Early Lung Cancer Detection Using the Self-Evaluation Scoring Questionnaire and Chest Digital Radiography: A 3-Year Follow-up Study in China

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Published online: 13 March 2012
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Abstract The standard definition of high-risk individuals for lung cancer was not uniform and the value of chest digital radiography (DR) in lung cancer screening was still unproven. The aim of this study was to assess whether the original questionnaire named as “Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer” combined with DR examinations could detect early stage of lung cancer effectively. The Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer had been designed in

previous studies. Subjects with scores over 116 points were regarded as high-risk individuals and underwent the current DR scans at least once a year from 2007 to 2009. Noncalcified nodules with a diameter over 30 mm, along with enlarged pulmonary hilus and atelectasis, were considered to be positive and subjected to further special examinations. Efficacy of the scoring questionnaire combined with DR scans was estimated by 3-year results. Among 1,537 subjects, 13, 11, and 7 were diagnosed with lung cancer in the first, second,

Funding This study was supported by the “The Eleventh Five-Year” Development Planning for Major Projects (Lung Cancer Prevention), Chengdu, China (grant #07YTYB961020) funded by the Chengdu Municipal Bureau of Science and Technology, Chengdu Municipal Bureau of Public Health and Chengdu Municipal Center for Disease Control and Prevention, China.

[The practice is registered as a clinical study at <http://www.chictr.org>, as number ChiCTR-DOC-10000975]

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and third year, respectively, indicating the detection rate of 2.02 % (31/1,537). In addition, 77.42 % (24/31) of the patients were in stage I and 51.61 % (16/31) were adenocarcinomas. For the 31 cases, 28 were defined as detected cancers, while the other three were interval ones, only accounting for 0.20 % (3/1,504) of individuals with negative judgments. The protocol of Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer combined with DR scans is a cost-effective and safe approach to detect early stage of lung cancer.

Keywords Lung neoplasm · Pulmonary nodule · Smoking · Screening

Introduction

Lung cancer is one of the most common malignant diseases in the world causing more than one million deaths every year [1]. The American Cancer Society estimated that in the USA, there would be approximately 222,000 new cases of lung cancer in 2010, and 157,000 patients die from the disease, making up 28 % of all cancer deaths [2]. Because of its hidden onset, most patients receive a diagnosis at an advanced stage with a poor prognosis [3]. It has been reported that the 5-year survival rate for non-small cell lung cancer patients in stage I was about 60 %, but it decreased to 2 % for stage IV [4]. As for small cell lung cancer, the 5-year survival rate for limited and extensive disease was 15 and 3 %, respectively [5]. It might be readily seen that the fundamental premise to make a progress in the prognosis of lung cancer is to carry out effective population screenings and improve early detection rate.

Some researchers advised high-risk individuals to take regular examinations, but the standard definition of high-risk individuals was not uniform; high-risk individuals are generally referred to heavy smokers or people with harmful occupational exposures [1, 6, 7]. However, many other factors, such as passive smoking, genetic susceptibility, and so on, also contributed to the development of lung cancer [6, 8]. There has not been an acknowledged assessment method for the risks of lung cancer.

With respect to screening methods, efficacy of chest X-ray (CXR) and computed tomography (CT) has been investigated in some large-scale studies. Since the 1970s, several randomized controlled trials, including the well-known Mayo Lung Project, has revealed CXR alone or combined with sputum cytology did not reduce the mortality of lung cancer [9, 10]. A recent meta-analysis even concluded a slightly higher mortality associated with frequent CXR examinations [11]. Subsequent experiences with CT, however, were more promising.

The high detection rate of early stage of lung cancer confirmed its significant effectiveness [12].

Unfortunately, the value of digital radiography (DR), more sensitive than CXR, less radioactive and much cheaper than CT, has never been evaluated. Thus, our current study was designed to assess the value of DR for early detection of lung cancer in high-risk human beings over a period of 3 years. High-risk individuals were identified by our recently developed Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer. We provide the evidence that the combined use of the scoring questionnaire and DR scans are an affordable, safe, and effective approach to detect early stage of lung cancer.

Methods

Participants

The Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer had been designed in separate studies and the threshold to confirm risk subjects was 116 points [14]. Individuals taking annual routine physical examinations in the Physical Examination Center of West China Hospital, Sichuan University, China, were recruited to participate in the current screening, but only high-risk volunteers identified by the questionnaire were satisfied. Furthermore, eligible candidates should not have undergone thoracic radiologic examinations at least 1 year before the enrollment and should be willing to take further examinations when necessary. Subjects with symptoms of lung cancer, such as thoracodynia, hemoptysis, and dyspnea, or too weak to accept invasive techniques, were also excluded. In addition, volunteers suffering from a previous pneumonectomy or with a history of malignant tumors in any part of the body were not qualified either. This study was approved by the Ethics Committee of Sichuan University, and each participant was given a written informed consent. It has been registered as a clinical study at <http://www.chictr.org> with the number ChiCTR-DOC-10000975.

Chest DR Scans

DR examinations consisted of a single anteroposterior view and were obtained with the Japanese Shimadzu digital X-ray photography system and PACS image processing system with 81 kV peak, 400 mA, and 0.25 ms of the scan time and at a tube-to-receiver distance of 150–180 cm. Images were taken at an inspiration phase. Two board-certified chest radiologists evaluated the scans independently. In case of a disagreement, a third senior radiologist was consulted to reach a consensus.

The site, size, and radiological features of each lesion were documented in detail.

Definition

Noncalcified Nodules

A nodule was a solid lesion and classified as noncalcified if it did not meet the previously published criteria for a benign lesion [15]. The diameter was the maximum length for the solid component.

Enlargement of Pulmonary Hilus

In normal circumstances, pulmonary hilus locates between the second and fifth intercostals space in the medial fields of thorax and the left side is often higher than the right by 1–2 cm. A diagnosis of enlargement of pulmonary hilus was made when it was beyond the above fields.

Atelectasis

Atelectasis is referred to as the shrinking of whole or part of the lung because of the reduction of gas content.

Screening Algorithm

All eligible participants received the baseline screening by DR in 2007. For noncalcified nodules, positive results meant those with a maximum diameter of over 30 mm, while negative results referred to nodules less than 5 mm. Of the remaining ones between 5 and 30 mm, at least one of the radiological features, such as spiculation, lobulation, vessel convergence, ground glass opacity, and cavity, were the evidence to make a positive determination; otherwise it is undetermined, which needed further follow-up examinations. The interval time was 6 or 3 months for those with diameters ranging from 5 to 15 and 16 to 30 mm, respectively. In the repeated examinations, diameter increase by at least 30 % or emerging malignant radiological features mentioned above indicated a positive result, or else negative.

Pulmonary hilus enlargement and atelectasis were always considered to be positive unless the radiologists declare it otherwise. If somebody possessed more than one lesion, the final result was defined as positive as long as there was one positive judgment, and they were advised to turn to a chest physician for further special workup. In the event that a diagnosis of lung cancer was made, the participant was treated for the disease and left the trial; otherwise, regular second-round screening, 12 months later after the baseline screening, was scheduled also for those who tested negative.

Principles for evaluating a new lesion in the second-round screening were inconsistent with the first round. For the existing nodules, diameter increase by 30 % or emerging malignant

radiological features indicated positive results, and further increase of the ever-detected pulmonary hilus enlargement and atelectasis suggested a positive result as well. The third round of screening was carried out after the second round.

Screen-detected cancers meant those diagnosed within a window extending 12 months from a positive result. Lung cancer identified in 1 year after a negative screening test was denoted as interval or nondetected cancer.

Statistical Analysis

Data analysis was performed with SPSS software for Windows version 13.0. Normally distributed data were summarized as means±standard deviation (SD). Diagnostic sensitivity, specificity, false-negative rate, false-positive rate, negative predicted value, positive predicted value, and their 95 % confidence intervals were introduced to access the effectiveness of the screening strategies. All the calculating formulae can be found in Table 1.

Results

The Scoring Questionnaire and Demographics Characteristics of the Participants

The scoring questionnaire is shown in Table 2. During 2007, 8,093 volunteers agreed to take part in the project, but only 1,537 (18.99 %) were eligible. The mean (±SD) age was 52.80±12.66 years old, and the characteristics of the studying cohort are summarized in Table 3.

Table 1 Definition and calculating formulae for the evaluating terms

		Final diagnosis of lung cancer (n)		Sum
		Positive	Negative	
Screening results (n)	Positive	a	b	a + b
	Negative	c	d	c + d
Sum		a + c	b + d	a + b + c + d

$$\text{Sensitivity} = a/(a+c) \times 100 \%$$

$$\text{Specificity} = d/(b+d) \times 100 \%$$

$$\text{False-negative rate} = c/(a+c) \times 100 \%$$

$$\text{False-positive rate} = b/(b+d) \times 100 \%$$

$$\text{Negative predicted value} = [(1-P) \times \text{Sp}] / [(1-P) \times \text{Sp} + P \times (1-\text{Se})] \times 100 \%$$

$$\text{Positive predicted value} = P \times \text{Se} / [P \times \text{Se} + (1-P) \times (1-\text{Sp})] \times 100 \%$$

As a general rule, predicted value means the probability of a participant with a positive or negative result to suffer from a particular disease or not, and the traditional formulae are as follows: negative predicted value = $d/(c+d)$, positive predicted value = $a/(a+b)$. But for lung cancer, its reported prevalence rate is about 0.035 % [14], which has a marked impact on the final result as well. Therefore in our opinion, the formulae applied in this practice probably were more accurate. P, Sp, and Se stand for the prevalence rate of lung cancer (0.035 %) [14], specificity, and sensitivity, respectively

Table 2 Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer

Self-evaluation Scoring Questionnaire

for High-risk Individuals of Lung Cancer ID: _____

Name: _____ Add: _____

Tel: _____ Date: _____

Risk factors	Classification	Risk assignments	Scores	Risk factors	Classification	Risk assignments	Scores
Sex	Male	7		Organ transplantation	Yes	36	
	Female	0		Connective tissue diseases	Yes	44	
Age (years)	<40	0		Chronic pulmonary diseases	Tuberculosis	14	
	40–60	19			Chronic bronchitis	15	
	>60	42			Emphysema	37	
Average daily cigarette consumption (cigarettes per day)	1–10	15		Exposure to cooking fumes (plates per day ^a years) ^c	≤150	0	
	11–20	44			≥151	36	
	21–40	54		Years for working as a miner	1–10	21	
	>40	72			10–25	25	
Smoking duration (years)	<20	5		Exposure to asbestos (years)	>25	36	
	20–40	43			<20	5	
	>40	70			20–29	21	
Initial Smoking Age (years)	≤15	100		Depression ^d	≥30	47	
	>15	32			Usually	37	
Female passive smoking (passive smoking cigarettes per day ^a years) ^b	1–199	0		Family history of lung cancer ^e	Yes	13	
	200–299	25		Family history of non-lung cancer tumors ^e	Yes	3	
	≥300	53		Total			

^b The female passive smoking (cigarettes per day × years) = average daily cigarette consumption of active smokers (cigarettes per day)/24 h × contact time between the active and passive smokers every day (hours) × contact years between the active and passive smokers (years)

^a Years = The average daily cooking plates × cooking duration (years)

^c Plates per day

^d Depression was defined as the feeling of unhappy sustained for over 3 days every week and existed for more than 1 year

^e Family history of malignant tumors means malignant tumor patient in first-degree relatives

Table 3 Demographic characteristics of the participants taking DR scans in 2007

Characteristics	Males (<i>n</i> =1,297, 84.39 %)	Females (<i>n</i> =240, 15.61 %)	Total (<i>n</i> =1,537)
Age, year			
20–39	158 (10.28 %) ^a	18 (1.17 %)	176 (11.45 %)
40–59	781 (50.81 %)	146 (9.50 %)	927 (60.31 %)
60–79	331 (21.54 %)	72 (4.68 %)	403 (26.22 %)
80–90	27 (1.76 %)	4 (0.26 %)	31 (2.02 %)
Scores			
116–129	144 (9.37 %)	13 (0.85 %)	157 (10.21 %)
130–144	60 (3.90 %)	108 (7.03 %)	168 (10.93 %)
145–159	645 (41.96 %)	44 (2.86 %)	689 (44.83 %)
160–249	416 (27.07 %)	75 (4.88 %)	491 (31.95 %)
250–325	32 (2.08 %)	0 (0.00 %)	32 (2.08 %)
Smoking status			
Current smokers	1,137 (73.98 %)	209 (13.60 %)	1,346 (87.58 %)
Former smokers	43 (2.80 %)	5 (0.33 %)	48 (3.12 %)
Never smoking	117 (7.61 %)	26 (1.69 %)	143 (9.30 %)
Family history of malignant tumors ^b			
Lung cancer	23 (1.50 %)	5 (0.33 %)	28 (1.82 %)
Other tumors	58 (3.77 %)	9 (0.59 %)	67 (4.36 %)
Negative	1,216 (79.12 %)	226 (14.70 %)	1,442 (93.82 %)

^aPercentage to the total 1,537 subjects

^bFamily history of malignant tumors in first-degree relatives

Results in Year 1

In the baseline screening, 230 subjects had 494 noncalcified pulmonary nodules by DR scans (Tables 4 and 5). Calcified lesions of benign appearance were detected in another 205 individuals. Of the undetermined 107 nodules between 5 and 30 mm, 14 displayed malignant signs. Following repeated examinations 3 or 6 months later revealed four persons with distinct growing-up or emerging malignant indications. On the part of other lesions, there were five pulmonary hilus enlargements, two of them with positive nodules as well, but no atelectasis was found.

Above all, 34 positive results were detected in the first year, promoting CT, contrast-enhanced CT, positron emission tomography/CT scans, even fiberoptic bronchoscopy and percutaneous transthoracic needle biopsy to make a definite diagnosis. Lung cancer was ultimately diagnosed in 11 of the participants, including two cases with pulmonary hilus enlargements. According to the latest Seventh Edition of the TNM Classification for Lung Cancer [16], 10 patients (90.91 %) were in

stage I, comparing with one (9.09 %) in a status of liver metastasis. Figure 1 showed a patient with a 15-mm noncalcified nodule in the baseline DR scan, and the following surgery confirmed a diagnosis of adenocarcinoma.

There were another two intervals or nondetected cancers, of which the period elapsed from initial negative screening results to the final diagnosis of lung cancer varying from 4 to 6 months. No abnormal lesion was found in one patient, but he developed pleural dissemination with hydrothorax 6 months later, and fiberoptic bronchoscopy confirmed an adenocarcinoma.

Results in Year 2

Except for the 13 cases of lung cancer and 31 people lost from the cohort, 1,493 participants underwent the second-year

Table 4 Noncalcified nodules detected by DR scans in the baseline

Diameters of the nodules (mm)	Subjects (<i>n</i>)
<5	110
5–15	64
16–30	43
>30	13
Total	230

Table 5 Subjects with different numbers of noncalcified nodules detected by DR scans in the baseline

Number of noncalcified nodules for each participant (<i>n</i>)	Subjects (<i>n</i>)	Total number of noncalcified nodules (<i>n</i>)
1	118	118
2	53	106
3	21	63
4	17	68
5	8	40
≥ 6	13	99
Total	230	494

Fig. 1 A patient diagnosed with lung cancer in 2007

screening. Altogether, 553 nodules were detected in 291 persons, of whom 84 were new cases. There were 1,369 subjects that revealed negative results and 28 were positive. For the rest of the patients with uncertain results, repeated scans were implemented to make further positive decisions in 15 subjects. Including the three cases of ever-detected pulmonary hilus enlargements and another three detected atelectasis, 46 participants were judged as positive in the second-year screening to promote specialized examinations. Finally, the diagnosis of lung cancer was made in eight subjects with pathological evidence, whereas no tissue could be obtained in two patients. Nonetheless, they were treated by chemotherapy because of the rapid nodule growth and positive diagnosis on contrast-enhanced CT scans. Four of the 10 patients did not have any lesions in the first-year screening, while remaining six were characterized by significantly enlarged nodules or pulmonary hilus. Another interval cancer was also detected, whose nodule had a benign appearance of about 10 mm in the previous screening, but increased suddenly and markedly.

Results in Year 3

By the end of December 2009, 1,441 participants had undergone the third-year screening. Including 39 new subjects, 394 individuals displayed 637 nodules. Added to the 30 positive individuals out of 93 undetermined subjects by extra scans, final positive results were in 55 persons and seven cases were diagnosed as lung cancer.

Conclusion and Comparison from the 3-Year Follow-up Study

A total of 31 lung cancer patients were found in the 3 years, and only five were women. The mean age was 65.35 years old (from 44 to 82). Besides, the average score by the questionnaire was 179.74 points, with one third over 200. The findings for the 3-year follow-up screening and characteristics of lung cancer patients are summarized in Tables 6 and 7.

In fact, we recruited a total of 8,093 subjects enrolled into the study for lung cancer following-up from 2007 to 2009. According to their scores by the self-assessment questionnaire, the other 6,556 ones were in the non-risk group, from which there were only five cases of lung cancer, with the detection rate of 0.08 % (5/6,556) [14], significantly lower than that of the risk group (2.02 %, 31/1,537), indicating screening for high-risk individuals might be more effective and economical.

Discussion

Although lung cancer screening is a controversial issue, mounting research has already shown its potential benefits, especially for high-risk populations. However, the criteria for determining high-risk groups have not yet been unified. Generally speaking, active cigarette consumption is the well-known principal respondent, so nearly all of the present studies focused on heavy smokers and the results were desirable [7, 17, 18, 28]. With the progress of research, passive smoking and exposure to cooking fumes have attracted more and more attention [19, 20]. Additionally, there has been a longstanding interest in genetic susceptibility to lung cancer, and recent studies have established its definite role [6, 21]. However, how to make a comprehensive evaluation about risks of lung cancer still remains a significant, but a little bit confusing, problem. Therefore, under separate studies, with the method of evidence-based medicine, our research team has established a brand new assessment system, namely the Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer, which took 15 risk factors and their effects into consideration altogether. Smoking was expectedly the most important factor, especially for those with initial smoking age younger than 15 years old. Moreover, subjects with psychological depression or family history of tumors were also incorporated into the high-risk group, which were not considered in previously documented

Table 6 Findings for the 3 years

Characteristics	Participants	Individuals losing from the study	Compliance rate (%)	Participants with nodules	Proportions of participants with nodules (%)	Total number of nodules	Participants with positive results	Proportions of positive results (%)	Detected lung cancers	Detection rates of lung cancer (%)	Interval lung cancers
2007	1,537	0	100	230	14.96	494	34	2.21	11	0.72	2
2008	1,493	31	97.97	291	19.49	553	46	3.08	10	0.67	1
2009	1,441	41	97.23	394	27.34	637	55	3.82	7	0.49	0

screening trials [1, 11–13]. Thus, we strongly believe that the scoring questionnaire represents an improved sensitive way to identify high-risk human beings for lung cancer.

Radiology is by far the main means for lung cancer screening. Value of CXR and CT has been evaluated over decades. With the help of computer processing system, DR can clearly show small lesions in lung fields with less radio-activation and less cost, even signs of lobulation or spiculation for a noncalcified nodule about only 2 mm. A recent small sample size case-control study, including 55 cases of lung cancer and 72 controls revealed the sensitivity of DR in suggesting a malignant diagnosis was close to 60 %, with specificity up to 90 % [22]. However, its efficacy for lung cancer screening in a much larger population has never been formally evaluated, which promoted us to carry out the current study.

In the baseline screening of our research, the nodule detection rate by DR was 14.96 % (230/1,537), lower than other trails with CT scans [23–25]. It was supposed that except for the screening method, special eligible subjects contributed to the difference substantially. Compared with heavy smokers in previous trails [23–25], approximately 10 % of the current volunteers were never smokers, probably indicating fewer nodules.

Although the initial detection rate of nodules in our study was slightly low, but with the excellent following-up protocols, the ultimate detection rate of early-stage lung cancer is comparable with the published results by using CT [12, 23]. Generally speaking, typical noncalcified nodules refer to solid lesions with diameters ranging from 8 to 30 mm [26, 27]. Malignant probability for the smaller ones are usually low, especially for those less than 5 mm, only about 0–1 % [27–29]. Accordingly, we overlooked nodules with a maximum diameter below 5 mm; but larger ones over 30 mm were considered to be positive. For the rest between 5 and 30 mm, spiculation, lobulation, and other imaging features determined the final results, which were almost ignored in other screening reports [1, 12, 30]. Our practice demonstrated that taking such imaging features into consideration was an effective approach to avoid missing important lesions. Furthermore, in the following-up strategies, an increase in nodules' diameters by 30 % indicated a malignant process as well. This was based on the assumption that the nodule was spheriform. So the expanding of diameter by 30 % meant the volume increased doubly, suggesting a volume-doubling time [13]. Beyond that, enlargement of pulmonary hilus and atelectasis were also identified as positive results in the practice for the first time. Either enlargement of pulmonary hilus or atelectasis might be one of the performances of hilus-occupying diseases. Among the nine subjects with enlargement of pulmonary hilus in our study, four were diagnosed with lung cancer. The high detection rate put another emphasis on the pulmonary hilus enlargement. However, none of the three participants with atelectasis obtained a positive diagnosis. As a matter of fact, to be more exact, all of

Table 7 Characteristics of lung cancer patients

	2007		2008		2009	
	Detected	Interval	Detected	Interval	Detected	Interval
Diagnostic methods						
Pulmonary lobectomy	7	1	2	1	4	
Percutaneous transthoracic biopsy	1		1			
Bronchoscopy	3	1	3		1	
Sputum cytology			2		1	
Contrast-enhanced CT			2			
Lymph node biopsy					1	
TNM stage						
I A	5	1	3	1	2	
I B	5		4		3	
II A						
II B			1			
IIIA					2	
III B			1			
IV	1	1	1			
Histopathological types						
Squamous carcinoma	4		2		4	
Adenocarcinoma	7	2	4	1	2	
SCLC			2		1	
Unclassified			2			

them were only a little poor in pulmonary air inflation and they were caused by heteroplasia or chronic inflammation. It probably gave us an indication that the extent of lesions was probably associated with the nature of diseases as well.

With the above protocols, 31 cases of lung cancer were detected in 3 years and the detection rate (2.02 %) was approximate to other trials [23, 25]. In terms of screening efficacy, sensitivity of protocol was over 85 %, with specificity about 96 %. Predicted value is another index to access a screening program. It means the risk of a person with a positive or negative result to suffer from a particular disease or not. Not only has the efficacy of a screening protocol but also the incidence rate of a particular disease had a marked effect on it. Unfortunately, almost all of the published reports have disregarded it [1, 32]. Accordingly, though the positive predicted value in our study was lower than others, we believe it ought to be more accurate.

At present, the major benefit of lung cancer screening is the high proportion of early cases. The Canadian experience from 2003 to 2005, one of the branches of the famous International Early Lung Cancer Action Program, demonstrated that 75 % of the detected patients (15/20) were in stage I and 70 % (14/20) received surgical excision [12], which were consistent with others [14, 30, 31]. Similarly, our study revealed 77.42 % (24/31) of screened patients were in stage I. However, there were three cases in stage IV and three interval cancers. This issue raised relevant

concerns: should we take repeated examinations more frequently or use other screening methods to take place of DR scans? What is noteworthy is that frequent CT scans perhaps induce excess radiation exposure and CT is more apt to make overdiagnosis, except for its higher cost. Data from the International Commission on Radiological Protection indicated three male or six female cases of radiation-induced cancer would occur in every 100,000 screened individuals over 15–20 years [33]. Recent estimates have suggested the false-positive rate of CT varied from 10 to 42 %, compared with 3 to 19 % for CXR [34, 35]. As a less radioactive method than CT, but much more sensitive than CXR, DR may integrate both of the advantages. Furthermore, two of the three advanced cases were detected in the first year, and the other three interval patients accounted for only 0.20 % (3/1,504) of all individuals with negative judgments and two were in stage I. From this point of view, increasing screening frequency or taking other screening methods appeared of no significant benefit. So we believe the current protocol is acceptable.

In conclusion, our findings suggest that DR, a much cheaper and less radioactive method than CT, has a great potential efficacy for early detection of lung cancer in high-risk individuals, identified by the Self-evaluation Scoring Questionnaire for High-risk Individuals of Lung Cancer. Most of the detected patients are in stage I and the current protocol is applicable, particularly in developing or under-developed regions/countries.

Acknowledgments This study was supported by the “The Eleventh Five-Year” Development Planning for Major Projects (Lung Cancer Prevention), Chengdu, China (grant #07YTYB961020) funded by the Chengdu Municipal Bureau of Science and Technology, Chengdu Municipal Bureau of Public Health and Chengdu Municipal Center for Disease Control and Prevention, China.

We heartily thank Prof. Zhou Xing (Department of Pathology and Molecular Medicine, McMaster University, Canada) for his kind help with revising the manuscript.

Role of the Funding Source Chengdu Municipal Bureau of Science and Technology, Chengdu Municipal Bureau of Public Health and Chengdu Municipal Center for Disease Control and Prevention, China implemented this study by providing financial and administrative support.

References

- Hocking WG, Hu P, Oken MM, Winslow SD, Kvale PA, Prorok PC, et al: Lung cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian (PLCO) screening trial. *J Natl Cancer Inst* 102(10):722–731, 2010
- American Cancer Society. Cancer facts & figures 2010. Atlanta: American Cancer Society 4–10, 2010
- Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, et al: Cancer statistics, 2008. *CA Cancer J Clin* 58(2):71–96, 2008
- Rami-Porta R, Crowley J, Goldstraw P: The revised TNM staging system for lung cancer. *Ann Thorac Cardiovasc Surg* 15(1):4–9, 2009
- Niho S, Kubota K, Yoh K, Goto K, Ohmatsu H, Ohe Y, et al: Survival improvement in patients (pts) with small cell lung cancer (SCLC): a historical comparison before and after amrubicin (AMR) approval in Japan [abstract]. *Am J Clin Oncol* 28(suppl 15):e18105, 2010
- Truong T, Hung RJ, Amos CI, Wu X, Bickeböller H, Rosenberger A, et al: Replication of lung cancer susceptibility loci at chromosomes 15q25, 5p15, and 6p21: a pooled analysis from the International Lung Cancer Consortium. *J Natl Cancer Inst* 102(13):959–971, 2010
- Doria-Rose VP, Marcus PM, Szabo E, Tockman MS, Melamed MR, Prorok PC: Randomized controlled trials of the efficacy of lung cancer screening by sputum cytology revisited: a combined mortality analysis from the Johns Hopkins Lung Project and the Memorial Sloan-Kettering Lung Study. *Cancer* 115(21):5007–5017, 2009
- Samet JM, Avila-Tang E, Boffetta P, Hannan LM, Olivo-Marston S, Thun MJ, et al: Lung cancer in never smokers: clinical epidemiology and environmental risk factors. *Clin Cancer Res* 15(18):5626–5645, 2009
- Peter B: Lung cancer screening. *J Natl Compr Canc Netw* 6(3):271–275, 2008
- Doria-Rose VP, Marcus PM, Miller AB, Bergstralh EJ, Mandel JS, Tockman MS, et al: Does the source of death information affect cancer screening efficacy results? A study of the use of mortality review versus death certificates in four randomized trials. *Clin Trials* 7(1):69–77, 2010
- Hunt I, Siva M, Southon R, Treasure T: Does lung cancer screening with chest X-ray improve disease-free survival? *Invest Cardiovasc Thorac Surg* 5(4):483–487, 2006
- Roberts HC, Patsios D, Paul NS, McGregor M, Weisbrod G, Chung T, et al: Lung cancer screening with low-dose computed tomography: Canadian experience. *Can Assoc Radiol J* 58(4):225–235, 2007
- Liu Y, Yang J, Zhao D, Liu J: A study of pulmonary nodule detection in three-dimensional thoracic CT scans. *Computer Modeling and Simulation*, 2010. doi:10.1109/ICCMS.2010.40
- Chen BJ, Cao HB, Wang DM, Liu D, Zeng J, Wang YJ, et al: Design and application of a self-evaluation questionnaire for individuals at a high-risk of lung cancer. *Thoracic Cancer* 3:60–67, 2012
- Lam B, Lam SY, Wong MP, Ooi CG, Fong DY, Lam DC, et al: Sputum cytology examination followed by autofluorescence bronchoscopy: a practical way of identifying early stage lung cancer in central airway. *Lung Cancer* 64(3):289–294, 2009
- Vallièrès E, Shepherd FA, Crowley J, Van Houtte P, Postmus PE, Carney D, et al: The IASLC Lung Cancer Staging Project: proposals regarding the relevance of TNM in the pathologic staging of small cell lung cancer in the forthcoming (seventh) Edition of the TNM classification for lung cancer. *J Thorac Oncol* 4(9):1049–1059, 2009
- Pedersen JH, Ashraf H, Dirksen A, Bach K, Hansen H, Toennesen P, et al: The Danish Randomized Lung Cancer CT Screening Trial—overall design and results of the prevalence round. *J Thorac Oncol* 4(5):608–614, 2009
- Dominioni L, Rotolo N, Poli A, Paolucci M, Sessa F, D’Ambrosio V, et al: Self-selection effects in smokers attending lung cancer screening: a 9.5-year population-based cohort study in Varese, Italy. *J Thorac Oncol* 5(4):428–435, 2010
- Alberg AJ, Ford JG, Samet JM, et al: Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 132(3):29S–55S, 2007
- Silvestri GA, Alberg AJ, Ravenel J: The changing epidemiology of lung cancer with a focus on screening. *BMJ* 339:451–454, 2009
- Young RP, Hopkins RJ, Hay B, Gamble GD: GWAS and candidate SNPs for COPD and lung cancer combine to identify lung cancer susceptibility: validation in a prospective study. *Am J Respir Crit Care Med* 181:A3738, 2010
- de Hoop B, Schaefer-Prokop C, Gietema HA, de Jong PA, van Ginneken B, van Klaveren RJ, et al: Screening for lung cancer with digital chest radiography: sensitivity and number of secondary work-up CT examinations. *Radiol* 255(2):629–637, 2010
- van Klaveren RJ, Oudkerk M, Prokop M, Scholten ET, Nackaerts K, Vernhout R, et al: Management of lung nodules detected by volume CT scanning. *N Engl J Med* 361(23):2221–2229, 2009
- Wang C, Tsai Y, Cheung Y, Ko H, Ni Y, Feng P, et al: Baseline results of lung cancer screening program for family lung cancer risk with low-dose spiral CT in Taiwan [abstract]. *Am J Clin Oncol* 28(suppl 15):7098, 2010
- Wilson DO, Weissfeld JL, Fuhrman CR, Fisher SN, Balogh P, Landreneau RJ, et al: The Pittsburgh Lung Screening Study (PLUSS) outcomes within 3 years of a first computed tomography scan. *Am J Respir Crit Care Med* 178(9):956–961, 2008
- Gould MK, Fletcher J, Iannettoni MD, Lynch WR, Midthun DE, Naidich DP, et al: Evaluation of patients with pulmonary nodules: when is it lung cancer? ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 132:108s–130s, 2007
- Wu YL, Jiang GL, Liao ML, Zhou QH, Lu S, Wang J, et al: Chinese consensus on treatment of solitary pulmonary nodule. *J Evid Base Med* 9(4):243–246, 2009
- Novello S, Fava C, Borasio P, Dogliotti L, Cortese G, Crida B, et al: Three-year findings of an early lung cancer detection feasibility study with low dose spiral computed tomography in heavy smoking. *Lung Cancer* 16(10):1662–1666, 2005
- Jeong YJ, Yi CA, Lee KS: Solitary pulmonary nodules: detection, characterization, and guidance for further diagnostic workup and treatment. *Am J Roentgenol* 188(1):57–68, 2007
- Infante M, Lutman FR, Cavuto S, Brambilla G, Chiesa G, Passera E, et al: Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. *Lung Cancer* 59(3):355–363, 2008

31. Gopal M, Abdullah SE, Grady JJ, Goodwin JS: Screening for lung cancer with low-dose computed tomography: a systematic review and meta-analysis of the baseline findings of randomized controlled trials. *J Thorac Oncol* 5(8):1233–1239, 2010
32. Xu DM, van Klaveren RJ, de Bock GH, Leusveld AL, Dorrius MD, Zhao Y, et al: Role of baseline nodule density and changes in density and nodule features in the discrimination between benign and malignant solid indeterminate pulmonary nodules. *Eur J Radiol* 70(3):492–498, 2009
33. Huppmann MV, Johnson WB, Javitt MC: Radiation risks from exposure to chest computed tomography. *Semin Ultrasound CT MR* 31(1):14–28, 2010
34. Block JP: High false-positive rate for lung cancer screening. *Ann Intern Med* 17(7):298–299, 2010
35. Croswell JM, Baker SG, Marcus PM, Clapp JD, Kramer BS: Cumulative incidence of false-positive test results in lung cancer screening: a randomized trial. *Ann Intern Med* 152(8):505–512, 2010