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Lung cancer screening study from a smoking population in Kunming

Q. CAO[1], Q. ZHANG[1,2], K.-X. ZHOU[1,3], Y.-X. LI[1,4], Y. YU[1,2], Z.-X. HE[1,5], Z.-B. XIANG[1,6], H.-R. GUAN[1], J.-C. ZHEN[1], R.-T. LIN[1], Y.-J. LIAO[1], Y. QIANG[7], X.-C. LI[8]

[1]School of Pharmacy, Macau University of Science and Technology, Macau, China
[2]Human Resource Management, School of Business Administration, Taishan University, Taian, China
[3]Hainan University Undergraduate Division, Hainan University, Hainan, China
[4]Faculty of Economics, Shandong University of Finance and Economics, Shandong, China
[5]School of Computer Science, The University of New South Wales, Wales, Australia
[6]Graduate School, The Second Xiangya Hospital of Central South University, Hunan, China
[7]Key Laboratory of Geohazard Forecast and Geoecological Restoration in Plateau Mountainous Area Ministry of Natural Resources of the People's Republic of China, Kunming University of Science and Technology, Kunming, China
[8]Department of Surgery, The Third Affiliated Hospital of Shandong First Medical University, Jinan, China

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 al[1] 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 disease[2]. 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.

Corresponding Authors: Li Xiaochen, MD; e-mail: lixiaochen202205@163.com
Qiang Yi, MD; e-mail: 20060136@kust.edu.cn

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±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 ≥ 6 mm solid and ≥ 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 (χ^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 (χ^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 I. Basic patient statistics.

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

*χ^2 test; **Student's *t*-test; ***Fisher's exact test.

Table II. Patient data on lung nodules.

	Solid lung nodules (n)			Ground glass nodules (n)		
Item	**≤6 mm**	**6 mm-8 mm**	**<8 mm**	**<5 mm**	**5 mm-10 mm**	**>10 mm**
No.	131	347	338	342	342	342
Single	67	25	35	22	31	29
≥2	177	3	2	11	2	4
Total	375	375	375	375	375	375

Table III. Statistics on the distribution of patients' nodules.

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

Table IV. SStatistics on nodule size and lung cancer detection rate.

Groups	**LC(n)**	**No-LC(n)**	**Total**	**Detection rate (%)**
A group (<6 mm SN+<5 mm GGN)	0	207	207	0
B group (≥6 mm SN+≥5 mm GGN)	10	74	84	11.91
Total	10	281	291	3.44

> 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 postoperative 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[3]. 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%[4]. 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[5]. 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[6]. 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[7]. There was a positive correlation between hand skin stains and oral tobacco stains and the patient's smoking age.

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 protection 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 molecules 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[46-49], 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 years 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 $\geq$ 6 mm or non-solid nodules $\geq$ 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.

Conflicts of Interest

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

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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.

ORCID ID
Cao Qiang, https://orcid.org/0000-0001-8160-8883
Zhang Qi, https://orcid.org/0000-0003-4078-6346
Zhou Kexuan, https://orcid.org/0000-0002-9005-3047
Li Yuxiao, https://orcid.org/0000-0001-9024-4970
Yu Ying, https://orcid.org/0000-0002-4051-1580
He Zixu, https://orcid.org/0000-0002-1742-3937
Xiang Zhibiao, https://orcid.org/0000-0002-4783-1536
Guan Haoran, https://orcid.org/0000-0001-5141-8392
Zhen Jingcheng, https://orcid.org/0000-0003-2174-9961
Lin Rongtian, https://orcid.org/0000-0002-5974-6371
Liao Yujie, https://orcid.org/0000-0002-7689-7075
Qiang Yi, https://orcid.org/0000-0002-9557-2268
Li Xiaochen, https://orcid.org/0000-0002-5281-0633

References

1) Whittaker J, Knight S, Barber P, Colligan D. Targeted lung cancer screening selects individuals at high risk of cardiovascular disease. Lung Cancer 2018; 124: 148-153.
2) Arenberg D, Greaves M, Howells J. Update on screening for lung cancer. Transl Lung Cancer Res 2019; 8: S77-S87.
3) Balata H, Duerden R. Targeted lung cancer screening selects individuals at high risk of cardiovascular disease. Lung Cancer 2018; 124: 148-153.
4) Baldwin D, Brain K, Quaife S. Participation in lung cancer screening. Transl Lung Cancer Res 2021; 10: 1091-1098.
5) Bhandari S, Tripathi P, Pham D. Performance of community-based lung cancer screening program in a Histoplasma endemic region. Lung Cancer 2019; 136: 102-104.
6) Brownlee A. Update on Lung Cancer Screening. Semin Respir Crit Care Med 2020; 41: 447-452.
7) Byrne M, Zhao W. Healthcare Use after Screening for Lung Cancer. Cancer 2015; 116: 4793-4799.
8] Field J. Lung cancer screening: the way forward. Br J Cancer 2008; 99: 557-562.
9) Ganti A. Lung cancer screening. Oncologist 2006; 11: 481-487.
10) Gohagan J, Marcus P, Pinsky P. Baseline findings of a randomized feasibility trial of lung cancer screening with spiral CT scan vs chest radiograph - The Lung Screening Study of the National Cancer Institute. Chest 2004; 126: 114-121.
11) Guichet P. Preliminary Results of Lung Cancer Screening in a Socioeconomically Disadvantaged Population. AJR Am J Roentgenol 2018; 210: 489-496.
12) Gutierrez A. Lung Cancer Screening. Radiology 2013; 30: 114-120.
13) Hasson R, Joseph D, Kayla A. Lung Cancer Screening in a Surgical Lung Cancer Population: Analysis of a Rural Quaternary Academic Experience. J Surg Res 2021; 262: 14-20.
14) Henschke C. Screening for lung cancer. J Thoracic Imaging 2000; 15: 21-27.
15) Heuvelmans M. Appropriate screening intervals in low-dose CT lung cancer screening. Transl Lung Cancer Res 2018; 7: 281-287.
16) Houston T. Screening for Lung Cancer. Med Clin North America 2020; 104: 1037.
17) Jazieh A. Saudi lung cancer prevention and screening guidelines. Ann Thorac Med 2018; 13: 198-204.
18) Kazerooni E. Lung cancer screening. European Radiol 2005; 15: D48-D51.
19) Kerpel F, Tammemagi M. Screening for Lung Cancer in Individuals Who Never Smoked: An International Association for the Study of Lung Cancer Early Detection and Screening Committee. J Thorac Oncol 2022; 17: 56-66.
20) Qiang C. Mechanisms of p2x7 receptor involvement in pain regulation: a literature review. Acta Med 2022; 38: 1187-1194.
21) Kvale P. Interval lung cancers not detected on screening chest X-rays: How are they different? Lung Cancer 2014; 86: 41-46.
22) Lake M, Shusted C, Juon H. Black patients referred to a lung cancer screening program experience lower rates of screening and longer time to follow-up. BMC Cancer 2020; 20: 122-132
23) Lee J. Feasibility of implementing a national lung cancer screening program: Interim results from the Korean Lung Cancer Screening Project (K-LUCAS). Transl Lung Cancer Res 2021;10: 723.
24) Maldonado S. Can autoantibody tests enhance lung cancer screening?-an evaluation of EarlyCDT (R)-Lung in context of the German Lung Cancer Screening Intervention Trial (LUSI). Transl Lung Cancer Res 2021; 10: 288-298.
25) Manse R. Lung cancer screening: screening frequency and lung cancer risk. Transl Lung Cancer Res 2016; 5: S1227-S1232.
26) Marcus M. Lung cancer screening: identifying the high risk cohort. J Thoraci Dis 2015; 7: S156-S162.
27) Martini K, Chassagnon G. Ongoing challenges in implementation of lung cancer screening. Transl Lung Cancer Res 2021; 10: 2347-2355.
28) Mazzone P. Proposed Quality Metrics for Lung Cancer Screening Programs A National Lung Cancer Roundtable Project. Chest 2021; 160: 368-378.
29) Midthun D. Update on screening for lung cancer. Critical Care Med 2008; 29: 233-240.
30) Minamimoto R, Senda M. Detection of Lung Cancer by FDG-PET Cancer Screening Program: A Nationwide Japanese Survey. Anticancer Res 2014; 34: 183-189.
31) Moldovanu D. Lung cancer screening and smoking cessation efforts. Transl Lung Cancer Res 2021; 10: 1099-1109.
32) Okamoto N. Cost-effectiveness of lung cancer screening in Japan. Cancer 2000; 89: 2489-2493.
33) Park S, Bhandari S. Factors related with colorectal and stomach cancer screening practice among

diseasefree lung cancer survivors in Korea. BMC Cancer 2017; 17: 321-333

34) Pastorino U. Lung cancer screening. British J Cancer 2010; 102: 1681-1686.

35) Pham D, Bhandari S. Lung Cancer Screening Registry Reveals Low-dose CT Screening Remains Heavily Underutilized. Clin Lung Cancer 2020; 21: E206-E211.

36) Prosch H. Screening for lung cancer. Curr Opin Oncol 2014; 26: 131-137.

37) Ravenel J. Screening for lung cancer. AJR Am J Roentgenol 2008; 190: 755-761.

38) Ravenel J, Joan W. Coronary artery calcification in lung cancer screening. Transl Lung Cancer Res 2018; 7: 361-367.

39) Roberts Hl. Screening High-Risk Populations for Lung Cancer Guideline Recommendations. J Thoracic Oncology 2013; 8: 1232-1237.

40) Sandler K. Women screened for breast cancer are dying from lung cancer: An opportunity to improve lung cancer screening in a mammography population. J Med Screening 2021; 28: 488-493.

41) Nanda H. Screening for lung cancer. Semin Oncol 2017; 44: 74-82.

42) Steliga M, P. Yang. Integration of smoking cessation and lung cancer screening. Transl Lung Cancer Res 2019; 8: S88-S94.

43) Tanner N. Screening Adherence in the Veterans Administration Lung Cancer Screening Demonstration Project. Chest 2020; 158: 1742-1752.

44) Tanoue L. Lung cancer screening. Curr Opin Pulm Med 2016; 22: 327-335.

45) Thalanayar P, Altintas N, Weissfeld J. Indolent, Potentially Inconsequential Lung Cancers in the Pittsburgh Lung Screening Study. Ann Am Thorac Soc 2015; 12: 1193-1196.

46) Van AL. Implementation of lung cancer screening: what are the main issues? Transl Lung Cancer Res 2021; 10: 1050-1063.

47) Wei M. Performance of lung cancer screening with low-dose CT in Gejiu, Yunnan: A population-based, screening cohort study. Thorac Cancer 2020; 11: 1224-1232.

48) Wilson DO. Doubling Times and CT Screen-Detected Lung Cancers in the Pittsburgh Lung Screening Study. Am J Respir Crit Care Med 2012; 185: 85-89.

49) Wilson DO, Weissfeld J. A simple model for predicting lung cancer occurrence in a lung cancer screening program: The Pittsburgh Predictor. Lung Cancer 2015; 89: 31-37.