**SUMMARY**

**Introduction**

Idiopathic pulmonary fibrosis (IPF) is a progressive, fatal disease, which is limited to the lungs and occurs in adult patients with a striking increase in prevalence in patients older than 60 years. Guideline documents published in the years 2000 and 2011 have refined the definition and diagnosis of IPF allowing a definite diagnosis of IPF across different countries and thus allowing large scale international multicenter treatment trials (1,2). Results of clinical trials and registries have led to an improved understanding of the natural history of the disease and have led to approval of two drugs for the treatment of this devastating disease.

**Etiologic and epidemiologic aspects of IPF**

In large scale epidemiological studies incidence of IPF ranged from 4.6 -16.3 /100,000/year and prevalence from 14.0 – 42.7 /100,000 (2-5). The results varied depending on case definition, gender, and ethnicity. There is an impression of increasing prevalence over time, while incidence remains quite stable.

The etiology of IPF is by definition unknown. However, recent advances in genetics and lessons from familial interstitial pneumonia (FIP) have revealed a number of predisposing genetic polymorphisms and mutations including surfactant protein A and C, telomerase complex, mucin 5B, tollip and others (2,6,7,8). Further risk factors are tobacco smoke, reflux and microaspiration, and potentially herpes viruses. The role misled wound healing and regeneration remains to be elucidated.

**Understand how to diagnose IPF**

In the IPF guideline document published in the year 2011 the diagnostic criteria have been newly defined. First of all there is no pathognomic finding for IPF, but the diagnosis of IPF needs to rule out all other reasons for lung fibrosis. Second, in a compatible clinical setting of IPF there is a pattern of "usual interstitial pneumonia" which can be identified radiologically on a high-resolution thin-section computed tomography (HRCT) or, in the absence of a conclusive HRCT, histologically on a surgical lung biopsy (SLB), which allow diagnosis of IPF (2). The dichotomy of his diagnostic algorithm would subject 30 – 50 % of patients suspected of IPF to SLB. This is not feasible for many reasons including a relatively high morbidity and mortality of SLB, severity of the disease at first diagnosis, multimorbidity of a mostly elderly population. Therefore, alternatives are needed and bronchoscopic transbronchial cryo-biopsy may allow obtain sufficient lung tissue for the pathologists to identify the heterogeneity of architectural distortion typical of UIP. The multidisciplinary team discussion between pneumologist, radiologist and pathologist should, therefore, include all available data of a patient beyond HRCT and histology, i.e. case history, exposures, course and treated course of the disease, BAL cytology and transbronchial biopsies, to find the correct diagnosis. Despite all efforts there will be 10-15 % unclassifiable cases even in experienced centres. In these cases, the multidisciplinary team is in the best position to decide on clinical grounds which is the most probable diagnosis and most appropriate therapy (2,9).
Understand therapeutic strategies in IPF

Treatment of IPF changed fundamentally since it became evident that immunosuppression plus N-acetylcysteine (NAC) and NAC monotherapy are not beneficial and potentially harmful for IPF patients (10,11). However, two antifibrotic drugs, pirfenidone and nintedanib, proved efficacious in IPF in randomised controlled clinical trials (12-15). Both drugs diminish the annual FVC decline by ca. 50 %; while pirfenidone also reduces the decline of the 6-minute walking distance and the progression free survival, nintedanib prolongs the time to first acute exacerbation and tends to improve quality of life. Both drugs have shown the potential to reduce overall mortality, although none of trials did provide a significant result. Consequently, both drugs have been approved in the EU and in the US and the updated IPF guideline recommends the use of these drugs in IPF patients (conditional recommendation) (16). The guideline also recommends to treat IPF patients with antacids, this conditional recommendation is, however, based on very low evidence and has been discussed controversially (16).

In addition to pharmacological therapy it is essential to assess and treat IPF patients for comorbidities which are frequently complicating the disease (17,18). Hypoxemia, pulmonary hypertension, cardiovascular diseases, emphysema, lung cancer, obesity and cachexia as well as gastro-oesophageal reflux, and depression need to be assessed and addressed. Pulmonary rehabilitation and long term oxygen therapy are important for many patients as well as palliative care in advanced disease (1).

Of great importance is the evaluation for lung transplantation in eligible candidates. IPF diagnosis per se is already an indication to refer the patient to a transplant center for a first evaluation (19). In progressive or advanced disease active listing for lung transplantation is indicated if there are no contraindications (19).

Since available therapies still do not offer satisfactory effects in IPF, patients should also be motivated to participate in clinical treatment trials (1,2).

Prognosis and monitoring of IPF

IPF is the most frequent idiopathic interstitial pneumonia and carries the worst prognosis of only two to three years median survival first after time of diagnosis (2). The individual course of disease, however, is variable and stable or slowly progressive phases may be interrupted by acute exacerbation. These are defined as respiratory worsening within 30 days with occurrence of new pulmonary infiltrates (on HRCT) and without an identifiable cause including infection. Acute exacerbations carry a high mortality of about 50 % in-hospital mortality and 80-90 % one-year mortality (20). High-dose methylprednisolone is used in these episodes, based on anecdotal reports (1). For prognostication the GAP index based on gender, age and physiology (FVC and diffusion capacity) is used to assess risk of death at first presentation (21).

REFERENCES


EVALUATION

1. Which of the following statements regarding the diagnosis of IPF is not correct?
   a. The UIP pattern on a surgical lung biopsy is sufficient to diagnose IPF.
   b. According to current guidelines patients suspected of having IPF with a possible UIP pattern on HRCT should undergo surgical lung biopsy.
   c. Patients with definite UIP pattern on HRCT in the presence of a diagnosis of rheumatoid arthritis cannot be diagnosed as having IPF.
   d. The multidisciplinary team can make a working diagnosis of IPF even in the absence of a UIP pattern or inconsistent features on HRCT or histology.
   e. Transbronchial cryobiopsies cannot yet serve as a substitute for surgical lung biopsies and carry significant risk of morbidity and potentially mortality.

Answer A

2. Which of the following pharmacological therapies received a conditional recommendation to use in the recent IPF guideline update (2015)?
   1) Prednisolone
   2) Anti-acids
   3) Nintedanib
   4) Pirfendone
   5) Bosentan
   a. All answers are correct
   b. Only 3 and 4 is correct
   c. Only 1, 2 and 5 are correct
   d. Only 2, 3 and 4 is correct
   e. Only 2, 3, 4 and 5 is correct.

Answer D

3. Which of the following statements regarding IPF is wrong?
   a. Median survival after first diagnosis of IPF is 2 – 3 years.
   b. Acute exacerbations are life threatening complications of IPF.
   c. Stable patients are not in danger of exacerbations.
   d. The GAP index uses gender, age and physiology to assess the prognosis of IPF.
   e. FVC decline of > 10 % within one year is associated with an increased risk of death.

Answer C
4. Which of the following mechanisms is not involved in IPF pathogenesis?
   a. Alveolar cell injury
   b. Aberrant healing/regeneration
   c. Genetic predisposition
   d. Exogenous noxes (e.g. tobacco smoke)
   e. Granulomatous inflammation

Answer E