# Core exploration of progress in diagnosis and treatment of solitary pulmonary nodules

# Lingling Fu

Pulmonary and Critical Care Medicine, Zhuji People's Hospital of Zhejiang Province, Zhuji, Zhejiang, 311800, China fu198609262021@sina.com

Abstract: Solitary pulmonary nodule (SPN) is a common imaging manifestation in clinic, which is usually found accidentally during routine physical examination or routine chest imaging examination in hospital due to other diseases. Solitary pulmonary nodules can be either benign or malignant, and the clinical treatment is different for different natures. Therefore, how to evaluate and accurately judge the nature of solitary pulmonary nodules is particularly important for the selection of treatment. This article reviews the literature on evaluation strategies, imaging diagnosis methods and treatment methods of solitary pulmonary nodules in recent years, and summarizes them as follows.

**Keywords:** solitary pulmonary nodules; diagnosis; treatment strategy; progress

Solitary pulmonary nodule disease has a certain complexity, and it can develop into lung cancer if it's not treated in time, further aggravating the adverse effects on patients [1,2]. The clinical diagnosis and treatment measures for this disease have the characteristics of multiple selectivity. Different diagnosis and treatment measures have different specific effects and impact on the prognosis of patients. This paper mainly analyzes common clinical diagnosis and treatment measures to select appropriate diagnosis and treatment measures for patients timely, so as to continuously improve the treatment effect and efficiency of patients' disease [3,4].

## 1. Brief introduction to solitary pulmonary nodule

In daily life, people are usually prone to develop solitary pulmonary nodule due to significantly poor air quality in living and working environment, bacterial infection, neoplastic diseases, autoimmune diseases, long-term smoking and other factors. In the early stage of this disease, patients usually have no obvious symptoms. With the continuous development of the disease, patients usually show cough, phlegm, chest pain, hemoptysis, body fever, weight loss and other related symptoms, which not only have a serious impact on patients' physical and mental health and quality of life, but even endanger their life safety [5,6].

Isolated nodules of the lung refers to the image of circular shadow, the shadow is simple, with a diameter of less than or equal to three centimeters, surrounded by solid or subsolid lesions of high and low density surrounded by qi lung tissue, without atelectasis, enlargement or pleural effusion. Isolated pulmonary nodules are pulmonary nodules without obvious symptoms, with very many causes, benign and malignant. At present, there are two kinds of solitary nodules of lung classification: the first one is classified according to the density, divided into solid nodules and subsolid nodules, the latter is divided into pure ground glass nodules and confounding pulmonary nodules, and some solid nodules. Second, nodules can also be classified according to the size of the lesion. The lesion diameter of less than 5mm is called micronodules, the lesion diameter of between 5 and 10mm is called small nodules, and the lesion diameter of less than 30mm is called pulmonary nodules.

## 2. Research of solitary pulmonary nodule

## 2.1 Routine chest radiography for solitary pulmonary nodule

Routine chest X-ray examination mainly refers to chest X-ray examination, which is characterized by simple operation and low examination cost, and can effectively reduce the diagnosis and treatment pressure of the client [7, 8]. Meanwhile, this examination method also has the characteristics of low

sensitivity and accuracy, and the incidence of false negative and false positive are significantly higher when it is used in the examination of solitary pulmonary nodule. Conventional chest radiograph can detect 0.09%~0.2% isolated pulmonary nodules, poor sensitivity, and has a high false negative rate and a certain false positive rate. One study showed benign nodules initially indicated on the chest radiograph, and about 20% were found in non-small cell lung cancer in a retrospective analysis. This examination method cannot achieve accurate location and nature determination of lesions, and thus has a great adverse impact on clinical diagnosis and subsequent treatment. The utilization rate in the diagnosis of solitary pulmonary nodules is significantly low [9].

#### 2.2 Chest CT examination of solitary pulmonary nodule

Compared with chest radiograph, chest CT has significantly higher sensitivity, specificity, accuracy and image resolution. In the examination of solitary pulmonary nodules, it can prompt medical staff to have a clear and comprehensive understanding of the two-dimensional shape, size of the patient's nodule and the influence characteristics on surrounding tissues timely [10]. At the same time, it can also prompt medical staff to compare the dynamic CT images of patients in different periods to analyze the changes and development status of patients' nodules, which has a significant promoting effect on improving the quality and efficiency of diagnosis. This examination method has the characteristics of non-trauma, non-radiation, repeatable operation and high safety, so as to promote the quality of diagnosis, safety and value can be effectively guaranteed. In the process of chest CT scanning, contrast-enhanced scanning can also be performed on patients with the help of contrast agents, so that doctors can timely and accurately understand the blood supply status of the lesion site of the patients, and accurately judge the nature and development phase of the disease, thus significantly improving the quality of diagnosis again [11].

#### 2.3 Positron emission tomography (FDG-PET) examination for solitary pulmonary nodule

FDG-PET examination is mainly used in the diagnosis of neoplastic diseases and the evaluation of treatment. The sensitivity and specificity range of FDG-PET examination is obviously larger when it is used to diagnose solitary pulmonary nodule. According to detailed classification studies, the sensitivity and specificity of FDG-PET examination for nodules with diameter less than 8-10mm are significantly lower, which affects the quality of subsequent diagnosis [12]. The sensitivity and specificity of FDG-PET for nodules with diameter of 8-10mm and above are significantly higher, which can realize the diagnosis and differential diagnosis of the nature of the patient's disease in time. In recent years, with the continuous improvement of our medical level, FDG-PET examination and CT examination are effectively combined in clinical practice, thus forming PET/CT examination [13]. The main principle of this examination method is to inject D-fluorodeoxyglucose-18 radioisotope (FDG) into the client, and then use CT to examine the level of FDG uptake in the nodule of the client, thus achieving diagnosis and differential diagnosis of the disease nature, and the evaluation of the metabolic status of the nodule. Generally, the intake of FDG in malignant nodules is obviously higher. PET/CT examination can also effectively display the nodule status of the client, thus promoting the continuous improvement of diagnostic quality, efficiency and safety.

## 2.4 CT-guided biopsy of solitary pulmonary nodule

CT-guided needle biopsy may be a good diagnosis when the risk of clinical assessment and the imaging findings of the patient's intention and / or the risk of surgery occur. Studies have shown that in people with high incidence of malignant nodules, the positive penetration rate of nodules of 2 to 4 cm in diameter is about 84%. In the population with a low incidence of malignant nodules, the diagnostic positive rate is only 36% to 43%. CT-guided needle biopsy may have a high positive rate when diagnose lung lesions greater than 4cm in diameter. The sensitivity depends on the size of the nodule, the thickness of the needle (especially in patients with lymphoma and benign nodules), the number of punctures, and the diagnostic ability of cytological pathology. Therefore, CT-guided needle biopsy is not a sensitive enough invasive examination method for isolated small pulmonary nodules of less than 3cm in diameter. In addition, considering the tissue heterogeneity of lung cancer cells, the sample size obtained by needle biopsy is relatively small, which sometimes cannot clearly classifies lung cancer. In particular, it should be noted that needle biopsy alone does not confirm the pathological diagnosis of adenocarcinoma in situ and early microinvasive adenocarcinoma. Biopsy is usually used as the gold standard for diagnosis of the disease, which enables doctors to timely understand the specific disease status of the client. However, previous biopsy is blind puncture, which is easy to cause unnecessary

trauma to the patient, and also has adverse effects on the quality and efficiency of diagnosis. The implementation of CT-guided biopsy can significantly improve the accuracy of puncture, as well as the diagnostic accuracy and efficiency [14, 15]. In this process, doctors also need to reasonably select puncture needle diameter and puncture times according to the size of nodules in time, so as to significantly improve the quality and efficiency of diagnosis again [16, 17].

In 2007, the American association of thoracic surgeons (ACCP) established guidelines for pulmonary isolated small nodules, mainly based on two factors: the risk of malignant tumors (age, previous malignant tumor history and smoking history is the high risk factor of malignant nodules) and nodules (enclosed size, morphology and doubling speed). The guidelines regulate the stratification of risk factors, the choice of imaging methods, the frequency of imaging follow-up, and the timing of surgical intervention. The National Cancer Institute (National Cancer Institu-te, NCI) of a 10-year lung cancer screening test latest results show that spiral CT screening for high-risk groups including smokers or former smokers can reduce lung cancer mortality by about 20%, this is a strong evidence-based medical evidence supporting lung cancer screening, in October 2010 through the NCI website, and on June 29, 2011, published online in the New England Journal of Medicine.

#### 2.5 MRI and dynamic MRI

The potential application value of MRI rapid imaging technology cannot be underestimated. Enhanced MRI has the characteristics of multi-level multi-sequence imaging and the characteristic signal enhancement characteristics, which can accurately reflect the characteristics of SPN, which is why it far exceeds CT technology. Enhanced MRI can provide better and more accurate information for clinical diagnosis and provide more feasible options for treatment. MRI dynamic enhanced scanning has proved well suited for assessing the nature of the SPN. Studies on dynamic MRI scanning to identify benign and malignant diseases have also been conducted in recent years. Kono et al studied the MRI enhancement characteristics of benign and malignant SPN by dynamic MRI method. The time to the maximum reinforcement rate of lung nodules was 4 min, and the maximum reinforcement rate of tuberculosis and hamartoma exceeded 4m in or gradual reinforcement without peak time. Cronin A Meta-analysis comparing the accuracy of CTMRI deoxy (FDC) -PET and SPECT for SPN showed that the diagnostic accuracy of dynamic MRI was comparable to dynamic CT, but the specific MRI was higher than CT. For the diagnosis of SPN, MRI is still at the research level due to the restriction of surgical preparation and economic factors.

## 2.6 Molecular imaging

Molecular imaging can clarify the staging and classification of the disease to determine the malignant degree and prognosis of the swelling, and improve the level of clinical diagnosis and treatment. Many scholars have tried to study SPN by using molecular imaging methods. Wang et al. showed that some CT signs of lung cancer were closely related to the DNA content of the nucleus, and the DNA content of tumors with spines increased, and the increase of alloploid cells had strong proliferation and invasion. With the development and progress of molecular and biotechnology in recent years, the targeted diagnosis and treatment of pulmonary nodules have become a new development of molecular imaging. In the early stage, some proteins called "tumor markers" are always overexpressed on the surface of tumor cells as targets for selective delivery of therapeutic drugs. With the deepening of research, it is currently believed that the effects of tumor markers such as growth factors and their receptors can be selectively targeted and blocked by pharmacologically active substances, such as monoclonal antibody toxins or radioisotopes, antisense cyribenzoan acid, immunolipososome dual specific antibodies, etc.

## 3. Treatment of solitary pulmonary nodule

## 3.1 Drug therapy

Drug therapy has high safety, but its treatment cycle is relatively long and the adaptation group is relatively limited. This kind of treatment is mainly used in patients with symptoms of fungal and tuberculosis infection, and the symptoms of patients can be improved timely by taking corresponding antibacterial drug treatment [18]. Before taking this examination method, the corresponding pathogen examination measures should be taken in time to promote the subsequent treatment effect to be effectively guaranteed.

#### 3.2 Surgical treatment

Surgery is still the "gold standard" for the diagnosis of benign and malignant isolated small nodules in the lung, and it can provide radical surgical treatment for early non-small cell lung cancer at the same time. However, the choice of surgery as a diagnostic strategy must weigh the benefits and surgical risks of a clear pathological diagnosis and further treatment. Surgical procedures should be avoided as far as possible. And biopsy, as a human operation, has certain risks and complications, and cannot make clear pathological diagnosis for a small number of patients. Follow-up observation of imaging can avoid the operation of some benign patients, but for patients with malignancy, follow-up observation may delay timely diagnosis and treatment.

Thoracoscopic surgery and thoracotomy are optional surgical methods for the diagnosis and treatment of isolated small nodules in the lung. The choice of surgical methods depends on the specific situation of the patient. In the medical center with conditions, thoracoscopic surgery is a more commonly used surgical method, while thoracotomy can also be selected in some cases where thoracoscopic surgery cannot be performed. When small nodules are diagnosed as primary lung cancer, surgery can achieve the purpose of further treatment and definite staging. The sensitivity and specificity of benign and malignant patients used to identify small pulmonary nodules are as high as 100%, while the mortality rate is about 1%. For small peripheral nodules diagnosed with nonsmall cell lung cancer, thoracoscopic lobectomy and mediastinal lymph node dissection are the standard radical surgery 16]. Thorthotomy is also the standard procedure for non-small cell lung cancer, but its complication rates and mortality are relatively high, reported as 34% and 4%, respectively. Of course, localized lung segment resection or wedge resection are also acceptable therapeutic strategies for patients with unsatisfactory cardiopulmonary function.

Surgery is one of the more effective measures for the treatment of solitary pulmonary nodule. With the continuous improvement of medical technology, clinical operations are mostly minimally invasive, which can effectively reduce the area of trauma, pain, intraoperative blood loss, etc., and promote the efficient recovery of patients. For solitary pulmonary nodule, video-assisted thoracoscopic (VAST) surgery is often used in clinical practice, either alone or in combination. It significantly reduces the treatment risk for patients [19]. During the surgical treatment of this disease, it is necessary to closely observe whether the patient has symptoms of nodule metastasis. If no symptoms of metastasis occur, thoracoscopic guided wedge resection is the preferred surgical method in the clinic. This surgical method is mainly used in patient group with lesion diameter less than 2cm, older patients, significantly poor lung function, previous history of lobectomy, incisal margin over 1cm, and lesions in 1/3 of the peripheral pulmonary zone. When the location of the patient's nodules is deep or the resection range is obviously small, accurate positioning should be performed on the patient in time before surgical method evaluation, and thoracotomy can be performed if necessary [20]. Existing evidence-based medical evidence suggests that anatomical segmental resection or wedge resection is currently only applicable to the following cases: a tumor diameter less than 2cm and located in 1/3 of the peripheral zone, resection margin> 1cm (smaller than tumor than 1) at 75 years or a history of previous lobectomy, or poor lung function to tolerate lobectomy, or lesions (preinvasive lesions or carcinoma in situ).

### 3.3 Other treatment measures

In addition to surgery and drug therapy, radiotherapy and radiofrequency ablation are also effective ways to treat solitary pulmonary nodule. Such surgery is mainly applied to patients with significantly poor cardiopulmonary function and patient's physical fitness that is too weak to receive surgical treatment [21]. The specific effect of this type of treatment needs to be further studied, and the follow-up relevant personnel can strengthen the research on this type of treatment in the future.

#### 4. Conclusions

In recent years, the incidence of isolated pulmonary nodules has increased, which is mainly closely related to people's daily work and living environment, air quality, living habits, and health awareness. In this regard, people need to pay more attention to this disease and timely take corresponding preventive measures according to the influencing factors. In addition, there are still some controversies about the surgical treatment method and effect of this disease. The safety and effectiveness of lung cancer screening have been supported by strong evidence-based medical evidence, and the standard lung cancer screening should be put into action immediately. More evidence-based medical evidence is

expected for the controversy over early lung cancer surgery. Under the guidance of preoperative CT, Hookwire positioning technology is safe and effective, and it is worth popularizing in qualified medical centers. New classification of lung adenocarcinoma: more specific and detailed, helpful for the implementation of individualized treatment decisions for lung cancer patients. In this regard, relevant institutions need to continuously strengthen the research on the treatment of such diseases to promote the continuous improvement of the treatment level.

#### References

- [1] Wu XY, Ding F, Li K, et al. Analysis of the Causes of Solitary Pulmonary Nodule Misdiagnosed as Lung Cancer by Using Artificial Intelligence: A Retrospective Study at a Single Center. Diagnostics (Basel), 2022,12(9).
- [2] Jokerst C, Adler C, Gotway M, et al. Dual Energy Technique Adds Value to Solitary Pulmonary Nodule Analysis with Dynamic Contrast-Enhanced CT: A 100 Nodule Experience. Curr Probl Diagn Radiol, 2023,52(1):25-30.
- [3] Wang Yubo, Cao Guoqiang. Early diagnosis of isolated pulmonary nodules. Journal of Clinical Pulmonary Science, 2012,17 (7): 1302-1303.
- [4]Liu Jilu, On the diagnosis of isolated nodules in the lungs. Guidelines for Health care, 2017, (2): 218.
- [5] Chen Ming, CT diagnosis and differential diagnosis of solitary nodules in the lungs. The World's Latest Medical Information Abstract (Continuous Electronic Journal), 2019,19 (51): 172,175.
- [6] Gu Mingzhong, Chen Jinbei, Wang Wencai, Qiu Aimin. Lung primary isolated small nodules of 62 cases of clinical analysis. Sichuan Medicine, 2008,29 (11): 1546-1547.
- [7] Duke JD, Fernandez-Bussy S, Reisenauer J. Combined portable cone beam computed tomography and robotic-assisted bronchoscopy impacting diagnosis of a solitary pulmonary nodule: a case report. AME Case Rep, 2022,6:23.
- [8] Yuan CT, Chen JS, Huang YL, et al. ALK-positive histiocytosis presenting as a solitary pulmonary nodule. Br J Haematol, 2022, 199(1):7.
- [9] Kosaka T, Iizuka S, Yoneda T, et al. Solitary pulmonary nodule as the initial manifestation of isolated metastasis from prostate cancer without bone involvement: A case report. Int J Surg Case Rep, 2022,90:106681.
- [10] Jiang Xinhua and Yu Dongping. Current status and progress of perfusion imaging of isolated pulmonary nodules. Jiangxi Medicine, 2011,46 (7): 670-673.
- [11] Kang L A, Yl A, Envelope P F C B P, et al. Assessing the impact of digital economy on green development efficiency in the Yangtze River Economic Belt[J]. Energy Economics, 2022, 112.
- [12] Huang J. Research on Tax Planning of PPP Projects in China: Based on the Perspective of Digital Economy. J. Journal of Financial Research (English), 2020, 4(2):7.
- [13] Zhuo Y, Zhan Y, Zhang Z, et al. Clinical and CT Radiomics Nomogram for Preoperative Differentiation of Pulmonary Adenocarcinoma From Tuberculoma in Solitary Solid Nodule. Front Oncol, 2021,11:701598.
- [14] Jiang Yifei. Clinical analysis of 42 cases of peripheral pulmonary solitary nodules with CT-guided percutaneous lung puncture biopsy. 2005.
- [15] Huang Feng, Chen Xiaoqi, Qi Le. Clinical study on the size of solitary pulmonary nodules and puncture biopsy. Journal of Clinical Medicine, 2006,(10):1023-1024.
- [16] Shangang L, Chengli L, Xuejuan Y, et al. Diagnostic accuracy of MRI-guided percutaneous transthoracic needle biopsy of solitary pulmonary nodules. Cardiovasc Intervent Radiol, 2015,38(2).
- [17] Govindraj R, Chowdhry F, Ang K, et al. Intra-operative frozen section diagnosis of the suspicious solitary pulmonary nodule, how can we improve the strike-rate. J Cardiothorac Surg, 2013,8(1suppl).
- [18] Li H, Zou J, Li J. Organizing pneumonia with solitary focal nodule and subsequent multiple pulmonary shadows. Am J Med Sci, 2022,364(1):e4-e5.
- [19] Cong CV, Luong DV, Anh TT, et al. Pulmonary arteriovenous malformation and inherent complications with solitary lung nodule biopsy-literature overview and case report. Radiol Case Rep, 2022,17(7):2353-2361.
- [20] Ko JP, Bagga B, Gozansky E, et al. Solitary Pulmonary Nodule Evaluation: Pearls and Pitfalls. Semin Ultrasound CT MR, 2022,43(3):230-245.
- [21] Yu L, Zhang B, Zou H, et al. Multivariate Analysis on Development of Lung Adenocarcinoma Lesion from Solitary Pulmonary Nodule. Contrast Media Mol Imaging, 2022,2022:8330111.