Original Research Article Study of body composition and systemic effects in Chronic Obstructive Pulmonary Disease

Susmita Saha¹, Jyotsana.R. Bharshankar², Akshay Berad^{3*}

¹Demonstrator, Department of Physiology, Diamond Harbour, Government Medical college, South 24th Paragana, West Bengal, India

²Professor, Department of Physiology, Government Medical College, Nagpur, Maharashtra, India ³Assistant Professor, Department of Physiology, Government Medical College, Nagpur, Maharashtra, India

Received: 12-10-2020 / Revised: 29-11-2020 / Accepted: 25-12-2020

Abstract

Chronic Obstructive Pulmonary Disease is a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive. Airflow obstruction in main feature of COPD . Body mass is divided into two compartments, fat mass and fat free mass. Fat free mass mainly contain metabolically active organs particularly skeletal muscle mass. Aim of study was to study spirometry in COPD patients & assess disease severity by GOLD criteria and to study the parameters of body composition in COPD patients The present study was a cross sectional study carried out in 100 stable male COPD patients with the aim of evaluating body composition and systemic effects in different stages (I-IV] of the disease according to GOLD criteria. Anthropometric parameters Weight, Standing height, Waist circumference, Hip circumference, Body mass index (BMI) were recorded. Parameters of spirometry (FEV1], (FVC], FEV1/FVC were included . Body composition parameters were Body Mass Index (BMI], Fat Free Mass Index (FFMI], Fat Mass Index (FMI]. In our study most of the COPD patients were in severe stage which mainly included elderly people of >60 years of age. Both BMI and FFMI was significantly decreasing as the severity of disease increased according to GOLD criteria. FMI decreased with higher COPD stages. Six-minute walking distance test was significantly decreasing as the disease severity increases. In patients of COPD there is loss of fat free mass thereby decreasing exercise capacity. High risked individuals must be regularly screened with spirometry for mild COPD so that necessary preventive measures can delay the onset of progression of disease.

Key words : COPD, Spirometry, Fat Mass Index (FMI], Fat Free Mass Index. This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0] and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read], which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a name coined for the diseases previously known as chronic bronchitis and emphysema. Recently the Global Initiative for Chronic Obstructive Lung Disease (GOLD) defined COPD as "a common preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases.

*Correspondence

Dr. Akshav Berad

Assistant Professor, Department of Physiology, Government Medical College, Nagpur, Maharashtra, India.

E-mail: akshay_berad@rediffmail.com

Exacerbations and comorbidities contribute to the overall severity in individual patient". [1] The global prevalence of physiologically defined chronic obstructtive pulmonary disease (COPD] in adults aged more than 40 year is approximately 9-10 % .[2] In India, the prevalence of COPD is 4.1% with a male-to-female ratio of 1.56:1 in the population of above 35 years of age. [3] COPD is the fourth-leading cause of mortality worldwide. Mortality from COPD is expected to increase further. It will rank at the third position causing 6 million deaths annually in 2020 [4]. Airflow obstruction in COPD is defined as a post bronchodilator forced expiratory volume in 1st sec (FEV1) to forced vital capacity (FVC) ratio less than 0.70. FEV1 is not only a marker for grading of COPD severity but also a marker of premature death from any

cause. . Weight loss and low body mass index (BMI), are part of the BODE (BMI, airflow Obstruction, Dyspnoea, and Exercise capacity) lindex, are also established negative prognostic factors for survival of COPD patients. [5] Body mass is divided into two compartments, fat mass and fat free mass. Fat free mass mainly contain metabolically active organs particularly skeletal muscle mass. Twenty five to forty percent of patients with advanced disease with a forced expiratory volume in 1st second (FEV1] less than 50% have weight loss, low body mass index (BMI) and low fat free mass index (FFMI) [6]However, recent data suggests that fat-free mass index (FFMI] provides information beyond that provided by BMI to compare weight loss in COPD patients. (7]The traditional marker for COPD progression, in the absence of other validated markers, has been lung function measurement specifically, forced expiratory volume in 1st second (FEV1]. So, the study was planned to observe weight loss, changes in body composition parameters, skeletal muscle dysfunction and limitation in exercise capacity. As a secondary outcome, it was also investigated whether BMI and FFMI could equally be associated to the recent staging of GOLD classification and which one better reflects weight loss in COPD patients. Available guidelines categorise the severity of COPD primarily by using forced expiratory volume in one second (FEV1], whereas symptoms play a minor role in the assessment. This tight link between FEV1 and COPD reflects the fact that spirometry is the standard for defining the presence of airway obstruction and the progressive loss of FEV1, the physiological variable that characterises COPD severity and predicts its mortality. Spirometry has become the standard procedure of choice for evaluating pulmonary function test because of good quality and inexpensive test[8]. Aim of present study was to study spirometry in COPD patients & assess disease severity by GOLD criteria and to study the parameters of body composition in COPD patients such as, Body Mass Index (BMI), Fat Free Mass Index (FFMI), Fat Mass Index (FMI).

Material and Methods

The present study was carried out in department of Physiology in collaboration with Chest and Tuberculosis department . The study protocol was approved by the Institutional Ethics Committee (IEC) of Indira Gandhi Government medical college , Nagpur.

Study design: Cross sectional study.

Study population

Male patients of age group 40-65 years, coming in Chest and Tuberculosis Out Patient Department, diagnosed as COPD by chest physicians, were included in the study. All patients with COPD were in stable state at the time of study. After registration of the subject, a detailed clinical history was obtained from each patient including history of occupation, smoking per pack-year, disease onset, exacerbations, associated co-morbidities, and current therapy. Clinical examination was done in all patients and findings were recorded.

Selection criteria

- 1. Male patients of age group 40-65 years.
- 2. Diagnosed as COPD by chest physicians.
- 3. Clinically stable on examination without any acute exacerbation.
- 4. On medication according to the stage of their disease.
- 5. No self-reported asthma or reversibility >12% of airway obstruction after administration of a $\beta 2$ agonist.

Exclusion criteria

Persons with following features were excluded from the study:

- 1. Diagnosed cases of bronchial asthma.
- 2. Respiratory infection in the last 4 weeks.
- 3. Active lesion of tuberculosis. Subjects with gross clinical abnormality of vertebral column, thoracic cage, neuro-muscular diseases.
- 4. Diagnosed cases of malignancy, drug addiction & alcoholism.
- 5. Subjects who had past abdominal or chest surgeries.
- 6. Known cases of Diabetes Mellitus, Coronary Artery Disease, Hypertension.

Study protocol

The selected patients were given appointment from 10: 00 am -12:00 pm in Physiology Department 2 days after their registration in chest OPD. They were asked to keep 4 hour fasting before coming for the study procedure on the day of appointment. Measurement of anthropometric parameters, spirometry, body composition and 6 Minute Walk Distance were done. The whole procedure of investigation and purpose of the study was explained to all subjects and informed written consent was obtained from them. After measuring standing height, weight, hip and waist circumference patients were subjected to spirometry with an electronic portable spirometer (MEDSPIRERrecorder and medicare system] . Then they were assessed for body composition test by bio-electrical impedance analysis QUADSCAN-4000, with BODYSTAT (Isle of Man] machine. 6MWD test was done by making the subject to walk in a 30m long

straight corridor marked in intervals of meters to observe the exercise capacity.

Anthropometric measurements included

Weight (Kg) , Standing height (cm) ,Waist circumference (cm) , Hip circumference (cm], Body mass index (BMI] (kg/m^2).

BMI was calculated as per following formula (9]

BMI = weight in kilogram / height in meter squared (kg/m2)

Spirometry

The technique of performing various lung function tests in the present study was based on operation manual of the instrument with special reference of American Thoracic Society. (10]The following parameters of spirometry were recorded:

1) Forced expiratory volume in one sec (FEV1] in % predicted.

2) Forced vital capacity (FVC] in % predicted.

3) FEV1/FVC ratio in % predicted.

The study subjects were staged as per GOLD guidelines, 2013 : Post bronchodilator [FEV1/FVC ratio<70% predicted], mild (FEV1≥80% predicted], moderate [50%≤FEV1<80% predicted], severe (30%≤FEV1<50% predicted], and very severe (FEV1<30% predicted] or FEV1<50% predicted plus the presence of signs of chronic respiratory failure. The patients were divided into four groups [I, II, III and IV] according to the severity by GOLD stages.

Body composition analysis

Patients were explained and assured about the safety of the procedure. Body composition analysis was performed by Quadscan 4000 machine as per guidelines given by the system providers[11]. Following parameters were taken for the study: 1.Body mass index (BMI) [Kg/m²]

2. Fat free mass index (FFMI) [Kg/m²]

3. Fat mass index (FMI) [Kg/m²]

Exercise Capacity

Exercise capacity was assessed by the six-minute walking distance test (6MWD] which is a reliable test for evaluation of physical activity in COPD patients. The 6MWT was performed according to the ATS guidelines, 2002. The test measures the distance that a subject can quickly walk on a flat, hard surface in a period of 6 minutes. Usually healthy subjects can walk 400-700m in 6 minutes. (12, 13]

Statistical analysis

The data were presented as mean (SD]. Statistical significance of differences in all study groups were estimated with one-way Analysis of Variance (ANOVA] with an appropriate post hoc test (Tukey's post hoc test] wherever necessary. For categorical variables Chi-square test was used. The associations between BMI and FFMI (dependent variables] and study parameters (independent variables] were determined using Pearson correlation coefficient analysis. Main Analysis was performed using statistical software SPSS version 22; p<0.05 considered significant.

Results

100 Subjects were divided in four groups from mild to very severe (GOLD stage I-IV) according to spirometry values based on FEV1% predicted and FEV1/FVC ratio <0.7. Then changes in body composition parameters in different stages of COPD were observed applying ANOVA test. P value <0.05 was considered statistically significant.

	Total	I	П	III	IV	P value
	n = 100	n = 13	n = 20	n = 41	n = 26	1 value
FEV1% predicted	46.16(19.05)	81.92(2.36)	61.25 (7.62)	40.41 (6.36)	25.73(2.30)	<0.0001

 Table 1: Showing values of FEV1 % predicted of COPD patients in different stages of severity by GOLD criteria

Data presented as mean (SD]. Results of ANOVA with p value <0.0001 considered highly significant. In our study, we observed there were 13 patients in stage I, 20 in stage II, 41 in stage III and 26 in stage IV. Most of the patients had advanced COPD (GOLD III, n = 41 and GOLD IV, n = 26]. Among 100 subjects, maximum were in severe stage [GOLD III] and minimum were in mild stage (GOLD I].

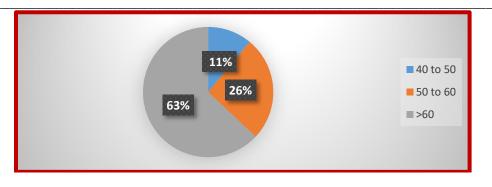


Fig 1: Pie diagram showing age wise distribution of COPD patients in different stages of severity by GOLD criteria

Figure 1 is the graphical representation of age wise distribution of COPD patients in different stages of severity by GOLD criteria. It was found only 11% of COPD patients in our study group were in the age group of 40-50 years, followed by 26% are aged between 50-60 years whereas 63% of them were above 60 years of age.

Table 2: General charac	teristics of COPD pati	ents in different stages o	of severity by GOLD criteria

	Total(n = 100)	I(n = 13)	II(n = 20)	III(n = 26)	IV(n = 41)	P value
Age (year)	58.69 (6.47)	52.38 (6.53)	56.45 (6.47)	60.44 (5.81)	60.81 (5.8)	< 0.0001
Height (cm)	161.38 (5.89)	161.54 (5.73)	163.80(5.64)	160.53(6.20)	160.62(5.56)	>0.05
Weight (kg)	47.51 (9.25)	57.15 (5.39)	53.75 (9.60)	45.59 (7.85)	40.92 (5.38)	< 0.0001

Data presented as mean (SD). Results of ANOVA with p value <0.0001 considered highly significant.Table- 2 shows the mean age of COPD patients in stage I was 52.38 ± 6.53 years, in stage II, 56.45 ± 6.47 years, in stage III, 60.44 ± 5.81 and in stage IV, 60.81 ± 5.8 years. Mean age of 100 COPD patients in our study was 58.69 ± 6.47 years. It was observed that with increasing COPD stage, the age presentation of the disease was also increasing significantly p (<0.0001). Our study presented most of the patients in stage III and IV were ≥ 60 years. The mean height of COPD

patients in GOLD stage I, II, III and IV was 161.54 ± 5.73 , 163.80 ± 5.64 , 160.53 ± 6.20 and 160.62 ± 5.56 cm respectively with no statistical difference (p value = 0.219).Table- 2 also shows the mean weight in stage I was 57.15 ± 5.39 kg, in stage II; 53.75 ± 9.60 kg, in stage III; 45.59 ± 7.85 kg and in stage IV; 40.92 ± 5.38 kg. Average mean weight in the 100 study population was 47.51 ± 9.25 kg. We observed, with increasing severity of COPD, there was significant weight loss where maximum weight loss was observed in GOLD stage IV (p<0.0001).

 Table 3 : Showing body composition parameters of the COPD patients in different stages of severity by

 GOLD criteria

Parameter	Total n = 100	I n = 13	II n = 20	III n = 41	IV n = 26	P value
$BMI(Kg/m^2)$	18.15 (3.06)	21.83(1.36)	19.90 (2.87)	17.58 (1.87)	15.87 (1.03)	< 0.05
FFMI(Kg/m ²)	11.25 (2.73)	15.11(1.95)	13.21 (1.46)	10.92 (1.87)	8.34 (1.03)	< 0.0001
FMI	6.27 (1.04)	7.33(0.84)	6.47 (1.07)	6.02 (0.99)	5.97 (0.89)	> 0.05

Data presented as mean (SD). Results of ANOVA with p value <0.05 significant; p <0.0001 highly significant. Mean BMI in the whole study group (n = 100) was $18.15 \pm 3.06 \text{ kg/m}^2$ whereas FFMI was $11.25 \pm 2.73 \text{ kg/m}^2$. In table 3 the mean BMI decreased significantly as disease severity increased (p<0.05). Mean FFMI also observed to be very significantly decreasing in

relation to GOLD staging as the disease severity increases. FFMI in stage I was significantly higher compared to the other three stages (p<0.0001). In contrast, FMI decreased in advanced disease state as in stage II, III and IV but it was not statistically significant (p>0.05).

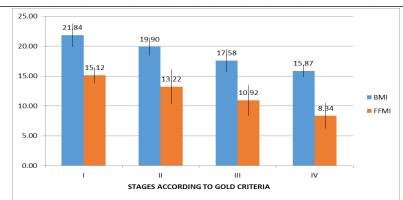


Fig 2: Bar diagram showing comparison of mean BMI (kg/m²) and FFMI (kg/m²) in different stages of COPD by GOLD criteria

Figure 2 is the graphical representation of comparison of BMI and FFMI in four stages of COPD.

Table 4: Showing distribution of COPD	patients in relation to BMI in different stages	of severity by GOLD

Classification					
Classification	I (n = 13)	II(n = 20)	III(n = 41)	IV(n = 26)	P value*
Underweight (BMI < 18.5 kg/m ²)	0	7	27	23	< 0.0001
Normal weight (BMI ≥18.5 kg/m ²)	13	13	14	3	HS

*Chi-square test with p value <0.0001 considered highly significant.

Table- 4 shows out of 100 COPD patients, 57 were underweight comprising maximum patients from severe and very severe group whereas 43 were of normal weight mainly coming from mild and moderate group. The undernourished BMI status was observed in 21.2% patients in early COPD (stage I and II, n = 33) whereas it was observed in 74.6% of patients in advanced COPD (stage III and IV, n = 67).

Table 5 : Showing 6MWD (m) performed by CO	D patients in different stages of severity by GOLD criteria

	Total n = 100	I n = 13	II n = 20	III n = 41	IV n = 26	P value
6MWD (m)	253.39(77.28)	356.62(9.95)	341.30(20.52)	233.63(42.42)	165.31(14.63)	< 0.0001

Data presented as mean (SD). Results of ANOVA with p value <0.05 considered significant

Exercise capacity of the patients measured by 6MWD following ATS guidelines 2002. Then it was subjected to ANOVA test and result is shown in the following table 5. It was observed in table 5 that 6MWD was significantly decreasing with the disease severity. Subjects with more advanced disease (stage III and IV) had lower mean of 6MWDT respectively 233.63 \pm

42.42 and 165.31 \pm 14.63 than primary disease state (stage I and II) respectively 356.62 \pm 9.95 and 341.30 \pm 20.52 meter.

The assessment of exercise capacity was done by observing the number of patients who could walk the distance more than 350 meter or less than 350 meters. The patients who could walk less than 350 meters distance were considered to have poor exercising capacity according to the ECLIPSE cohort study.

		criter	ria		
6MWD(m)	Ι	Π	III	IV	P value*
	n = 13	n = 20	n = 41	n = 26	P value*
<350m	2	11	41	26	< 0.0001
>350m	11	9	0	0	HS

Table 6: Showing distribution of 100 COPD patients in relation to 6MWD (m) in different stages by GOLD

*Chi square test; p<0.0001 highly significant.

From the table 6 it was observed that 41 patients in stage III performed 6MWD test <350m followed by 26 patients in stage IV. In stage III and IV no patient performed 6MWD test more than 350 meter. Only 11 patients in stage I (n = 13) and 9 patients in stage II (n = 20) have shown better exercise capacity by walking more than 350 meter distance in 6 minutes. Our observation was only 20 patients could walk >350m whereas 80 patients walked a distance <350 m in 6 minutes in total 100 study population.

Discussion

Although COPD is primarily a disease reflecting lungs, it produces wide range of systemic consequences such as nutritional changes, skeletal muscular dysfunction, abnormal body composition and reduced exercise capacity. Malnutrition is a frequent complication in COPD and an important predictor of functional capacity, mortality and morbidity. Several studies have confirmed lower values of body composition parameters (BMI, FFMI) in COPD patients. The change in these parameters keeps on increasing with increased severity of disease. Hence our study was conducted to observe changes in body composition markers in stable COPD patients according to disease severity by GOLD criteria. It was a cross sectional study including 100 stable COPD patients. They were divided in four groups according to FEV1% predicted as mild (GOLD-I), moderate (GOLD-II), severe (GOLD-III) and very severe (GOLD-IV). Only male patients of age group 40-65 years were included in the study to avoid gender and age variation in spirometry and body composition. As shown in table 1 the mean FEV_1 decreased significantly (p<0.0001) with the disease severity by GOLD criteria. In our study mean FEV₁ was 81.92 ± 2.36 in stage I, 61.25 ± 7.62 in stage II, 40.41 \pm 6.36 in stage III and 25.73 \pm 2.30 % predicted in stage IV. As shown in figure 1, among 100 participants, 13 cases were found in mild stage (GOLD-I), 20 cases were in moderate stage (GOLD-II), 41 cases were in severe stage (GOLD-II) and 26 were in very severe stage (GOLD-IV). The findings of our study are in accordance with the studies by Schols et al (2005). Most of the patients they had in advanced COPD (GOLD II, n = 71; GOLD III, n = 134; and GOLD IV, n=207) which was supporting our finding[14]. Rufino R. et al (2007) also found similar distribution of patients including 3 cases as mild, 18 as moderate, and 17 as severe in total 38 COPD patients[15]. As shown in table 2, the mean age of COPD patients in stage I was 52.38 ± 6.53 , in stage II, 56.45 ± 6.47 , in stage III, 60.44 ± 5.81 and in stage IV, 60.81 ± 5.8 years. Mean age of 100 COPD patients in our study was 58.69 ± 6.47 years. De et al (2012) observed the average age of COPD patients in their study was 62.1 ± 10.4 years. In another study, Gupta et al (2014) demonstrated the mean age of the patients was 55.66 ± 9.73 years in their study that is similar to our finding. They suggested COPD is a disease of middle aged to elderly people involving more patients in severe and very severe stage[16]. As shown in table 2, mean values of weight decreased significantly in stage I, stage II, stage III and stage IV respectively 57.15 \pm 5.39, 53.75 \pm 9.60, 45.59 \pm 7.85 and 40.92 \pm 5.38 kg (p <0.0001). Mean weight of overall 100 COPD patients was 47.51 ± 9.25 kg. The mean weight was observed to be decreasing in relation to GOLD staging, where maximum weight loss was observed in GOLD stage IV followed by stage III. As shown in table 4 out of 100 COPD patients, 57 patients were underweight, 43 were of normal weight. The nourishment status from BMI as per WHO classification, observed in our study was like this: in stage I all patients were normal weight; in stage II (n =20) 35%, in stage III (n = 41) 65.8% and in stage IV (n = 41)= 26) 88.4 % were underweight that were highly statistically significant (p<0.0001). It was observed that with increasing COPD stage the proportion of undernourished subjects increased significantly. It was observed that 21.2% patients in early disease (stage I and II) were underweight and 74.6% patients in advanced disease (stage III and IV) were underweight. Our result is supported by study done by Schols et al (1993), where they found approximately 50% patients suffered from weight loss in severe COPD whose FEV₁ was <50%. (17) According to severity (stage I - IV) mean FFMI of the study group was 15.11 ± 1.95 , 13.21 \pm 1.46, 10.92 \pm 1.87 and 8.34 \pm 1.03 kg/m² respectively which was decreasing very significantly with p value <0.0001 (table - 4). Overall mean FFMI was 11.25 \pm

2.73 kg/m². It was observed mean FMI was 7.33 ± 0.84 in stage I, 6.47 ± 1.07 in stage II, 6.02 ± 0.99 in stage III and 5.97 ± 0.89 kg/m² in stage IV. In relation to staging, mean FMI though decreased GOLD progressively as disease severity increased but it was statistically not significant (p>0.05). Other studies with similar finding are those by Schols et al (2005), Ischaki et al (2007), Sabino PG (2010), T. M. L Eagan et al (2010), Park J. E. et al (2012), D. Gologanu et al (2014), Mann R. (2014)[18-21]. There is chronic weight loss and malnutrition in COPD patients as the disease severity increases suggested by many authors. The overall weight loss can be correlated with low BMI and low FFMI observed in our study. Low BMI and FFMI are independent predictor of COPD related mortality, morbidity and health related quality of life (HRQL) studied by previous investigators[22]. The result of present study showed that 6MWD covered by COPD patients in mild to very severe group (stage I-IV) was significantly decreasing according to severity of disease with mean of 356.62 ± 9.95 , 341.30 ± 20.52 , 233.63 ± 42.42 and 165.31 ± 14.63 m (p < 0.05) respectively. Subjects with more advanced disease (stage III and IV) had lower mean of 6MWDT than primary disease state (stage I and II). The mean of 6MWD in total 100 patients was 253.39 ± 77.28 m. Only 20 patients showed 6MWD >350m whereas 80 patients walked a distance <350 m in 6 minutes in total 100 COPD patients .Casanova C. et al (2007) evaluated the temporal change of 6MWD in patients of COPD for a 5 year follow-up period. They found 6MWD declined over time but the decline was really significant in only in patients with severe airflow obstruction (FEV₁ <50%). ⁽²³⁾Spruit M. A. et al (2010) have shown patients with a 6MWD <350 m generally had more severe airflow limitation (GOLD Stage IV). We found similar observation that more advanced disease (stage III and IV) had lower mean of 6MWDT than the primary stages due to more airway obstruction. Chronic obstructive pulmonary disease (COPD) is associated with a progressive loss of muscle mass and function and a systemic inflammatory process that can cause sarcopenia. There is a 24.6% prevalence of sarcopenia in patients with COPD[24]. The study showed that, in patients with COPD, the decrease in BMI and is related to impaired body composition and functional capacity[25]. Study examined the changes in total and segmental body composition with aging and COPD severity. It found that aging and COPD altered the body composition differently, and the effect was most pronounced in leg lean mass. Remarkably, differences in appendicular lean masses were seen in mild COPD although no changes in body weight. In

contrast, fat depot changes were only observed in severe COPD [26]. Garcia-Aymerich J. (2015) observed patients with greater exercise capacity actually had lower systemic inflammation which potentially attenuated muscle dysfunction. Our study, which included COPD patients with a wide range of severity, shows FFMI provides information beyond BMI regarding variables expressing disease severity, systemic inflammation and exercise capacity. Hence, FFMI can be a good predictor of recent staging of disease compared to BMI suggested by Ischaki et al.

Conclusion

In patients of COPD there is a state of chronic systemic inflammation which is associated with loss of fat free mass (skeletal muscle mass) thereby decreasing exercise capacity which acts in a vicious cycle to deteriorate the condition landing the patients into complications. High risked individuals must be regularly screened with spirometry for mild COPD so that necessary preventive measures can delay the onset of progression of disease. Once diagnosed as case of COPD, proper therapeutic regimen should be advised along with the non-pharmacological approach of treatment such as proper diet plan including food with high protein and minerals along with nutritional supplements. The specific regular exercise should be targeted towards the respiratory muscles as well as to the peripheral skeletal muscles which may improve the overall health status of COPD patients.

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