Literature Review

The Solitary Pulmonary Nodule: Is It Benign or Malignant?

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Abstract

Solitary pulmonary nodules (SPN) are round-shaped opacities with or without firm borders and ≤3 cm in diameter. 40% of solitary pulmonary nodules in high-risk populations are malignant and >10 mm in diameter. With the high incidence of pulmonary cancer, diagnosing pulmonary nodules is essential for clinicians. This review aims to discuss more solitary pulmonary nodules based on multiple recommendations for diagnosis and management. Malignancy probability assessment is the first step in evaluating each patient with new pulmonary nodules, as it significantly affects the prognosis of the disease. The assessment depends on the risk factors present in the patient, which are cigarettes, age, history of cancer, and family history. Radiological evaluation is the second phase in pulmonary nodule evaluation. Predictors of malignant nodules that should be assessed are nodule size, growth rate, nodule morphology, location, and enhancement. Many guidelines have been published regarding treating solitary pulmonary nodules, including the Fleischner Society, ACCP, and BTS guidelines.

Keywords: benign, malignant, pulmonary nodule management, solitary pulmonary nodule

INTRODUCTION

Solitary pulmonary nodules (SPN) are defined as round-shaped opacities with or without firm borders and ≤3 cm in diameter. Spherical lesions with a more than 3 cm diameter are associated with lung masses and can be indicated as lung cancer until proven otherwise histologically.[1] Solitary pulmonary nodules are generally lesions due to benign abnormalities such as infections, inflammations, and vascular and congenital abnormalities. However, 40% of solitary pulmonary nodules in high-risk populations are malignant and >10 mm in diameter. With the high incidence of pulmonary cancer, diagnosing pulmonary nodules is essential for clinicians.[2]

The initial identification process in cases of malignant nodules significantly affects the prognosis of the disease.[3] The initial step in the nodule assessment is the evaluation of clinical parameters such as signs and symptoms, the patient's age, smoking history, exposure to carcinogens, family history of cancer, clinically related

lung disease, and previous history of the disease. The next step is the evaluation of the radiological picture. The main parameters assessed in the radiological evaluation are the nodule's size and speed of growth. Other parameters that can be assessed are spiculated, lobulation, vascular convergence, and pleural retraction.[2]

Supporting examinations are also needed to identify cases of pulmonary nodules. Some modalities that can be done include Thin-section Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), Positron emission tomography (PET), and PET/CT integration to help diagnoses become more accurate in nodule characterization. Clinical follow-up is still needed to help establish a diagnosis in cases of small nodules, and a definitive diagnosis still requires a tissue biopsy.[2,3]

Pulmonary nodules can be divided into solid and subsolid with different morphological and pathological features based on density.[1] Most subsolid nodules are transient and arise due to infection or bleeding. Granulomas, lymph nodes, primary malignancies, or metastases can cause solid nodules. Subsolid nodules are more likely to exhibit indolent growth patterns, and subsolid nodules diagnosed with malignancy have a high overall cure rate.[4,5]

In a systematic study, 712 lung cancer cases with ground-glass opacity manifestations were stage I adenocarcinomas with a five-year survival rate of 100%.[4] In contrast, malignant solid nodules have a worse prognosis than malignant subsolid nodules with rapid growth and earlier metastases.[3]

With the complications associated with the biopsies or repeated "unnecessary" CT scans of the chest, a systematic approach becomes essential in evaluating these nodules.[6] Many guidelines have been published regarding the treatment of solitary pulmonary nodules. The Fleischner Society guidelines are guidelines for pulmonary nodules found incidentally.[7]

Meanwhile, the American College of Chest Physicians (ACCP) and British Thoracic Society (BTS) guidelines do not distinguish between incidental and screening-detected nodules. There are some differences between the three guidelines. The Fleischer Society recommendations emphasize the initial inspection, whereas the ACCP and BTS guidelines include the evaluation and treatment.[2]

This literature review discusses more solitary pulmonary nodules based on multiple recommendations for diagnosis and management.

DEFINITION, EPIDEMIOLOGY, AND RISK FACTORS OF SOLITARY PULMONARY NODULE

The Fleischner Society defines solitary pulmonary nodules as a single nodule, round-shaped, well-defined with an opaque appearance and a diameter of less than or equal to 3 cm, and surrounded by normal lung parenchyma without other abnormalities such as enlarged lymph nodes, atelectasis, or pleural effusions.

Lung masses with a diameter of >3 cm are considered lung cancer until proven otherwise.[1]

Pulmonary nodule is seen in 150,000 Americans annually. Thoracic CT scans in clinical practice increased pulmonary nodule detection. In 2006 and 2012, U.S. thoracic CT scans detected 3.9 to 6.6/1000 lung nodules yearly. Baseline screening found 20% of nodules in a 2012 systematic study. Eight randomized controlled studies reported a 3%–30% prevalence, while 13 cohort studies reported 5–51%. Most studies report <5-10% malignant nodules, meaning 90-95% are false positives.[4] It poses a challenge for clinicians and radiologists to eliminate the diagnosis of malignant nodules, but they want to avoid invasive examinations and procedures.[8]

Malignancy probability assessment is the first step in evaluating each patient with new pulmonary nodules. The assessment depends on the risk factors present in the patient, including the following.

Cigarette

Smoking causes lung cancer and 85% of cancer fatalities. Smoking number and duration affect lung cancer risk. According to the meta-analysis, men's lung cancer risk increased with the number of cigarettes they smoked daily: <10 cigarettes (4.97 times), 10-20 (8.93 times), and > 20 (14.61 times). Smoking duration also increases lung cancer risk, 0-20 years 1.23 times, 20-30 years 2.98 times, 30-40 years 7.84 times, 40-50 years 12.82 times, and >50 years 28.94 times.[2] Passive smokers were also at risk for malignancy.[9]

Age

Older age is associated with an increased likelihood of malignancy in patients with pulmonary nodules. The majority of cancer cases (>50%), including lung cancer, are found at the age of >70.[1] SPN is a rare finding in the pediatric population and, as a result, when the finding is incidental, it is difficult to narrow down the differential diagnosis, especially for the untrained eyes.[10]

History of Cancer

Individuals who have survived lung cancer have a heightened likelihood of developing subsequent primary lung cancer. According to research on patients with early-stage non-small cell lung cancer (NSCLC) who underwent resection surgery, second lung cancer was nearly 7x higher during the initial year following the surgery. The risk remains 4x higher after ten years. Patients with squamous cell carcinoma or other cigarette-related malignancies (pancreatic or bladder cancer) are at a heightened risk of developing primary lung cancer.[1]

Family History

The familial background of an individual is a noteworthy determinant of risk. Individuals who have a first-degree family history of lung cancer are at a twofold increased risk of developing lung cancer. Individuals with multiple family

members diagnosed at a young age are at an increased risk.[1]

Another risk factor for lung cancer, such as exposure to carcinogens (asbestos, uranium, radon), has been described in studies. Prolonged exposure to coal dust or mineral dust (silica or beryllium) can also cause the appearance of lung nodules.[11] Emphysema and chronic obstructive pulmonary disease were also evaluated as risk factors for lung malignancy.[12,13]

CLASSIFICATION OF SOLITARY PULMONARY NODULES

The categorization of pulmonary nodules is based on their density (Figure 1), which classifies them as either solid or subsolid. Subsolid pulmonary nodules can be classified into two categories: non-solid or pure ground glass nodules, which do not obstruct broncho-vascular structures, and part-solid nodules, which consist of ground-glass opacity with solid components. The pulmonary parenchyma underlying subsolid nodules remain observable. The term ground-glass opacity is commonly used to describe this phenomenon.[3] Solid nodules are the most common type, with radiodensity characteristics in the form of homogeneous soft tissues.[1]

Granulomas, lymph nodes, primary malignancies, or metastases can cause solid nodules. Subsolid nodules are predominantly transient and manifest as a result of infection or hemorrhage. If subsolid nodules persist, they result in adenocarcinoma pathology. Non-solid nodules can be non-invasive, minimally invasive, or lepidic-predominant adenocarcinomas. The majority of part-solid nodules, meanwhile, are invasive adenocarcinomas. Most of the nodules detected by screening have solid characteristics.[4]

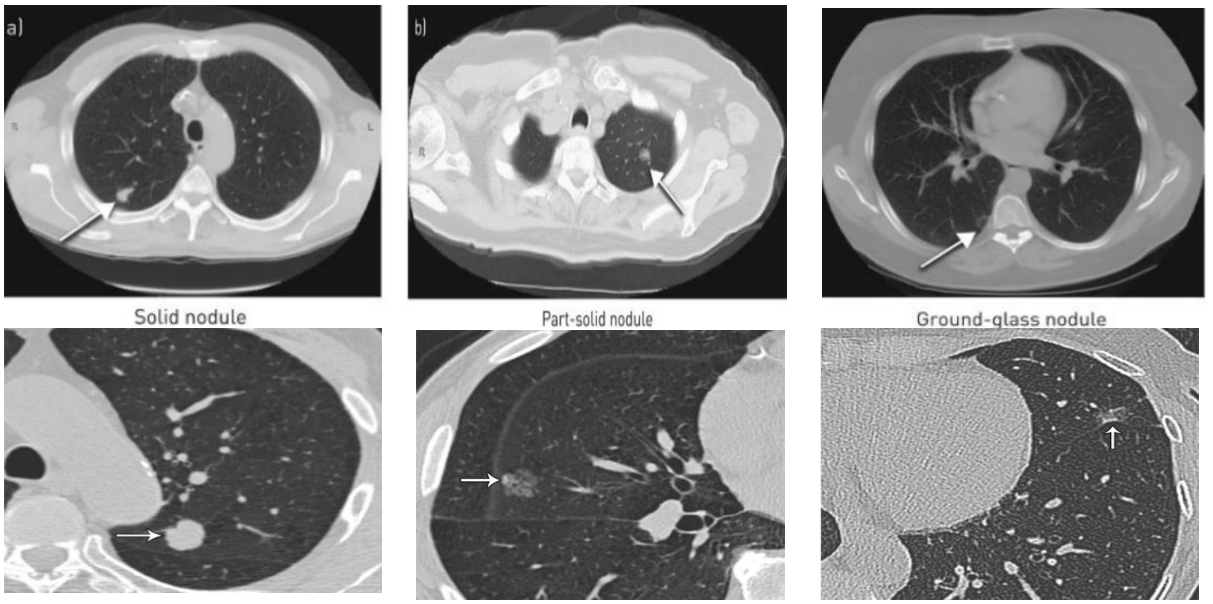

Figure 1. Classification of pulmonary nodules by density
(A) solid nodule; (B) part-solid nodule; (C) ground-glass nodule.[14]

According to Henschke et al's research, the probability of malignancy is higher in sub-solid or part-solid nodules than in solid nodules. Most pulmonary solid nodules are benign. The majority of solid nodules, approximately 80%, are granulomas and intrapulmonary lymph nodes. Hamartomas account for approximately 10%, while the remaining 10% are attributed to other benign lesions.[15]

Based on their clinical presentation, SPNs can be divided into three groups: incidental SPNs, symptom-associated SPNs, and screen-detected SPNs. This classification method is helpful since the clinical presentation affects the likelihood that the nodule is malignant. An SPN can be seen on imaging performed for nonpulmonary clinical indications, termed an incidental SPN.[16]

Symptom-specific SPNs are those identified after chest imaging that was explicitly done to determine the origin of respiratory complaints. Screen-detected SPNs are SPNs that are found on a screening LDCT (low-dose computed tomography).[16]

DIAGNOSIS OF SOLITARY PULMONARY NODULES

Non-solid nodules tend to grow slowly. Overall, malignant non-solid nodules have a high cure rate.[4] Due to their rapid growth and early metastasis, malignant solid nodules have a worse prognosis than non-solid ones. Therefore, the early identification of malignant solid nodules significantly affects the prognosis.[3] Radiological evaluation is the second phase in pulmonary nodule evaluation. Assessment of lung cancer risk is based on nodule size and growth rate. Other imaging features have been identified as predictors of benign and malignant nodules.[1]

Using screening CT scans, men are more likely than women to have an SPN of 18.8% versus 16.3%, respectively. Men still had more SPN findings than women when a chest X-ray was used for screening, with incidence rates of 2.5% and 1.6%, respectively. On the other hand, in the non-smoking group, women did have a higher incidence of having an SPN than men.[17]

Predictors of Benign Nodules

Several benign nodule predictors exist. Perifisural nodules are solid nodules in contact with the fissure or pleural surface. These nodules are considered benign nodules and most likely describe intrapulmonary lymph nodes. After long-term follow-up, no patients with these nodules developed lung cancer.[3]

Calcified pulmonary nodules are rarely cancerous. However, some preliminary research indicated calcification in 10% of lung cancer cases. Thus, the calcification pattern should be prioritized. Diffuse, central, laminated, and popcorn calcification patterns indicate benignity. In contrast, punctate, eccentric, and amorphous calcification patterns cannot rule out malignancy.[1]

The BTS guideline advised not investigating small, homogenous, well-defined perifissural and subpleural nodules. However, the Fleischner Society Guideline states that perifissural and subpleural locations do not rule out malignancies. Other risk factors, such as morphology and clinical condition, should be considered when determining treatment.[1]

Predictors of Malignant Nodules

Size

Malignancy is closely correlated with nodule size. The current guideline proposes a low-risk indicator (<1%) of <6 mm based on high-risk patients' lung cancer screenings. The threshold works for single and multiple solid nodules. The second clinically relevant threshold is >8 mm in diameter. According to the NELSON study, solid nodules of 8 mm had a 9.7% chance of lung cancer, whereas those of 5-8 mm had a 1% chance.[1]

The Fleischner Society classified pulmonary nodules into acinar, which usually measures 5-8 mm and shows consolidations in the acinus. Opacities ≤3 mm, are called micro nodules.[18] A CT scan is needed to detect nodules under 1 cm.[19] Wahidi et al. examined several studies that compared nodule size with malignancy frequency.[20]

Solitary pulmonary nodules <5 mm have a malignancy rate of less than 1%, even in the high-risk category, while 5-10 mm and >2 cm nodules had 6-28% and 64-82%, respectively. Pulmonary nodules >10 mm have a 33-60% probability of cancer, according to other research.[20] Malignancy is more likely in lesions larger than 3 cm.[21]

Growth Rate

Pulmonary nodules are often cancerous. Incidentally detected nodules should be compared with previous imaging data. Nodules may not need further investigation if they are stable. CT surveillance for pulmonary nodules is based on the rapid growth of lung cancer lesions. Volume-doubling time (VDT), the most sensitive marker of nodule growth, is rarely used in clinical practice. One VDT shows 26% nodule diameter growth. Most lung cancers have a VDT of 400 days, with the highest malignancy risk at 100 days. However, a VDT of >400 days does not exclude the possibility of malignancy.[1]

In the NELSON research, VDT >600 days had 0.8% malignancy risk, 400-600 days 4%, and <400 days 9.9%. Cruickshank et al. found that lung cancer VDT averages 139 days. Bronchial carcinoma VDT is 1-18 months. VDT <20 days suggests infection. VDT over 500 days predicts malignancy 98% negatively. BTS guidelines recommend VDT for lung nodules over 6 mm.[18,21]

Since only 1% of malignant nodules maintain growth stability or size for two years, solid pulmonary nodule growth stability is measured over two years. Adenocarcinoma in situ and minimally invasive cancer had VDTs of 457-812 days, while sub-solid nodules grew slower. Sub-solid nodules require extended follow-up.[21]

Morphology and Location

Nodule morphology can also predict cancer. Spiculated nodule margins have

consistently been linked to lung cancer risk.[22] Lung cancer has been associated with lobulated margins, as in Figure 2.[3] Upper lobe lung cancer is the most common location. Pleural retraction, vascular convergence, and air bronchogram are less common malignancies characteristic.[1]

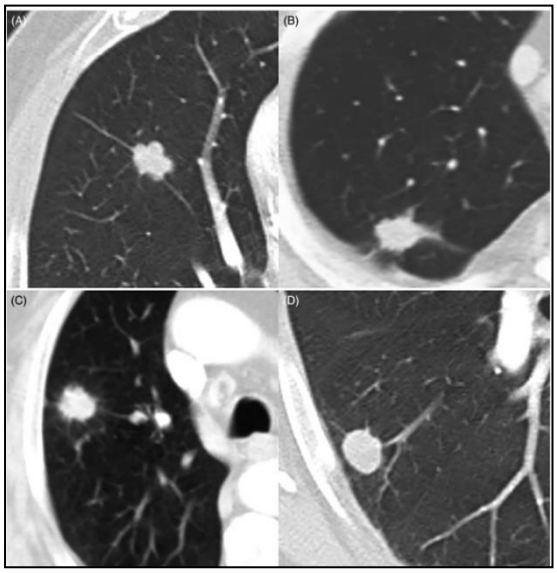

Figure 2. The morphology of the margin of a solitary pulmonary nodule. (A) lobulation, (B) irregular, (C) spiculated, (D) well-defined round-shaped. [21]

There is calcification or fat attenuation in pulmonary nodules. Calcified solitary pulmonary nodules are most likely benign.[15,18] Non-contrast CT images reveal calcifications with >200 HU attenuation. Calcification characteristics include dense central nodules, solid diffuse, laminated, popcorn, punctate, and dendriform structures. Pulmonary hamartomas exhibit calcification resembling popcorn, whereas the first three forms indicate benign lesions. Calcified nodules are also present in primary central lung carcinoid, metastasis, and primary bronchogenic carcinomas.[21]

Amorphous, punctate, and reticular calcifications characterize primary lung cancer calcification. Dystrophic calcifications result from granulomas or tumor necrosis. Mucinous adenocarcinoma may first calcify. In malignant solitary pulmonary nodules, calcifications may present in larger sizes and are usually stippled and eccentric.[15,18] Pulmonary metastasis from bone malignancies is usually also characterized by solid calcifications.[15] Calcification rate in carcinoid cancers is approximately 8-35%.[21]

Fat in the solitary pulmonary nodule indicates benign lesions like pulmonary hamartomas, lipoid pneumonia, and lipomas.[18,23] CT scans show fat in 50% of pulmonary hamartomas.[17] Imaging criteria for benign pulmonary nodules include nodule stability for at least two years or calcification with specific characteristics like in Figure 3 (calcification in all nodules, central/bull's-eye calcification, eggshell calcification). A 30-150 HU density test confirms fat in the nodule and reliably identifies benign lung lesions.[18,23]

The cavity is an air-filled space that appears as a lucency or low attenuation picture in lung consolidation, mass, or nodule. Cavities occur in benign lesions like infections and inflammation and malignant single lung nodules like squamous cell carcinoma.[18,21,24]

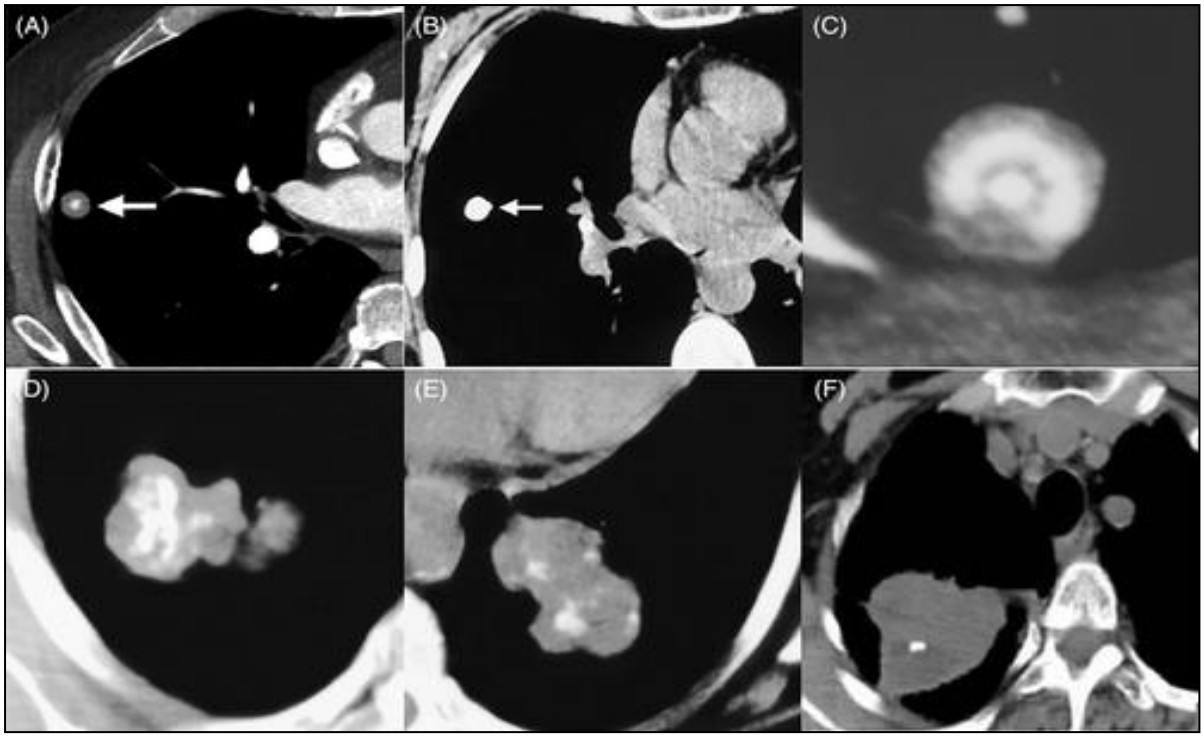

Figure 3. Calcification descriptions in pulmonary nodules. (A) central or "bull's eye" calcifications in benign granulomas; (B) diffuse calcification in benign granulomas; (C) laminated calcification in benign granulomas; (D) popcorn calcification in pulmonary hamartoma; (E) punctate calcification in malignant carcinoid tumor; (F) eccentric calcification in primary pulmonary adenocarcinoma.[21]

Pulmonary tuberculosis abscesses, histoplasmosis, aspergilloma, Wegener granulomatosis, Churg-Strauss syndrome, and rheumatoid arthritis can create benign lesion cavities. Central necrosis causes malignant lesion cavities. Wall thickness indicates cancer risk. Malignant tumors have thick, uneven walls, while benign lesions have thin, smooth walls. 95% of cavity nodules with walls thicker than 15 mm are malignant, while 92% with walls thinner than 5 mm are benign. Because 51% are benign and 49% are malignant, the 5-15 mm cavity wall thickness cannot tell whether the nodule is cancerous or benign.[18,21,24]

Air bronchograms show an air-filled bronchus surrounded by a solid, airless lung, frequently due to illness. The air bronchogram sign is common in malignant solitary pulmonary nodules such as adenocarcinomas.[21]

Solitary pulmonary nodules are usually circular or oval. Round solid nodules are less likely to be malignant, although subsolid round nodules are more likely to be malignant.[24] Perifisural nodules (PFN) are linked to intrapulmonary lymph nodes. Intrapulmonary lymph nodes (IPN) are commonly characterized by fissures or interlobular septa associated with solid nodules featuring smooth borders and shapes such as triangular, polygonal, oval, or lentiform.[18,24]

Perifisural nodules are frequently below the carina and 15 mm from the fissure or pleura. Atypical IPN is a nodule with a less evident fissure or a lesion with a convex and rounded side. PFN, a benign solid lung nodule, can double in size like

malignant ones. However, spiculated or fissure-crossing PFN should be followed.[18,24]

One-third of pulmonary nodules metastasize in the lower lobes, but most are in the upper lobes, notably the right. Nodules in the upper lobes of the lung had a 1.9-fold higher risk of malignancy, with the right upper lobe having the highest rate at 45%. In smokers, higher airflow in the right upper lobe during inspiration increases carcinogen exposure. 60% of pulmonary nodules are peripheral, mainly subpleural. Granulomas and IPNs also prefer subpleural locations. Perifissural nodules are oval or triangular solid nodules near the pleural fissure that are usually benign and do not need further imaging. Perifissural nodules with considerable risks, such as irregular spiculated margins and fissure distortion, require further imaging.[24]

A nodule's margin also influences its malignancy. Benign lesions have smooth, rounded edges. 21% to 33% of smooth-edged nodules had lung cancer or metastases.[24–26] Malignant cells invade the lung interstitium, causing irregular borders like spiculated or lobulated nodules.[24] The spiculated edges are observed, commonly called corona radiata or sunburst signs. Fibrosis is attributed to tumors in the lymphatic channels or pulmonary blood arteries. Spiculated edges have a 90% positive predictive value for cancer. Lobulated edges are moderately cancerous.[18,24]

Nodules with lobulation grow irregular patterns. It is linked to cancer. Lobulated edges within part-solid nodules may indicate the likelihood of invasive carcinoid tumors. Benign lobulation is a result of connective tissue hyperplasia and scar shrinkage. CT scans must distinguish satellite micro nodules from nodule edges. Benign nodules exhibiting lobulation are associated with hamartomas and granulomatous diseases that display a "notch sign".[24]

Enhancement

Enhancement after intravenous iodine contrast injection distinguishes benign from malignant nodules. Swensen et al. discovered that an enhancement value of >15 Hounsfield units (HU) had 98% sensitivity, 58% specificity, 68% positive predictive value, and 96% negative predictive value for malignancy. MDCT increased the enhancement value threshold. Yi et al found a 99% sensitivity and 54% specificity for cancer detection at >30 HU.[1]

Small Nodule

The previously described characteristics of malignancy help differentiate between benign and malignant nodules. However, these characteristics are usually absent in small lung nodules, making diagnosis more difficult. Increased nodule size makes the lesion more regular, with more apparent signs of edge lesions and invasion of surrounding tissues. Siegelman et al found that lung cancer tumor boundaries were rougher than benign lesions. Chu et al found that tumor-lung boundary roughness increased with nodule size, probably due to

tumor cell infiltration into peripheral tissue.[3]

Solid lung cancer growth is a gradual process. Tumor cells accumulate slowly, and lesion size increases continuously. According to the theory, tumor density becomes more homogeneous on CT scans as lesion size increases. Recent studies have found that more small nodules (especially those with a diameter <1 cm) have heterogeneous densities. Lung cancer is suspected if the density of such nodules increases and becomes homogeneous.[3]

In general, nodule characteristic changes in follow-up using a CT scan effectively differentiate the nature of small solid nodules. Knowing the regular changes in small solid nodules will make identifying suspected malignant nodules easier during follow-up.[3]

DIAGNOSIS OF SPN BASED ON RADIOLOGY EXAMINATION

A fluorodeoxyglucose (FDG) PET/CT improves lung nodule diagnosis by providing anatomical and morphological information from CT components. Yi et al compared PET/CT and High-Definition Computed Tomography (HDCT) for solitary pulmonary nodules. PET/CT outperformed HDCT with 96% sensitivity, 88% specificity, and 93% accuracy. Thus, PET/CT was recommended as the first imaging method for lung nodules.[2]

Fluorodeoxyglucose PET/CT can distinguish benign from malignant solid lung nodules and avoid unnecessary procedures. Malignant solid nodules had higher Standardized Uptake Values (SUVs) than benign ones. Slow-growing malignant tumors have minimal FDG absorption. Pneumonia, TB, amyloidosis, and sarcoidosis also absorb FDG. FDG-PET paired with CT is less specific for malignancy in populations with endemic lung infections, according to a meta-analysis by Deppen et al.[27]

MRI has better soft tissue contrast and spatial resolution; however, motion, respiratory artifacts, and low proton density can affect it. Using gadolinium chelates and new approaches has enhanced MRI lung cancer detection and staging. Diffusion-weighted and perfusion MRI sequences provide morphological and functional information. CT, FDG PET/CT, and MRI characterize nodules non-invasively.[2] The MRI results can also help follow the patients without sufficient PET-CT results.[28]

Artificial neural networks (AI) power deep learning (DL) can detect lung nodules well. Gong et al. found lung nodules with 93.6% sensitivity and one false positive per scan using 3D deep convolutional neural networks. Conventional approaches cannot attain 90% sensitivity. DL research currently classifies lung nodules by histology. Ciompi and Nishio classified nodules with DL models. DL models had 68% classification accuracy versus 55.9% for conventional approaches.[2] Radiomics quantitatively extracts medical picture features (volume, shape, density) for clinical decision-making. Radiomics enhances cancer diagnosis, prognosis, and prediction.[2,29,30]

MANAGEMENT OF SOLITARY PULMONARY NODULE

Accurate measurement is crucial in the management and decision-making process of lung nodules. It can help estimate baseline risk, appropriate management algorithms, and optimize follow-up for lesion growth during subsequent examinations. The evaluation of lung nodules begins with distinguishing solid and subsolid lesions using appropriate techniques.[2]

Fleischner Society

The Fleischner Society advises low-dose radiation CT with a 1.0 mm-section thickness and rigorous comparison of previous CT images for appropriate interpretation. The Fleischner Society criteria for accidental nodules have been revised. The minimal size criteria for solid nodule follow-up have been increased, and periods rather than intervals are recommended.[7]

The Fleischner Society (Table 1) categorizes risk into high-risk (>5%) and low-risk groupings. High-risk variables include older age (>55 years), heavy smoking (>30 pack-years), large nodule size, uneven or spiculated borders, and upper-lobe placement. High-risk patients have emphysema, lung fibrosis, family history, and carcinogen exposure.[2]

The ACCP Guideline

The ACCP recommends serial CT scans based on nodules and patient conditions, as shown in Table 2. This guideline suggests sampling intermediate-risk nodules with or without surgery, considering patient preferences and surgical risks.[2]

Table 1. Treatment Guideline for Lung Nodule according to The Fleischner Society[7]

Initial size	Solitary		Multiple	
	Low Risk	High Risk	Low Risk	High Risk
Solid Nodul				
< 6 mm (<100 mm^3)	No routine follow-up	Optional CT in 12 months	No routine follow-up	Optional CT in 12 months
6-8 mm (100-250 mm^3)	CT in months 6-12, consider CT in months 18-24	CT in months 6-12, consider CT in months 18-24	CT in months 3-6, consider CT in months 18-24	CT in months 3-6, consider CT in months 18-24
> 8 mm (>250 mm^3)	Consider CT in month 3, PET/CT, or tissue sampling	Consider CT in month 3, PET/CT, or tissue sampling	CT in months 3-6, consider CT in months 18-24	CT in months 3-6, consider CT in months 18-24
Ground-glass				
< 6 mm (<100 mm^3)	No routine observation		CT in 3-6 months. If stable, consider CT in 2 and 4 years.	
≥6 mm (>100 mm^3)	CT in 6-12 months to confirm persistence, then CT every 2-5 years		CT in 3-6 months. Further treatments are based on the suspicious nodule.	
Partly-solid				
< 6 mm (<100 mm^3)	No routine observation		CT in 3-6 months. If stable, consider CT in 2 and 4 years.	
≥6 mm (>100 mm^3)	CT in 3-6 months to confirm persistence. If there is no change and the solid component is still <6 mm, annual CT is suggested for 5 years.		CT in 3-6 months. Further treatments are based on the suspicious nodule.	

Table 2. Treatment Guideline for Lung Nodule from ACCP[2]

Initial size	Solitary and Multiple	
	Low Risk	**High Risk**
Solid Nodul		
≤4 mm	Follow-up optional	Follow-up in 12 months. If there is no change, no follow-up is required.
5-6 mm	Follow-up in 12 months. If there is no change, no follow-up is required	Follow-up in 6-12 months. If stable, follow-up in 18-24 months.
6-8 mm	Follow-up in 6-12 months. If there is no change, follow up in 18-24 months.	Follow-up in 3-6 months. If there is no change, follow up in 9-12 and 18-24 months.
>8 mm	Low risk: CT or FDG-PET surveillance Moderate risk: PET or functional imaging High risk: Biopsy or refer for a surgery	
Ground-glass		
≤5 mm	No Follow-Up	
>5 mm	Annual CT surveillance for ≥3 yr	
Part Solid		
≤8 mm	Repeat CT at 2, 12, 24 month	
>8 mm	Repeat CT at 3 months. If persistent: PET-CT, biopsy, or resection	

Table 3. Treatment Guideline for Lung Nodule from BTS[2]

Initial size	Solitary and Multiple	
	Risk <10%	**Risk ≥10%**
Solid Nodul		
<5 mm	No follow-up	No follow-up
5-6 mm	Follow-up CT scan 1 year If stable: a) Based on the volumetric: discharge; b) Based on the 2D non-automated diameter value: follow-up 1-year If unstable: a) VDT >600 days: discharge; b) VDT 400-600 days: consider CT surveillance or biopsy; c) VDT ≤400 days: further examinations and definitive treatments.	
6-8 mm	Follow-up CT scan in 3 months. If stable, follow-up 1 year and estimate VDT. Treatment is based on the recommendations for nodules of 5-6 mm.	
>8 mm	CT surveillance, according to the recommendation for 6-8 mm	PET/CT with risk assessment using the Herder model; a) <10%: CT surveillance; b) 10-70%: biopsy; c) >70%: Surgical resection or non-surgical treatment.
Ground-glass		
≤5 mm	No Follow-Up	No Follow-Up
>5 mm	Follow-up CT at 3 months to confirm the persistence	
	Annual CT x 4 yr	Consider Follow-Up CT, biopsy, non-surgical treatment, or resection.
Part Solid		
Any	Repeat CT at 1, 2, 4 year	Repeat CT, biopsy, or surgical resection.

Risk factors are low (<5%), moderate (5-65%), and high (>65%). Nonsmoking, age <40, no cancer history, well-defined borders, and middle or lower lobe location are low-risk factors.[2]

Smoking >30 pack-years, age >60, history of cancer, spiculated nodule margins, and upper lobe location are high-risk factors. Moderate risk features combine the other two groups.[2]

The BTS Guideline

Brock and Herder risk models and volumetric analysis determine a nodular doubling time in the BTS recommendation. Brock evaluates solid and subsolid nodules; meanwhile, Herder's risk stratification. Computed tomography (CT) should evaluate nodules that exceed the size of 5 mm or 80 mm^3. Stable solid nodules require a one-year follow-up. VDT results guide unstable solid nodule management. PET/CT is essential for controlling nodules with a Brock model malignancy risk of 10% and a diameter or volume of 8 mm or 300 mm^3.[2,19]

The Herder model uses FDG uptake (none, mild, moderate, high) and additional risk factors (age, smoking, cancer history, suspicious nodule morphology) to predict nodule malignancy risk. Based on PET/CT malignancy risk, nodules are treated with CT, tissue samples without surgery, excision surgery, or non-surgical therapy.[2,19] Treatment guidelines for lung nodules can be seen in Table 3.

CONCLUSION

The early detection of lung nodules significantly impacts the prognosis of the disease. The increased utilization of thoracic CT scans in routine clinical settings has led to increased case detection, enabling prompt intervention. Several variables affect the likelihood of malignancy in solitary pulmonary nodules, including clinical and metabolic evaluation, evaluation of nodule characteristics from CT scan images, nodule size, and growth rate. Determining the likelihood of malignancy presents a formidable challenge, yet it remains a crucial step in devising a course of action for subsequent monitoring and treatment.

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