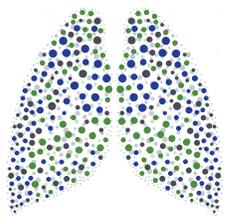


Idiopathic Pulmonary Fibrosis



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Why Family Physicians Should Know About IPF

As front-line health care providers, family physicians play an essential role in the early detection of idiopathic pulmonary fibrosis (IPF) and the timely referral to a pulmonologist. The disease is rare and includes signs and symptoms that make it difficult to distinguish among other interstitial lung diseases (ILDs). By identifying suspected cases of IPF at primary care visits, family physicians have an opportunity to refer patients earlier and enable diagnosis and treatment sooner. This makes education about IPF a key factor in early detection, which can potentially lead to better health outcomes. Diagnostic criteria and treatment options presented in this brochure are based on specialist guidelines that have not been reviewed or endorsed by the AAFP. However given the limited guidance for IPF, the information is presented for consideration in management of this disease.

Introduction to IPF

Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing interstitial lung disease (ILD) of unknown cause.¹ ILDs may be a result of a number of insults to the lungs (e.g., medication, connective tissue disease, occupational or environmental exposures).²

Idiopathic pulmonary fibrosis is characterized by a progressive breathlessness and cough, as well as a decline in lung function.¹

Symptoms

The most common symptoms of IPF are dyspnea and cough.² Dyspnea is usually exertional and associated with walking up inclines or steps.² The cough is typically described as “dry” and “hacking,” and may start with a tickle in the throat.³ The severity of these symptoms varies.

Other possible symptoms of IPF are fatigue and problems with sleeping.³ Symptoms that have not been associated with IPF include chest pain, fever, rash, weight loss, and myalgia or arthralgia,⁴ although these may be seen in various other forms of ILD.

History

Knowledge of a patient’s medical history and exposures is vital to diagnosing IPF and essential to excluding other ILDs. Questions should focus on the following:

- **Smoking history.** Cigarette smoking is strongly associated with IPF, especially individuals with a history of more than 20 pack-years.^{2,4}
- **Other medical conditions.** Gastroesophageal reflux disease, hiatal hernia, pulmonary malignancy, coronary artery disease, obstructive sleep apnea, obesity, emphysema, and pulmonary hypertension are comorbid conditions frequently associated with IPF.^{2,4}
- **Occupational and environmental exposures.** Chronic, repeated exposure to metal dusts (brass, lead, and steel), wood dust (pine), and aerosolized organic antigens (primarily, molds, bacteria, and bird antigens) have been associated with IPF. Relevant occupations with associated exposures include farming, raising birds, hair dressing, and stone cutting/polishing.^{2,4}
- **Medication history.** Some medications may have pulmonary fibrosis as a potential toxicity.⁵

Physical Examination

The physical examination should focus on two key signs:

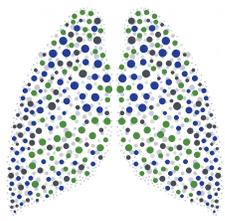
- **Inspiratory crackles.** This sign may be the earliest clinical finding and is the hallmark feature of IPF, reported in more than 90% of patients.⁴ These crackles sound like the ripping apart of Velcro and are heard at the posterolateral, basal aspects of the lungs.³ It is best to listen with the stethoscope applied directly to the skin.³ Inspiratory “squeaks” and wheezes are uncommon in IPF, and should prompt consideration of other diagnoses.⁶
- **Finger clubbing.** This sign occurs in 25% to 50% of patients.⁴

Idiopathic pulmonary fibrosis is unlikely in the presence of signs of connective tissue disease, such as joint deformity, synovitis, muscle weakness, and rash.⁴ Instead, these signs should prompt a workup for rheumatologic disease.⁴

Risk Factors

The cause of IPF is unknown, but some patients have a higher risk, including those who:

- Are older than 55 years⁷
- Are male⁷
- Have a history of smoking⁴
- Have been or are currently exposed to occupational or environmental antigens⁴



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No one clinical factor indicates IPF. Rather, a patient's entire clinical context should be considered when making a diagnosis of IPF.

Epidemiology

While IPF is rare, a lack of large-scale studies makes it difficult to estimate the incidence of the disease. We do know that the incidence of IPF increases with age, occurring most often after 55 years, and slightly more often in men.⁷ Among all individuals 55 to 64 years old, the incidence is 19.3 cases per 100,000 person-years.⁷

Challenges

Misdiagnosis and delays in diagnosis of IPF are common. In one study, IPF was most often misdiagnosed as asthma (13.5%), pneumonia (13.0%), or bronchitis (12.3%).⁸ Delays in diagnosis have been reported to be from one year to as long as three years, with longer delays associated with an increased risk of death.^{4,7}

Idiopathic pulmonary fibrosis is difficult to diagnose for several reasons, including:²

- Symptoms (breathlessness on exertion or at rest, and a dry cough) are nonspecific
- Clinical presentation is similar to that of many other pulmonary diseases
- Many interstitial lung diseases may mimic IPF
- Diagnostic criteria for IPF have changed over the past few years
- No biomarkers of the disease are available

Diagnosis

The diagnosis of IPF is challenging and one of exclusion. No one clinical factor indicates IPF. Rather, a patient's entire clinical context should be considered when making a diagnosis of IPF. Currently, standards for diagnosis include: a multidisciplinary discussion (MDD) among pulmonologists, radiologists, and pathologists discussing all features of the patient's presentation, radiographic findings, and pathologic findings (if available). The discussion should address the following:⁹

- Exclusion of other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity)

- Presence of usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) in patients who do not have surgical lung biopsy
- Specific combinations of HRCT and surgical lung biopsy pattern (in patients who have surgical lung biopsy)

MDD enhances the accuracy of diagnosis, with family physicians playing a vital role through early detection and timely referral. Excluding other causes of disease relies on recognizing the signs and symptoms of the disease, as well as:⁹

- Documenting risk factors
- Taking a detailed, comprehensive history
- Carefully performing a physical examination
- Ordering appropriate diagnostic testing

Referrals should include a complete documentation of findings.^{10,11} Diagnosing IPF requires not only knowledge of the signs and symptoms of IPF, but also the ability to distinguish it from other diseases with similar clinical presentations.

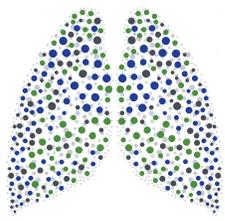
Diagnostic Testing

Most objective testing is not part of the recommended diagnostic criteria. Nevertheless, the results of some tests can help exclude other diagnoses and/or add to the clinical context of IPF.

Although laboratory testing is not useful in diagnosing IPF, guidelines recommend serologic testing for most patients to exclude underlying connective tissue disease.⁹ Such testing may include rheumatoid factor, anti-cyclic citrullinated peptide, and anti-nuclear antibodies.⁹ An extractable nuclear antigen panel is often times helpful to identify other connective tissue diseases, such as Sjögren's syndrome, systemic lupus erythematosus, and scleroderma, all of which are also associated with ILDs.¹²

The sensitivity of chest radiographs for the detection of subtle interstitial changes is low.⁴ An indication of IPF is symmetric peripheral, basilar reticular opacity with loss of volume in the lower lobe.⁴ However, some patients with IPF may have normal findings on chest radiographs.⁴

Pulmonary function tests are integral to monitoring progression of IPF and staging of disease severity.⁴ The results may also be helpful in establishing an initial diagnosis of IPF. The forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide are usually decreased, but these values may be normal early in the disease course.⁴



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When to Consider IPF

Idiopathic pulmonary fibrosis should be considered for all patients with unexplained chronic exertional dyspnea, and those who present with a cough, bibasilar inspiratory crackles, and finger clubbing.⁹ The disease most often occurs in individuals older than 50, men, and smokers.^{4,9} The index of suspicion for connective tissue disease should be high for women younger than 60 years.⁹

An HRCT should be ordered for any patient who has abnormal findings on chest radiographs and clinical findings that are consistent with an ILD.⁴

The radiographic standard for the diagnosis of IPF is an HRCT of the chest.⁹ An HRCT is a special, non-contrast chest computed tomography (CT) that obtains thin slice (< 2 millimeters), volumetric images of the lungs enhanced with special software algorithms. A pattern of UIP on HRCT is characterized by a subpleural, basilar predominance, and honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis with a relative paucity of ground-glass opacities.^{4,9}

The UIP pattern on HRCT is highly accurate for a UIP pattern on histologic examination of a surgical lung biopsy specimen.⁹ Thus, surgical lung biopsy is needed only when the findings on HRCT are not “classic” for UIP.⁹

It is essential for HRCT images to be interpreted by a radiologist experienced with ILDs. The decision to pursue surgical lung biopsy is best left to the providers in the MDD, as many factors go into this decision.

Documenting Referrals

A complete report of the family physician’s findings is an important aspect of a referral to confirm IPF. A thorough referral report should include the following:¹¹

- Symptoms and their duration
- Smoking history
- Comorbidities
- Family history
- Medication history
- Occupational history
- Environmental exposures, including hobbies, pets, and other exposures outside of work

- Results of physical examination, primarily the presence of inspiratory crackles and finger clubbing
- Findings on chest radiographs
- Description of previous treatments
- Results of pulmonary function tests
- Results of HRCT (plus images), if available

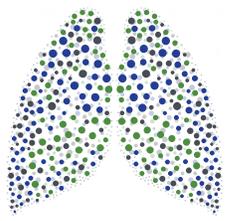
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Pathogenesis and Complications

The pathogenesis of IPF is unknown.⁴ It was believed that IPF was caused by generalized inflammation that progressed to widespread parenchymal fibrosis.^{13,14} This was questioned when IPF failed to respond to anti-inflammatory drugs and immune modulators.¹³ Studies now suggest that exposure to external stimuli (e.g., smoke, environmental agents) can lead to damage of alveolar epithelial cells, subsequent activation of mesenchymal cells, and excess accumulation of extracellular matrix.^{13,14} A genetic basis for IPF is still being explored.

Patients with IPF are at an increased risk for several comorbidities, including coronary artery disease, lung cancer, obstructive sleep apnea, emphysema, pulmonary hypertension, pulmonary infection, gastroesophageal reflux disease, hiatal hernia, and diabetes mellitus.^{2,4,15}

The course of IPF is unpredictable, and many people experience acute exacerbations of the disease. In one study, 72% of 1,735 patients with IPF sought urgent, outpatient care because of a suspected exacerbation of the disease, and 39% of the patients had at least one all-cause hospitalization.¹⁶ These disease-related interruptions diminish patients’ quality of life.



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Treatment of IPF

The goals of treatment are to slow progression of the disease, reduce symptoms, and improve the quality of life. IPF is currently treated with a combination of antifibrotic drugs and pulmonary rehabilitation.^{2,4,17} The need for oxygen therapy should be assessed, and lung transplantation is an option for moderate to severe disease in select patients.^{2,4} Clinical trials and registries may be available for patient involvement in your area.

Antifibrotic Drugs

Until 2014, no approved drugs were available for the treatment of IPF. Now, two first-in-class antifibrotic drugs are approved by the Food and Drug Administration (FDA). Studies have shown both drugs slow disease progression in patients with IPF, as measured by the decline in FVC.¹⁸⁻²⁰

Overall, adverse events were tolerable.^{19,20} The most common were gastrointestinal- or skin-related adverse events.^{19,20}

The goals of treatment are to slow progression of the disease, reduce symptoms, and improve quality of life.

Pulmonary Rehabilitation

A systematic review of nine studies demonstrated that pulmonary rehabilitation is beneficial for people with interstitial lung disease, including IPF.²¹ According to the findings, pulmonary rehabilitation was safe and was associated with short-term improvements in functional exercise capacity, dyspnea, and quality of life.²¹

A more recent systematic review and meta-analysis (five randomized controlled trials) focused on only IPF and showed that pulmonary rehabilitation was associated with increased exercise tolerance and improved quality of life.²²

Patients derive the most benefit from pulmonary rehabilitation early in the course of the disease.²³ As such, pulmonary rehabilitation should begin immediately after diagnosis.

Oxygen Therapy

Patients with IPF should be assessed for the need for oxygen therapy. This is best accomplished by a six-minute walk study. If the patient's oxygen saturation drops below 88%, then an oxygen titration component should be performed.² This can help determine the least amount of oxygen necessary to maintain saturations above 88% with exertion.²

Management of Comorbidities

Most specialty centers advocate for aggressive management of comorbidities.

Lung Transplantation

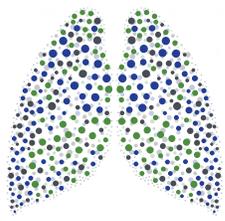
Lung transplantation is a potential option for patients with moderate to severe IPF, and it is the only treatment associated with prolonged survival.^{2,4,24} While the number of single-lung transplantations has remained steady, the number of double-lung transplantations has increased since the mid-1990s.²⁵ There is no evidence showing the benefit of single- versus double-lung transplantation.¹⁷

Living With IPF

Idiopathic pulmonary fibrosis has a substantial impact on health-related quality of life, primarily attributed to a high-symptom burden and functional limitations. People with IPF have reported that the most troublesome symptoms are dyspnea, severe coughing, and persistent fatigue.²⁶ Limited mobility is also an issue.²⁶ One study reported that individuals with IPF were sedentary for more than nine hours per day.²⁷ People with IPF become frustrated as they lose the ability to engage in activities they once enjoyed.²⁶

Difficulty interacting with friends and family, and the financial strain are also primary challenges.²⁶ Depression is common and is also a substantial factor of health-related quality of life.²⁸⁻³⁰ In one study, nearly 26% of patients with IPF experienced symptoms of depression.³⁰

Diagnosing IPF is challenging, but guidelines are available to help primary care physicians identify patients with IPF and make earlier referrals. Early referral means earlier treatment, which can help improve patient outcomes.



The Role of Family Physicians in Treatment

In addition to their vital role in early detection and referral, family physicians play an important role in the ongoing care of their patients with IPF. Family physicians can contribute to the care of patients with IPF in the following ways:

- Oversee the treatment of comorbidities
- Encourage participation in pulmonary rehabilitation and monitor progress
- Vaccinate against influenza, pneumococcus, and pertussis
- Assess emotional and mental health
- Recommend support groups for patients and their caregivers
- Monitor the need for oxygen therapy
- Discuss treatment preferences and end-of-life care

Patients value a trusted source of information and may ask their family physician for information and advice. Family physicians should provide their patients with guidance for self-management of their disease and recommend credible resources for patient education.

Resources for Patient Education on IPF

American Thoracic Society: www.thoracic.org

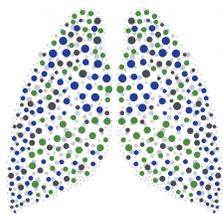
Action for Pulmonary Fibrosis: www.actionpulmonaryfibrosis.org

American Lung Association: www.lung.org

Breathless: www.breathlessipf.com

Lungs & You: www.lungsandyou.com

Pulmonary Fibrosis Foundation: www.pulmonaryfibrosis.org



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