

STUDY ON THE EFFECT OF 6 ITEMS OF THE DETECTION OF LUNG CANCER MARKERS COMBINED WITH MYRIAN IN SCREENING EARLY LUNG CANCER IN SMOKING POPULATION

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ABSTRACT

Objective: it is to investigate the clinical effect of serum CEA, CA153, CYFRA21-1, CA125, NSE, and CA199 in the application of Myrian imaging reconstruction technique in screening early lung cancer after multislice spiral CT examination in smoking population.

Methods: select a total of 100 smoking patients suspected of having early lung cancer after the screening of CEA, CA153, CYFRA21-1, CA125, NSE, and CA199 in Department of Respiratory Medicine of our hospital from January 2006 to 2007. First, 512-slice spiral CT was used for detection and screening. Then, Myrian image reconstruction technique was applied for testing and screening. The patients were followed up for 5 years and their incidence of lung cancer was counted. The specificity, accuracy and sensitivity of Myrian imaging reconstruction and conventional 512-slice spiral CT were evaluated.

Results: the sensitivity, specificity, Youden index and accuracy of Myrian reconstruction were 95.45%, 81.82%, 77.27% and 82%, respectively; the sensitivity, specificity, Youden index and accuracy of 512-slice spiral CT were 92.42%, 63.64%, 56.06% and 90% respectively. However, the different has no statistical significance.

Conclusion: The use of Myrian image reconstruction technique can be used as one of the tools for clinical auxiliary diagnosis in the diagnosis of early lung cancer.

Keywords: lung cancer, Myrian imaging reconstruction system, spiral CT, early diagnosis of lung cancer, smoking population, 6 items of lung cancer detection.

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Introduction

Lung cancer, also known as primary bronchial lung cancer, is a malignant tumor originating from bronchial mucosa or glandular tissue. According to epidemiological studies⁽¹⁾, there were 1.6 million cases in the world in 2008, of which 1.4 million died. Both morbidity and mortality have become the first among cancers in the world. Studies in China have shown that lung cancer is the leading cause of death in cancer patients⁽²⁾. Statistics over the past 30 years show that the death rate has increased by 464.8%, and the number of patients is still rising. As the problem of smoking and air pollution in China has worsened, the number of patients with lung cancer is expected to go beyond 1 million.

By then, China will be a big country with lung cancer. With the development of medical technology, new chemotherapeutic drugs, targeted therapeutic drugs and biotherapy have made brilliant achievements in the treatment of lung cancer. More and more clinical reports show that the prognosis of lung cancer patients is not poor if they can be diagnosed early and treated in time.

However, most patients with lung cancer have little or no symptoms at the early stage, which increases the difficulty of clinical diagnosis of lung cancer. Therefore, the diagnosis of early lung cancer has gradually become the main research direction of clinical workers. It has been shown that six tests, including serum CEA, CA153, CYFRA21-1, CA125, NSE, and CA199, can effectively screen out early lung cancer patients in smoking popula-

tion⁽⁴⁾. However, there are still errors in serological tests. Thus, as for how to further confirm the conclusion of early lung cancer patients in the next step of detection, so far, there is no effective screening method. Myrian CT image reconstruction system is a newly developed CT image processing system in recent years. In many studies, it has been shown that Myrian CT image reconstruction system can effectively provide some convenience for the diagnosis of patients, and can also be used to guide future treatments⁽⁵⁾. But whether the Myrian CT imaging reconstruction system can provide a certain reference for the diagnosis of early lung cancer patients, so far there is still no effective conclusion to confirm. Therefore, this experiment will use Myrian image reconstruction technology to compare with the traditional 512-slice spiral CT, and explore the value of this examination in patients with early lung cancer, hoping to summarize the experience to provide some reference for clinical work in the future. The report is as follows:

Information and methodology

Basic information

A total of 100 smoking patients suspected of having early lung cancer after the screening of CEA, CA153, CYFRA21-1, CA125, NSE, and CA199 in Department of Respiratory Medicine of our hospital from January 2006 to 2007 were selected, including 67 males and 33 females, aged 45-82, with an average age of 65.84 ± 11.28 . There were 48 patients with cough which had blood occasionally, 36 patients with cough accompanied with chest pain and 22 patients without obvious symptoms. Before the experiment, all the patients understood the procedure of the experiment with the explanation of the nursing staff and voluntarily signed the informed consent. The specific contents of all the experiments were reported to the ethics committee for the record, and the experiment was carried out in the case of a multi-party authorization, and the relevant documents were stored in Beijing Dehong Law firm (Room 1006, Baiyan Building, No. 238, Bei Sihuan Zhong Road, Haidian District, Beijing).

Inspection methods

Six tests for lung cancer

Six tests for lung cancer include carcinoembryonic antigen (CEA), tumor associated antigen

(TRA), cytokeratin 21-1 fragment (CYFRA21-1), carcinoantigen 125 (CA125), neuron-specific enolase (NSE) and tumor-associated antigen (CA199). The patients' peripheral blood was extracted from the coagulant tube at 5 ml when they were on an empty stomach, and then stored at room temperature for 30 minutes. After that, the blood was centrifuged by a super speed centrifuge (Tianjin Instrument Factory). After extracting the serum, it was stored in the environment of -80°C for 1 hour. After preparation, the chemiluminescence detector Berthold LB 942 microporous plate multifunctional enzyme marker was started, and the kit provided by Roche was prepared, which was operated one by one according to the specification.

CT scan

The patients were examined with spiral CT after the detection of six tumor markers in the serum of lung cancer with suspected possibility of lung cancer. The method of detection was multislice spiral CT (GE Light Speed Plus multislice CT scanner). The specific operating parameters are 120kVr, 50mA, screw pitch of 6, 0.8s / r, bed speed of 15mm / r, layer thickness of 2.5mm, and interval of 2.5mm. Before the examination, nurses taught the patient how to practice calm breathing and apnea, and the patient was examined in a supine position. First of all, a complete lung scan was performed under the patient's calm breathing condition. The scanning area included the area between the tip of the lung and the bottom of the costal angle. When the lesion was discovered, the local area was scanned thinly, with the parameters of 120 kv, 150 mA, and screw pitch of 1. A contrast agent was injected, and at the rate of 3 ml / s, 100 ml opaque was injected through the elbow vein. The focus was scanned once at 25 seconds after the injection. After the CT image information was collected, it was sent to two chief physicians who had worked for more than 35 years of the imaging department of our hospital to read and record the enhanced and plain scan images by double blind method. When there were different opinions, group meetings would be conducted to resolve problems.

Using Myrian image reconstruction

After the patient's lung scanning image acquisition was finished, the image was reconstructed by 1mm and imported into the workstation software of the Myrian XP-Liver medical image analysis system (provided by Intracense, France)

in Dicom format. The image was shared by two imaging physicians for image processing. The concrete operation includes: first, use the image analysis software to reconstruct the three-dimensional structure; second, calculate the volume of each anatomical structure inside the lung, tumor volume, and the whole lung volume; third, assess the patient's prognostic risk and treatment means.

Reference standard

Diagnostic criteria of six tumor markers for lung cancer

The diagnostic criteria for six tumor markers in patients with serological lung cancer are as follows: CA125 0.01-35 U / ml, CA1530.01-25 U / ml, CA199 0.01-37 U / ml, CEA 0-5 U / ml, NSE 0-25 U / ml, and CYFRA211 0.1-3.3 U / ml.

Judgment standard of CT

The width of pulmonary window was 1700 HUU, and the window position was -600HU. The width of mediastinal window was 350HU, and the window position was 40HU. The CT value was 1/2 radius region of the center of the maximum plane diameter. If the short diameter of mediastinal lymph nodes exceeded 1cm, the mediastinal lymph nodes were considered to be significant. The maximum radius of the section was used as the diagnostic criterion for the size of the tumor. The signs of lung cancer were based on the CT findings of the patients. The relative enhancement value was based on the difference between the average CT value in the middle and adjacent upper and lower layers of the tumor and the plain CT value of the same plane.

Data processing

The patient's data were input into the Microsoft Office Excel 2010 software, and then the data were programmed into the database by Microsoft Access software and analyzed statistically by SPSS 20.0 software. The results were expressed in the form of mean ±standard deviation. Then the χ^2 test and the sensitivity, specificity, Youden index and accuracy of the metrological data were calculated. The specific formula is: Sensitivity = the number of true positive patients / (the number of true positive patients + the number of false negative patients); specificity =the number of true negative patients/ (the number of true negative patients + the number of false positive patients); accuracy =

(the number of true positive patients + the number of true negative patients) / the total number; and Youden index =(sensitivity + specificity)-1.

The higher the sensitivity, the greater the probability of detecting patients is; the higher the specificity, the less the possibility of misdiagnosis is; the closer the value of Youden index to 1, the higher the detection value is; and the higher the accuracy, the better the effect of diagnostic screening is.

Results

Patients' diagnosis and actual prevalence

There were 67 cases of lung cancer diagnosed in the later diagnosis, including 32 cases of squamous cell carcinoma, 24 cases of adenocarcinoma, 6 cases of large cell lung cancer, 5 cases of small cell lung cancer, 32 cases of death, and 35 cases survived. The diagnosis and actual condition of the patients were shown in Table 1. The screening data of traditional spiral CT and that of Myrian reconstruction were statistically analyzed, and the difference was not statistically significant (P > 0.05).

True positive	False positive	True negative	False negative	
Traditional spiral CT	61	12	21	6
Myrian reconstruction	63	6	27	4
χ^2	3.182			
P	0.36441			

Table 1: Table 1 Patients' diagnosis and actual prevalence.

Sensitivity, specificity, Youden index, and accuracy of both tests

The sensitivity, specificity, Youden index, and accuracy of the two screening methods are shown in Table 2. The sensitivity, specificity, and Youden index of the Myrian reconstruction imaging system were all higher than those of the conventional spiral CT, and the accuracy of conventional spiral CT was slightly higher than that of Myrian reconstruction imaging system. The statistical analysis showed that the difference between the two groups was not statistically significant (P > 0.05).

With the development of medical technology, more and more software tools are used in computer-aided image diagnosis. Especially in the early diagnosis of lung cancer, respiratory physicians

can effectively understand the anatomical changes of patients and can utilize these changes in the later surgical treatment plans⁽⁶⁾, and can also calculate the effect of operation on blood supply of patients' residual lung tissue.

	Sensitivity	Specificity	Youden index	Accuracy
Myrian reconstruction	95.45%	81.82%	77.27%	82%
Traditional spiral CT	92.42%	63.64%	56.06%	90%
χ^2	4.224			
P	0.23827			

Table 2: Sensitivity, specificity, Youden index, and accuracy of Myrian reconstructed imaging system and conventional spiral CT.

In this experiment, it used the Myrian XP-Liver medical image analysis system developed by Intracense Company of France to reconstruct the lung tumor and internal blood flow according to the image data obtained by 512 MSCT. The system is characterized by its ability to avoid complicated images and spatial images in the brain by surgical respirators only based on the results of two-dimensional images⁽⁷⁾, and it can ensure that clinicians can visualize the lungs of patients in three-dimensional conditions. Thus, they can further simulate early lung cancer of patients and further analyze the postoperative risk of patients. The system can effectively assist doctors to provide accurate operation plans and provide more specific individualized information⁽⁸⁾.

Serological detection of tumor markers in patients is a rapid, economical and simple method, which has important diagnostic significance for tumor occurrence, development and prognosis. The carbohydrate structure on the surface of the tumor also plays an important role in the progression of the tumor. There is a close relationship between the occurrence of lung cancer and smoking. Therefore, the screening of smoking population is of great clinical significance. For this experiment, it is of great significance to use the six serological tumor markers, including CEA, CA153, CY-FRA21-1, CA125, NSE and CA199 for the screening in the smoking population. By using these six tests, the preliminary screening on patients can be completed with simple operation, so it is very important for the patients with abnormal indicators in these six examinations to carry out the next examination.

The patient was tested by measuring the volume of both lungs, tumor volume and blood flow, which is of great significance for future surgical treatment, pulmonary function assessment and risk assessment of recurrence. Traditional spiral CT examination results in the radiation errors in target volume and target area radiation dose due to the effect of tail shadow of respiratory movement. Previous studies have found that suspend breathing during examination can effectively reduce the effects of the tail shadow in the respiratory state, but it still cannot completely eliminate the negative effects of the tail shadow, nor can we study the changes of chest organs over time. At the same time, because of the influence of tail shadow, the effect of treatment in the future has also been affected. In related studies, a dose deviation of up to 47.8% was found in CT guided small radiotherapy errors⁽⁹⁾.

In this experiment, Myrian imaging reconstruction technique was found to be more specific and sensitive than traditional spiral CT in diagnosis, which was similar to that of Myrian image reconstruction in other diseases. This indicates that Myrian imaging reconstruction technique has a high application value in the screening of early lung cancer. Three-dimensional reconstruction of pulmonary tissue, simulated surgery and prognostic risk analysis of Myrian imaging system can accurately calculate the volume and blood flow of patients with early lung cancer, and play an important role in the later combined therapy. In addition, Myrian imaging reconstruction system is highly sensitive in the diagnosis of mediastinal lymph nodes. Mediastinal lymph node metastasis is one of the important imaging indications of malignant tumors, usually referring to lymph nodes which are more than 1 with structural abnormalities. The results of Myrian reconstruction system showed that the incidence rate and the screening rate of mediastinal lymph node metastasis was higher, which also had some effective value in the treatment of patients.

Three-dimensional medical imaging reconstruction software is one of the most widely used methods in the diagnosis of early lung cancer in China. It is widely used in the clinical work of orthopaedics, general surgery and neurosurgery. Research and application of this technology in the Department of respiratory medicine for early diagnosis of lung cancer is relatively few and the merits are not clear. Myrian XP-Liver medical im-

aging systems have the advantage that clinicians through MSCT multi-phase scan examination can easily access the image and import it into the office computer⁽¹⁰⁾. The patient's anatomical changes, lesions, blood flow channels and other factors can be three-dimensionally reconstructed and dynamically demonstrated, and through rotation, the tumor and the surrounding tissue change relationship can be observed, providing intuitive and accurate spatial information for the future surgery. But based on two-dimensional CT images, in the layer-by-layer resection of planning the operation, adjusting the coronal and sagittal view, the operation is very complicated. The virtual surgical planning software based on windows XP platform can be used in personal computer. By analyzing the structure and the volume of resection, we can specify an effective treatment plan. Accordingly, German's MeVis system has similar functions, but the operation of this system is very difficult and it is expensive, so there is no corresponding application value in the domestic market.

To sum up, six serological tumor markers (CEA, CA153, CYFRA21-1, CA125, NSE and CA199) were detected in smokers suspected to have tumors. Using 512-slice spiral CT combined with Myrian imaging reconstruction system, it can provide a certain reference value for the screening of patients and future treatment plans such as surgery and radiotherapy.

References

- 1) Mahnken A H, Wildberger J E, Sinha A M, et al. Value of 3D-volume rendering in the assessment of coronary arteries with retrospectively ECG-gated multislice spiral CT.(J). *Acta Radiologica*, 2015, 44(3): 302-309.
- 2) De-Zhong M A, Zhi-Zheng L I, Miao Y J, et al. Effect of low-dose spiral CT combined with tumor markers detection on screening of high-risk lung cancer in community(J). *Chinese Journal of Clinical Oncology & Rehabilitation*, 2017.
- 3) Fengzhang L I, Zou N, Hanming H U. Low-dose spiral CT combined tumor markers for lung cancer screening high-risk groups(J). *Jiangxi Medical Journal*, 2015.
- 4) Wang W J, Tao Z, Gu W, et al. Clinical observations on the association between diagnosis of lung cancer and serum tumor markers in combination(J). *Asian Pacific Journal of Cancer Prevention Apjcp*, 2013, 14(7):4369-71.
- 5) Pozzi P, Munarini E, Bravi F, et al. A combined smoking cessation intervention within a lung cancer screening trial: a pilot observational study.(J). 2015.
- 6) Villanti A C, Jiang Y, Abrams D B, et al. A Cost-Utility Analysis of Lung Cancer Screening and the Additional Benefits of Incorporating Smoking Cessation Interventions(J). *Plos One*, 2013, 8(8): e71379.
- 7) Kim Y, Kim D H. CpG Island Hypermethylation as a Biomarker for the Early Detection of Lung Cancer(J). *Methods in Molecular Biology*, 2015, 32(1238):141-171.
- 8) Guldbbrandt L M. The effect of direct referral for fast CT scan in early lung cancer detection in general practice. A clinical, cluster-randomised trial.(J). *Danish Medical Journal*, 2015, 61(3).
- 9) Healey G F, Lam S, Boyle P, et al. Signal stratification of autoantibody levels in serum samples and its application to the early detection of lung cancer(J). *Journal of Thoracic Disease*, 2013, 5(5): 618-25.
- 10) Hou H, Xu Z, Zhang H, et al. Combination diagnosis of multi-slice spiral computed tomography and secretory phospholipase A2-IIa for solitary pulmonary nodules. (J). *Journal of Clinical Laboratory Analysis*, 2017.

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