Screening for lung cancer using thin-slice low-dose computed tomography in a Chinese physical examination population: a population-based real-world study

Jiaxuan Wu  
Sichuan University

Ruicen Li  
Sichuan University

Huohuo Zhang  
Sichuan University

qian Zheng  
Sichuan University

Wenjuan Tao  
Sichuan University

Ming Yang  
National Clinical Research Center for Geriatrics (WCH), Sichuan University

Yuan Zhu  
Sichuan University

Guiyi Ji  
Sichuan University

Weimin Li  
weimin003@163.com

Sichuan University

Research Article

Keywords: Low-dose computed tomography (LDCT), Thin slice scan, Pulmonary nodule, Lung cancer, Screening, Early diagnosis

Posted Date: April 2nd, 2024

DOI: https://doi.org/10.21203/rs.3.rs-4181242/v1
License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.
Abstract

Objectives

Lung cancer is one of the most common malignant tumors threatening human life and health. At present, low-dose computed tomography (LDCT) screening for high-risk population to achieve early diagnosis and treatment of lung cancer has become the first choice recommended by many authoritative international medical organizations. Therefore, in order to further optimize the lung cancer screening method, we conducted a real-world study of LDCT lung cancer screening in a large sample of healthy physical examination population, comparing the differences in lung nodules and lung cancer detection between thin and thick-slice LDCT scanning.

Methods

A total of 29,296 subjects who underwent low-dose thick slice CT scan (5mm thickness) from January 2015 to December 2015 and 28,058 subjects underwent low-dose thin-slice CT scan (1mm thickness) from January 2018 to December 2018 in West China Hospital were included. The positive detection rate, detection rate of lung cancer, pathological stage of lung cancer, and mortality rate of lung cancer were analyzed and compared between the two groups.

Results

The positive rate of LDCT screening in thin slice was significantly higher than that in thick slice scan group (20.1% vs 14.4%, P < 0.001). In addition, the lung cancer detection rate in the thin-slice LDCT screening positive group was significantly higher than that in the thick slice scanning group (78.0% vs 52.9%, P < 0.001).

Conclusions

The screening positive rate of low-dose thin-slice CT scan is higher, and more early stage lung cancer (IA1 stage) can be detected in the screen-positive group.

1. INTRODUCTION

Lung cancer is known to be a major global public health challenge because of its high incidence, high treatment costs, high mortality rates, and low 5-year survival rates, hovering between 10% and 20% in most countries. (Allemani et al., 2018; Bray et al., 2018; Siegel et al., 2024). The death rate for lung cancer in China has soared about seven-fold in recent decades and projections suggest that the number of lung cancer-related deaths could reach or exceed 850,000 by 2030, an increase of 42.7 percent.(Fang et al., 2023; Wei et al., 2020; Zhao et al., 2010). An important reason for the poor prognosis of lung cancer is the
lack of specific symptoms and signs. Most patients are diagnosed at an advanced stage when the disease has already locally spread or metastasized (Chen et al., 2014; Nooreldeen and Bach, 2021). The 5-year relative survival rate for stage IA1 Non-small cell lung cancer (NSCLC) is 90%, but falls below 10% for stage IV NSCLC (Pirker, 2020). Therefore, recent efforts to improve patients’ outcomes have focused on screening. Previous studies have shown that chest X-ray (CXR) and sputum cytology can detect advanced-stage lung cancer, but the detection rate of early lung cancer is low, and can not effectively improve the survival rate of patients (Marcus et al., 2000). Several studies have evaluated the effectiveness of LDCT as a screening tool for high-risk individuals (Oudkerk et al., 2021; Wei et al., 2020). With the popularization of LDCT, a growing number of pulmonary nodules were detected. In the United States, lung nodules are found in 1.6 million patients each year, while in China there are more than 100 million cases (Mazzone et al., 2022). Studies in our country have shown similar results. In a UK randomized CT screening study for lung cancer, the detection rate of non-calcified lung nodules was 56% (Field et al., 2016). Previous studies have found that nodule recognition is slightly more common in women than men, and that the incidence increases dramatically with age, moreover, the detection rate of lung nodules is higher in patients with a history of smoking or passive smoking (Gould et al., 2015; Tang et al., 2024). However, recent studies have found that non-smokers with lung nodules also have a high incidence of lung cancer, so LDCT screening is very necessary (Kang et al., 2019). Pulmonary nodules are common manifestations of early lung cancer. NELSON study had shown that about 4% of non-calcified lung nodules have the potential to become malignant (Heuvelmans et al., 2017), of new pulmonary nodules, about 9% are malignant (Walter et al., 2018). In addition, for patients with potentially malignant tumors, pulmonary nodules may also be manifestations of tumor metastasis to the lungs. Therefore, the detection of pulmonary nodules and the judgment of benign and malignant appear to be very important.

If imaging features can accurately and satisfactorily predict the benign or malignant nature of nodules, unnecessary follow-up CT scans can be reduced. Studies have shown that for nodules smaller than 6-7mm in diameter, the sensitivity of conventional scanning is less than 70%, and many small pulmonary nodules can not be detected (Diederich et al., 1999; Wormanns et al., 2000). Thin slice CT improves spatial resolution, reduces volume effects, and enhances detection of small pulmonary nodules. Additionally, it offers clearer visualization of nodules’ internal, marginal, and subtle relationships with surrounding structures, aiding in precise depiction and crucial differential diagnosis of pulmonary nodules (Diederich et al., 1999; Wormanns et al., 2000). Currently, there is limited research on the use of thin-slice CT (1mm slice thickness) in the detection and differentiation of benign and malignant pulmonary nodules, especially the lack of large-scale studies on the application of thin-slice CT in lung cancer screening.

Therefore, in order to further comprehensively explore the role of thin-slice CT in lung cancer screening, this study intends to compare the detection of lung nodules and lung cancer by unified follow-up time between thin-slice and thick-slice chest LDCT scanning, so as to provide a theoretical basis for better optimization of lung cancer screening methods.

2. METHODS
2. Study participants

This study included individuals who underwent low-dose thick-slice chest CT scans (5mm slice thickness) at the Health Management Center of West China Hospital, Sichuan University, from January 2015 to December 2015, and low-dose thin-slice CT scans (1mm slice thickness) at the same center from January 2018 to December 2018, with complete follow-up information.

2.1.1 Inclusion criteria: Voluntarily signing informed consent forms, participants expressed their willingness to undergo chest LDCT scans to complete this screening; The clinical and imaging data of the subject were complete, and the CT images were clear without artifacts; Clear pulmonary nodules on CT images for easy observation; No symptoms or signs such as cough, sputum, hemoptysis, chest tightness and dyspnea appeared or worsened in the past 18 months from the date of enrollment; No chest imaging examination was performed within 18 months from the date of enrollment; The above five points must be met simultaneously.

2.1.2 Exclusion criteria: Participants with poor CT image quality (e.g. with severe metal artifacts, motion artifacts, etc.); Participants with underlying lung lesions such as diffuse metastases, large patchy consolidation, diffuse interstitial changes, and massive pleural effusion; Participants with previous history of lung cancer; Participants who had undergone total or partial lobectomy for various reasons; Participants with a previous history of pulmonary nodules of unknown nature, malignant pulmonary nodules, masses, hilar enlargement, and atelectasis; Participants who have experienced unexplained weight loss of more than 5kg within the past year. Participants who met one of the six criteria were excluded from the study.

2.2 Study Design

This was a cohort study based on a real-world physical examination population. This study was designed with reference to the NLST study (Moyer, 2014) and included subjects who underwent low-dose thin-slice CT scan in the Health Management Center of West China Hospital, Sichuan University. At the time of enrollment, the subject confirms whether to undergo screening with low-dose chest CT scan. Medical history information, low-dose thin-slice CT scan of the chest and other physical examinations were performed by the staff of the Health Management Center of our hospital for all study participants. The collection of medical history information includes current history, previous history, surgical history, infectious history, family history, smoking and drinking history, etc. Other medical examinations include blood tests, abdominal color ultrasound, electrocardiogram and urine tests. After the completion of baseline data collection, follow-up was conducted for all study participants. For the assessment of chest CT scans, two chest imaging specialists with over 5 years of experience each independently reviewed the LDCT images with 1mm and 5mm slice thicknesses using a blinded method. Subsequently, the diagnostic team was composed of more than 2 experienced experts from the Department of respiratory medicine and thoracic oncology in our hospital. The diagnostic team integrated the recommendations from the chest imaging specialists with other physical examination results for a comprehensive assessment.
The specific study design was as follows: First, we calculated the screening positivity rates of LDCT thin-slice and thick-slice scanning. Participants were then categorized into a screening positive group and a screening negative group according to the results. We then analyzed the pathological features and the detection rate of stage IA1 lung cancer in the two groups of participants under thin and thick slice scanning. Second, we further categorized the groups based on the time of lung cancer detection (baseline/follow-up), and examined the pathological characteristics of lung cancer, the detection of stage IA1 lung cancer, and the histological types across different tumor stages within the two groups. The flowchart of this study is shown in Figure 1.

2.3 Analysis and recording of images

2.3.1 CT Scanner and Scanning Parameters

All subjects underwent low-dose thin-slice chest scan using Somatom Emotion Duo (Somatom double-slice spiral CT). Before the examination begins, the participants were trained to take deep breaths and hold their breath. The client was placed in the supine position and scanned with breath holding at the end of deep inhalation. The scan ranged from the lung apex at the thoracic entrance level to the lower margin of the bilateral costophrenic Angle.

Scanning parameters: Tube voltage 120 kV, automatic milliampere second, pitch set 1.2cm, rotation time 0.5s, scanning matrix set 512 x 512, slice spacing 1 mm, using the standard algorithm for 1 mm and 5mm reconstruction, using the large field of view (FOV=L), according to the inspector's situation appropriate adjustment, The scanning time ranges from 4 to 6s. All chest CT images were uploaded and archived in the Picture archiving and communication systems (PACS).

2.3.2 CT image analysis

Chest CT images were analyzed independently by two radiologists with more than 5 years of experience in chest CT diagnosis, and the conclusion was reached by consensus. Lung window (WW1200Hu, WL-600Hu) was used to observe the tumor edge signs and changes in the surrounding lung field, mediastinal window (WW400Hu, WL40Hu) was used to observe the tumor edge signs and internal structure.

2.3.3 Judgment of image results

The diagnostic team including more than 2 experienced experts from the Department of respiratory medicine and thoracic oncology in our hospital integrated the recommendations from the chest imaging specialists with other physical examination results for a comprehensive assessment. Specific evaluation criteria and classification criteria based on nodule density are detailed in the supplementary materials.

2.3.4 Nodular analysis and recording

The slice numbers of nodules were analyzed and recorded in detail. The location, density, size, shape, internal features (such as cavities and calcification) and marginal signs (such as smooth edges, lobed,
burrs, vascular cluster signs and pleural depression) of pulmonary nodules were also recorded in detail, and clear follow-up advice was given. When multiple follow-up CT scans are performed, the changes of nodules should be compared, including whether the nodule density changes, whether the size changes, whether the volume increases, and whether new signs appear. At the same time, other pulmonary lesions (such as lymph node enlargement, pleural changes, pulmonary fibrosis, emphysema, etc.) were recorded, and extrapulmonary lesions (such as mediastinum and heart abnormalities) were detected within the scan range.

2.4 Evaluation and follow-up strategy of pulmonary nodules detected by LDCT

The diagnostic team including more than 2 experienced experts from the Department of respiratory medicine and thoracic oncology in our hospital. Further intervention and treatment plans were formulated according to the Chinese Guidelines for the Classification, Diagnosis and Treatment of Pulmonary Nodules (2016 edition)(Zhou et al., 2016). Pulmonary nodules are generally divided into two broad categories. Classification details are in the supplementary materials.

2.5 Lung cancer diagnostic criteria

2.5.1 TNM stage:

All lung cancer patients are staged based on the size of their tumor, lymph node involvement, and distant metastasis, according to the 8th edition of the Tumor-Node-Metastasis (TNM) staging system established by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) in 2017(Amin et al., 2017). Lung cancer is classified into stages I, II, III, and IV based on these criteria.

2.5.2 Histological classification:

The histological classification of lung cancer in this study was performed according to the 2015 World health organization (WHO) histological classification of lung cancer(Travis et al., 2015).

2.6 Quality control:

In order to ensure the quality of the entire screening experiment, strict quality control must be implemented at every stage of baseline screening and follow-up. The quality control process is listed in the supplementary materials.

2.7 Ethical conduct of research

2.7.1 Informed consent:

This study will ensure that participants receive adequate and adequate oral and written information about the nature, purpose, possible risks and benefits of the program. Participants were informed that
they could withdraw from the study at any time. No specific procedures or investigations regarding the study will be conducted until the patient signs and dates the informed consent form.

2.7.2 Participant withdrawal:

All participants may withdraw from the study at any time. However, researchers should do their best to complete the final evaluation and record their efforts. The results of these evaluations and observations, along with a description of the reasons for withdrawing the subject, must be documented in detail in the original data.

2.8 Loss of follow-up

Loss of follow-up refers to patients dropping out of the study for various reasons during the screening period. A high rate of loss of follow-up may overestimate the benefits of a screening program, so loss of follow-up should be controlled to the maximum extent possible throughout the study. In general, the loss of follow-up rate should be less than 20%. In order to reduce the loss of follow-up rate, the following conditions should be met as far as possible during the implementation of the program: First, before registration, the participants who were unwilling to follow up or had greater migration were excluded as far as possible; Second, a dedicated person is responsible for the follow-up of the same person; What’s more, we provided necessary and simple medical consultation services to the examinee and we obtained other contact information such as the phone number of the participant’s family and work unit, so as to avoid the situation of loss of visit due to the inability to contact the client directly.

2.9 Statistical analysis

In this study, Statistical Product and Service Solutions (SPSS) 22.0 was used for statistical analysis. For comparison between groups, t test or ANOVA was used for measurement data and Chi-Squared Test was used for classification data. \( P \leq 0.05 \) was considered statistically significant.

3. RESULTS

3.1 Baseline characteristics analysis of the health examination population undergoing LDCT lung cancer screening.

This study included a total of 29,296 subjects who underwent low-dose thick slice CT screening for lung cancer at the Health Management Center of West China Hospital of Sichuan University from January 2015 to December 2015. A total of 28,058 patients who underwent chest low-dose thin slice CT screening for lung cancer at the Health Management Center of West China Hospital of Sichuan University from January 2018 to December 2018 were also included. Demographic characteristics, smoking status, family history of lung cancer, and chronic lung disease of all subjects are shown in Table 1. The average age of participants in the thick-slice LDCT scan group at baseline was 46.15 \pm 13.10 \text{ years old}, with 30.3\%
of participants being under the age of 40. The average age of participants in the thin-slice LDCT scan group at baseline was 44.45 ± 12.60 years old, with 36.6% of participants being under the age of 40.

Table 1
Baseline characteristics of lung cancer screening cohort in healthy physical examination population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Thin slice (%)</th>
<th>Thick slice (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>28,058 (100.0)</td>
<td>29,296 (100.0)</td>
<td>-</td>
</tr>
<tr>
<td>Age(years) 𝑎</td>
<td>44.45 ± 12.60</td>
<td>46.15 ± 13.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;40</td>
<td>10,275 (36.6)</td>
<td>8872 (30.3)</td>
<td></td>
</tr>
<tr>
<td>40~</td>
<td>4196 (15.0)</td>
<td>5004 (17.1)</td>
<td></td>
</tr>
<tr>
<td>45~</td>
<td>4401 (15.7)</td>
<td>4771 (16.3)</td>
<td></td>
</tr>
<tr>
<td>50~</td>
<td>3684 (13.1)</td>
<td>3863 (13.2)</td>
<td></td>
</tr>
<tr>
<td>55~</td>
<td>1993 (7.1)</td>
<td>2295 (7.8)</td>
<td></td>
</tr>
<tr>
<td>60~</td>
<td>1627 (5.8)</td>
<td>1845 (6.3)</td>
<td></td>
</tr>
<tr>
<td>65~</td>
<td>887 (3.2)</td>
<td>965 (3.3)</td>
<td></td>
</tr>
<tr>
<td>70~</td>
<td>506 (1.8)</td>
<td>680 (2.3)</td>
<td></td>
</tr>
<tr>
<td>75~</td>
<td>283 (1.0)</td>
<td>602 (2.1)</td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>206 (0.7)</td>
<td>399 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.818</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>8171 (29.1)</td>
<td>8506 (29.0)</td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>19,887 (70.9)</td>
<td>20,790 (71.0)</td>
<td></td>
</tr>
<tr>
<td>Family history of lung cancer</td>
<td>0.721</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>764 (2.7)</td>
<td>812 (2.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27,294 (97.3)</td>
<td>28,484 (97.2)</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease 𝑏</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>932 (3.3)</td>
<td>676 (2.3)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27,126 (96.7)</td>
<td>28,620 (97.7)</td>
<td></td>
</tr>
</tbody>
</table>

a Mean ± standard deviation.

b Chronic lung diseases include a history of chronic obstructive pulmonary disease, diffuse pulmonary fibrosis, and tuberculosis.

3.2 Screening results:
3.2.1 Results of chest LDCT screening in healthy physical examination group

A total of 29,296 participants participated in thick-slice baseline LDCT screening, 4212 (14.4%, 4212/29,296) had at least one positive finding, and a total of 121 lung cancer cases were screened, with a lung cancer detection rate of 0.4% and a false positive rate of 97.1% in the healthy population. Among them, 48 cases of stage IA1 lung cancer were screened, accounting for 0.16% of the total number of lung cancers. A total of 28,058 participants participated in thin-slice LDCT baseline screening, and 5638 (20.1%, 5638/28,058) had at least one positive finding, which was higher than that in the thick-slice scan group, with a statistically significant difference (20.1% vs 14.4%, P < 0.001). A total of 132 cases of lung cancer were screened, the detection rate of lung cancer in healthy people was 0.5%, and the false positive rate was 97.7%. Lung cancer detection rates were higher in the thin-slice scan group than in the thick-slice scan group (0.5% vs 0.4%). Among them, 65 cases of stage IA1 lung cancer were detected, accounting for 0.23% of the total number of lung cancer patients, which was higher than that of the thick scanning group (0.23% vs 0.16%, P = 0.068). Detailed results are shown in Table 2 and Fig. 2.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>thin-slice (%)</th>
<th>thick-slice (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening number</td>
<td>28,058 (100.0)</td>
<td>29,296 (100.0)</td>
<td>-</td>
</tr>
<tr>
<td>Screening positive</td>
<td>5638 (20.1)</td>
<td>4212 (14.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of screened cases of lung cancer</td>
<td>132 (0.5)</td>
<td>121 (0.4)</td>
<td>0.302</td>
</tr>
<tr>
<td>Number of screened cases of stage IA lung cancer</td>
<td>65 (0.23)</td>
<td>48 (0.16)</td>
<td>0.068</td>
</tr>
<tr>
<td>Screening negative</td>
<td>22,420 (79.9)</td>
<td>25,084 (85.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

3.2.2 The pathological characteristics of lung cancer in different screening result groups of healthy individuals undergoing chest LDCT for physical examination.

Among 121 cases of lung cancer detected by LDCT thick-slice screening, 64 cases (52.9%) were detected in the positive group, of which 25 cases (40.3%) were stage IA1 lung cancer. 57 (47.1%) cases of lung cancer were detected in the screening negative group, including 23 (46.0%) cases of IA1 stage lung cancer. Of the 132 cases of lung cancer detected by LDCT scanning, 103 cases (78.0%) were detected in the positive group, of which 54 cases (52.9%) were stage IA1 lung cancer. In the negative group, 29 cases (22.0%) of lung cancer were detected, including 11 cases (45.8%) of stage IA1 lung cancer. The lung cancer detection rate in the positive LDCT scan group was significantly higher than that in the thick LDCT scan group, and the difference was statistically significant (78.0% vs 52.9%, P < 0.001). Detailed results are shown in Supplementary table 1 and Table 3.
### Table 3
Pathological characteristics of lung cancer in different screening result groups of healthy individuals undergoing chest LDCT for physical examination.

<table>
<thead>
<tr>
<th>Stage and histological type</th>
<th>Thin-slice</th>
<th>Thick-slice</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screening positive</td>
<td>Screening negative</td>
</tr>
<tr>
<td></td>
<td>(N = 103)</td>
<td>(N = 29)</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA1</td>
<td>54/102 (52.9)</td>
<td>11/24 (45.8)</td>
</tr>
<tr>
<td>IA2</td>
<td>31/102 (30.4)</td>
<td>10/24 (41.7)</td>
</tr>
<tr>
<td>IA3</td>
<td>11/102 (10.8)</td>
<td>1/24 (4.2)</td>
</tr>
<tr>
<td>IB</td>
<td>4/102 (3.9)</td>
<td>2/24 (8.3)</td>
</tr>
<tr>
<td>II</td>
<td>1/102 (1.0)</td>
<td>0/24 (0.0)</td>
</tr>
<tr>
<td>III</td>
<td>1/102 (1.0)</td>
<td>0/24 (0.0)</td>
</tr>
<tr>
<td>IV</td>
<td>0/102 (0.0)</td>
<td>0/24 (0.0)</td>
</tr>
<tr>
<td><strong>Histological type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>89/103 (86.4)</td>
<td>23/29 (79.3)</td>
</tr>
<tr>
<td>Squamous carcinoma</td>
<td>1/103 (1.0)</td>
<td>2/29 (6.9)</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>2/103 (1.9)</td>
<td>0/29 (0.0)</td>
</tr>
<tr>
<td>Other types</td>
<td>11/103 (10.7)</td>
<td>4/29 (13.8)</td>
</tr>
</tbody>
</table>

#### 3.2.3 Detection of stage IA1 lung cancer in different screening result groups of healthy individuals undergoing chest LDCT for physical examination.

Table 4 shows that among 48 cases of stage IA1 lung cancer detected by LDCT thick-slice screening, 25 cases (52.1%) were detected in the positive screening group and 23 cases (47.9%) were detected in the negative group. Of 65 patients with stage IA1 lung cancer detected by LDCT thin-slice screening, 54 cases
(83.1%) were detected in the positive group. In the negative group, 11 cases (16.9%) were detected. The detection rate of stage IA1 lung cancer in the thin-slice LDCT screening positive group was significantly higher than that in the thick-slice scan group (83.1% vs 52.1%, P < 0.001). Further analysis showed that there were significant differences in the detection rates of stage IA3 lung cancer, adenocarcinoma, small cell carcinoma and other types of cancer between thin-slice and thick-slice CT (P < 0.05 for all).

Table 4
Detection of stage IA1 lung cancer in different screening result groups of healthy individuals undergoing chest LDCT for physical examination.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>thin-slice (%)</th>
<th>thick-slice (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of stage IA1 lung cancers detected</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Screening positive</td>
<td>54 (83.1)</td>
<td>25 (52.1)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>11 (16.9)</td>
<td>23 (47.9)</td>
<td></td>
</tr>
<tr>
<td>Number of stage IA2 lung cancers detected</td>
<td></td>
<td></td>
<td>0.488</td>
</tr>
<tr>
<td>Screening positive</td>
<td>31 (75.6)</td>
<td>31 (68.9)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>10 (24.3)</td>
<td>14 (31.1)</td>
<td></td>
</tr>
<tr>
<td>Number of stage IA3 lung cancers detected</td>
<td></td>
<td></td>
<td>0.019</td>
</tr>
<tr>
<td>Screening positive</td>
<td>11 (91.7)</td>
<td>4 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>1 (8.3)</td>
<td>7 (63.3)</td>
<td></td>
</tr>
<tr>
<td>Number of adenocarcinoma detected</td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Screening positive</td>
<td>89 (79.5)</td>
<td>48 (58.5)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>23 (20.5)</td>
<td>34 (41.5)</td>
<td></td>
</tr>
<tr>
<td>Number of Squamous carcinoma detected</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Screening positive</td>
<td>1 (33.3)</td>
<td>2 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>2 (66.7)</td>
<td>6 (75.0)</td>
<td></td>
</tr>
<tr>
<td>Number of Small cell carcinoma detected</td>
<td></td>
<td></td>
<td>0.386</td>
</tr>
<tr>
<td>Screening positive</td>
<td>2 (100)</td>
<td>1 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>0</td>
<td>3 (75.0)</td>
<td></td>
</tr>
<tr>
<td>Number of other types detected</td>
<td></td>
<td></td>
<td>0.114</td>
</tr>
<tr>
<td>Screening positive</td>
<td>11 (73.3)</td>
<td>13 (48.1)</td>
<td></td>
</tr>
<tr>
<td>Screening negative</td>
<td>4 (26.7)</td>
<td>14 (51.9)</td>
<td></td>
</tr>
</tbody>
</table>
3.2.4 Pathological characteristics of lung cancer detected by chest LDCT during baseline screening and follow-up in healthy physical examination population

Of 121 cases of lung cancer detected by LDCT thick-slice screening, 65 cases (53.7%) were detected by baseline screening, of which 24 cases (39.3%) were stage IA1 lung cancer. During the follow-up, 56 cases of lung cancer were detected, accounting for 46.3% of the total, of which 24 cases of stage IA1 lung cancer were detected, accounting for 47.1%. Of the 132 cases of lung cancer detected by LDCT thin-slice screening, 87 cases (65.9%) were detected by baseline screening, including 39 cases (45.3%) of stage IA1 lung cancer. During the follow-up period, 45 cases (34.1%) of lung cancer were detected, including 26 cases (65.0%) of stage IA1 lung cancer. The baseline lung cancer detection rate in the thin-slice scan group was significantly higher than that in the thick-slice scan group, and the difference was statistically significant (65.9% vs 53.7%, P = 0.048). Details are provided in Supplementary table 2 and Supplementary table 3.

3.2.5 Detection of stage IA1 lung cancer in the baseline screening and follow-up of chest LDCT in healthy physical examination population

Supplementary table 4 shows that 48 cases of stage IA1 lung cancer were detected by LDCT thick-slice screening of the chest, and 24 cases were detected by baseline screening, accounting for 50.0%. During the follow-up period, 24 cases of lung cancer were detected, accounting for 50.0%. Of 65 patients with stage IA1 lung cancer detected by LDCT thin-slice screening, 39 cases (60.0%) were detected by baseline screening. During the follow-up, 26 cases of lung cancer were detected, accounting for 40.0%. The baseline detection rate of stage IA1 lung cancer in the thin-slice scan group was significantly higher than that in the thick-slice scan group, but the difference was not statistically significant (60.0% vs 50.0%, P = 0.290).

3.2.6 The histological types of lung cancer detected by chest LDCT screening in different tumor stages of the healthy physical examination population

The vast majority of adenocarcinoma and squamous cell carcinoma can be detected at stage I on both thick and thin slice LDCT scans. Among 121 cases of lung cancer detected by LDCT thick-slice screening, 82 cases (67.8%) were adenocarcinoma, of which 74 cases were stage IA. There were 8 cases of squamous cell carcinoma (6.6%), of which 4 cases were stage IA and 1 case was stage IB. Among 132 cases of lung cancer detected by LDCT scanning, 112 cases (84.8%) were adenocarcinoma, of which 102 cases (93.6%) were stage IA, and 6 cases (5.5%) were stage IB. There were 3 cases of squamous cell carcinoma (2.3%). See Supplementary table 5 for details.

3.3 Follow-up results of the screening positive group

All the physical examination population with positive findings in each screening were followed up immediately. The thick-slice LDCT group was followed up from January 1st, 2015 to October 1st, 2018, the shortest follow-up time was 0.1 year, the longest follow-up time was 2.9 years, and the average follow-up time was 1.0 year. One patient died of stage IIA lung adenocarcinoma, and the mortality rate
was 0.8%. Thin-slice LDCT scanning group follow-up started on January 1st, 2018, and ended on October 1st, 2021, with the shortest follow-up time being 0.1 years and the longest follow-up time being 2.9 years. The average follow-up time was 0.9 years, with zero death recorded.

4. DISCUSSION

In this study, the subjects who had undergone low-dose spiral computed tomography screening for lung cancer in the Health Management Center of West China Hospital of Sichuan University were selected as the study participants. By comparing the incidence of lung cancer, early disease rate and pathological classification of lung cancer in thin slice and thick slice CT scan, the screening effect of LDCT with different slices was evaluated.

It is well known that LDCT plays an important role in improving lung nodules, early lung cancer detection rates and reducing lung cancer mortality (Becker et al., 2020). Using LDCT to screen high-risk groups of lung cancer and realize early diagnosis and treatment of lung cancer has become the first choice recommended by many authoritative international medical organizations (Chinese Thoracic Society, 2023; Jaklitsch et al., 2012; Naidich et al., 2013; Wender et al., 2013; Wood et al., 2015).

However, most of the lung cancer screening projects in China are currently small sample and retrospective studies, large sample, especially prospective cohort studies are urgently needed to explore lung cancer screening guidelines suitable for China's national conditions. Studies have shown that many small nodules cannot be detected by routine scanning (Diederich et al., 1999; Wormanns et al., 2000). With the widespread application of CT as a routine screening method for lung cancer (Barton et al., 2018; McWilliams et al., 2013), long-term and multiple CT follow-up is often required to determine the benign and malignant nodules of small nodules or nodules that are difficult to identify. This not only led to increased radiation measurement, psychological burden and complication risk for patients (Brenner, 2004; Kummer et al., 2020), but also led to a rapid increase in the number of chest CT images and a sharp increase in the workload faced by radiologists. Coupled with subjective fatigue, different diagnostic levels and other factors, lung cancer screening had a certain rate of missed diagnosis, misdiagnosis and regional differences (Berlin, 2007; Godoy et al., 2022; Kim et al., 2020; Ko et al., 2022). Therefore, in order to further optimize the screening program for lung nodules and lung cancer in the Chinese population, we conducted a real-world screening program for a large sample in the Health Examination Center of West China Hospital of Sichuan University to provide better guidance for lung cancer screening. Our findings suggest that thin-slice chest LDCT screening in people over 40 years of age can detect more stage IA1 lung cancer.

Studies have shown that thin-slice spiral chest CT images increase the spatial resolution, reduce the volume effect, can obtain more slices, and is more conducive to the detection of small pulmonary nodules. Currently, sub-millimeter resolution has been achieved, and it has high sensitivity to the detection of small nodules and hidden nodules. Thin-slice CT scan can also improve the accuracy of the measurement of nodule size (Goo et al., 2005; Lancaster et al., 2022; Winer-Muram et al., 2003). In
addition, thin-slice CT can find more subtle lung structure and pathological changes, which can provide more basis for the differentiation of benign and malignant lesions (Diederich et al., 1999; Li et al., 2023; Wormanns et al., 2000). This study found that the screening positive rate of thin-slice LDCT was significantly higher than that of the thick-slice scanning group, and the detection rate of lung cancer in the thin-slice scanning group was also higher than that in the thick-slice scanning group, and more early stage (IA1 stage) lung cancer could be detected. Fischbach et al. also found that thin-slice scanning had a higher detection rate of nodules less than 5 mm in diameter than thick slice scanning, which is similar to our findings (Fischbach et al., 2003). There also exist some limitations in this study. First of all, the retrospective study in this study may have some selective bias, so further prospective studies are needed. Second, the short follow-up time of our study resulted in fewer observed outcome events (including death from any cause, death from lung cancer, loss to follow-up, etc.). Follow-up time should be extended in the future to specify reasonable screening strategies for lung cancer.

5. CONCLUSION

This study systematically and comprehensively studied the optimization and application of low-dose spiral CT screening for lung cancer for the first time, and clearly pointed out that thin-slice LDCT scanning is more beneficial to lung cancer screening. In addition, we used very large sample sizes, and the research results can fully and accurately reflect the real clinical situation. This can provide a reliable reference and theoretical basis for the further development of optimized lung cancer screening methods and guidelines.

Abbreviations

AJCC, American Joint Committee on Cancer
CXR, chest X-ray
COPD, chronic obstructive pulmonary disease
DICOM, Digital Imaging and Communications in Medicine
LDCT, low-dose spiral CT (LDCT)
PACS, Picture archiving and communication systems
SPSS, Statistical Product and Service Solutions
TNM, Tumor-Node-Metastasis
UICC, Union for International Cancer Control
WHO, World health organization
Declarations

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

HUMAN ETHICS APPROVAL DECLARATION

The West China Hospital Research Ethics Committee and ethics committees approved the study (2019 Trial No. 195), which did not interfere with clinical management. Informed consent (oral or written) was obtained from study participants according to local requirements, except for cases in which a local committee granted a waiver or exemption. We adhered to the Declaration of Helsinki and Good Clinical Practice guidelines.

Author Contribution


ACKNOWLEDGEMENTS

We extremely appreciate the all members’ contribution to this study. This study was supported by National Natural Science Foundation of China (Nos. 92159302 to W Li), the Science and Technology Project of Sichuan (2022ZDZX0018 to W Li), 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University (ZYGD22009 to W Li), Natural Science Foundation of Sichuan Province (grant 2023NSFSC1458), Sichuan Province Science and Technology Support Program (2022YFS0130), the Science and Technology Project of Sichuan (2020YFS0573), Post-Doctor Research Project, West China Hospital, Sichuan University (2019HXBH085), Investigator-Initiated Clinical Trial, West China Hospital, Sichuan University (HXCR20001). These agencies did not play any part in study design; in collection, analysis or interpretation of data; in writing the report; or in submitting the article for publication.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.
References


Figures

Flowchart of study participants. The participants who underwent LDCT in the health examination center of West China Hospital of Sichuan University were included.
Figure 2
Cumulative number of lung cancers. The number of lung cancer patients showed an increasing trend over time.

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- SUPPLEMENTALMATERIALS.docx