Chapter

Nutritional Status and COPD

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Abstract

Since chronic obstructive pulmonary disease COPD and obesity became global public health challenges, the nutritional status evaluation is more important. How malnutrition and obesity will impact COPD prognosis and treatment is relevant and we considered need a separate approach. The new adiposity based chronic disease concept explains the role played by adiposity, and important studies, like European Community Health Survey ECRHS are highlighting the correlation between adiposity and lung function decline. On the other side, malnutrition decreases effort capacity and impairs the strength of respiratory muscles. Foods, nutrients and dietary patterns are influencing COPD prognosis and Mediterranean Diet, integrated in a healthy lifestyle should be part of COPD management. The important benefic role played by fibers, whole grains, combined with anti-inflammatory and antioxidant effects of fruits and vegetables, together with poly-unsaturated fatty acids PUFA, fish, vitamins and minerals, is detailed below, in contrast with the detrimental role of Western Diet. A multidisciplinary approach in COPD should be considered, integrating lifestyle interventions as important tools in COPD management.

Keywords: obesity, lung function, malnutrition, COPD, nutritional intervention, lifestyle

1. Introduction

Nutritional status and chronic obstructive pulmonary disease COPD.

COPD definition & prevalence. A global public health challenge that can be prevented and treated, COPD is the 4th leading cause of death, estimated to become the 3rd. According to Global Initiative for Chronic Obstructive Lung Disease GOLD 2020, "COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development" [1].

Prevalence- Worldwide, COPD is underdiagnosed and under-recognized, with a medium of <6% of the adult population described in studies. However, most of the studies define COPD by spirometry, not combining symptoms, limiting prevalence description [1].

Nutritional status evaluation. Body mass index BMI (weight per square height) is not the only criteria which defines nutritional status, moreover other measurements, like bioimpedance will describe better the muscle mass, lean mass and

adipose tissue. In COPD, the challenge will be to preserve, muscle mass, in order to support lung function. In scientific research dual energy X ray absorptiometry DXA, magnetic resonance imaging MRI are also used to evaluate body composition, but in daily clinical practice, bioimpedance is widely used.

Importance in COPD. Malnutrition, cachexia, obesity represent important co-morbidities, with impact on COPD evolution, treatment and mortality.

2. Obesity

Definition- Adiposity based chronic disease; Abdominal obesity. The concept of cardiometabolic chronic disease, elaborated by Rippe [2] and Mechanick [3] some years ago gain more acceptance. It defines 4 stages: risk, pre-disease, disease and complications for 3 entities: Adiposity based chronic disease ABCD, dysglycemic based chronic disease DBCD, cardiometabolic based chronic disease CMBCD. Practically, instead of obesity, a more complex approach is suggested, named ABCD. The risk stage combines genetics, environment with behavior. The second stage pre-disease describes the increased amount of adipose tissue with abnormal function and distribution. The third stage is classifying obesity based on BMI, with antropometrics and biochemical tests. The fourth stage is defining complications which are cardiometabolic and biomechanical. This more detailed approach is suggesting better the multifactorial interdependence in obesity and the important role played by adiposity.

Prevalence. Worldwide, overweight prevalence is 39% and obesity 13%, meaning 650 mil obese people and 2 bil overweight [4] being an important health-care issue. In order to better understand the impact of obesity on COPD evolution, analyzing actual studies results is important.

3. Lung function decline and obesity

3.1 European Community Respiratory Health Survey ECRHS

ECRHS is the longest prospective populational study, multicentric that involved 18000 adults along 20 years in 3 phases [5]. Very detailed information have been obtained on forced vital capacity FVC, forced expiratory volume in first second FEV1 as lung function markers. Weight changes were considered as: moderate weight gain 0,25–1 kg/year; stable weight +/− 0,25 kg/year; weight loss −0,25 kg/year. As pulmonary disease diagnosis, asthma was noted. Records about lifestyle were available: smoking status, physical activity, leisure time. Results are summarized below in **Table 1**.

How these data may be interpreted? Weight gain is leading to an accelerated decline of FVC and FEV1, independent of initial weight, normal, overweight or underweight. Clinically, an accelerated decline of pulmonary function was noticed. FEV1/FVC ratio was not altered during weight gain, suggesting the possible restrictive syndrome associated with obesity. For underweight group, surprisingly, FEV1 and FVC decline is attenuated, but the decline of FEV1/FVC ratio is accentuated, concluding that the airflow limitation typical for obstructive pulmonary syndrome may be favorized. Obese people who lost weight during the study period have an attenuated FVC and FEV1 decline suggesting the role played by obesity in the respiratory function and the importance of including obese people in comprehensive lifestyle interventions for restoring a good pulmonary function.

Baseline- young adulthood	Follow- up for 20 years	FVC, FEV1 at the end of the study	FEV1/FVC at the end of the study
Normal BMI, overweight and obese	Increase Weight	FVC and FEV1 accelerated decline	Without decline
Obesity	Decrease Weight	FVC and FEV1 attenuated decline	Without decline
Underweight as teenagers	Stable weight	FVC and FEV1 attenuated decline	FEV1/FVC ratio in an accelerated decline

Adapted after [5].

Table 1.
Conclusions from ECRHS results.

3.2 The Chinese study

A very large Chinese study included 452259 participants with diagnosed COPD, with a follow-up period of 10.1 years [6]. 10739 hospitalization events and deaths have been reported. The study concluded that underweight, with a BMI < 18,5 represents an increased risk of COPD, adjusted hazard ratio HR 1.78 (95% CI, 1.66–1.89). Abdominal obesity was positively associated with COPD risk, after adjustment for BMI. In conclusion, both, abdominal adiposity measures and BMI should be considered for COPD prevention.

3.3 Adipose tissue is not inert, but is acting like an endocrine organ

Adipose tissue may be considered a systemic modulator, influencing the response to environmental exposures and should be considered a potential target for future therapeutic interventions. As an endocrine organ, adipose tissue secretes adipokines, which are adipocyte derived factors that could affect airways function. Not only the inflammatory role recognized for leptin, but the anorexigenic role, accelerated metabolism, modulating immune function together with driving ventilatory regulation will influence pulmonary function [7, 8]. Leptin is supposed to increase bronchial hyperreactivity [9] . In contrast, adiponectin is the anti-inflammatory adipokine, exclusively produced by adipocytes. In lean persons their activity is normal, but decrease in obese patients. Hypoxia, adipose tissue inflammation, macrophage infiltration in adipose tissue will induce finally insulin resistance [9].

3.4 Obesity paradox

Many years ago, in 2002 Gruberg used for the first time the term" obesity paradox" to characterize the lower risk of complications and mortality observed for overweight and obese people versus normal weight or underweight patients in coronary heart disease, pulmonary hypertension, heart failure, stroke, hypertension [10]. Not well elucidated, the concept of obesity paradox is still a subject for study. Increased risk of developing obesity is characterizing patients with COPD, since long term treatment with systemic glucocorticoids is administered [11] and usually a decreased physical activity is seen. Loss of free fat mass FFM, accompanied by muscle weakness and exercise capacity decrease is seen in COPD patients, leading to the conclusion that FFM may be a better predictor than BMI. FFM and weight loss will impact prognosis in COPD [12]. Landbo, Jee [13, 14] described a lower mortality risk for COPD patients with higher BMI. Moreover, Cao [15]

described for underweight patients higher risk of mortality compared to leaner counterparts. (HR:0.78; 95% CI:0.65–0.94 and HR:0.69; 95% CI: 0.54–0.89). In this context, the importance of cardiorespiratory fitness CRF should not be neglected. Findings from Aerobic Center Longitudinal Study proved that CRF modify the association between adiposity and results on survival. Fogelholm [16] found a lower all cause/cardiovascular CVD mortality risk for individuals with high BMI and improved aerobic capacity, but this protective effect disappear for BMI > 35 kg/m^2. In a study concluded by Sabino [17] for 32 patients with COPD, higher FFM and exercise capacity lead to better functional outcomes for overweight and obese patients. Practically, obesity paradox is mainly related to CRF and FFM. The role of physical activity PA is well proved in type 2 diabetes, CVD but not well documented in COPD, suggesting potential future correlations and research PA-obesity paradox-CRF and COPD.

In COPD, considering obesity paradox, a question arise: To treat or not to treat? Best strategy is under research, clinicians dilemma is to recommend weight reduction which will improve cardiac performance but may worsen respiratory performance and increase mortality? Which could be the ideal intervention to loose weight? [18].

A new study published in 2020 may propose new answers [19]. The relationship between exacerbation frequency in COPD should be investigated in detail in order to understand better the obesity paradox [20, 21]. This is an observational, retrospective study performed in Netherlands [19] that included 604 patients with COPD, stratified based on BMI level. Lowest five year survival rate was found for underweight and normal weight patients (35%, 41%, p = NS not significant). Survival increased at 47% (p = 0.028) for overweight group, 51% (p = 0.046%) for moderately obese and 63% for severely obese (p = 0.003) patients, versus normal weight patients. Cox regression analysis showed that the effect was independent by other variables and HR = 0.962 (95% CI 0.940–0.984) p = 0.001. The study demonstrated a significant reduction in the exacerbation frequency that required hospitalization in obese patients. Moreover, a significant decrease by 34–40% of readmissions for obese patients was noticed together with a decreased mortality. In contrast with other studies, were the" protective" effect was lost for BMI > 32 kg/m^2, in this study, the group with BMI > 35 kg/m^2 was more protected. The fact that cardiovascular comorbidities, atherosclerosis, is causing a higher mortality rate for leaner patients with COPD should be discussed [22]. Fat reserve, offering a protective source of energy along hospitalization in critical illness should be considered, too. This is supported by better survival rate for critically ill patients with a higher BMI [23, 24]. Preserved muscle mass mean a better prognosis influencing stroke volume and cardiac output [25]. Furthermore, lower systemic vascular resistance is described for obese patients. On the other side, underweight patients, in this study, had an increased mortality, attributed to decreased CRF in the context of lower muscle mass, decreased cardiac output and limited energy storage [23, 24]. Underweight is associated with an increased readmission time in this study, in line with previous data about malnourished patients. How the results of this study should be interpreted? They are limited to specific groups of patients suffering from a disease and should not be considered guidelines for preventive measures at populational level, as authors are mentioning. But, best explanation of this paradox will help the specific approach for future interventions. In conclusion, exacerbation frequency reduction in obese patients with COPD may partially explain obesity paradox, but more prospective research is needed.

4. Malnutrition

4.1 Prevalence

Malnutrition is represented in COPD with a prevalence of 30–60% [26]. Daily energetic expense with respiratory effort is 36–72 kcal/day, normally, but this value may increase by 10 times in COPD. Malnutrition is produced by increased basal metabolic rate, low nutritional intake, or both. The energy spent may be increased more by infections associated with fever.

4.2 The diagnosis of malnutrition

The diagnosis of malnutrition will be based on Global Leadership Initiative on Malnutrition GLIM [27] criteria for the Diagnosis of Malnutrition: a consensus report from the Global Clinical Nutrition Community. There are described 3 phenotypic criteria: low BMI, decrease intake or assimilation of food, unintentional weight loss; and 2 etiologic criteria: disease severity, inflammation and muscle mass decrease. For diagnosis, one etiologic and one phenotypic criteria will be mandatory.

Being an unfavorable prognosis in COPD, malnutrition predispose to infections, lead to weight decrease, decrease effort capacity and the strength of respiratory muscles. Moreover infections decrease surfactant production.

Issues to be addressed in COPD: loss of muscle mass is a strong negative prognosis factor, as has been discussed in previous paragraph and should be addressed by a correct medical nutrition therapy that will be detailed later in this chapter.

5. Lung function and individual foods and nutrients in the context of COPD

5.1 Fibers and whole grains

Larger research focused on wholegrain has been done in relation with cardiovascular disease CVD and cancer [28], but independent benefits have been reported in observational studies on lung function [29, 30] and COPD. Synergic effects of phenolic acids, phytic acid, selenium, vitamin E, essential fatty acids, found in whole grains explain documented benefits on respiratory disease, observed in nonrespiratory diseases, too. Large prospective studies [31] revealed a 40% reduction in the COPD risk after higher fiber intake. Epidemiological data associated fiber intake with lower serum levels of C reactive protein and cytokines (interleukin IL 6, tumoral necrosis factor TNF) and high adiponectine levels, with well-known anti-inflammatory effect. Protective effects are seen mainly for cereal fiber intake in current smokers and ex-smokers, but fruits and vegetable fibers are evidenced, too [31, 32].

5.2 Antioxidant and anti-inflammatory foods - fruits and vegetables

The inflammatory/oxidative pathogenetic implications in COPD, as well as nutritional status and the dietary quality in COPD lead to verify the relations between respiratory effects of antioxidants and anti-inflammatory dietary components. In 2 recent Swedish populational studies, beneficial role of high consumption

of fruits and vegetables on long term was reflected in a decreased incidence of COPD, 35% decreased risk in men ($p < 0,0001$) and 37% lower risk for women ($p < 0,0001$) consecutive high consumption of fruits (boths) and vegetables (men). This benefit was mainly obvious in smokers [33, 34]. In conclusion fresh, hard fruits and vegetables provide benefits on lung function decline, COPD symptoms, COPD incidence and mortality. Specific, the protective effect in the men cohort was limited to current smokers or ex-smokers, explained probably by increased antioxidative stress level in smoking. Individual food items observed: apples, pears, peppers, green leafy vegetables [33].

5.3 Vitamins

Limited evidence is reported about any benefit of vitamin D supplementation in COPD progression and immune responses. A conclusion can be drawn, for patients with baseline low level of (OH) D < 25 nmol/L supplementation is beneficial in preventing COPD exacerbations [35]. There are described genetic mutations of vit D binding protein associated with decreased vit D levels linked with a higher risk of COPD [36]. Conflicting results are reported with vit D supplementation but in conclusion they pointed out a benefit for patients with low baseline levels of (OH) D < 25 nmol/L, the active metabolite of vitamin D [37]. The antioxidative effect of vitamin E is revealing promising options for lung function decline associated with age. Well recognized action for vitamin C, which protects lung tissue, focusing on lung function maintenance mediated by vitamin C may lead to a greater success in exploring potential targets in preventing pulmonary diseases [38].

5.4 Minerals

Intake of calcium, phosphorus, potassium, iron and selenium are positively associated with lung function measures (measured by FEV1) based on a case control study published in Japan. 35% reduction of COPD risk is inversely correlated with Calcium intake [39]. An independent positive correlation is found between FEV1 and selenium, calcium, iron and chloride but inverse correlation with sodium and potassium in the general population [40]. Cooper and selenium serum levels are also related to higher lung function in other cross-sectional studies [41]. Through its protective effect against bronchoconstriction and inflammation, Magnesium may play a beneficial role in pulmonary function [42]. Further studies are warranted to prove protective effects of some minerals, explained mainly by antioxidant and anti-inflammatory properties.

5.5 Polyunsaturated fatty acids & fish

Higher intake of ω3-PUFA is related to lower levels of cytokine TNF (OR = 0.46, $p = 0.049$) in stable patients with COPD. The same study mentioned the association between a high intake of ω 6-PUFA with high inflammatory markers, for example C reactive protein CRP, interleukin 6, IL6. (OR = 1.96 for IL-6, $p = 0.034$; for CRP OR = 1.95, $p = 0.039$) [43]. Lower FEV1 after higher consumption of ω6-PUFA was evidenced in a large population based cross sectional study, mainly in smokers, with a higher risk of COPD but without relation to ω3-PUFA [44]. Potential fish benefits in the diet might be obvious within the whole diet, as a recent analysis of two large cohorts is suggesting [45]. 4 servings of fish/week were associated with lower risk of newly diagnosed COPD in 2 large US cohorts. A healthy diet including fish and vegetable sources of ω3-PUFA may be beneficial for COPD, as fish intake could reduce the risk of COPD when plant sources of ω3-PUFA intake is high.

5.6 Foods with negative effects on lung function and COPD

A cross sectional analysis of NHNES [46] associated independently an obstructive pattern in spirometry with increased intake of cured meat but also with newly diagnosed COPD patients, independently of Western dietary pattern or other associations [46, 47]. A more recent large populational study from Sweden confirmed the detrimental effect of processed red meat [48, 49] but not unprocessed. Another reference showed an increased risk of readmission from COPD associated with cured meat intake. A meta-analysis, recently summarized results indicating that higher consumption of red processed meat (more than 75-785 g/week) is leading to a 40% increased risk of COPD [50, 51].

6. Dietary patterns and COPD

In COPD pathogenesis, pollution, genetics, smoking, aging, play a role in developing inflammation, oxidative stress, mucus hypersecretion, antioxidant

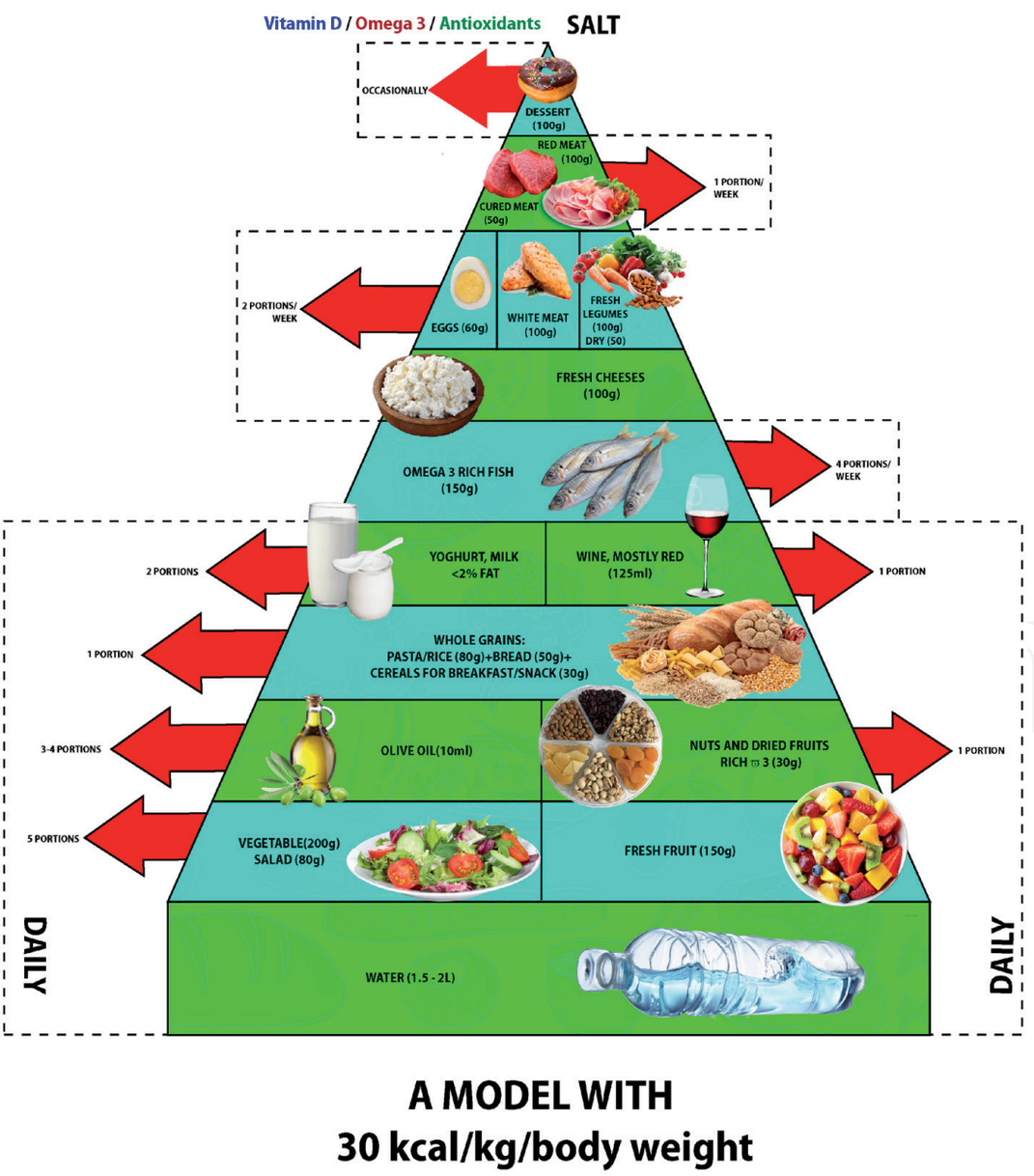

Figure 1.
Food pyramid for subjects with COPD.

depletion, airway remodeling [28] . But lung function is influenced by dietary factors, too. Detrimental role for lung function of Western type diet, characterized by high energy dense food, red and processed food, added sugar, high salt intake, preservatives, low antioxidants, high glycemic index and saturated fats is already proven. By contrast, fruits, vegetables, whole grains, alcohol, wine, legumes, nuts, coffee, fish, high antioxidants, low glycemic index and unsaturated fats, as part of a mediterranean healthy pattern are a support of a healthy lung function. As dietary patterns, is clearly proved the detrimental role of Western model and the protective role of Mediterranean model in COPD.

A special pyramid was designed for COPD patients, represented below, in **Figure 1**, adapted after International Journal of COPD, 2020 [52].

7. Medical nutrition therapy MNT in COPD

Daily energy has to be adapted to activities and requirements calculated by bio-impedance and calorimetry in order to maintain BMI below 30–32 kg/m^2. (special situation in malnutrition is detailed separately). Recommended macronutrients proportion is: 15–25% proteins, 30–45% fats, 40–55% carbohydrates. It has to be underlined that the % of macronutrients is important to maintain (respiratory quotient)RQ, the marker for respiratory tolerance of the pattern recommended. Respiratory quotient, defined as CO_2 volume expired/O_2 volume consumed is the respiratory parameter that indicates food mix metabolized. RQ is 1 for carbohydrates, 0.85 in mixed diets, 0,82 for proteins and 0.7 for fat. The macronutrient percentage is important, correct diet, but not overconsumption will be critical for COPD patients which have compromised ability for gas exchanges, because excess calories produce CO_2 that must be expired and will influence the respiratory process [26]. Considering drug-food interactions, special attention should be considered for salt intake during oral corticosteroid treatment, that should be minimized. Meanwhile, due to increased risk for metabolic disorders, especially high glycaemia, sugar intake should be limited [26].

7.1 MNT in obesity

Muscle mass decrease is a risk factor for mortality from COPD and muscle mass maintenance is important. Considering these, the recommended daily protein intake is 1,2–1,5 g/kgb/day, combined with physical exercises, much more compared to general population recommendations of 0.75–1 g/kgb/day [53]. General recommendations, specified in the 2019 obesity guidelines [54] should be emphasized: decreasing food energetic density, avoid skipping meals, but also snacking, eating just as response to hunger sensations and stop eating when satiety appears, eating slowly and mindfully, as an assumed responsibility, not as a restriction.

7.2 MNT in malnutrition

the objective is to address hypermetabolism in order to prevent weight decrease and lean mass decrease. Practically lean mass/muscular mass maintenance is the key for a good prognosis in COPD [26]. From clinician perspective, MNT should address appetite decrease and improper food intake. Main recommendations are: small meals, frequent, nutritional dense. The main meal should be at the time when the energetic level is the highest. It is recommended to rest before meal. The proper caloric intake will be adjusted in order to maintain a BMI of 20–24 kg/m^2. Availability of food which request minimum time to be prepared, eventually pre-prepared is important. To limit alcohol intake <2 portions/day, 30 g is mandatory.

8. Lifestyle recommendations in COPD

All these nutritional recommendations should be integrated in a healthy lifestyle. Mandatory tobacco cessation, gradual increase in physical activity, according to cardiorespiratory fitness score, optimal sleep and mindfulness, seen as a harmony between mind, body, thoughts and feelings will be beneficial for COPD patients. Despite a great interest in managing COPD, there is a gap in recommendations for physical activity (PA), the most commonly prescribed PA is: walking, cycling, strength training and nonspecific aerobic training. Physical activity PA should be part of lifestyle, may be performed in groups, social or independently. People with COPD should be active until breathless or as per their capacity. Recommended PA durations are ranging from 20 to 45 min/day, depending on guideline. For severe patients, to add short intervals rather than a continuous activity is mentioned. No specific guidelines are mentioning sedentary behaviors. Despite the fact that no specific sleep recommendations are in COPD guidelines, we encourage a referral to a sleep specialist [55].

9. Post-COVID 19

Post COVID 19 pulmonary rehabilitation measures, which start in the hospital for moderate cases, will improve symptoms like dyspnea, anxiety, depression and should continue as part of a healthy lifestyle after recovery, for future. A healthy lifestyle, normalizing body weight by adopting a healthy model adapted to caloric and nutritive requirements daily physical activity and an optimal sleep, mindfulness, will remain key principles for COPD patients after SARS-COV2 infection.

10. Conclusion

New concept of cardiometabolic disease reflects in a more appropriate way the role of adipose tissue in all comorbidities developed in obesity. Lung function decline associated with obesity, as it is revealed by important studies may be an interesting relation to be considered in COPD obese patients. Moreover, malnutrition, with the worst prognosis on COPD development will influence patients management. The importance of a healthy dietary pattern in COPD, designed in the new COPD pyramid are suggesting the strong correlation between foods, nutrients in order to achieve best therapeutical results. Medical nutrition therapy in COPD, based on Mediterranean model, with a high % of proteins, integrated in a healthy lifestyle should be part of COPD management. Nutritional status play an important role in future COPD prognosis and a multidisciplinary team with pneumologist, nutritionist and kinetotherapist should cooperate in order to achieve best long term outcomes.

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