least 20 pack-years of cigarette smoking history, including currently smoking or giving up smoking for less than 15 years; 2) passive smoking; 3) a history of occupational exposure, including asbestos, beryllium, uranium, radon, etc; 4) a history of cancer or a family history of lung cancer; and 5) a history of chronic obstructive pulmonary disease (COPD) or diffuse pulmonary fibrosis [8].

Screening

Participants were invited to undergo a base-line screening. We conducted annual screenings from the next year. Participants with positive screening would be followed up, and those with negative screening would be screened in the next round.

All screening tests were conducted in accordance with a standard protocol developed by the medical physicists associated with the trial, which specified the acquisition variables and the acceptable

characteristics of the machine [20-22]. All computed tomography (CT) scans were performed on double row spiral CT (Somatom Emotion Duo, Siemens, Germany). Thin slice scanning with 1mm was performed on the local lesions. All scans were obtained using a low-dose regimen, with the machine set at 120 kVp, 16 (20 mA/0.8 s) ~ 40 (50 mA/0.8 s) mAs, pitch ≤ 1cm, and 0.8 seconds rotation time. Chest radiographs were obtained with the use of digital equipment. All the machines used for screening met the technical standards [5].

Radiologic technologists and radiologists were certified by appropriate agencies. Radiologic technologists completed training in image acquisition. Radiologists also completed training in standardized image interpretation. Two radiologists with at least 5 years of experience in thoracic radiology assessed all chest images independently. Images were assessed first in isolation and then in comparison with available historical and screening images. The comparative analysis was used to determine the outcome of the chest examination. When the interpretations of these two radiologists were different, they need to analyze repeatedly and negotiated the judgment. In addition, at least two qualified respiratory medicine and chest tumor experts from our hospital formed a diagnosis team. Based on the recommendation of radiologists and other results of physical examination, the diagnosis team made a further plan of intervention treatment. LDCT scans that could reveal any non-calcified nodule with at least 4 mm diameter were classified as positive, suspected lung cancer. Other abnormalities such as obstructive atelectasis, soft tissue or patchy clouding opacity could be classified as a positive result as well.

Medical-Record Abstraction

Data regarding diagnostic evaluation procedures and any associated complications for patients with positive screening tests and lung cancer were extracted from the medical records. At the same time, the pathology reports and records of operation and treatment of lung cancer patients were also obtained. Metastatic lung cancer was excluded. The classification of histologic characteristics of the lung cancer were conducted according to the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) [23], and the clinical stages were conducted according to the eighth edition of the Cancer Staging Manual of the American Joint Committee on Cancer (AJCC) [24].

Vital Status

We have trained professionals to follow-up. A special follow-up team is responsible for ascertaining probable vital status and determining whether the cause of death was lung cancer. We have carefully distinguished between lung cancer-related deaths and those caused by diagnostic evaluation or treatment of lung cancer.

Statistical analysis

SPSS was adopted for statistical analysis. Comparisons between the group of patients with lung cancer and the group of patients without lung cancer were calculated by the chi-square test (categorical data) or

the T-test (numerical data). P value < 0.05 was considered as statistically significant. Survival analysis was performed by Kaplan-Meier with ungrouped data.

Results

Characteristics of the Participants

The 15,996 subjects completed baseline lung screening with LDCT from June 30, 2006 through June 30, 2017. The baseline demographic characteristics of the 15,996 participants are summarized in Table 1. The age of participants was distributed in all ages, but it was mainly over 40 years old. 70.3% individuals did not smoke.

Positive Resultsof Screening

In the lung cancer screening with LDCT, positive results are shown in Table 2. Of the 15996 participants with physical examination who completed the baseline screening, 6779 subjects had at least one positive finding, with a positive rate of 42.4% (Table 2).

Incidence of Lung Cancers

The detection rates of lung cancer are summarized in Table 2. A total of 142 cases of lung cancer were screened out from the physical examination population initially recruited in this research, the detection rate of lung cancer was 2.1%, and the false positive rate was 97.9% (Table 2).

We conducted this analysis in high-risk population of lung cancer. The analysis showed that based on the guidelines of the lung cancer screening proposed by the USPSTF [6,7], of the 142 cases of lung cancer, 72 patients were aged 55-80, and 70 patients did not meet the age-standard (Table 3). In addition, the proportion of patients who met the smoking and quit-smoking standards were 8.5% and 2.1% respectively (Table 3). Only 13 cases of lung cancer met all criteria of screening (Table 3). The rate of missed diagnosis was as high as 90.8% according to the guideline of the lung cancer screening proposed by the USPSTF (Table 3).

Moreover, we did the similar research in high-risk population of lung cancer based on the Chinese screening guidelines. According to the guidelines of the lung cancer screening in China [8], of the 142 cases of lung cancer, the proportion of patients who met the standards, including age, smoking, tumor history and chronic lung diseases, was 53.5%, 12.7%, 18.3% and 14.7%, respectively (Table 4). Just 25.4% people with lung cancer met all criteria of this guideline. The rate of missed diagnosis was 74.7% (Table 4).

Analysis of high-risk factors in lung cancer stratified by gender

Previous studies have shown that there were differences in the high-risk factors of lung cancer between different genders [12,16-17]. Therefore, we further investigated the high-risk factors of lung cancer by gender.

As shown in Table 5, age and smoking status were high-risk factors of lung cancer in women, while in men, besides these factors, there were some other high-risk factors, such as COPD, diffuse pulmonary fibrosis, and previous history of malignant tumor (all $P < 0.05$). In addition, we found that the detection rate of lung cancer in women was 1.1%, significantly higher than that in men 0.7% ($P=0.021$) (Table 5). In order to explore the correlation between different age stages and lung cancer, we further analyzed the risk factor of age (Table 5). The proportion of lung cancer in men under 50, 50-55, 55-75, 75-80 and over 80 years old were 23.2%, 11%, 42.5%, 12.3% and 11.0% respectively, and those in women were 33.3%, 14.5%, 33.4%, 8.7%, 10.1% respectively (Table 5). At the same time, we also found that among lung cancer patients in male, the proportion of smokers was 75%, and that in female lung cancer cases was only 5.8% (Table 5).

Mortality

Participants were followed-up from January 1, 2007 to January 31, 2020. The shortest follow-up time was 2.5 years, and the longest was 13 years. Up to the end of follow-up, 963 people lost their visit, the rate of which was 6.0%. There were 18 deaths of all the lung cancer patients. The mortality rate was 12.7%. Lung cancer accounted for 55.5% of all the deaths in the study (Table 6). In addition, we plotted survival curves for lung cancer patients (Figure 1).

Discussion

The current lung cancer screening guidelines define high-risk groups in terms of age, smoking and so on [6–8, 25]. However, the high-risk factors of lung cancer are different between countries and regions [6–8, 25]. In order to know whether the current screening guidelines of lung cancer will cause missed diagnosis of lung cancer cases in the physical examination population, we firstly conducted a real-world prospective study using these screening guidelines in this Chinese population. Our results suggested that the current screening guidelines of lung cancer might miss some of the high-risk population in the physical examination population. Several factors as following may contribute to this.

On the one hand, of 142 lung cancer patients in our study, non-smokers accounted for 67.6%. In female patients with lung cancer, the proportion of non-smokers was even as high as 94.2%. Therefore, according to the current lung cancer screening guidelines, this part of lung cancer cases will be missed diagnosis, especially female patients. Researches have shown that the incidence of lung cancer is related to many factors including genetic factors, smoking, environmental exposure, air pollution, and so on [10,28–35]. Generally, the vast majority (80%) of lung cancer cases are attributable to tobacco smoking [26,27]. However, the global statistics estimate that 25% of all lung cancer cases worldwide are not due to smoking [12]. Furthermore, with the successful implementation of smoking prevention and cessation programmes, the proportion of lung cancer in non-smokers is expected to increase [9]. In addition, the smoking prevalence of female patients with lung cancer was very low in our study which was consistent with previous study and significantly lower than that in Caucasian female patients [36–43]. Therefore, this

may be the main reason why the missed diagnosis rate of lung cancer in this study is higher than that in previous studies abroad [12,36–44].

On the other hand, of all lung cancers detected in our study, 28.1% patients were younger than 50 years, and 10.6% patients were older than 80 years. After further analysis by age and gender, we found that according to the age standard of lung cancer screening guidelines in China, the proportion of patients with lung cancer in men who met the criterion was 53.5%, and that in women was 47.9%. In other words, according to the Chinese standards, the proportion of male and female lung cancer patients missed diagnosis were 46.5% and 52.1% respectively. In addition, according to age standard of lung cancer screening guidelines recommended by USPSTF, the proportion of lung cancer cases in male who met the criterion was 54.8%, and that in female was 42.1%. That is to say, based on the American Standards, the proportion of lung cancer cases missed diagnosis in men and women were 45.2% and 57.9% respectively. It can be seen that no matter which lung cancer screening guidelines you choose, there were many lung cancer patients missed according to the age standard, especially female patients. Previous studies showed that the incidence of lung cancer in young adults were around 1.2–6.2% (less than 40 years), 5.3% (under 45 years), and 13.4% (less than 50 years) [45–49]. Therefore, with an increasing incidence of lung cancer in young people, it have gradually become a disease group that can not be ignored [50,51].

In addition, our study found that compared with lung cancer patients in male, female lung cancer patients have the following characteristics. Firstly, the detection rate of lung cancer in women is higher than that in men. Secondly, the prevalence of non-smoking lung cancer in women was much higher than that in men. Previous studies have also found that the proportion of women with non-smoking lung cancer is higher than that of men [12]. Global statistics estimate that 53% of lung cancers in female and 15% in male are not attributable to smoking [12]. Thirdly, the proportion of young people among female lung cancer patients is higher than that among male lung cancer patients. The feature in our study is consistent with earlier result reported in previous studies [16,17].

Meanwhile, the result showed that there was a high rate of false positive in lung cancer screening with LDCT in our study. This was consistent with the results of the National Lung Screening Trial (NLST) [5]. Most of the false positive results might be due to the presence of non-calcified granulomas or benign intrapulmonary lymph nodes.

To our knowledge, this is the first real-world study to explore whether the current lung cancer screening guidelines are applicable to the physical examination population in China. The missed diagnosis rate is very high whether using American or Chinese screening guidelines of lung cancer. Moreover, our study was a prospective cohort study with large sample size and was less affected by certain biases such as recall bias.

Our research also has some limitations. First, the study population mainly came from Chengdu and surrounding areas. Relevant research that includes other regions is needed. Second, our research population is mainly the staff of enterprises and institutions. Personnel structure is relatively single. We

need to further enrich our personnel structure to reflect the situation more realistically. Finally, the follow-up time is too short to calculate the 5-year and 10-year survival rates together. Thus, we should extend the follow-up time to know the long-term survival rate of lung cancer.

Conclusions

This real-world study is the first prospective cohort research applied the current lung cancer screening guidelines to the physical examination population in China. The results suggested that the rate of missed diagnosis was very high. In addition, our study also found that female patients with lung cancer have some characteristics when compared with lung cancer patients in male. As shown in our data, further study to determine screening guidelines for targeted populations, is warranted.

Abbreviations

USPSTF = U.S. Preventive Services Task Force; LDCT = low-dose computed tomography; CT = computed tomography; COPD = chronic obstructive pulmonary disease; ICD-O-3 = International Classification of Diseases for Oncology, 3rd Edition; AJCC = American Joint Committee on Cancer; NLST = National Lung Screening Trial.

Declarations

Acknowledgments

We thank all study participants for their cooperation.

Authors' contributions

GJ had full access to all of the data in this study, take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the acquisition, analysis and interpretation of data, and the drafting of the manuscript. All authors contributed to the intellectual content. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors.

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Availability of data and materials

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

Ethics approval and consent to participate

The Ethics Committee of the West China Hospital of Sichuan University, China, provided authorization for our study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1

Selected Baseline Characteristics of the Study Participants

Parameter	Man, n (%)	Woman, n (%)	Total, n (%)
Total	9801 (61.3)	6195 (38.7)	15996 (100.0)
Age at inclusion (years)[a]	51.26±14.76	48.80±14.76	50.31±14.81
<30	545 (5.56)	586 (9.5)	1131 (7.0)
30~	1361 (13.9)	872 (14.1)	2233 (14.0)
40~	3119 (31.8)	2224 (35.9)	5343 (33.4)
50~	2363 (24.1)	1196 (19.3)	3559 (22.2)
60~	1033 (10.5)	605 (9.8)	1638 (10.2)
70~	832 (8.5)	475 (7.7)	1307 (8.2)
≥80	548 (5.6)	237 (3.8)	785 (5.0)
Smoking status			
smoking	4697 (47.9)	52 (0.8)	4749 (29.7)
non-smoking	5104 (52.1)	6143 (99.2)	11247 (70.3)
Smoking volume (pack year)[a]	19.24±14.84	13.95±25.04	19.20±14.93
<10	894 (19.0)	13 (25.0)	907 (19.1)
10~	1080 (23.0)	8 (15.4)	1088 (23.0)
20~	841 (17.9)	1 (1.9)	842 (17.7)
30~	488 (10.4)	1 (1.9)	489 (10.3)
40~	225 (4.8)	0 (0)	225 (4.7)
50~	45 (1.0)	0 (0)	45 (0.9)
≥60	100 (2.1)	1 (1.9)	101 (2.1)
Unknown	1024 (21.8)	28 (53.8)	1052 (22.2)
Family history of lung cancer			
Yes	163 (87.2)	181 (84.6)	401 (2.5)
No	24 (12.8)	33 (15.4)	15595 (97.5)
Chronic lung disease[b]			
Yes	5868(59.9)	3450(55.7)	9318 (58.3)

No	3933(40.1)	2745(44.3)	6678 (41.7)

a Values are presented as mean ± SD (range). b Chronic lung diseases include the chronic obstructive pulmonary disease, diffuse pulmonary fibrosis, history of pulmonary tuberculosis and other respiratory diseases.

Table 2

Results of Screening

Parameter	**Physical Examination**
	Population
	n(%)
Total No. Screened	15996
Positive Result	6779 (42.4)
Lung cancer confirmed	142(2.1)
T0a	86 (1.9)
T1	31 (1.9)
T2	20 (3.9)
T3	4 (3.5)
T4	1 (4.2)
Lung cancer not confirmed	6637 (97.9%)
T0c	4441 (98.1)
T1	1574 (98.1)
T2	490 (96.1)
T3	109 (96.5)
T4	23 (95.8)
Negative Result	9217(57.6)

a The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization.

Table 3

The results of lung cancer screening according to the USPSTF screening guidelines

Parameter	Number of lung cancer (n=142)	
	Met the inclusion criteria, n(%)	Not met the inclusion criteria, n(%)
Age at inclusion (years)		
A. 55~80	72(50.7)	70(49.3)
Smoking volume (pack year)		
B. ≥ 30	12(8.5)	130(91.5)
Quit smoking time (years)		
C. < 15	3(2.1)	139(97.9)
AB or AC	13(9.2)	129(90.8)

Table 4

The results of lung cancer screening according to the Chinese screening guidelines

Parameter	Number of lung cancer (n=142)	
	Met the inclusion criteria, n(%)	Not met the inclusion criteria, n(%)
Age at inclusion (years)		
A. 50~75	76(53.5)	66(46.5)
Smoking volume (pack year)[a]		
B. ≥ 20	18(12.7)	124(87.3)
History of cancer[b]		
C. Yes	26(18.3)	116(81.7)
Chronic lung disease[c]		
D. Yes	45(14.7)	145(85.3)
A(B or C or D)	36(25.4)	106(74.7)

a: This includes current smoking and quitting smoking less than 15 years. b: This includes a history of cancer or a family history of lung cancer. c: This includes the chronic obstructive pulmonary disease, diffuse pulmonary fibrosis, history of pulmonary tuberculosis and other respiratory diseases.

Table 5

Analysis of high-risk factors in lung cancer stratified by gender

Characteristic	Male			Female		
	Patients with lung cancer, n(%)	Patients without lung cancer, n(%)	P value	Patients with lung cancer, n(%)	Patients without lung cancer, n(%)	P value
Total	73(0.7)	9728(99.3)		69(1.1)	6126(98.9)	0.021 [b]
Age (years) [a]	62.10±13.51	51.18±14.74	<0.0001	59.17±13.44	48.69±14.73	<0.0001
<30	0(0)	545(5.6)		0(0)	586(9.6)	
30~	0(0)	627(6.4)		0(0)	397(6.5)	
35~	2(2.7)	732(7.5)		1(1.4)	474(7.7)	
40~	6(8.2)	1497(15.4)		8(11.6)	1158(18.9)	
45~	9(12.3)	1607(16.5)		14(20.3)	1044(17.0)	
50~	8(11.0)	1288(13.2)		10(14.5)	710(11.6)	
55~	4(5.5)	1063(10.9)		4(5.8)	472(7.7)	
60~	7(9.6)	591(6.1)		6(8.7)	363(5.9)	
65~	13(17.8)	422(4.3)		5(7.2)	231(3.7)	
70~	7(9.6)	446(4.6)		8(11.6)	192(3.1)	
75~	9(12.3)	370(3.8)		6(8.7)	269(4.4)	
80~	8(11.0)	540(5.6)		7(10.1)	230(3.8)	
Smoking history	55(75.3)	5299(54.5)	0.000	4(5.8)	52(0.8)	0.003
Chronic obstructive pulmonary disease	24(32.9)	1821(18.7)	0.002	9(13.0)	606(9.9)	0.384
Diffuse pulmonary fibrosis	17(23.3)	1440(14.8)	0.042	6(8.7)	732(11.9)	0.407
Previous pulmonary tuberculosis	4(5.5)	357(3.7)	0.346	1(1.4)	168(2.7)	1.000
Previous history of	11(15.1)	268(2.8)	<0.0001	12(17.4)	691(11.3)	0.112

malignant tumor						
Family history of cancer	5(6.8)	723(7.4)	0.850	10(14.5)	751(12.3)	0.574
Number of first-degree relatives with cancer	5(6.8)	653(6.7)	0.371	10(14.5)	655(10.7)	0.478
Family history of lung cancer	2(2.7)	185(1.9)	0.651	1(1.4)	213(3.5)	0.733
Number of first-degree relatives with lung cancer	1(1.4)	162(1.7)	0.287	1(1.4)	180(2.9)	0.888
a Values are reported as mean ± SD (range). b The detection rate of lung cancer in women is compared with that in men.						

Table 6

Causes of Death among Lung Cancer Patients

Cause of Death [a]	**Number/Total number (%)**
Neoplasm of bronchus and lung	10/18 (55.5)
Respiratory illness	4/18 (22.2)
Multiple organ failure	3/18 (16.7)
Other	1/18 (5.6)
a Causes of death were categorized according to the codes in the International Classification of Diseases, 10th Revision (ICD-10).	

Figures

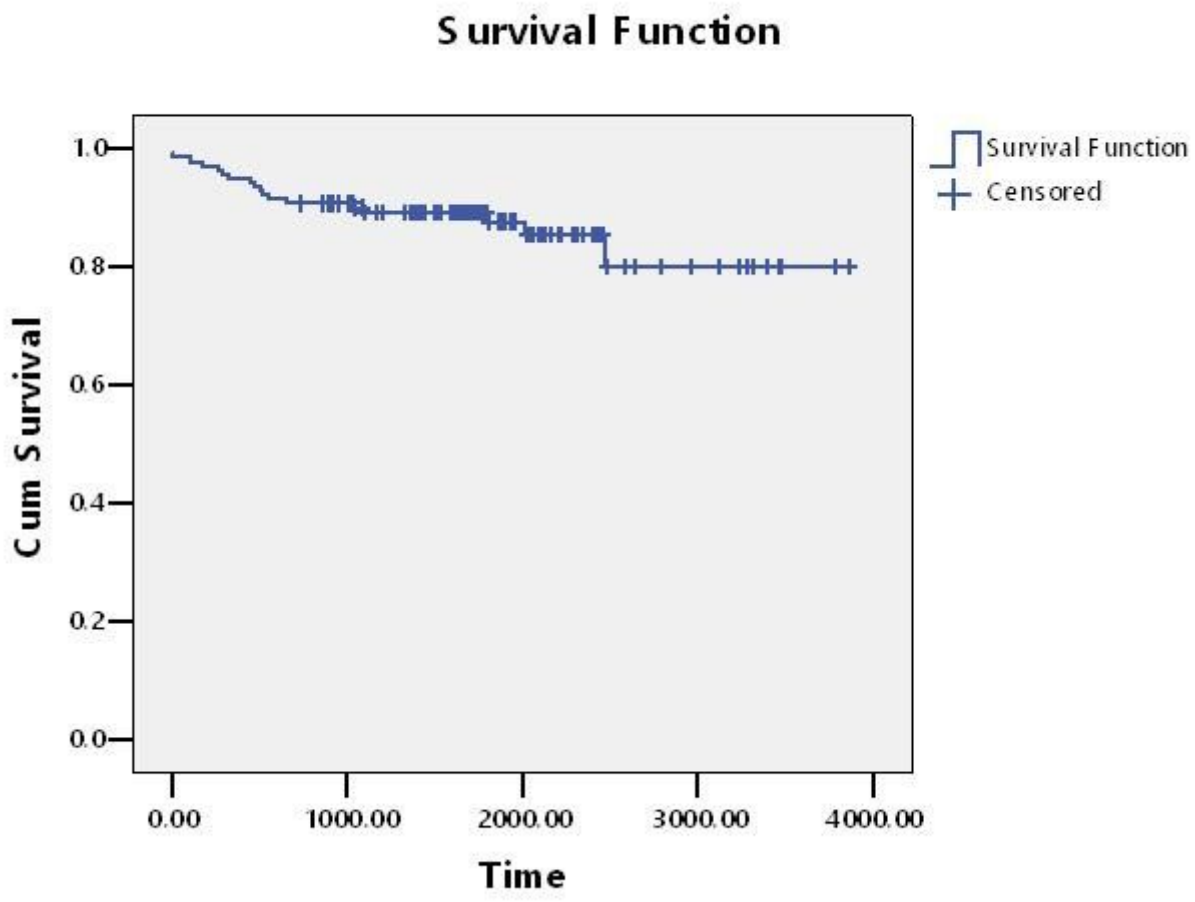

Figure 1

Survival curve of lung cancer patients

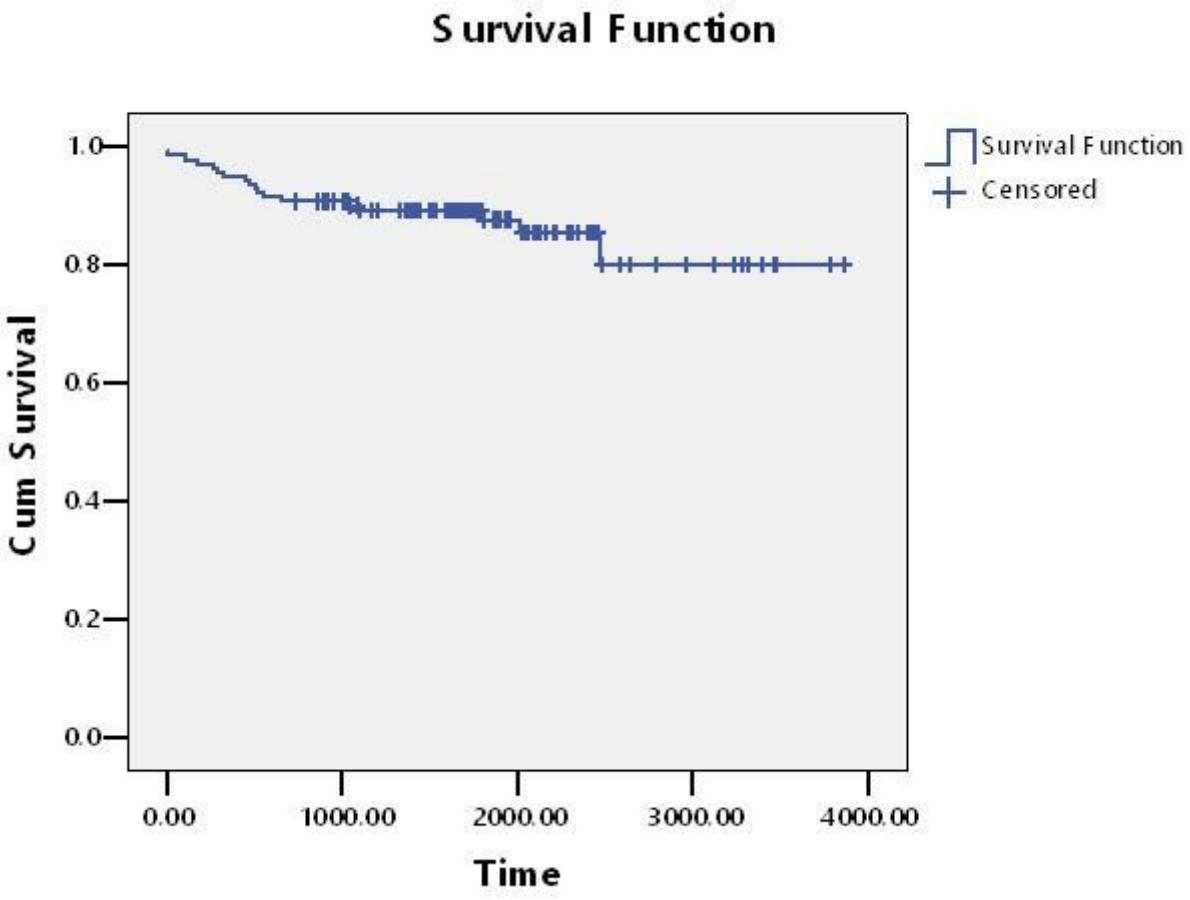

Figure 1

Survival curve of lung cancer patients