Lung cancer screening study from a smoking population in Kunming

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Abstract. – OBJECTIVE: Yunnan, China, is a central tobacco-producing region with a large smoking population and an increasing incidence of lung cancer in recent years. This study aimed to understand the incidence of lung cancer and the characteristics of lung nodules on low-dose computed tomography (LDCT) scans of the chest in a long-term smoking population in Kunming.

PATIENTS AND METHODS: Long-term smokers in Kunming who were not at risk of evident lung disease symptoms were recruited through recommendation and publicity by the Kunming University of Science and Technology.

RESULTS: Among 375 cases eligible for inclusion, 14 cases of lung cancer were detected with a detection rate of 3.73% (95% CI: 2.55%-4.27%), including one case of squamous carcinoma, one case of small cell lung cancer, seven cases of adenocarcinoma of the lung and five cases of early-stage lung cancer (35.71%). In the group of <6 mm solid nodules and <5 mm non-solid nodules, no lung cancer was detected in 201 cases; lung cancer was detected in 14 cases in 61 cases, and there was a statistical difference between the two groups (p<0.05).

CONCLUSIONS: The lung cancer detection rate in long-term smokers was high, with the type predominantly adenocarcinoma and a high incidence of lung nodules, and increased when solid nodules ≥6 mm or non-solid nodules ≥ 5 mm were present. It is recommended that screening for lung cancer by LDCT of the chest be introduced in the male smoking population who meet the risk factors and that screening for lung cancer in women should be redefined as a high-risk factor.

Key Words: Colostrum, Sodium bicarbonate, Oral care, Neonatal ventilator-associated pneumonia.

Introduction

The incidence of lung cancer is rising annually in East Asia. The World Trade Organization’s annual cancer report reveals that lung cancer is the most prevalent malignancy in China, with the highest incidence and mortality rate. Whittaker et al¹ have shown that low-dose chest computed tomography scans have a detection rate of up to 80% for lung cancers less than 1 cm in diameter. Timely screening can reduce lung cancer mortality by 20%. As an economically developed city, Kunming has approximately 10% or more of its smoking population with varying degrees of lung disease, making it important to screen smokers in the Kunming area for lung disease². By understanding the status of lung nodules and lung cancer in smokers in Kunming, we can also provide a reference for the development of lung cancer screening in China.
Patients and Methods

Study Object

Heavy smokers without significant lung disease symptoms in Kunming were recruited through recommendations from Kunming University of Science and Technology and Publicity from July 2019 to January 2022. Those who met the inclusion criteria were screened by questionnaire and included in the study group for chest LDCT scans.

Inclusion criteria: (1) 55-70 years of age; (2) the patient’s smoking age (in years) multiplied by the number of packs the patient smokes per day gives a result of 30 or more; (3) smokers who smoked more than 30 packs per year and met one of the following criteria: (1) long-term work in a confined environment with high levels of dust particles for more than five years; (2) history of tuberculosis. Two of (1)+(2), or any one of (1)+(3) (1)-(3), were satisfied and included in the study group.

Screening Process

Postgraduate students from Kunming University of Science and Technology (KMUST) are trained to recommend that long-term smokers visit the KMUST Health Screening Centre to complete the Lung Cancer Risk Factor Screening Form. Upon completing the form, a specialist doctor at the Health Screening Centre will explain the purpose of the screening, its significance, and the benefits and possible risks of taking part. The doctor at the screening center will also answer any questions that the subject does not understand.

The subject understands the procedure and its contents and agrees to voluntarily sign an informed consent form. The doctor will also test the patient for risk factors for lung cancer, such as the patient’s smoking history and the patient’s family history of cancer and examine the patient’s physical signs resulting from smoking.

LDCT Method

They were following Chinese Health Care Commission standards. Tube voltage used 100 KVP-140 KVP; tube current <60 mAs. Total radiation exposure dose ≤5 mSv, scan parameters: 130 kVP; 50 mAs; pitch 0.975; reconstruction layer thickness 1.15 mm constant (reconstruction interval 0.1 mm), scan layer thickness 1.15 mm. scan range: from the lung tip to the angle of the rib diaphragm (including all lungs), patient. The scan is completed in one breath-hold at the end of inspiration, with a scan sampling time of ≤8 s. The CT scan detector is 64 rows. Image storage: transfer of 1.15 mm layer thickness continuous image reconstruction images into PACS.

Image observation

The images are observed by an experienced attending radiologist or above at the CT workstation using a standard lung window. The lung window has a window width of 1,500 HU and a window position of 700 HU.

Nodule measurement

The nodule’s longest diameter and wide diameter are measured with an electronic measuring tape through the most significant section of the nodule. Note that the longest diameter is the largest diameter of the most significant section; the wide diameter is the largest diameter perpendicular to the longest diameter. Solid nodules include partially solid nodules, and the diameter measurement includes the non-solid portion. All ≥ 2 mm solid and non-solid nodules are described in the report. Solid nodules ≥ 6 mm and non-solid nodules ≥ 5 mm were considered suspicious for lung cancer.

Follow-Up Consultations

For those with suspected malignant nodules in the lungs on first chest LDCT, positron emission tomography (PET), chest CT review, bronchoscopic lung biopsy, ultrasound endoscopy-guided transbronchial needle aspiration biopsy (EBUS-TBNA), or thoracoscopic pneumonectomy will be arranged according to the risk of lung cancer and LDCT imaging features after discussion by the lung cancer screening team to clarify the diagnosis and perform.

The doctors will follow the subjects at the Kunming University of science and Technology Health Screening Centre for two years after the LDCT examination. The immediate follow-up will include the subject’s smoking status and the presence of other respiratory symptoms or diseases, and the timing of the subsequent LDCT examination. For those diagnosed with lung cancer at the first LDCT, the immediate follow-up was the subject’s treatment plan and survival.

Statistical Analysis

The results of this study were statistically analyzed using SPSS statistics 23 software (IBM, Armonk, NY, USA). Measurements were expressed as mean±standard deviation (Mean±SD). The lung cancer size and the cancer detection rate
in the multiple nodule group were compared with that in the single nodule group using the Chi-square test. Pearson's bivariate correlation analysis was used to test the correlation between the results of this study, and if a final $p < 0.05$ was obtained, then the difference between the two could be considered statistically significant.

## Results

### General Information and High-Risk Factors for Lung Cancer

The mean age was $(62.47 \pm 6.94)$ years in 375 cases who were eligible and completed LDCT of the chest. The sex ratio, age distribution, smoking signs, family history of tumors, education and work history, and patient history of the disease are shown in Table I. 94 of the patients quit smoking on their initiative. Seventy-two had a family history of tumors, including 28 fathers, 21 mothers, 14 siblings, 8 with more than two members in the family, and one other case.

### Pulmonary Nodule Characteristics

Pulmonary nodules were detected in 279 cases and not in 96 cases, with a detection rate of 74.4% (95% CI: 67.8%-78.0%). The size and distribution characteristics of the nodules are shown in Table II. As observed in Table II, the detection rate of $< 6$ mm multiple solid nodules was the highest, followed by $< 6$ mm single solid nodules. There were 44 suspected lung cancer nodules of $\geq 6$ mm solid and $\geq 5$ mm non-solid nodules, with a detection rate of 15.1% (95% CI:11.0%-19.20%) as shown in Table III. The lung cancer detection rate was higher in the suspected lung cancer nodule group than in the $< 6$ mm solid nodule and $< 5$ mm non-solid nodule groups ($\chi^2=29.8, p < 0.05$), as shown in Table IV. The nodule size was correlated with the detection rate of lung cancer, $r=0.51, p<0.01$. Seventy-four cases of single nodules and no lung cancer were detected; 205 cases of multiple nodules and 14 cases of lung cancer were detected, with no statistical difference between the two groups ($\chi^2=1.68, p > 0.05$). Further correlation analysis revealed no correlation between the number of nodules and the detection rate of lung cancer, $r=0.14, p > 0.05$.

### Diagnosis and Treatment of Patients with Lung Cancer

Fourteen lung cancer cases were detected, pathologically confirmed, with a detection rate of 3.73% (95% CI: 2.55%-4.27%). Early-stage lung cancer (TNM stage I) was detected in 5 cases, accounting for 35.71% of lung cancer cases. Of the ten lung cancer patients, 8 had solid nodules, all $> 8$ mm in diameter, 7 of which were combined with $< 6$ mm solid nodules. 2 hairy glass nodules, both

<table>
<thead>
<tr>
<th>Items</th>
<th>Characteristic</th>
<th>Data [n (%)]</th>
<th>LC [n]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>329 (87.74)</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>46 (12.26)</td>
<td>0</td>
</tr>
<tr>
<td>Age groups (yr)</td>
<td>55-59</td>
<td>99 (26.68)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>60-64</td>
<td>121 (32.61)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>65-69</td>
<td>104 (28.03)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>70-75</td>
<td>51 (12.66)</td>
<td>2</td>
</tr>
<tr>
<td>Education level</td>
<td>No</td>
<td>28 (7.54)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Primary school</td>
<td>112 (29.11)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Journal high school</td>
<td>121 (32.61)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>High school</td>
<td>91 (24.52)</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>University or higher</td>
<td>23 (6.1)</td>
<td>1</td>
</tr>
<tr>
<td>Smoking</td>
<td>PACK-years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$\geq 30$</td>
<td>324 (85.99)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>20-29</td>
<td>52 (14.01)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15-19</td>
<td>8 (2.15)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>20-29</td>
<td>47 (12.66)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$\geq 30$</td>
<td>330 (85.17)</td>
<td>12</td>
</tr>
<tr>
<td>Family cancer history</td>
<td>Yes</td>
<td>47 (12.13)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>328 (87.87)</td>
<td>12</td>
</tr>
<tr>
<td>lung disease history</td>
<td>Yes</td>
<td>137 (35.85)</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>238 (64.15)</td>
<td>6</td>
</tr>
</tbody>
</table>

* $\chi^2$ test; ** Student’s $t$-test; *** Fisher’s exact test.
>10 mm in diameter, were also combined with <6 mm solid nodules. In one patient with adenosquamous carcinoma, LDCT revealed five GGO >10 mm in diameter, multiple solid nodules <6 mm and non-solid nodules <5 mm, and bronchial stenosis in the left upper lung. The pathological diagnosis was adenosquamous carcinoma, and post-operative radiotherapy was administered. After total excision of the left lung, the pathology showed adenosquamous carcinoma, small intrapulmonary nodules with adenocarcinoma in situ, and one lymph node with metastasis of squamous carcinoma, which was counted as a solid nodule group.

**Discussion**

In 2021, there were 20051 new lung cancer cases in Kunming, 17,427 cases in men aged 55 years or older, with a crude incidence rate of 41.48 per 100,000. A total of 14 cases of lung cancer were detected in this study, all of which were male, with a detection rate of 3.44%. This detection rate is higher than the Chinese average lung cancer detection rate of 1.1%-2.4% published by the Chinese Health Planning Commission. Possible reasons for this analysis are related to the fact that the smoking history of the subjects included in this study was reliable. In order to avoid the inclusion of ineligible individuals, smoking-related questions were set, and smoking-related signs were examined so that subjects could be identified. The first diagnosis was made by a physician at the Kunming University of Science and Technology Physical Examination Centre, who found that 89.8% and 94.4% of the subjects had smoking stains on the skin of their hands and in their mouths, respectively. There was a positive correlation between hand skin stains and oral tobacco stains and the patient’s smoking age.

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**Table II.** Patient data on lung nodules.

<table>
<thead>
<tr>
<th>Item</th>
<th>≤6 mm</th>
<th>6 mm-8 mm</th>
<th>&lt;8 mm</th>
<th>&lt;5 mm</th>
<th>5 mm-10 mm</th>
<th>&gt;10 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>131</td>
<td>347</td>
<td>338</td>
<td>342</td>
<td>342</td>
<td>342</td>
</tr>
<tr>
<td>Single</td>
<td>67</td>
<td>25</td>
<td>35</td>
<td>22</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>≥2</td>
<td>177</td>
<td>3</td>
<td>2</td>
<td>11</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>375</td>
<td>375</td>
<td>375</td>
<td>375</td>
<td>375</td>
<td>375</td>
</tr>
</tbody>
</table>

**Table III.** Statistics on the distribution of patients’ nodules.

<table>
<thead>
<tr>
<th>Item</th>
<th>Single [n]</th>
<th>≥2 [n]</th>
<th>&lt;5 mm</th>
<th>5mm-10mm</th>
<th>&gt;10mm</th>
<th>GGN [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 mm SN</td>
<td>69</td>
<td>137</td>
<td>16</td>
<td>4</td>
<td>3</td>
<td>229 (5.6%)</td>
</tr>
<tr>
<td>6 mm-8 mm SN</td>
<td>5</td>
<td>12</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>21 (5.6%)</td>
</tr>
<tr>
<td>&gt;8 mm SN</td>
<td>3</td>
<td>13</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>21 (5.6%)</td>
</tr>
<tr>
<td>&lt;5 mm GGN</td>
<td>2</td>
<td>3</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>5 (1.3%)</td>
</tr>
<tr>
<td>5 mm-10 mm GGN</td>
<td>3</td>
<td>0</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>3 (0.8%)</td>
</tr>
<tr>
<td>&gt;10 mm GGN</td>
<td>0</td>
<td>0</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>0</td>
</tr>
<tr>
<td>Total [n (%)]</td>
<td>83 (22.1)</td>
<td>165 (44.4%)</td>
<td>22 (5.8%)</td>
<td>5 (1.3%)</td>
<td>5 (1.3%)</td>
<td>279 (74.4%)</td>
</tr>
</tbody>
</table>

**Table IV.** Statistics on nodule size and lung cancer detection rate.

<table>
<thead>
<tr>
<th>Groups</th>
<th>LC[n]</th>
<th>No-LC[n]</th>
<th>Total</th>
<th>Detection rate [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>A group (&lt;6 mm SN+&lt;5 mm GGN)</td>
<td>0</td>
<td>207</td>
<td>207</td>
<td>0</td>
</tr>
<tr>
<td>B group (≥6 mm SN+≥5 mm GGN)</td>
<td>10</td>
<td>74</td>
<td>84</td>
<td>11.91</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>281</td>
<td>291</td>
<td>3.44</td>
</tr>
</tbody>
</table>
However, in similar studies\(^8,^9\), the inclusion of patients with signs of smoking is often not judged, which often results in the inclusion of people who have smoked for a short period or rarely, resulting in a lower detection rate of lung cancer in the group. The high lung cancer detection rate in this study may also be explained because most of the subjects in this group live in the second ring road, which has the highest population density and car ownership in Kunming, where patients live in a small space. The air is heavily polluted by car exhaust\(^10\). Domestic epidemiological surveys have found a strong correlation between air pollution indices and lung cancer incidence\(^11\). The early-stage lung cancer detection rate in this study was 35.71%, which was lower than the baseline level at home and abroad\(^12-14\). It was related to the low literacy level, and poor awareness of lung cancer prevention among the patients included in this study. Lung cancer patients in this group were detected between 55 and 70 years. If this group of people with high-risk factors for lung cancer were to undergo annual LDCT after the age of 55 years, as recommended by the World Health Organization, early diagnosis and treatment of lung cancer would be possible, and the cure rate of lung cancer would be improved\(^15,^16\). Therefore, increasing health education and participation in lung cancer screening among smokers is essential\(^17-19\).

There are studies that found that the incidence of lung adenocarcinoma is high in Asian women. In this study, all seven lung adenocarcinoma patients were male\(^20,^21\), higher than smoking-related squamous and small cell lung cancers\(^22-25\). This is associated with the high use of filtered cigarettes by tobacco consumers in Kunming. Filtered cigarettes alter the composition of tobacco smoke, reducing the amount of nicotine, tar, and carbon monoxide inhaled by patients. However, because smokers often increase the perception of smoking by blocking the air holes in the filter and increasing the amount of smoke inhaled, filtered cigarettes do not reduce the amount of nicotine and tar ingested by smokers. Instead, it makes it easier for small particles of smoke to reach the peripheral airways of patients. This results in a high incidence of adenocarcinoma. In addition, the combustion agents in tobacco increase the patient’s intake of nitric oxide, which in turn promotes the formation of nitrosamines, and nitrosamines-4-(methylated nitrosamines)-1-(3-pyridyl)-1-butanone are strongly associated with lung adenocarcinoma\(^26-28\).

Lung adenocarcinoma production in Asian women is associated with EGFR gene variants in the epidermal growth factor receptor, accounting for more than 50% of cases. However, there was only one case of EGFR gene variation in lung adenocarcinoma patients, accounting for 20%, which was lower than in women\(^29-32\). It is presumed to be related to men’s different variants of the adenocarcinoma gene locus.

A trend study of lung cancer in men diagnosed and treated from 2012 to 2020 by the Chinese Academy of Sciences found that lung adenocarcinoma in smokers increased from 41.61% to 61.49%, increasing at a level of 5.02% per year\(^33-35\). Therefore, the pathogenesis of lung adenocarcinoma in men who smoke deserves attention and research. The detection rate of lung nodules varies widely between national and international reports, with the UKLS project in the UK in the United Kingdom, with 1,994 participants and a detection rate of lung nodules of 50.9%. In Shanghai in a community of 2,972 people aged 60-75 years who underwent LDCT, the nodule detection rate in the smoking group was 33.7%\(^36-40\). The high detection rate of 74.4% for pulmonary nodules in this study was related to the above factors, such as smoking and dust, but also to the fact that the scan layer in this study was 1.15 mm thick and the reconstruction the layer was 1.15 mm thick, which could detect tiny nodules of 2 mm and above. A study by Nanda\(^41\), concluded that <6 mm solid nodules and <5 mm non-solid nodules have a low incidence of lung cancer and a lung cancer risk of <1%, and such nodules are referred to as false positive nodules.

The risk of lung cancer increases as the nodules increase in size. The present study had similar results to this. The lung cancer detection rate was significantly higher in the suspicious nodule group than in the false-positive nodule group\(^42-44\). This suggests that nodule size is associated with lung cancer risk. It is also consistent with the Greer’s results\(^45\).

**Conclusions**

Lung nodules in this study were predominantly multiple solid nodules, accounting for 74.6%, which was higher compared to the 49.5% found in the previous study. There was a trend towards an increased lung cancer detection rate in the multiple lung nodule groups, but there was no statistical difference. This study demonstrates no significant correlation between the number of nodules and the incidence of lung cancer. Currently, 97%
of lung cancers in patients with multiple nodules in Asia occur in the most critical nodes.

All 14 lung cancer patients in our group had multiple nodes, and postoperative pathology confirmed that all lung cancers were in the most critical nodes. Recent studies have shown that in high-risk groups, even if only false-positive nodes occur, the incidence of lung cancer over the subsequent 4-10 years is significantly higher than in low-risk groups and should be of particular concern when new nodules appear in the same lung segment. Therefore, in this high-risk group, LDCT should be performed once a year after the age of 55, regardless of the presence or absence of nodules and regardless of their size, in order to detect lung cancer at an early stage. However, LDCT, with its radiological risks, still requires continuous research to develop more sensitive and specific screening techniques to control the risks and improve the detection rate of lung cancer.

The women in this group accounted for 12.26% of the 46 cases, and no lung cancer was found in any of them. It is related to the low number of female smokers in Kunming. To the Kunming Tobacco Control Assessment Report, the smoking rate for women aged 45 and above in 2020 is only 4.4%; this compares with 1084 new cases of lung cancer in women in Kunming in 2021, and 728 new cases over the age of 50, which is only 5.22% of lung cancer in men (13,929 cases over the age of 50 in men). Therefore, inclusion criteria based on smoking can result in some female lung cancer patients being missed. There is a need to redefine risk factors for lung cancer in women, such as the family history of lung cancer, history of secondhand smoke exposure, and history of dust exposure in the work environment.

In summary, multiple small solid nodules dominated LDCT findings in the smoking population. Lung cancer types were dominated by adenocarcinoma, with an increased incidence of lung cancer when solid nodules ≥ 6 mm or non-solid nodules ≥ 5 mm were present. It is recommended that screening for lung cancer by chest LDCT be introduced in the male smoking population who meet the risk factors and that screening for lung cancer in women should redefine the risk factors.

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Data Availability
The data used to support the findings of this study are included within the article.

Availability of Data and Material
All data are included in the article and are available from the corresponding author.

Informed Consent
Informed consent was obtained from all patients included in this study prior to submission of data.

Ethics Approval
This study was designed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Macau University of Science and Technology School of Pharmacy. Approval number: SP2021062128.

Authors’ Contributions
Conceptualization: Cao Qiang, Zhang Qi and Li Xiaochen, Methodology: Cao Qiang and Qiang Yi, Validation: Zhou Kexuan and Li Yuxiao, Formal analysis: Yu Ying, He Zixu and Xiang Zhibiao, Investigation: Guan Haoran, Zhen Jingcheng, Lin Rongtian and Liao Yujie, Resources: Cao Qiang and Zhang Qi, Data Curation: He Zixu and Liao Yujie, Writing - Original Draft: Cao Qiang, Writing - Review & Editing: Zhang Qi and Qiang Yi, Supervision: Li Xiaochen and Qiang Yi, Project administration: Qiang Yi and Zhang Qi.

Conflicts of Interest
The authors declare that there is no conflict of interest regarding the publication of this paper.
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