Editorial



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Nutritional status in patients with Idiopathic Pulmonary Fibrosis

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Idiopathic Pulmonary Fibrosis (FPI) is an interstitial pneumonia of unknown origin. Its respiratory symptoms are very limiting and its prognosis, despite the advent of new antifibrotic treatments (i.e. nintedanib, pyrfenidone), still remains poor [1,2]. The interest in IPF has increased in recent years due to both the appearance of these therapies and the important advances that have occurred in the knowledge of its pathophysiology and the imaging techniques. However, this interest has focused almost exclusively on the pulmonary involvement, characterized by mechanical changes derived from the rigidity of the lung parenchyma and the presence of areas with low ventilationperfusion ratios and a decrease in oxygen transfer through the alveolocapillar interphase [3]. Less known are the systemic manifestations of IPF. One of the most frequent is the presence of abnormalities in the nutritional status and/or body composition, which in turn can lead to muscle and bone problems. The prevalence of nutritional disorders has been estimated at 30% in hypoxemic IPF patients [4], almost doubling the percentage in those who are already candidates for lung transplantation [5]. The typical nutritional profile in patients with advanced FPI is a conserved body weight but with a decrease of more than 60% in lean mass [5], a circumstance generally associated with muscle dysfunction [6]. This disparity between body weight and lean mass can be explained by the frequent presence of a relatively high fat percentage in these patients [7]. Nevertheless, combined losses of body weight and lean mass can also be seen in some individuals [5]. It is worth noting that both body weight and lean mass loss are independent prognostic factors in IPF [5,8], making an early and full evaluation of these circumstances essential in all patients. The latter implies that the assessment should not be limited to the calculation of the Ideal Body Weight percentage (% IBW) or the Body Mass Index (BMI), but must be completed with blood analyses and determination of body composition, especially of the fat-free mass index (FFMI, usually obtained through bioelectric impedance). An important consequence of lean mass loss is muscle dysfunction. In fact, the weak relationship between pulmonary function and exercise capacity observed in many IPF patients already suggests the presence of this, and other additional factors. In spite of that, only a few studies have devoted their attention to muscle function in IPF patients. These studies have clearly demonstrated that there is muscle weakness both in respiratory and peripheral muscles [9-11], which undoubtedly contributes to the reduction in physical activity and worse quality of life shown by the patients [9,12].

However, as already demonstrated in other chronic respiratory diseases, the cause of the nutritional abnormalities and muscle dysfunction observed in IPF is probably multifactorial. On the one hand, there is a reduction in the level of physical activity that initially results from pulmonary involvement and its psychological consequences (basically anxiety and depression), but subsequently leads to deconditioning of different body components, such as the cardiovascular system, limb muscles and bones, further limiting physical capacity. On the other hand, IPF patients can have difficulties in feeding as a result of severe dyspnea. However, there are other possible etiological factors, such as pulmonary and systemic oxidative stress and inflammation [13,14] and hypoxia, all of them are able to induce protein content loss, due to both decreased synthesis and increased catabolism [15,16]. It is interesting to note here that the "spill over" theory (systemic extension of inflammation from a predominantly pulmonary location to other organs through the blood stream) has also been invoked in IPF and would be especially important during exacerbations [17]. Hypoxia also hinders the action of certain hormones and active peptides, such as leptin and ghreline (an endogenous secretagogue of the growth hormone) [6]. Furthermore, aging and the most frequent comorbidities of IPF can also favor nutritional abnormalities. This is the case of diabetes mellitus type II, present in up to 35% of patients with IPF, even after the exclusion of those who have received systemic corticosteroids for a long time [18,19]. It is also well known that some patients with COPD (an entity in which nutritional disturbances are also frequent) associate areas of fibrosis [20], and vice versa up to one third of IPF patients also exhibit pulmonary emphysema [21,22]. Vitamin D deficiency, with a prevalence of 20-40% in these patients [23,24], can also contribute to muscle and bone mass loss, and also seems to contribute to the negative prognosis of the pulmonary disease [25]. This vitamin deficit is probably being the result of both an inappropriate diet and the restriction in daily outdoor activities due to the primarily respiratory limitation [26]. Moreover, since IPF usually appears after the age of 50, the loss of muscle mass and function characteristic of elderly patients (sarcopenia) can be added to previous factors [27]. Finally, we should mention the deleterious effects of some treatments commonly used in IPF, such as systemic corticosteroids, which can produce nutritional alterations through a reduction in protein synthesis and an increase in their degradation [28,29], as well as induce acute and chronic myopathies, both characterized by muscle weakness [29,30]. On their own both nintedanib and pirfenidone could facilitate body weight and lean mass wasting due to their anorexic and gastrointestinal side effects [31]. However, pirfenidone could also have a positive effect on the nutritional status, since it inhibits transforming growth factor beta (TFG- β) [31], which has been implicated in weight loss in various disorders [32].

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Surprisingly, and despite all these evidences, the clinical guidelines for IPF management do not give specific recommendations for nutritional abnormalities associated with this disorder [33,34]. However, it appears reasonable to propose general measures related to lifestyle, such as appropriate diet and level of physical activity. It is interesting to note that there are some reports showing the effects of some diet schedules even in the occurrence and prognosis of IPF. Miyake et al. in particular, have shown the effects of a diet rich in fruit for the prevention of this lung disease [35], while the intake of saturated fatty acids seems to have the opposite effect, increasing the risk of suffering IPF [36]. The use of nutritional supplements can be useful when diet recommendations become insufficient. It is also recommendable to try to achieve a good control of the lung disease [6], controlling hypoxemia and avoiding exacerbations due to the effect they have on systemic inflammation and physical activity, as well as refraining from an improper use of systemic corticosteroids. Rehabilitation programs in turn, and especially those that include general and muscle training, have proven to be beneficial at least for muscle function [10,37] although their results can be further improved ensuring first a good nutritional substrate. Finally, even though anabolic drugs (eg, androgenic derivates or growth hormone secretagogues) have demonstrated no benefits in IPF patients in particular, it seems reasonable to use them in cases of severe malnutrition.

As a summary, abnormal nutritional status and/or body composition are frequent in IPF patients, and since they influence prognosis, clinicians must be alert for an early detection. Once the problem has been identified, healthy habits, including an appropriate diet and a good level of physical activity, should be recommended. The use of nutritional supplements may also be necessary in some cases. Moreover, the lung disease should be well controlled, improving oxygenation, avoiding exacerbations and harmful treatments, and initiating training with programs adapted to the patient's possibilities. Although their effects are controversial, anabolic drugs may be recommended in the most serious nutritional depletions.

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