

ORIGINAL ARTICLE

Status and perspectives of detection by low-dose computed tomography or computed radiography in surgical patients with lung cancer, based on a five-year study

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Keywords

Computed radiography; low-dose computed tomography; lung cancer; rural patients; urban patients.

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Abstract

Background: A retrospective study involving 502 lung cancer patients who had received pulmonary resection from 2009–2013 was conducted in order to compare the clinical characteristics of patients whose diagnosis was detected by low-dose computed tomography (LDCT) and computed radiography (CR).

Methods: Two groups were established, based on the method of detection: the LDCT group included 172 lung cancer patients; the CR group included 330 lung cancer patients. The evolution of proportions of patients in urban and rural regions was also analyzed, according to detection method.

Results: The percentage of patients with stage I was higher in the LDCT group than in the CR group (77.3%, 133/172 vs. 53.6%, 177/330). The incidence of postoperative complications within 30 days was significantly lower in the LDCT than in CR group (25.0% vs. 33.6%). The proportion of patients detected by LDCT or CR in urban regions was constantly higher than in rural regions (with an increase of 13.0% vs. 5.9%); the proportion of LDCT-detected patients in urban regions was constantly higher than in rural regions (with an increase of 8.7% vs. 5.9%).

Conclusions: LDCT contributes to a higher proportion of early lung cancer diagnoses and a lower incidence of postoperative complications in surgical patients. The proportions of patients detected early and by LDCT have both increased steadily during the last five years. These two trends are more pronounced in urban compared with rural patients.

Introduction

Malignant tumors represent the most life-threatening diseases to humans. The morbidity and mortality rates of lung cancer in 2014 in China were 46.08/100 000 and 37.00/100 000, respectively, with the mortality rate ranking highest among all types of tumors, regardless of gender or region.¹ The primary treatment for lung cancer is surgery. Improved surgical techniques, combined with effective adjuvant chemotherapy, can significantly benefit lung cancer patients.^{2,3} Despite advances in treatment, advanced lung cancer remains incurable upon the time of diagnosis, and pre-malignant or early lesions (intermediate stages) are not amenable to resection or cure.

Early detection or screening, which helps with the diagnosis of lung cancer, is an important and effective treatment strategy. According to some large-scale early detection trials,

low-dose computed tomography (LDCT) can detect a larger number of lung cancers compared with chest radiography; most of these lesions were detected at early and resectable stages (IA to IB).⁴ It has been proven that lung cancer-related mortality can be reduced by 20% by screening high-risk individuals with LDCT.⁵ Nevertheless, problems still exist, such as defining the high-risk population, proper timing, interval and methods of screening, and, particularly, cost-effectiveness in relation to other lung cancer prevention strategies.^{6–9} Advances in imaging technology enable the detection of more asymptomatic lung cancers via LDCT or computed radiography (CR), which may offer beneficial effects to relevant treatments.

Concerned with the increasing number of lung cancer patients detected by LDCT or CR in our thoracic department, we performed a five-year retrospective study to compare the clinical characteristics between patients detected via these

two techniques. The evolution of proportions of LDCT-detected patients in cities and townships (rural regions) were analyzed separately.

Our intention for this study was not only to confirm or emphasize the advantages of LDCT from a surgical perspective, but also to unveil the evolution in utilization of LDCT among urban and rural patients in our department from 2009–2013.

Materials and methods

A retrospective database of patients who underwent lobectomy with detection via LDCT or CR at our department from 2009–2013 was analyzed.

Population

From a total of 2571 lung cancer patients identified in our department from 2009–2013, we selected patients who: (i) made a medical visit mainly as a result of detection via LDCT or CR, (ii) finally accepted surgical treatment, and (iii) were diagnosed with primary non-small-cell lung cancer (NSCLC). Finally, 502 patients were included.

The time duration from detection to diagnosis was also recorded and stratified into four periods: <1 month, 1–6 months, 6–12 months, and >1 year.

Demographic, clinical, and surgical data of the included patients were retrospectively analyzed. Pathological stages were determined according to the 6th Union for International Cancer Control (UICC) tumor node metastasis (TNM) staging system.^{10,11}

Grouping criterion

A cohort of 502 surgical lung cancer patients hospitalized at our department were stratified into two groups according to lung cancer detection method: LDCT or CR.

Regions of residence and urban-rural gaps in medical and health public services

According to the new standard of urban and rural region division promulgated by the State Council of China, regions of residence were classified by the following criteria: (i) signing the register at the administration concerned; (ii) residing there for at least one year; and (iii) having local medical insurance.^{12,13} The imbalance of health expenditure and resources between urban and rural regions has directly resulted in the excessive concentration of medical resources in urban regions. In 2009, the in-patient beds in urban regions accounted for 81.38% of total beds, four-fold higher than in rural regions; similarly, the ratio of the number of medical personnel in urban to rural regions was 5.83:1.¹⁴

Surgical approaches

Video-assisted thoracic surgery (VATS) lobectomy has been recognized as an option for peripheral NSCLC smaller than 5 cm, or central NSCLC with pathological minimal invasiveness. As reported, VATS offers advantages such as relieved postoperative pain, shorter in-hospital duration, and higher compliance with adjuvant chemotherapy. VATS lobectomy is also a better option than open lobectomy for gerontal patients with poor heart function or low surgical tolerance. Open lobectomy is recommended for patients after chemotherapy or radiotherapy; central NSCLC patients with lesions invading the initial portion of the bronchus; patients with lymphatic metastasis; or NSCLC patients at T3 or T4. Moreover, selection of the optimal method also depends on the opinions of patients, the feasibility and availability of surgical approaches, and other factors.

Statistical analysis

Data analyses were performed on SPSS 19.0 (IBM Corp., Armonk, NY, USA)

and Stata 12.0 (Stata Corp, College Station, TX, USA). All statistical tests were two-sided. Numerical variables were expressed as means \pm standard deviations (SD), while discrete variables were compared using chi-square or Fisher's exact tests. The time durations from detection to diagnosis between the two groups were analyzed by non-parametric test. All results were considered significant at $P < 0.05$.

Results

In total, 502 lung cancer patients aged 18–82 years (mean 58.8 \pm 10.5), including 306 (61.0%) men and 196 (39.0%) women, were included in the analysis (details are listed in Table 1). There were 162 (32.2%) smokers, 52 (10.4%) ever-smokers, and 288 (57.4%) non-smokers. The proportions of urban and rural patients were significantly different (63.7%, 320/502 vs. 36.3%, 182/502; $P = 0.031$).

Of the included patients, 34.3% (172/502) were allocated to the LDCT group, and 65.7% (330/502) to the CR group.

The major portion (410/502, 81.2%) of patients were asymptomatic, but the proportions of asymptomatic patients were not significantly different between the LDCT and CR groups ($P = 0.272$).

The proportion of patients with stage I in the LDCT group was 77.3% (133/172), significantly higher than in the CR group (53.6%, 177/330) ($P < 0.001$).

Concerning surgical approaches, a higher percentage of patients in the LDCT group (121/172, 70.3%) underwent pulmonary VATS resection, compared with 63.3% (209/330) in the CR group ($P = 0.116$).

Table 1 Baseline characteristics

	LDCT	CR	P value
Age, mean \pm SD	58.5 \pm 10.6	59.6 \pm 10.2	0.765
Gender			
Male	102 (59.3)	204 (61.8)	0.325
Female	70 (40.7)	126 (38.2)	
Smoking			
Never	103 (59.9)	185 (56.1)	0.037
Current	45 (26.2)	117 (35.4)	
Former	24 (13.9)	28 (8.5)	
Clinical manifestations			
Asymptomatic patients	145 (84.3)	265 (80.3)	0.272
Patients with symptoms	27 (15.7)	65 (19.7)	
Regions of residence			
Urban regions	121 (70.3)	199 (60.3)	0.031
Suburban or rural regions	51 (29.7)	131 (39.7)	

CR, computed radiography; LDCT, low-dose computed tomography; SD, standard deviation.

The distributions of time duration from detection to diagnosis were not significantly different between the groups ($P=0.759$) (Table 2).

The incidence of postoperative complications within 30 days was significantly lower in the LDCT than in the CR group (25.0% vs. 33.6%) (Table 3).

From 2009–2013, the proportion of patients detected by LDCT or CR in urban regions was constantly higher than in rural regions (Fig 1, Table 4) (an increase of 13.0% vs. 5.9%; average speed of increase: 13.4% vs. 12.1%). The proportion of LDCT-detected patients in urban regions was constantly higher than in rural regions (Fig 2, Table 5) during the same period (an increase of 8.7% vs. 5.9%, average speed of increase: 28.7% vs. 53.4%).

Table 2 Clinical characteristics in LDCT group and CR group

	LDCT	CR	P value
Time duration from detection to diagnosis			
<1 month	66 (38.4)	134 (40.6)	0.759
1–6 months	81 (47.1)	146 (44.2)	
6–12 months	13 (7.5)	26 (7.9)	
>1 year	12 (7.0)	24 (7.3)	
Surgical approaches			
VATS	121 (70.3%)	209 (63.3%)	0.116
Open	51 (29.7%)	121 (36.7%)	
Pathologic staging			
Stage 0 or I	133 (77.3%)	177 (53.6%)	0.000
Other			
Stage II	23 (13.4%)	79 (23.9%)	
Stage III	14 (8.1%)	64 (19.4%)	
Stage IV	2 (1.2%)	10 (3.0%)	

CR, computed radiography; LDCT, low-dose computed tomography; VATS, video-assisted thoracic surgery.

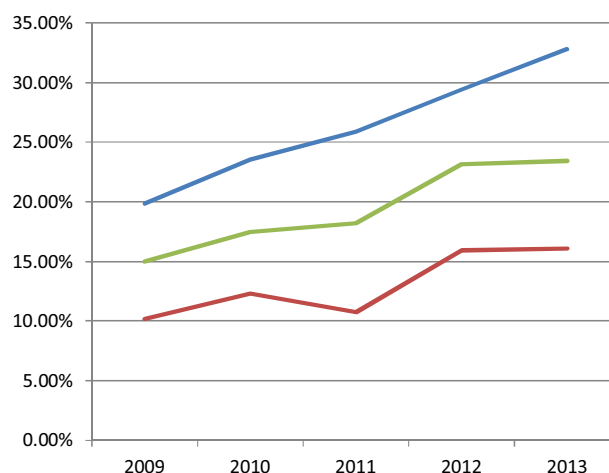


Figure 1 Evolution of the proportion of patients detected by low-dose computed tomography or computed radiography. (—) Urban patients, (—) rural patients, (—) total.

Discussion

Surgery is considered the principal method for lung cancer treatment; however, the expected survival rate of NSCLC patients is low, partly because many patients are diagnosed at advanced stages when curative treatments are infeasible. Periodic physical examination or lung cancer screening with effective methods (e.g. LDCT and chest radiography) and strategies (e.g. activities aimed at high-risk groups to promote public awareness or increase the possibility of detection of inchoate lung cancer) contribute to early diagnosis. Since the 1990s, abundant research has been conducted to reveal the significance or advantage of LDCT on the screening or detection of lung cancer, and many of the findings are promising.^{4,15,16} However, there are insufficient studies and data regarding the comparison between LDCT-based and CR-based detections. There is also little research available on the evolution of the prevalence of LDCT-detected lung cancers in China. Our study provides data, analytic findings, and conclusions that may contribute to policy-making and provides a scientific basis for better understanding the prevalence of LDCT.

For asymptomatic patients, especially those with risk factors, periodic physical examination or screening is an effective method for the early detection or observation of lung cancer. We believe that using LDCT or CR methods to check asymptomatic patients will ensure more frequent early diagnoses of lung cancer. In our study, 81.2% of the detected surgical patients were asymptomatic. This high percentage makes physical examination or screening indispensable, as a large proportion of lung cancer patients do not show any manifestation before diagnoses. Chest LDCT has been investigated intensively in the last two decades. Compared with

Table 3 Complications (in 30 days) in two groups

	LDCT group		CR group		Entire group	
	<i>n</i>	<i>n</i> /172 (%)	<i>n</i>	<i>n</i> /330 (%)	<i>n</i>	<i>n</i> /502 (%)
No. of patients with complications	43	25.0	111	33.6	154	30.7
Respiratory complications						
Pneumonia/chest infection	20	11.6	35	10.6	55	11.0
Severe dyspnea	6	3.5	9	2.7	15	3.0
Atelectasis	4	2.3	9	2.7	13	3.0
Respiratory failure	1	<1.0	3	<1.0	4	<1.0
Pneumonema	10	5.8	16	4.8	26	5.2
Pleural effusion (>500 mL)	6	3.5	16	4.8	22	4.4
Pulmonary embolism	0	0	4	1.2	4	<1.0
Hemoptysis (>100 mL/d)	5	2.9	7	2.1	12	2.4
Cardiovascular complications						
Severe arrhythmia	7	4.1	9	2.7	16	3.2
Surgical complications						
Aerodermection (>7 days)	15	8.7	46	13.9	61	12.2
Air leak (>7 days)	9	5.2	14	4.2	23	4.6
Wound infection/cellulitis	6	3.5	10	3.0	16	3.2
Chylothorax	3	1.7	7	2.1	10	2.0
Bronchopleural fistula	1	<1.0	2	<1.0	3	<1.0
Hemothorax	2	1.2	7	2.1	9	1.8
Severe electrolyte abnormality	2	1.2	3	<1.0	5	<1.0
Alimentary complications						
Abdominal distension or diarrhea	4	2.3	6	1.8	10	2.0
Severe vomiting	2	1.2	8	2.4	10	2.0
Other						
Retention of urine	2	1.2	3	<1.0	5	<1.0
Urinary tract infection	1	<1.0	3	<1.0	4	<1.0
Perioperative transfusion	1	<1.0	5	1.5	6	1.2
Venous thrombus	1	<1.0	9	2.7	10	2.0
Reoperation (in 30 days)	0	0	3	<1.0	3	<1.0
Stroke	0	0	1	<1.0	1	<1.0
ARDS	1	<1.0	1	<1.0	2	<1.0
Back to ICU	1	<1.0	3	<1.0	4	<1.0
Death	1	<1.0	2	<1.0	3	<1.0

ARDS, acute respiratory distress syndrome; CR, computed radiography; ICU, intensive care unit; LDCT, low-dose computed tomography.

chest radiography, this technique is more sensitive in the detection of early lung cancers manifested as small, non-calcified, and solitary pulmonary nodules (Fig 3).^{17,18} Among the 502 lung cancer patients in the present study, the majority (65.7%, 330/502) were detected by chest radiography, rather than LDCT (34.6%, 172/502). The use of LDCT was not as

popular as expected. We suggest three reasons for this outcome. (i) Few randomized controlled trials have been performed in China to confirm the advantage of LDCT in reducing lung-cancer-specific mortality (in other words, there is no data or analysis specific to China), which may complicate the establishment of criteria for LDCT-based detection of lung

Table 4 Proportion of patients detected by LDCT or CR

Year	Urban patients			Rural patients			Total		
	<i>n</i>	<i>N</i>	<i>n</i> / <i>N</i> (%)	<i>n</i>	<i>N</i>	<i>n</i> / <i>N</i> (%)	<i>n</i>	<i>N</i>	<i>n</i> / <i>N</i> (%)
2009	44	222	19.8	23	226	10.2	67	447	15.0
2010	49	208	23.6	30	244	12.3	79	452	17.5
2011	68	263	25.9	29	270	10.7	97	533	18.2
2012	80	272	29.4	51	320	15.9	131	592	22.1
2013	79	241	32.8	49	305	16.1	128	546	23.4

CR, computed radiography; LDCT, low-dose computed tomography.

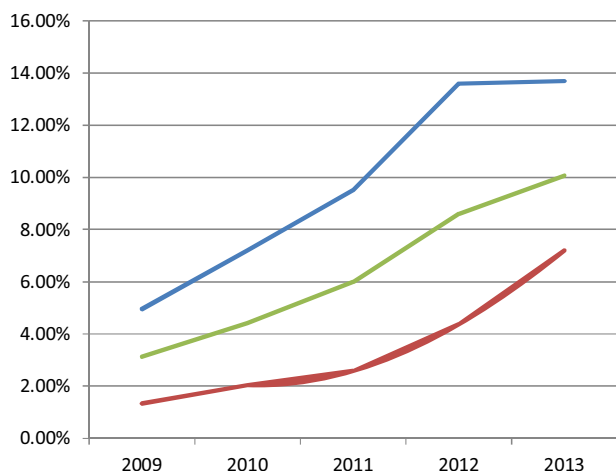


Figure 2 Evolution of the proportion of patients detected by low-dose computed tomography. (—) Urban patients, (—) rural patients, (—) total.

cancer. (ii) The cost of LDCT is relatively high and is not covered by national basic medical insurance. (iii) Problems exist that need to be solved urgently, such as defining the high-risk population, proper timing, interval and methods of screening, and, particularly, cost-effectiveness in relation to other lung cancer prevention strategies.

We suspect that the duration from detection to diagnosis may be shorter in LDCT-detected patients than CR-detected patients, indicating that more time and money could be saved. Moreover, earlier diagnosis may be offered, leading to early treatment, and, subsequently, a more propitious outcome. The basis for our determination that LDCT likely leads to shorter time from detection to diagnosis may be attributed to the fact that LDCT-based detection offers better and more specific evidence for a diagnosis of lung cancer. Thus, patients are more prone to further medical visits with advice from a physical examination organization or social hospital. Moreover, patients can even visit tertiary referral centers through a fast-track route, without referral or transfer. Further studies are needed to confirm whether LDCT-based detection can help to save more money and time, and prevent referral or transfer. However, the time durations from

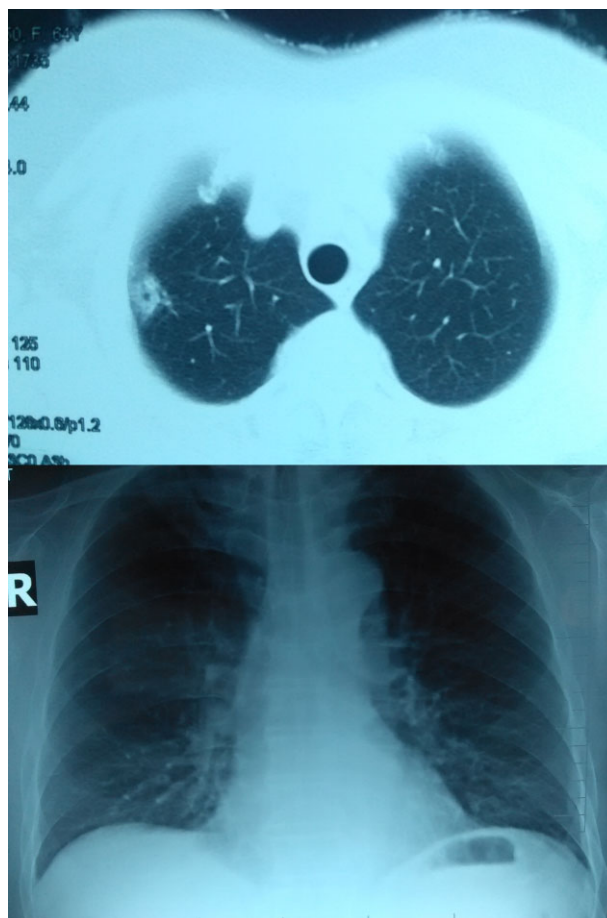


Figure 3 Comparison between low-dose computed tomography (above) and computed radiography (below). The images are from two different patients treated in our department.

detection to diagnosis were not significantly different between the LDCT and CR groups in our study. We suggest three reasons for this finding: (i) once CR-based detection indicates a pulmonary abnormality, the patient immediately undergoes other precise examinations or methods under suggestions from medical personnel; (ii) our sample size was small; and (iii) potential factors with non-negligible effects were not considered.

Table 5 Proportion of patients detected by LDCT

Year	Urban patients			Rural patients			Total		
	<i>n</i>	<i>N</i>	<i>n/N</i> (%)	<i>n</i>	<i>N</i>	<i>n/N</i> (%)	<i>n</i>	<i>N</i>	<i>n/N</i> (%)
2009	11	222	5.0	3	226	1.3	14	447	3.1
2010	15	208	7.2	5	244	2.0	20	452	4.4
2011	25	263	9.5	7	270	2.6	32	533	6.0
2012	37	272	13.6	14	320	4.4	51	592	8.6
2013	33	241	13.7	22	305	7.2	55	546	10.1

LDCT, low-dose computed tomography.

Patients in the LDCT group had a lower postoperative incidence of complications within 30 days, compared with the CR group. Although this result may be influenced by many factors, LDCT contributes to a higher proportion of early-stage lung cancer diagnoses compared with CR. Compared with chest radiography, LDCT is more sensitive for the detection of lung cancers manifested as small, non-calcified, and solitary pulmonary nodules, enabling early detection in more patients. These advantageous factors of LDCT in the detection of lung cancer, indicating better outcomes after surgical resection, may better rationalize the application of LDCT in physical-examination or screening.

The developments of regional economy, education, and medical systems are significantly different between urban and rural regions. Better medical resources are offered in cities; therefore, urban residents have more access to screening programs or physical examination. These benefits potentially contribute to early detection in urban patients. In this study, we analyzed the evolution of a proportion of lung cancer patients who had been detected in early stage (including CR or LDCT), particularly the proportion of LDCT-detected patients from 2009–2013. We also compared evolutions in urban and rural patients. Results show that the proportion of both early detected and LDCT-detected patients has steadily increased during the five year period of study. It should be noted that these two trends are more pronounced in urban patients. These results indicate that screening and utilization of LDCT is more prevalent in urban compared with rural patients. Regarding such differences, relevant administrations and medical and health institutions are advised to invest more manpower and resources into rural regions to promote health awareness in these areas. Rural residents need to understand reasons for utilizing LDCT and the significance of periodic physical examination or screening programs.

Strengths and limitations

Numerous studies have been published to verify or confirm the advantages of LDCT in the scanning of high risk groups, but there are insufficient data concerning a comparison between LDCT and CR-based detections. We hope that an analysis of the evolution of imaging-based detection (particularly by LDCT) in our department can contribute to policy-making in clinics and the public health system. Nevertheless, there are some issues that cannot be ignored.

Our analysis was a retrospective evaluation, rather than a prospective randomized trial. All patients were enrolled from a population who had been surgically treated from 2009–2013 by a small group of surgeons in our department, and limitations, such as a lack of generalization, cannot be avoided from a single-center study. Bias caused by the analysis of a single center cannot be ignored. Asymptomatic patients account for the majority, and there was no significance

between the LDCT and CR groups when comparing the proportion of asymptomatic patients. However, for the remaining patients with symptoms, we cannot discern whether it was their symptoms or other reasons which compelled them to participate in screening or physical-examination. Other factors, such as a floating population, were not considered, which may confound the study, reduce its generalizability, and, inevitably, impact the results.

Future multi-variable analysis, which could better evaluate and refine our conclusions, is needed.

In summary, the proportion of both early detected and LDCT-detected patients has steadily increased from 2009–2013. These two trends are more pronounced in urban compared with rural patients.

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Disclosure

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