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Review of Clinical Characteristics and Early Screening Strategies for Idiopathic Pulmonary Fibrosis Complicated with Lung Cancer

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Abstract: Patients with idiopathic pulmonary fibrosis (IPF) exhibit a significantly elevated risk of developing lung cancer and poorer prognosis compared to those with pure IPF. Based on existing literature, this study provides a systematic review of the clinical characteristics and early screening strategies for IPF complicated by lung cancer. This complication is characterized by distinctive demographic distribution, specific lung cancer sites and pathological types, as well as nonspecific clinical manifestations. Early screening should focus on high-risk population identification, regular imaging surveillance, and dynamic biomarker monitoring. Establishing standardized screening protocols is crucial for improving patient outcomes.

Keywords: Idiopathic pulmonary fibrosis; Lung cancer; Clinical characteristics; Early screening; Risk factors

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1. Introduction

Idiopathic pulmonary fibrosis is a chronic progressive fibrotic interstitial pneumonia of unknown etiology, with its association with lung cancer recognized by the academic community since the 1960s. Epidemiological studies have confirmed it as an independent risk factor for lung cancer development. The disease exhibits nonspecific clinical manifestations, and pulmonary fibrosis lesions often mask early-stage lung cancer imaging changes, leading to delayed diagnosis and shorter survival periods after confirmation. A deeper understanding of the clinical characteristics of idiopathic pulmonary fibrosis complicated by lung cancer, along with the development of effective early screening strategies, holds significant clinical value for improving outcomes in this special patient population.

2. High-risk population characteristics of IPF complicated by lung cancer

2.1. Demography and Behavioral Risk Factors

Patients with idiopathic pulmonary fibrosis (IPF) complicated by lung cancer exhibit distinctive demographic

characteristics. Relevant studies indicate that the incidence of this condition is higher in males than in females, with the majority of cases occurring in middle-aged and elderly individuals. Most IPF patients with concurrent lung cancer have a history of long-term smoking[1]. Li Na et al. (2024) observed that the age distribution of IPF-associated lung cancer patients is generally advanced, with aging playing a significant role in disease progression. The study also revealed that IPF patients exhibited lower preoperative serum albumin levels and higher C-reactive protein levels, reflecting poorer nutritional status and more pronounced inflammatory manifestations[2]. Kong Wei (2026) conducted research on antifibrotic agents, with baseline data showing that IPF patients had an average age exceeding 60 years, with a slightly higher male predominance compared to females—characteristics consistent with the high-risk profile of IPF complicated by lung cancer[3].

2.2. Pulmonary Function and Disease Progression Characteristics

The rate of disease progression in patients with idiopathic pulmonary fibrosis (IPF) is associated with the risk of lung cancer development. Lu Qiangwei et al. (2022) concluded that rapid deterioration of forced vital capacity (FVC) is a risk factor for lung cancer in IPF patients. IPF patients with concurrent emphysema exhibit an even higher risk of lung cancer[1]. An accelerated decline in pulmonary function can serve as an indicator of IPF disease progression and for predicting potential lung cancer risk. In clinical follow-ups, IPF patients showing accelerated deterioration in pulmonary function require heightened attention to concurrent lung cancer during diagnosis and treatment. Li Hongmei (2022) noted in a review that pirfenidone and nintedanib exert anti-fibrotic effects, delaying IPF progression. Standardized anti-fibrotic therapy can help control the rate of pulmonary function decline in these patients. However, existing studies have not provided definitive conclusions regarding lung cancer risk in such patients; even with standardized anti-fibrotic treatment, continuous lung cancer screening remains essential[4].

3. Oncological Characteristics of IPF Complicated with Lung Cancer

3.1. Anatomical Location and Distribution Characteristics of Lung Cancer

Idiopathic pulmonary fibrosis (IPF) complicated by lung cancer exhibits a distinctive distribution pattern at the site of disease onset. Current studies indicate that lung cancer lesions are predominantly concentrated in areas with severe pulmonary fibrosis, particularly in the peripheral regions of the lungs where honeycomb lung and transitional fibrosis lesions are commonly observed. In their study on IPF patients with non-small cell lung cancer (NSCLC), Xiao Ting et al. (2022) noted that NSCLC lesions often develop progressively from the honeycomb areas of IPF[5]. At the lobar level, lesions predominantly occur in the lower lobes, followed by the upper lobes, with peripheral lung cancers accounting for an exceptionally high proportion of lung field distributions, while central-type cases are relatively rare. This distribution pattern closely aligns with the pathological changes observed in IPF, suggesting that the fibrotic microenvironment provides favorable conditions for the initiation and progression of lung cancer.

3.2. Pathological Type Characteristics of Lung Cancer

The existing literature reports inconsistent findings regarding the pathological types of idiopathic pulmonary fibrosis (IPF) complicated by lung cancer. Most studies identify squamous cell carcinoma as the most common type, while some studies indicate a higher prevalence of adenocarcinoma. Lu Qiangwei et al. (2022) proposed in a relevant review that regional variations in study populations, sample selection criteria, and diagnostic standards may contribute to these discrepancies[1]. Small cell carcinoma, large cell carcinoma, and mixed carcinoma are less frequently observed clinically. The pathological manifestations of lung cancer in IPF patients differ from those in the general lung cancer population, with malignant lesions often adjacent to areas of pulmonary fibrosis. He Xing et al. (2021) conducted a molecular analysis revealing a higher detection rate of TP53 mutations in this patient cohort, suggesting that genetic abnormalities play a role in the pathological progression from IPF to lung cancer[6]. Kong Wei (2026) noted in anti-fibrotic treatment studies that nintedanib exhibits both anti-angiogenic effects on fibrosis progression and antitumor activity[3].

3.3. Clinical Staging and Prognostic Characteristics

Patients with idiopathic pulmonary fibrosis (IPF) complicated by lung cancer are often diagnosed at intermediate or advanced stages. A meta-analysis by Shi Xiaoyan et al. (2021) demonstrated that the proportion of stage III and IV patients was significantly higher than that of stage I and II patients. This phenomenon stems from multiple factors: the cough and dyspnea symptoms of IPF overlap with those of lung cancer, making early-stage lung cancer signs easily overlooked; additionally, the scar tissue formed by pulmonary fibrosis can mask the imaging features of early-stage lung cancer, increasing diagnostic difficulty[7]. Such patients exhibit shorter survival compared to those with isolated IPF. Li Na et al. (2024) reported that NSCLC patients with IPF had lower overall survival and recurrence-free survival rates postoperatively than those without IPF, with causes of death including progression of lung cancer itself, acute exacerbations of IPF, and complications such as pulmonary hypertension[2]. Lu Qiangwei et al. (2022) further indicated that IPF patients with lung cancer face a higher risk of acute exacerbation after chemotherapy compared to those receiving chemotherapy alone, which further deteriorates their prognosis[1].

4. Early Screening Strategies for IPF Complicated with Lung Cancer

4.1. Identification and Stratified Management of High-Risk Populations

Based on existing literature, elderly male smokers with a long-term smoking history, patients with rapidly declining pulmonary function, those with concurrent emphysema, and IPF patients exhibiting dynamic elevation of serum tumor markers should all be prioritized for screening. Li Na et al. (2024) investigated the nutritional status and inflammatory levels in IPF patients[2]. Decreased albumin levels and elevated C-reactive protein often indicate poor prognosis. Clinicians should implement risk stratification for IPF patients based on these risk factors, with high-risk individuals requiring closer follow-up and more aggressive screening interventions. Shi Xiaoyan et al. (2021) emphasized that IPF patients presenting with relatively specific symptoms such as hemoptysis, chest pain, or weight loss—regardless of severity—should undergo timely lung cancer-related examinations[7]. Zhang Xiaoli's (2024) study evaluated the efficacy of the Feiwu Decoction combined with pirfenidone in treating IPF. The study's design, which included a regular follow-up protocol, provides a reference for establishing a routine monitoring framework for IPF patients in clinical practice[8].

4.2. Standardized Application of Imaging Screening

High-resolution CT serves as the core imaging modality for follow-up in IPF patients and lung cancer screening. In IPF complicated with lung cancer, lesions predominantly concentrate in fibrotic areas, particularly in the honeycomb lung and peripheral zones, necessitating focused imaging interpretation in these regions. A study by Lu Qiangwei et al. (2022) demonstrated that lung cancer frequently occurs in areas with honeycomb-like or transitional fibroblast lesions, presenting as newly formed nodules, masses, or consolidation shadows against an existing fibrotic background[1]. Fibrotic scars may obscure early tumor morphology, and newly detected lesions or morphological changes in pre-existing lesions during follow-up—regardless of small size—should be highly vigilant. Shi Xiaoyan et al. (2021) emphasized that regular pulmonary CT re-examinations and close monitoring of dynamic changes are critical for early diagnosis[7]. Experienced radiologists should be responsible for imaging interpretation, with contrast-enhanced scans performed when necessary to improve diagnostic accuracy. Li Hongmei (2022) noted in a review that characteristic pathological changes in IPF include honeycomb-like and reticular interstitial fibrosis, which also constitute fundamental background features requiring meticulous evaluation during imaging follow-up[4].

4.3. The Value of Dynamic Monitoring of Biomarkers

Serum tumor markers can provide auxiliary support for early screening of IPF complicated with lung cancer. A meta-analysis by Shi Xiaoyan et al. (2021) found that carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA19-9), carbohydrate antigen 125 (CA125), and neuron-specific enolase (NSE) were frequently elevated in patients with IPF

complicated by lung cancer[7]. Lu Qiangwei et al. (2022) similarly emphasized the need for heightened vigilance for potential lung cancer complications when CEA and CA125 levels show significant elevation in IPF patients[1]. Elevated levels of a single marker cannot serve as definitive diagnostic criteria, whereas combined detection of multiple markers and their dynamic trends can provide critical insights. For IPF patients with persistent or progressive marker elevation, even in the absence of definitive imaging findings, follow-up intervals should be shortened and further investigations considered. Gene alterations such as TP53 and TERT, reviewed by He Xing et al. (2021), have not yet been incorporated into routine screening protocols[6]. Future research may explore novel molecular-level screening approaches for high-risk populations. Zhang Xiaoli's (2024) study investigated inflammatory and fibrosis-related factors, including TNF-α, IL-8, and TGF-β at the mechanistic level[8]. These factors not only reflect disease activity status in IPF but also correlate with lung cancer development, potentially offering dual diagnostic implications through dynamic changes.

5. Challenges in Screening and Corresponding Strategies

5.1. Identification difficulties caused by symptom overlap

Interstitial Pulmonary Fibrosis (IPF) primarily manifests as progressive dyspnea and dry cough, which closely overlap with early symptoms of lung cancer. When coexisting with lung cancer, pre-existing cough and shortness of breath may worsen, leading clinicians to often attribute these symptoms to IPF disease progression. Lu Qiangwei et al. (2022) emphasized the need for heightened vigilance for potential lung cancer involvement when IPF patients present with relatively specific symptoms such as chest pain, hemoptysis, or weight loss[1]. This possibility should also be considered in patients whose symptoms persist despite conventional antifibrotic therapy. Zhang Xiaoli's (2024) study found that combining Pulmonary Weil Formula with pirfenidone improved Traditional Chinese Medicine syndrome scores in IPF patients, but showed no corresponding changes in objective indicators like pulmonary function[8]. This "symptom-indicator dissociation" phenomenon suggests that even when patients experience subjective improvement, objective disease progression—including potential lung cancer development—may still occur. Clinicians should establish dynamic assessment awareness for symptom changes in IPF patients, and promptly initiate lung cancer-related diagnostic procedures when symptoms exceed the typical IPF disease course**.**

5.2. Technical challenges in imaging interpretation

Shi Xiaoyan et al. (2021) noted that scar tissue formed during pulmonary fibrosis can obscure the morphology of early-stage lung cancer lesions, increasing diagnostic difficulty in early detection[7]. Newly identified nodular and mass-like manifestations in IPF patients during follow-up stages should be differentiated from fibrotic progression, infections, and organizing pneumonia. Xiao Ting et al. (2022) highlighted the potential risk of immune checkpoint inhibitors inducing acute exacerbations of IPF during lung cancer treatment, adding complexity to imaging surveillance[5]. Li Hongmei (2022) summarized that typical IPF pathological changes primarily involve honeycomb-like and reticular interstitial fibrosis, emphasizing the need for radiologists to master these fundamental pathological features to accurately identify occult early tumor lesions[4].

5.3. Interaction between Treatment and Screening

IPF therapeutic agents may exert certain impacts on the occurrence and screening of lung cancer. Kong Wei (2026) demonstrated that the combination of pirfenidone and nintedanib can reduce inflammatory cytokine levels and optimize pulmonary-related functional status in IPF patients[3]. Lu Qiangwei (2022) noted that nintedanib was initially developed as an antineoplastic agent, exhibiting antitumor effects through its inhibition of angiogenesis, and was subsequently approved for clinical use in IPF treatment[1]. Li Hongmei (2022) similarly proposed that anti-fibrotic interventions are associated with a reduced risk of lung cancer development in IPF patients, emphasizing the need to consider potential regulatory effects of treatment measures on screening-related biomarkers when interpreting imaging and tumor marker data in IPF

patients treated with anti-fibrotic regimens[4].

6. Conclusion

In clinical practice, a screening model can be established based on stratification of high-risk populations, with regular HRCT examinations as the core and combined with dynamic monitoring of serum biomarkers. Multidisciplinary collaboration can address diagnostic challenges related to symptom overlap, imaging interpretation, and therapeutic interventions, enabling early identification and timely intervention of IPF complicated by lung cancer. Existing anti-fibrotic agents can delay disease progression in IPF but cannot fully replace lung cancer screening. Patients receiving pharmacological treatment should still be included in standardized follow-up management systems.

Disclosure statement

The author declares no conflict of interest.

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