Lung cancer imaging methods in China from 2005 to 2014: A national, multicenter study

Dong-Hui Hou†, Shi-Jun Zhao†, Ju-Fang Shi†, Le Wang, De-Bin Wang, Yun-Chao Huang, Xian-Zhen Liao, Xiao-Jing Xing, Ling-Bin Du, Li Yang, Yu-Qin Liu, Yong-Zhen Zhang, Dong-Hua Wei, Yun-Yong Liu, Kai Zhang, Ni Li, Wan-Qing Chen, You-Lin Qiao, Jie He, Min Dai#, Ning Wu, & LuCCRES Group

1 Department of Diagnostic Radiology, National Cancer Center/ National Clinical Research Center for Cancer/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
2 Office of Cancer Screening, National Cancer Center/ National Clinical Research Center for Cancer/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
3 School of Health Services Management, Anhui Medical University, Hefei, China
4 Department of Thoracic Surgery, Yunnan Cancer Hospital, Kunming, China
5 Hunan Office for Cancer Control and Research, Hunan Cancer Hospital, Changsha, China
6 Liaoning Office for Cancer Control and Research, Liaoning Cancer Hospital & Institute, Shenyang, China
7 Zhejiang Office for Cancer Control and Research, Zhejiang Cancer Hospital, Hangzhou, China
8 School of Public Health, Guangxi Medical University, Nanning, China
9 Cancer Epidemiology Research Center, Gansu Provincial Cancer Hospital, Lanzhou, China
10 Department of Epidemiology, Shanxi Provincial Cancer Hospital, Taiyuan, China
11 Medical Department, Anhui Provincial Cancer Hospital, Hefei, China
12 Department of Cancer Prevention, National Cancer Center/ National Clinical Research Center for Cancer/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
13 Department of Cancer Epidemiology, National Cancer Center/ National Clinical Research Center for Cancer/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
14 Department of Thoracic Surgery, National Cancer Center/ National Clinical Research Center for Cancer/ Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China
15 PET-CT Center, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Keywords
China; imaging method; lung cancer; trend.

Abstract

Background: The study was conducted to examine changes in diagnostic and staging imaging methods for lung cancer in China over a 10-year period and to determine the relationships between such changes and socioeconomic development.

Methods: This was a hospital-based, nationwide, multicenter retrospective study of primary lung cancer cases. The data were extracted from the 10-year primary lung cancer databases at eight tertiary hospitals from various geographic areas in China. The chi-squared test was used to assess the differences and the Cochran–Armitage trend test was used to estimate the trends of changes.

Results: A total of 7184 lung cancer cases were analyzed. Over the 10-year period, the utilization ratio of diagnostic imaging methods, such as chest computed tomography (CT) and chest magnetic resonance imaging (MRI), increased from 65.79% to 81.42% and from 0.73% to 1.96%, respectively, while the utilization ratio of chest X-ray declined from 50.15% to 30.93%. Staging imaging methods, such as positron emission tomography-CT, neck ultrasound, brain MRI, bone scintigraphy, and bone MRI increased from 0.73% to 22.95%, from 8.77% to 40.71%, from 42.40% to 62.22%, and from 0.88% to 4.65%, respectively; abdominal ultrasound declined from 83.33% to 59.9%. These trends were more notable in less developed areas than in areas with substantial economic development.
Introduction

Among all malignant tumors, the incidence and mortality rates of lung cancer have become a particularly critical threat to worldwide human health. In China, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death. In the United States, lung cancer incidence rates have declined in recent years, but it remains the leading cause of cancer death in people aged ≥ 40 years. Although lung cancer mortality has remained high for decades, the associated survival rate has improved as a result of increasingly standardized and reasonable diagnoses and therapies. Imaging examination is the primary method for the diagnosis and staging of lung cancer. Chest X-ray has long served as the major imaging examination method. With technological advances, additional imaging methods have become available.

There are no national data regarding the use of various imaging examinations for lung cancer in China. The present study represents part of an ongoing, multicenter, retrospective, hospital-based research effort focused on Chinese people with primary lung cancer. The analysis involved the assessment of demographic characteristics, exposure to risk factors, radiographic examinations, pathological characteristics, and therapeutic modalities. During the 10-year period analyzed in this study (2005–2014), the incidence of lung cancer has increased, while the diagnosis and treatment methods have improved; therefore, these data may help to clarify the current status of lung cancer in China and improve its management. As part of a series of further analyses of the original data, this study was conducted to describe the imaging methods for lung cancer in China and the shift in these methods during the period of 2005–2014 via a multicenter analytical approach.

Methods

This multicenter, hospital-based, 10-year (2005–2014), retrospective, clinical epidemiological study of primary lung cancer cases was performed via medical chart review.

According to the traditional National Bureau of Statistics administrative district definition, China is stratified into seven geographic regions (North, Northeast, Central, South, East, Northwest, and Southwest). The sampling framework comprised the highest level cancer hospital in each region. Finally, eight tertiary hospitals from seven regions were included in this study using convenience sampling: Shanxi Cancer Hospital (Shanxi Province, North China), Liaoning Cancer Hospital (Liaoning Province, Northeast China), Zhejiang Cancer Hospital (Zhejiang Province, East China), Anhui Cancer Hospital (Anhui Province, East China), Hunan Cancer Hospital (Hunan Province, Central China), Guangxi Cancer Hospital (Guangxi Autonomous Region, South China), Yunnan Cancer Hospital (Yunnan Province, Southwest China), and Gansu Cancer Hospital (Gansu Province, Northwest China). Notably, two hospitals were chosen from the East region because it includes more provinces than other regions. One month was randomly selected from 2005 onwards to represent the whole year in each hospital, and patients in the selected month were included as the representatives for that particular year. The following year, patients in the subsequent month were recruited, and this was repeated until 2014. January and February were excluded from random selection to remove any confounding effects of the longest and most celebrated holiday (the Spring Festival) in China. In each selected month, if < 100 patients were admitted, additional patients from the neighboring months were reviewed until the total number in that hospital reached 100; if the inpatient number in the selected month exceeded 100, all patients were recruited. Enrollment criteria were as follows: (i) pathologically confirmed primary lung cancer; (ii) inpatient admission date within the selected month in the study hospital; and (iii) the patient had received or was receiving treatment (surgery, chemotherapy, and/or radiotherapy) for lung cancer. The Ethics Committee of the Cancer Foundation of China approved this study. Patient consent was not required as there were no anticipated risks to participants.

Trained interviewers from each hospital collected data from the medical records. The socioeconomic levels of the eight selected hospitals were classified on the basis of socioeconomic status (SES). The details of SES in those areas have been described previously. Liaoning, Hunan, Zhejiang, and Anhui were designated as high economic areas while Gansu, Shanxi, Guangxi, and Yunnan were designated as low economic areas.

Conclusion: Overall, chest CT was the most common radiological diagnostic method for lung cancer in China. Imaging methods for lung cancer tend to be used in a diverse, rational, and regionally balanced manner.
Statistical analyses

SPSS version 21 (IBM Corp., Armonk, NY, USA) was used to analyze the data. The Cochran–Armitage trend test was used to estimate changes in the trends of various surgical treatment options during the 10-year period. Differences in the treatments between high and low economic areas were estimated by chi-squared test. All analyses were two-sided tests with a significance level of 0.05. Missing data were not counted in the sample size.

Results

From 2005 to 2014, 7,184 patients with lung cancer treated in the eight hospitals were selected, including 3,369 in high economic regions and 3,715 in low economic regions. The annual distribution of each region is shown in Table 1.

The utilization ratios of each method in the different regions are shown in Table 2. Overall, chest X-ray and bone magnetic resonance imaging (MRI) were used more frequently in low economic areas (P < 0.05); by contrast, chest computed tomography (CT), positron emission tomography (PET)-CT, abdominal ultrasound, brain MRI, brain CT, and bone scintigraphy were used more frequently in high economic areas (P < 0.05). Chest MRI was used in < 1% of cases in both high and low economic areas; however, this difference was not significant (P = 0.085). The difference in the usage rate of neck ultrasound was also not significant (P = 0.738).

The trends of different imaging methods from 2005 to 2014 are shown in Figure 1. The rates at which diagnostic methods were performed from 2005 to 2014 were as follows: chest CT and chest MRI increased from 65.79% to 81.42%, and from 0.73% to 1.96%, respectively; while the rate of chest X-ray use declined from 50.15% to 30.93%. The rates at which staging tests were performed were as follows: PET-CT, neck ultrasound, brain MRI, bone scintigraphy, and bone MRI increased from 0.73% to 9.17%, 22.95% to 47.92%, 8.77% to 40.71%, 42.40% to 62.22%, and 0.88% to 4.65%, respectively; while the use of abdominal ultrasound declined from 83.33% to 59.90%. Changes in the trends of use of these tests were more obvious in less developed areas. Changes in the trends of brain CT use differed between the two types of areas: they increased in low economic areas and declined in high economic areas.

Discussion

This is the first multicenter, hospital-based investigation of radiological diagnosis methods for lung cancer to assess trends over time. The imaging approach to lung cancer can be divided into different processes: screening, detection, diagnosis, staging, and follow-up. The focus of this study was inpatient pretreatment imaging methods, therefore the imaging methods we included were: diagnosis (chest X-ray, chest CT, chest MRI) and staging (PET-CT, neck ultrasound, abdominal ultrasound, brain MRI, brain CT, bone scintigraphy, and bone MRI). The data retrospectively covered a 10-year period to assess changes in lung cancer imaging diagnosis in tertiary hospitals.

We found that imaging methods for lung cancer diagnosis have become more comprehensive and varied; moreover, the usage rates of various examinations shifted between 2005 and 2014. The utilization ratios of chest X-ray and abdominal ultrasound decreased while the ratios for chest CT, chest MRI, PET-CT, brain MRI, neck ultrasound, bone scintigraphy, and bone MRI increased. Brain CT showed a decreasing trend in the whole country and in high economic areas in China, but use increased in low economic regions. All changes were more pronounced in low economic areas.

Imaging diagnosis and staging methods are related to lung cancer stage. Cancers, such as small lesions without chest lymph node metastasis, tend to require simple examination. In contrast, larger primary lesions with intrapulmonary metastases or chest lymph node metastasis are more likely to require comprehensive and systematic examination. We also considered the stages of lung cancer in cases occurring over the past 10 years. Based on the 7th edition of lung cancer staging, there were no significant changes in the proportion of early (stages 1 and 2) and advanced (stages 3 and 4) lung cancer, although the proportion of stage 1 lung cancers increased from 15.79% to 18.53%. This shows that the diversification and rationalization of imaging methods did not result from an increase in the number of cases with higher stage lung cancer.

We summarize the reasons for these changes as follows. Firstly, because of economic constraints, cheaper examination methods, such as chest X-ray, have been applied more
widely in past years, particularly in underdeveloped areas.\(^12\) In contrast, expensive and less readily available methods, such as PET-CT, have been applied less frequently. However, because of overlapping anatomical structure, the accuracy of the X-ray is low for central lung cancer and mediastinal lesions; moreover, its detection rate is poor for ground-glass opacity and small nodules.\(^{17,18}\) Secondly, with the improvement of living standards and the ability of patients to pay for better healthcare, as well as the increased national health insurance coverage and the emergence and popularity of relatively advanced imaging methods, people have more opportunities to use quality medical resources. Thirdly, doctors increasingly focus on comprehensive and accurate pretreatment diagnosis and staging, which is the basis for clinically standardized treatment; therefore, the sensitivities and accuracies of examination methods are more closely scrutinized. CT and PET-CT are recommended for lung cancer diagnosis and staging.\(^19\) Lung cancer exhibits predilections for particular metastatic sites, such as lymph nodes, pleura, bone, liver, brain, and the adrenal glands.\(^20\) Notably, different inspection methods involve specific sensitivities: CT has a unique advantage in lung tissue examination and is recommended for lung cancer diagnosis;\(^21\) PET-CT has a salutary effect in detecting metastasis and is recommended for staging;\(^6,22\) MRI exhibits a consistently higher qualitative diagnostic rate in soft tissue lesions and could distinguish pulmonary neoplasm from obstructive atelectasis, as well as assessing chest wall or mediastinal invasion;\(^23\) ultrasound is highly sensitive to metastatic lymph nodes;\(^24\) and bone scintigraphy is sensitive to bony metastases, such that it is complementary to bone MRI.\(^25,26\) As a result, the utilization rates of these examinations have increased and their diagnosis and staging accuracy for lung cancer have improved. As thoraco-abdominal applications become increasingly common, the use of separate abdominal exams, such as abdominal ultrasound, has decreased. Furthermore, with the implementation of national policies, the distribution of medical resources has tended to become more balanced; accordingly, medical treatment in less developed areas has developed rapidly, such that the relevant changes were more obvious.\(^27\) Finally, although lung cancer mortality has remained high for decades, the corresponding survival rate has improved. The five-year survival rate of lung cancer patients increased from 8% to 18% in China from 1995–1999 to 2005–2009\(^4\) and increased from 15% to 18% in America from 2004 to 2014.\(^5\) This change is related to systemic, normative, and combination therapy. The basis of standardized treatment is the accurate diagnosis and staging of lung cancer by imaging examination. For example, the specific location of the lesion, the adjacent vascular condition, and whether metastases have been observed are critical to the choice of treatment. In addition, the National Lung Screening Trial reported that low-dose CT screening reduced lung cancer-specific mortality by 20%, compared to chest X-ray.\(^28\) Therefore, we believe that these improved imaging methods may partially account for the improved survival rate among lung cancer patients.

Although this was an epidemiologic study with an extensive retrospective review, there were several limitations. We selected inpatients in tertiary hospitals in seven regions to represent the entire country. Selection bias might exist in the catchment of lung cancer patients in the selected hospitals; these were some of the best hospitals in each region and all could provide comprehensive cancer therapies. This may only reflect the trends and capabilities of the tertiary hospitals in the seven districts and not of the corresponding primary or secondary hospitals. However, we believe that these data reflect the imaging methods used in lung cancer diagnosis in China because most Chinese cancer patients choose high level medical institutions for better therapy. An additional limitation was that the medical examination records could not be fully accessed and the medical system

| Imaging methods             | Nationwide N (%) | High economic level areas N (%) | Low economic level areas N (%) | \(\chi^2\) | \(P\) |
|-----------------------------|------------------|---------------------------------|-------------------------------|--------|------|
| Chest X-ray                 | 2691 (37.46%)    | 896 (25.83%)                    | 1795 (48.32%)                 | 387.27 | < 0.001 |
| Chest CT                    | 5552 (77.28%)    | 3026 (87.23%)                   | 2526 (67.99%)                 | 378.05 | < 0.001 |
| Chest MRI                   | 57 (0.79%)       | 34 (0.98%)                      | 23 (0.62%)                    | 2.97   | 0.085 |
| PET-CT                      | 448 (6.24%)      | 296 (8.53%)                     | 152 (4.08%)                   | 60.51  | < 0.001 |
| Abdominal ultrasound        | 4993 (69.50%)    | 2596 (74.83%)                   | 2397 (64.52%)                 | 90.00  | < 0.001 |
| Neck ultrasound             | 2638 (36.72%)    | 1267 (36.52%)                   | 1371 (36.90%)                 | 0.11   | 0.738 |
| Brain CT                    | 2509 (34.92%)    | 1284 (37.01%)                   | 1225 (32.97%)                 | 12.88  | 0.002 |
| Brain MRI                   | 2211 (30.78%)    | 1510 (43.53%)                   | 701 (18.87%)                  | 512.00 | < 0.001 |
| Bone MRI                    | 319 (4.44%)      | 121 (3.49%)                     | 198 (5.33%)                   | 14.34  | 0.001 |
| Bone scintigraphy           | 4238 (59.00%)    | 2485 (71.63%)                   | 1753 (47.19%)                 | 443.20 | < 0.001 |

\(^\dagger\)The number and \(\dagger\)portion of patients examined via the imaging method in the region. CT, computed tomography; MRI, magnetic resonance imaging; PET, positron emission tomography.
itself is unable to perform intelligent analysis; moreover, the results of imaging tests involving patients in other hospitals could not be included in the statistical analysis. Patients who underwent imaging examinations at other facilities might have been missed. Therefore, it is possible that we may have underestimated the use of particular imaging
methods in this study. With the development of the Integrating the Healthcare Enterprise, this weakness can be avoided in future.29

In China, the most common radiology method for lung cancer analysis is CT. Imaging methods for lung cancer tend to be diverse, rational, and regionally balanced. Improvement in lung cancer prognosis over the past decade may be partly ascribed to the advancement and popularization of various imaging methods.

Acknowledgments

This work was supported by the National Key R&D Program of China (No.2017YFC1308700), the National Key R&D Program of China (No.2017YFC1308705), the Chinese Academy of Medical Sciences Initiative for Innovative Medicine Program (No.2017-12M-I-005), and Cancer Screening Program in Urban China, National Health and Family Planning Committee (currently National Health Commission) of P. R. China.

We sincerely thank all of the members of this survey from the National Cancer Center of China, field provinces, and the expert panel.

Disclosure

No authors report any conflict of interest.

References

1 Torre LA, Siegel RL, Jemal A. Lung cancer statistics. Adv Exp Med Biol 2016; 893: 1–19.
2 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017; 67: 7–30.
3 Chen W, Zheng R, Baade PD et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115–32.
4 Allemani C, Weir HK, Carreira H et al. Global surveillance of cancer survival 1995–2014: Analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 2015; 14: 977–1010.
5 Jemal A, Tiwari RC, Murray T et al. Cancer statistics, 2004. CA Cancer J Clin 2004; 54: 8–29.
6 Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. (Published erratum appears in CA Cancer J Clin 2014; 64: 364.). CA Cancer J Clin 2014; 64: 9–29.
7 Collins LG, Haines C, Perkel R, Enck RE. Lung cancer: Diagnosis and management. Am Fam Physician 2007; 55: 56–63.
8 Yang RM, Li L, Wei XH et al. Differentiation of central lung cancer from atelectasis: Comparison of diffusion-weighted MRI with PET/CT. PLoS One 2013; 8: e60279.
9 Kim HS, Lee KS, Ohno Y, van Beek EJ, Biederer J. PET/CT versus MRI for diagnosis, staging, and follow-up of lung cancer. J Magn Reson Imaging 2015; 42: 247–60.
10 Kitajima K, Doi H, Kanda T et al. Present and future roles of FDG-PET/CT imaging in the management of lung cancer. Jpn J Radiol 2016; 346: 387–99.
11 Qi ZY. The value of spiral CT examination and chest X-ray examination in the diagnosis of lung cancer. China Contin Med Educ 2016; 28: 44–5.
12 Gu P, Yu SY, Chen Q et al. The application research of chest X-ray, CT and fibrobronchoscope in the diagnosis of lung cancer. Shaanxi Med J 2007; 5: 548–51.
13 Chen WQ, Zheng RS, Zhang SW et al. Report of incidence and mortality in China cancer registries, 2008. Chin J Cancer Res 2012; 24: 171–80.
14 Chen WQ, Zheng RS, Zeng HM, Zhang S, He J. Annual report on status of cancer in China, 2011. Chin J Cancer Res 2015; 27: 2–12.
15 Li Y, Shi J, Yu S et al. Effect of socioeconomic status on stage at diagnosis of lung cancer in a hospital-based multicenter retrospective clinical epidemiological study in China, 2005–2014. Cancer Med 2017; 6: 2440–52.
16 Shi JF, Wang L, Wu N et al. Clinical characteristics and medical service utilization of lung cancer in China, 2005–2014: Overall design and results from a multicenter retrospective epidemiologic survey. Lung Cancer 2019; 128: 91–100.
17 Turkington PM, Kennan N, Greenstone MA. Misinterpretation of the chest xray as a factor in the delayed diagnosis of lung cancer. Postgrad Med J 2002; 78: 158–60.
18 Nagatani Y, Nitta N, Ikeda M et al. Ability of chest X-ray to detect faint shadows documented as ground-glass attenuation in images of computed tomography: A comparison between flat-panel detector radiography and film-screen radiography. Eur J Radiol 2010; 75: 384–90.
19 Lee WK, Lau EW, Chin K, Sedlaczek O, Steinke K. Modern diagnostic and therapeutic interventional radiology in lung cancer. J Thorac Dis 2013; 5: S51–23.
20 Rühimäki M, Hemminki A, Fallah M et al. Metastatic sites and survival in lung cancer. Lung Cancer 2014; 86: 78–84.
21 Hollings N, Shaw P. Diagnostic imaging of lung cancer. Eur Respir J 2002; 19: 722–42.
22 Kitajima K, Doi H, Kanda T et al. Present and future roles of FDG-PET/CT imaging in the management of lung cancer. Jpn J Radiol 2016; 34: 387–99.
23 Ohno Y, Sugimura K, Hatabu H. MR imaging of lung cancer. Eur J Radiol 2002; 44: 172–81.
24 Prosch H, Strasser G, Sonka C et al. Cervical ultrasound (US) and US-guided lymph node biopsy as a routine procedure for staging of lung cancer. Ultraschall Med 2007; 28: 598–603.
25 Takenaka D, Ohno Y, Matsumoto K et al. Detection of bone metastases in non-small cell lung cancer patients: Comparison of whole-body diffusion-weighted imaging (DWI), whole-body MR imaging without and with DWI,
whole-body FDG-PET/CT, and bone scintigraphy. *J Magn Reson Imaging* 2009; **30**: 298–308.

26 Michel F, Solèr M, Imhof E, Perruchoud AP. Initial staging of non-small cell lung cancer: Value of routine radioisotope bone scanning. *Thorax* 1991; **46**: 469–73.

27 An YF. Characters and improvement strategies of distribution of high-quality medical resources. *Chin Health Qual Manage* 2011; **18**: 110–3.

28 National Lung Screening Trial Research Team, Aberle DR, Adams AM et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011; **365**: 395–409.

29 Zheng XC, Wu YZ, Hu B. The challenge and evolution of image sharing in regional medical collaborative business process. *China Med Device Inf* 2009; **10**: 57–61.