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The efficacy of pulmonary rehabilitation in improving the clinical status in idiopathic pulmonary fibrosis

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Abstract

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, fatal lung disease with a median survival rate of 2-4 years after diagnosis, occurring primarily in older adults. The diagnosis is suggested by histology or radiologic evidence of a usual interstitial pneumonia (UIP) pattern and exclusion of known cases of pulmonary fibrosis. There are some comorbidities associated with IPF such as pulmonary hypertension, emphysema, chronic obstructive pulmonary disease (COPD), asthma, lung cancer, cardiovascular disorders, gastroesophageal reflux disease (GERD), sleep disorders and psychiatric disturbances. The management of IPF focuses on the amelioration of symptoms, preserving lung function, improving health status, minimizing the adverse effects of therapy and improving survival. Pulmonary rehabilitation is suggested for IPF patients when adequate medical therapy controls poorly the disease progression and mental, physical or social consequences of the illness persist during daily life. Currently, there are only two approved available antifibrotic therapies, pirfenidone and nintedanib, capable to reduce disease progression and physical deterioration, but cure is elusive and improvements are hardly observed. In addition, there is a continuous need of non-drug therapy components which should be included in IPF patient management: education, psychosocial support, exercise training, nutrition, symptom management and palliative care, non-invasive ventilation and pulmonary transplant. These complementary therapies have been proven to improve dyspnea, exercise capacity, fatigue and quality of life.

Key words: *idiopathic pulmonary fibrosis, rehabilitation, quality of life, palliative care,*

Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic fibrotic lung disease with poor prognosis and rapid progression, with a median survival rate between 2-5 years after diagnosis (1). IPF is characterized by fatigue and dyspnea, which impairs daily living by decreasing the quality of life. As fibrosis evolves, these symptoms worsen, patients becoming unable to perform physical activities. Also, these subjects associate skeletal muscle deconditioning, depression and social isolation (2). IPF has a limited response to pharmacological treatment and new approaches and complementary therapies to improve IPF control are urgently required (3).

Prevalence

IPF affects about 3 million people worldwide, with an incidence increasing dramatically with age (4). IPF is more prevalent in males, but it can also affect women, especially the heaviest smokers (5). A recent analysis based on healthcare claims data of a large health plan in the United States yielded a prevalence estimate of between 14.0 and 42.7 per 100,000 persons depending on the used case definition (6). Generally, the prevalence is higher in America than in Europe or Asia, and it is unclear whether this is due to differences in geographic, ethnic and cultural aspects or due to different types of disease management (5).

Etiology

Even though idiopathic pulmonary fibrosis is, by definition, a disease of unknown etiology, a number of potential risk factors have been described such as cigarette smoking, environmental exposures, microbial agents, chronic viral infections and certain comorbidities (4, 6). Smoking is strongly associated with the development of IPF, especially for individuals with a smoking history of more than 20

packs/year (6). It is a well-known fact that cigarette smoking is the main factor responsible for the development of IPF, but there are some debates regarding the implication of this exposure on the evolution of this disease. King Jr. et al. reported a better survival in subjects who were current smokers at the time of diagnosis, explained by the earlier presentation because of smoking-related symptoms, facilitating an accurate diagnosis in a mild stage of the disease (7, 8). Numerous environmental exposures that target the lung epithelium increase the risk of IPF, the most important being cigarette smoking. Also, an increased risk has been linked to exposures such as agriculture and farming, metal and wood dust, stone dust and silica (4).

Taking into account the microbial agents, it is known that the Epstein-Barr virus has primarily been detected in the alveolar epithelia of IPF patients (4, 6). Viruses include cytomegalovirus, human herpes viruses (HHV-7, HHV-8), which have been associated with IPF development. Several studies have also suggested that bacteria might play a part in the pathogenesis of IPF. The lungs of patients with IPF have higher bacteria loads and significant differences in the composition of their microbiota compared to healthy subjects. The most common pathogenic bacteria are Staphylococcus spp and Streptococcus spp. These modifications have been associated with the clinical markers of disease evolution (4).

An association between serum Helicobacter Pylori (HP) antibody positivity and more severe diseases was recently described. In a recent study, the prevalence of HP infection in IPF was compared between two groups: HP-positive IPF patients and HP-negative IPF patients and revealed that those with HP positive infection had significantly lower FVC, FEV1 than the other group (9).

Pathophysiology

Despite the fact that lungs are exposed to many external factors, they possess a great ability to recover through various mechanisms. But, in an individual with susceptible state, a repetitive alveolar injury causes a premature and persistent epithelial damage, a release of pro-fibrotic mediators and a cascade of mesenchymal cell activation, all these mechanisms conducting to an ongoing development of IPF.

Ageing is the most important demographic risk factor, affecting epithelial type 2 cells (AEC2s) which have epigenetic changes, genomic instability, mitochondrial dysfunction, altered intercellular communication, deregulated nutrient sensing, loss of proteostasis, genomic instability and a lower secretory capacity with a loss of surfactant (10,11). Moreover, in IPF the function of the epithelial type 1 cells (AEC1s) is affected, influencing the epithelial turnover. Besides ageing, in one-third of cases, the major risk factors are genetic variants (12, 13). Even if the certain mechanism of developing IPF is not clear, there are some multidirectional interactions between the risk factors and genetic susceptibility, causing alterations in the epithelial cells, extracellular matrix and mesenchymal cells, so all individuals diagnosed with IPF are considered mechanistically similar (14).

Comorbidities

Pulmonary and extra pulmonary comorbid conditions are progressively being recognized as important in patients with IPF (4). Comorbidities may differently influence prognosis of IPF patients (15).

IPF has been correlated with a considerable number of comorbidities such as pulmonary hypertension, emphysema, COPD, asthma, lung cancer, cardiovascular disorders, gastroesophageal reflux disease (GERD), sleep disorders and psychiatric disturbances (16). Kreuter et al. described the "comorbidome" of IPF, a new tool that can help clinicians to predict the survival in patients with IPF, which include cardiovascular (atherosclerosis, arterial hypertension, coronary arterial disease, pulmonary hypertension), metabolic (diabetes), gastroenterological (GERD) and neoplasia diseases (lung cancer) (16, 17).

Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF) are two severe multifactorial pulmonary disorders characterized by quite distinct clinical and pathological features. COPD is characterized by a poorly reversible and progressive airflow limitation that is determined by the concurrence of airways inflammation and emphysema, whereas in IPF a restrictive pattern of lung volume abnormality is associated with impaired diffusion capacity. During imaging and pathological examinations COPD and IPF exhibit different appearances, as far as the involved pulmonary regions (upper lobes versus lower lobes), and the occurring parenchyma modifications are concerned (alveolar emphysematous dilation and bronchiolar

inflammation in COPD, versus interstitial fibrosis and honeycombing in IPF) (18).
Nevertheless, a number of similarities can be recognized between the two disorders. Firstly, both COPD and IPF are chronic and progressive diseases of elderly people (with male predominance), that severely affect the lung function and both are related to long term inhalation of external noxious agents (mainly tobacco smoking). Secondly, in both diseases a progressive loss of alveolar parenchyma takes place leading to severe impairment of respiratory function. Variants of pulmonary fibrosis associated with emphysema have been described and these cases have been grouped in a newly defined syndrome of combined pulmonary fibrosis and emphysema (CPFE). In CPFE, lung volumes are commonly within normal limits due to the opposing effects of hyperinflation and fibrosis. The CPFE syndrome is more frequent in male smokers and pulmonary hypertension can complicate all these disorders.
Finally, both IPF and COPD are associated with an increased risk of cancer development and several lines of evidence suggest that this increase is independent from the effect of cigarette smoking (18, 19).

Lung cancer (LC)
One of the most impacting comorbidity is the appearance of LC in the course of IPF. Interestingly, IPF itself increases the risk of LC development by 7% to 20%. There are various common molecular, genetic and cellular processes that associate lung fibrosis with LC like oxidative stress, myofibroblast activation and uncontrolled proliferation, myofibroblast/mesenchymal transition, alterations of growth factors expression, endoplasmic reticulum stress and other genetic and epigenetic variations that lead to the development of IPF and LC (20). The risk of developing LC of patients with IPF is up to 5 times greater than in the general population, with a prevalence ranging between 3% and 48% depending on different cohort studies (5, 20). The reason of this bizarre association is still unclear. Some studies demonstrated that both diseases share common risk factors such as aging, smoking history and male gender and similar pathogenic mechanisms. Usually lung cancer develops as nodules close to fibrotic areas and the most diagnosed subtypes are the adenocarcinoma and squamous cell carcinoma, worsening the evolution of IPF patients (21, 22).

Pulmonary hypertension (PH)
Pulmonary hypertension is a frequent complication of IPF and is now defined as mean pulmonary arterial pressures (mPAP) more than or equal to 25mm Hg at rest, confirmed by right heart catheterization (RHC) (23). Patients with PH and IPF presents a very poor survival rate with reduced quality of life. Usually they tend to have reduced exercise tolerance, lower arterial oxygen at rest, lower lung diffusion of carbon monoxide (DLCO) values, right ventricular hypertrophy and/or pulmonary artery enlargement on imaging scans. Currently, the only approved treatment for PH in IPF is lung transplant in selected cases (15).

Obstructive Sleep Apnea (OSA)
Sleep apnea is increasingly evident in patient with IPF. The relationship between obstructive sleep apnea (OSA) and IPF is complex. The restrictive condition can reduce upper airway tone increasing their collapsibility and the nocturnal oxygen desaturation leads to an increased oxidative stress (25), both of these conditions leading to a poor prognosis of IPF. By using therapy with continuous positive air pressure we can see significant improvements in activities of daily living, quality of sleep, survival and ultimately quality of life (15, 21, 24, 25).

Gastroesophageal reflux disease (GERD)
The finding of GERD in the context of IPF is not rare. However, how this mechanism has a pathogenic role in IPF is not clear. It is known that micro aspiration can cause a repetitive alveolar cell injury, leading to an irregular wound healing process and finally to lung fibrosis (15). Antacid therapy, mainly proton pump inhibitors (PPI) might decrease the frequency of acute exacerbations of IPF (AE-IPF) by reducing the acidity of the micro aspirate (16).

Asthma
Both asthma and IPF affect the architecture of the lung parenchyma and even if there is no connection between these two diseases, environmental triggers can determine hypersensitivity pneumonitis, which in evolution can cause pulmonary fibrosis. In an individual, both asthma and IPF can coexist, sharing common risk factors, even if in IPF lung injury is more important, progressing to destroyed lung tissue and respiratory failure (26).

Cardiovascular comorbidities (CVD)

Numerous cardiovascular comorbid conditions like arrhythmias, congestive heart failure and ischemic heart disease are very often associated with IPF (4, 27). Amongst them, an increased incidence of Atrial Fibrillation (AF) and Atrial Flutter (AFL), which have been the most commonly reported arrhythmias in patients with IPF, comorbidities that persist after a lung transplant according to Nielsen et al. (23, 28). Kizer et al. showed that pulmonary fibrosis was associated with an increased incidence of coronary artery disease (CAD) (17, 29). The causal relation where pulmonary fibrosis promotes atherosclerosis is evidenced by the increasing serum levels of interleukins, cytokines, circulating immune complexes and development of fibrosis in extra-pulmonary organs like the digits and mediastinum (4). Cardiovascular impairments among IPF patients are considered a significant limiting factor during physical exertion and are associated with exercise intolerance, severe signs and symptoms and lower prognosis outcomes (1).

Depression and anxiety

Symptoms like anxiety and depression are commonly observed in patients with IPF. Also they are related to the functional status of patients and can cause an increase in dyspnea, physical disability and mortality and decrease exercise tolerance (21).

Given that, comorbidities should be systematically explored in IPF because an appropriate treatment and an early recognition may help in optimizing the management and improving quality of life (15).

Diagnostic

IPF is a fibro proliferative disease of unknown case, associated with histopathological and/or high resolution computed tomography (HRCT) pattern of usual interstitial pneumonia. To establish the diagnosis of IPF, an exclusion of other known cases of interstitial lung disease (ILD) is required, through a multidisciplinary discussion between pulmonologists, radiologists and pathologists experienced in the diagnosis of ILD (in particular those linked to the environment exposures, drug toxicity and connective tissue disease). The confirmation of the certain IPF diagnosis is challenging and it is based mainly on the radiological pattern. Given the high-quality evidence regarding HRCT specificity for the recognition of histopathologic UIP pattern (reticular opacities, honeycombing, secondary bronchiectasis), surgical lung biopsy (SLB) is not essential. When surgical lung biopsy is indicated, the diagnosis is established in the presence of SLB aspects showing up a UIP pattern and specific combinations of HRCT (6, 30).

Management

The main goals of IPF management focuses on the amelioration of symptoms, preserving lung function, improving health status, minimizing adverse therapy effects and improving survival (4). The 2011 American Thoracic Society/European Respiratory Society/ Japanese Respiratory Society/Latin American Thoracic Association (ATS/ERS/JRS/ALAT) consensus guidelines recommend long-term oxygen therapy if hypoxemia is present, the treatment of comorbidities, pulmonary rehabilitation (PR), lung transplant for selected patients and clinical follow-up every 4–6 months. Also, an important aspect of care is the management of cough, dyspnea and psychological suffering, symptoms which nearly all patients with IPF develop as the disease evolves (31).

A comprehensive care approach that includes nonpharmacological and pharmacological treatment, patient education, palliative care and increased support throughout the course of the illness is needed.

Antifibrotic therapy

Apart from lung transplant, long term efficient treatment is still limited for most patients with IPF, despite some recent encouraging findings in pharmacotherapy. Currently, there are only two available approved antifibrotic therapies: pirfenidone (dose 801 mg 3 times daily) and nintedanib (dose 150 mg twice daily). Both antifibrotics are capable of reducing disease progression and physical deterioration, but improvements are hardly ever observed and cure is elusive (31).

Oxygen therapy

In individuals with resting hypoxemia, the 2011 ATS/ERS/JRS/ALAT treatment guidelines advise the initiation of long-term oxygen therapy, maintaining a SaO2 between 92–95% at rest and around 88% during physical activity (6). In evolution, the titration of oxygen therapy is required every 60-90 days, or more frequently if needed (32). Also, patient education is required in order to encourage self-monitoring at home by pulse oximetry, both at rest and with exertion, to provide

the sufficient supply of oxygen in order to achieve the individual need (31). The current guidelines do not encourage clinicians to perform cardiopulmonary exercise testing for routine monitoring, but the 6-minute walking test (6MWT) instead, a useful tool to appreciate the physical exercise capacity of the patient. This test should be done at baseline and at an interval of 3 to 6 months, moreover because IPF subjects which are not hypoxic at rest in the early stage of the disease can experience a fall in oxygen saturation during minimum exercise (6).

Smoking cessation

Since tobacco exposure is the main risk factor in IPF, and it is involved in pathogenesis, prognosis and evolution, smoking cessation needs to be implemented in all active smoker subjects. In order to obtain smoking cessation, the clinicians should adopt an individualized management plan including behavioral support and necessary pharmacotherapy. Also, the medical team is encouraged to give intensive cessation advice that has been proven to be more helpful in making smokers quit compared with brief advice. In addition, it was proved that these methods can be augmented by telephone quit-lines, group-based counseling programs, self-help materials and internet-based interventions. Recommendations are based on relaxation training, problem-solving skills and group counseling adding elements of peer support (33, 34). In subjects with IPF, smoking addiction should be avoided because nicotine and other excipients of the cigarette smoke interact with the action mechanism of antifibrotic therapy, resulting in lower medication concentration with a lack of efficiency (35, 36).

Rehabilitation Programs

Pulmonary rehabilitation has become a multidisciplinary approach which includes a routine of education, exercise training and behavior modification techniques, used to improve symptomatology and self-management and to enhance the participation of these subjects in daily life activities, even if in the majority of clinical trials regarding PR programs patients with IPF have not been distinguished from other restrictive lung diseases, such as bronchiectasis, scoliosis and neuromuscular disease (37). Since the prognosis, the disease progression and the response to therapy of IPF subjects are heterogeneous, therefore the ideal moment to initiate a PR program is still unknown and requires further studies (3).

Education

Comprehensive pulmonary rehabilitation plays a significant role in the management of patients with IPF, including its educational intervention. Patients should be informed about disease progression and health deterioration and need to be prepared for the future (31). It has been suggested that educational programs should cover exacerbation and symptom management, oxygen therapy, mood disorders, medications, lung transplantation, energy conservation and end of life care (38).

Psychosocial support

A priority of IPF patient management is psychosocial support in order to improve the quality of life and to reduce the symptomatology. In this group of patients, depression and anxiety affects the daily living, especially in those with a severe, progressive form of IPF. Psychosocial programs need to provide individual and group support to increase the adherence to antifibrotic and symptomatic therapy (39). Subjects who live in rural areas or have limited mobility may benefit from online support groups, such as the Pulmonary Fibrosis Foundation website. Also, an efficient tool in monitoring is represented by the community medical support system with specialists that can detect the decline of clinical status or the need of additional measures, before the next clinic visit. This means that, for the management of an IPF individual, the intervention of a multidisciplinary team is required (40).

Exercise training (ET)

In literature, the majority of studies proposed a training program based on a combination of strength and endurance exercises with a duration between 6 and 12 weeks. The majority of the programs include aerobic exercise (walking, cycling), resistance training and flexibility exercises for peripheral skeletal muscles (41), besides breathing exercises and respiratory muscle training (42). In patients with IPF, due to reduced daily physical activity, a significant loss of muscle strength and endurance was observed, especially of the quadriceps muscle (43). The changes in quadriceps strength in IPF patients was evaluated by Kozu et al. during an 8-week outpatient PR program and an increase of 10% in the maximal isometric knee extension maneuver (41) was observed. After the exercise training program, Nishiyama et al. concluded that there were no significant effects on the arterial blood gases,

dyspnea scale or lung function, but the 6-minute walking distance (6-MWD) had been 46,3 m higher in patients who had physical activity as recommendation (44). These findings are confirmed by Huppmann et al., which found an improvement of 45 ± 55 m of the 6-minute walking distance in patients receiving rehabilitation programs (45).

It has been stipulated that physical activity and regular exercise have an important effect on patients with mild-moderate IPF than in more severe IPF conditions so, as Kozu et al. demonstrated that in patients with severe dyspnea, a home-based rehabilitation program had no effect on 6-MWD, dyspnea or the quality of life (41). The heterogeneity of these findings can be explained by the differences between certain exercise programs, proving that home-based training is not so efficient in patients with IPF which require a more supervised management. Vainshelboim et al. observed that patients included in a supervised exercise training program showed an improvement in exercise tolerance, pulmonary function (FVC), ventilatory response, dyspnea, functional capacity and quality of life. So, since these parameters influence the prognosis of IPF subjects, the ET has an impact on the morbidity and mortality of these individuals (42).

IPF patients usually have a restrictive pathophysiology, with inefficient breathing and lower lung compliance (46). It is plausible that the stretching of thoracic muscles, chest expansion during deep breathing and repetitive stimulus of high ventilation demands that were used in several programs to be responsible of the effectiveness of the breathing pattern with the decreasing of dyspnea. Nykvist et al. demonstrated that by adding inspiratory muscle training on the PR program in patients with IPF, an improvement of dyspnea, exercise capacity, fatigue and quality of life was obtained (47).

Management of IPF and Comorbidities

COPD

COPD is a frequent comorbidity in patients with IPF and the rehabilitation programs have proven their efficacy. In these subjects, there were improvements in dyspnea, functional exercise-capacity (measured by 6MWT) and health-related quality of life (44, 48). Despite the fact that the mechanism of exercise intolerance differs between COPD and IPF, the rehabilitation therapies approved for COPD patients are effective to achieve a suitable exercise capacity in patients with IPF. The management of COPD and IPF should include a multidisciplinary approach, including individualized rehabilitation intervention as an adjuvant to the medical treatment, through effective methods such as muscular training, speleotherapy, soft tissue manual therapy, neuromuscular electrostimulation and halotherapy (49, 50).

ASTHMA

Asthma is a heterogeneous condition that is associated with IPF, influencing the prognosis of these patients and remaining poorly controlled despite optimum management. The additional interventions in asthma and IPF management, such as physical training, smoking cessation, environmental control practices, inspiratory muscle training, breathing techniques, speleotherapy and halotherapy have been proven to improve muscle strength, symptomatology, exercise capacity and quality of life (15,51).

OSA

The reason of association between OSA and IPF remains unclear. Some possible interactions are explained by the reduction of upper airway tone which determines an increased collapsibility, and by the alterations of the respiratory drive found in subjects with IPF. As showed by Bosi et al., the presence of OSA in IPF patients influences the prognosis by worsening the nocturnal oxygen desaturations (52, 53). In these conditions, the continuous positive pressure treatment (CPAP) is highly advised in patients diagnosed with OSA and IPF, despite the fact that the efficacy of this treatment in reducing disease progression and mortality is not yet proven in large clinical trials (15,54).

LUNG CANCER

The patients diagnosed with IPF have a high risk of developing lung cancer, diseases with several common risk factors, which shares many pathogen mechanisms. Individualized pulmonary rehabilitation in patients with IPF and lung cancer has been shown to increase exercise tolerance, reduce symptomatology and improve quality of life. Complementary therapies include adequate nutrition, physical activity, smoking cessation and psychosocial support. However, at this moment, there is a lack of evidence in the benefit of these therapies on the survival period, symptomatology and the health-related quality of life (55, 56).

Symptom management and palliative care

IPF is a progressive, disabling disease responsible for the deterioration of lung function which determines a progressive increase in fatigue, shortness of breath, and cough. As the pathology evolves, this symptom management represents a major point of interest, the purpose being maintaining an adequate quality of life (57). Even if it is known that the disease has a fatal prognosis, it is challenging for the patient and the caregivers to accept the poor outcome despite maximum conventional and additional therapy (58).

The main goal of palliative care focus is to reducing the symptomatology and to provide comfort for patients, decreasing the physical and emotional distress by introducing the psychological and spiritual support. The persistence of symptoms such as dyspnea and cough affects the daily living of IPF patients, which can be managed with corticosteroids, thalidomide or chronic opioids, but there is a lack of data in this direction (59). Patients with IPF with severe physiological impairment and important co morbid conditions should benefit from advanced directives and end-of-life plan (6).

Nutrition

Patients with IPF which associate gastro-esophageal reflux have an inappropriate nutritional status, so the BMI should be taken into consideration in the management decision. Nutritional support refers to the optimization of calorie intake, with a rigorous adjustment of protein and fat content. Dietary control includes the management of symptoms and of the weight with a focus on reducing the body weight, especially because obesity is a contraindication for lung transplant. An important direction is the management of symptoms related to antifibrotic therapy, such as nausea and reduced appetite, which can require symptomatic therapy and reduction of antifibrotic therapy doses (31).

Non-invasive ventilation (NIV)

NIV is used as a first line respiratory management for AE-IPF, especially because there is an extremely poor prognosis of subject treated with invasive mechanical ventilation (IMV). Although mechanical ventilation has become an indispensable support for critically ill patients with acute respiratory failure, it is well known that MV can initiate and exacerbate lung lesions and can increase the patient morbidity and mortality. Non-invasive ventilation was used in CPAP mode or BiPAP S/T mode in all patients, but it seems that CPAP is less effective in acute respiratory failure, despite the fact that many patients can be successfully managed by using CPAP mode. The patients with IPF have a poor prognosis, with a controversial evolution, as Yokoyama et al. highlighted in their study, a mean duration of NIV of 12.3 days and a high rate of mortality. However, almost half of the subjects can avoid intubation and have a greater survival rate with the application of NIV, initiated to avoid the severe hypoxemia in acute exacerbation (60, 61).

Pulmonary transplant

Taking into account that the patients with IPF have a poor prognosis and there is a lack of therapy that can reduce mortality, pulmonary transplant has to be taken into consideration. The International Society for Heart and Lung Transplantation (ISHLT) recommends that lung transplant should be indicated in chronic lung disease in subjects who have a high (> 50%) risk of death within two years. Worldwide, the percentage of IPF patients which benefit from lung transplant has gradually increased and even if most evidence supports both lung transplants, the single lung transplant has the advantage of a lower waiting time and can also prevent the higher rates of mortality. During clinical evaluation of IPF patients, a prognosis assessment should be completed in order to refer for lung transplant at the most appropriate moment. Factors that can determine a poor prognosis include older age, low pulmonary function, higher dyspnea score (Modified Medical Research Council, Scala Borg), history of respiratory exacerbation, higher oxygen need, low six-minute walk distance, especially if there is a decline of these parameters over a 6-12 month time period (62). Contrary, higher body mass indices, better pulmonary function and lower mean pulmonary artery pressures have been associated with a better survival five years after the initial diagnosis (63). Clinical prediction models incorporating these variables have been formulated in an effort to improve a clinician's ability to predict prognosis (64).

Conclusion

The management of patients diagnosed with IPF is challenging and integrate disease-specific strategies for slowing disease progression and extending patient survival, simultaneously with palliative care, in order to improve symptom management and quality of life. The major components of the treatment are represented by: early initiation of

antifibrotic therapy, oxygen therapy, psychosocial support, adequate nutrition, education of patient and family, symptom management and palliative care and specific rehabilitation programs, designed in order to prolong the survival period and to enhance the quality of life.

Declaration of conflict of interests

The author does not have any financial interest involving the companies and materials mentioned in this article.

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All authors have equal rights as the first author of this paper.

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