

## **AIM OF THE WORK**

To assess skeletal muscle dysfunction in patients with stable COPD and to find out if there is relationship between muscle dysfunction and ventilatory impairment, arterial gasometry and systemic inflammation in these patients.

## MATERIALS AND METHODS

This study was conducted on 30 patients with stable COPD. Diagnosis and grading severity of COPD were according to Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD guidelines 2013). Patients were recruited from Chest disease department, Alexandria University, faculty of medicine, from september 2013 to April 2014.

Also, 12 healthy subjects were included as control group.

### **Exclusion criteria:**

1. Presence of a disease that could contribute to dyspnea, exercise limitation, or muscle weakness (cardiovascular, neuromuscular, orthopedic, endocrinal or other respiratory diseases).
2. Metabolic diseases(Renal failure and liver failure).
3. Patients receiving chronic regular treatment with systemic steroids.

### **All cases were subjected to**

#### **• Thorough history taking:**

a) **Age.**

b) **Smoking history** which include:

- i) Number of cigarettes per day.
- ii) Duration of smoking.
- iii) Smoking index using pack year index formula.

Pack year index= number of packs per day x number of years.<sup>(163)</sup>

c) **Dyspnea** was asked for as a main complaint for cases only. Dyspnea index score was estimated for cases.<sup>(164)</sup>

### **Modified Medical Research Council Questionnaire for Assessing the Severity of Breathlessness (MMRC).<sup>(114)</sup>**

- 1) I only get breathless with strenuous exercise.
- 2) I get short of breath when hurrying on the level or walking up a slight hill.
- 3) I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.
- 4) I stop for breath after walking about 100 meters or after a few minutes on the level.
- 5) I am too breathless to leave the house or I am breathless when dressing or undressing.

d) **Cough** was asked for as a main complaint for cases only.

- e) **Wheezes** were asked for within past 2 months.
- f) **Chest pain, hemoptysis**, other complaints to exclude other diseases.
- g) **Medical history** including detailed drug history (Corticosteroids).

• **Full clinical examination:**

a) **Local examination:**

- i. To confirm the disease.
- ii. To exclude other chest disease and exacerbation.

b) **General examination**

- i. To exclude other organ involvement.
- ii. To assess complications.

c) **Body mass index:**

- i. To assess height in meters and weight in kilograms.
- ii. To estimate BMI using this formula: <sup>(174)</sup>

$$\text{BMI}^{(174)} = \frac{\text{Weight in kilograms}}{\text{Height in meters}^2}$$

• **Laboratory investigations:**

- **Routine investigations:**

- Complete blood count was done to exclude infections and blood diseases .
- Hepatic and renal functions tests.

- **Arterial blood gases ( for patients only)**

Arterial blood gases: samples were drawn from radial artery and analyzed for:

1. **PaO<sub>2</sub>**: Partial pressure of arterial oxygen
2. **PaCO<sub>2</sub>**: Partial pressure of arterial carbon dioxide
3. **HCO<sub>3</sub>**: Bicarbonate level
4. **SaO<sub>2</sub>** : arterial Oxygen saturation
5. **pH**

- **Assessment of serum level of CRP in patients with COPD.**

CRP is a marker of systemic inflammation. Serum CRP levels were estimated with original reactive analyzers. Rapid latex agglutination test used to detect human serum CRP. Venous blood samples were centrifuged and serum were separated and preserved at - 20° .

▪ **Chest X ray ( postero-anterior view):**

Plain x ray was done for all cases aiming to confirm the diagnosis, to exclude other chest pathologies and to detect pulmonary hypertension and cor pulmonale.

▪ **Electrocardiography (ECG):**

ECG was done to exclude the presence of ischemia, other heart diseases.

▪ **Pulmonary function tests (PFT)**

PFT were performed by spirometer. The best from three consecutive tests was accepted. The following parameters were measured:

- FVC “forced vital capacity”% of predicted
- FEV<sub>1</sub> “forced expiratory volume in 1 second % of predicted.
- FEV<sub>1</sub>/ FVC %

**BODE index for staging COPD**

The BODE Index was calculated using the following variables: BMI, degree of airway obstruction with FEV<sub>1</sub>% in the value predicted, dyspnea through the MMRC scale and ability to exercise by walking distance in 6MWT. The subjects received scores according to the results obtained in each of the four variables (0–3 for FEV<sub>1</sub>, dyspnea and walking distance in 6MWT; 0–1 for BMI) and these results were added up to a total score ranging from 0 to 10. The individuals’ classification was divided into quartiles, where: Quartile 1 is the score from 0 to 2; Quartile 2 from 3 to 4; Quartile 3 score from 5 to 6; and Quartile 4 from 7 to 10. The higher the score, the greater was the severity and the likelihood of mortality for individuals with COPD.<sup>(142)</sup>

**Table II. BODE index for staging COPD:**<sup>(142)</sup>

Parameter	0 Points	1 Point	2 Points	3 Points
Body: BMI	>21	<21		
Obstruction: FEV <sub>1</sub> (% predicted)	>65%	50–64%	36–49%	<35%
Dyspnea: MMRC score	0–1	2	3	4
Exercise: 6 minute walk distance (meters)	>350	250–349	150–249	<149

BMI, body mass index; MMRC, Modified Medical Research Council score.

▪ **Functional assessment of exercise capacity**

• **6 minute walk test (6MWT) :**

It was carried to assess exercise intolerance.<sup>(140)</sup>

1. 6MWT was performed indoors, the walking course was 30 m in length, a flat straight with a hard surface corridor was used .
  2. Each patient was instructed to walk from one end to the other, covering as much ground as possible during the 6 minute time.
  3. Patients were prohibited to exercise vigorously within 2 hours of beginning the test
  4. The six minute walked distance was measured for all cases.
  5. The patients' usual medications were continued.
  6. All patients were given standardized encouragement during the test.
- **Peak oxygen consumption (VO<sub>2</sub> peak):**

Peak VO<sub>2</sub> is considered an index of cardiovascular performance and a measure of aerobic capacity .VO<sub>2</sub> peak was assessed via a modified Rockport formula. During the exercise test, the duration of running any distance were calculated, no oxygen were administered to the subjects.

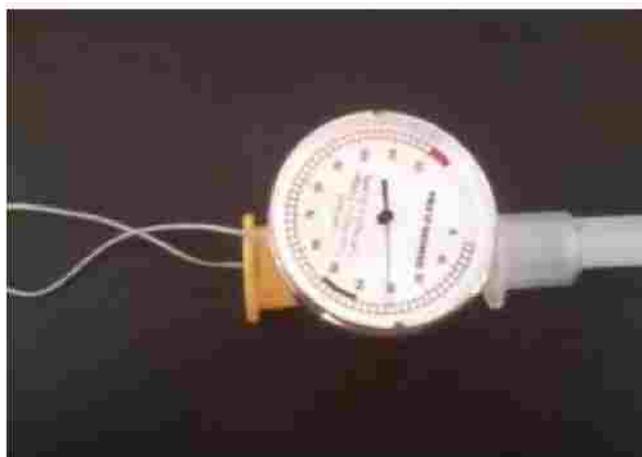
The formula used to calculate the VO<sub>2</sub> peak was:

$$132.853 - (0.0769 \times \text{Weight}) - (0.3877 \times \text{Age}) + (6.315 \times \text{Gender}) - (3.2649 \times \text{Time}) - (0.1565 \times \text{Heart rate}).$$

Where: Weight was in pounds (lbs), Gender Male = 1 and Female = 0, Time was expressed in minutes and 100ths of a minute, It required a continuous 3- to 5-minute “supermaximal” effort, but it usually consisted of increments in effort (graded exercise) to the point where a person was no longer continue to exercise, heart rate was in beats/minute, age was in years.<sup>(139)</sup>

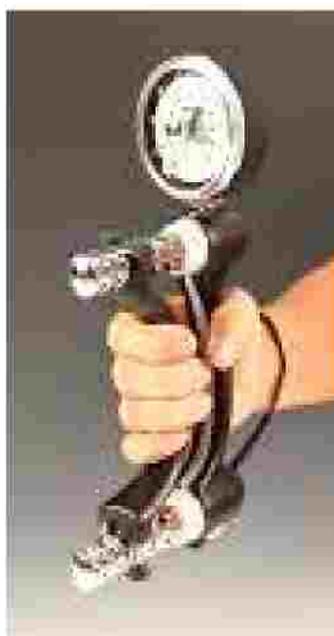
▪ **Assessment of skeletal muscle dysfunction:**

- Respiratory muscle strength has been assessed at the mouth by measuring maximal respiratory pressures generated during forced inspiratory (PI<sub>max</sub>) and expiratory (PE<sub>max</sub>) efforts performed against an occluded airway. Maximum inspiratory pressures were measured from functional residual capacity and maximum expiratory pressures were measured from total lung capacity, in the standard way with the patient seated, wearing a nose-clip and using a flanged mouthpiece . Repeated efforts were made until consistent results were achieved and the numerically largest pressure noted.<sup>(146)</sup>



**Fig. (9):** Apparatus used for measuring maximal respiratory pressures generated during forced inspiratory ( $PI_{max}$ ) and expiratory ( $PE_{max}$ ) efforts.

- Hand grip strength was determined using hand dynamometer. After explaining the procedure to the study subject and giving a demonstration, they were asked to hold the handgrip dynamometer in the dominant hand in sitting position. The forearm was extended over a table and elbow flexed at  $90^\circ$ . Subjects were asked to hold the dynamometer in such a way that the second phalanx was against the inner stirrup, and were then asked to grip the dynamometer handle with as much force as they possibly could apply. The handgrip muscle strength was recorded in kilograms as indicated by the pointer on the dynamometer. Three recordings were taken with a gap of two minutes between each effort and the maximum value was recorded for the analysis. <sup>(147)</sup>



**Fig. (10):** The hand dynamometer.

- Biceps and quadriceps muscle strength was assessed by determining the 1 repetition maximum. The UL and LL (maximum muscle strength) was determined by the 1RM test on the muscle toning station. Knee extension by sitting position, where the individual is instructed to extend the knee of the dominant leg, starting from a 90° knee flexion position to a 180° extension, which works the thigh muscles and especially, the quadriceps. This test was to determine the greatest amount of weight that the individual could move in a single repetition, with a random initial load that was increased or reduced in accordance with the individual's ability to perform or not a repetition; this could be repeated again or not, with a three-minute interval between each load and 30 minutes between each exercise trial. Up to six attempts were carried out to obtain the 1RM value for each of the exercises. The performance order for the UL exercises was determined by 1 RM of arm flexors (biceps muscle) of the dominant limb as the LL testing. The individual was monitored throughout the test by questioned about dyspnea and fatigue or pain in UL and LL, using the same aforementioned equipment.<sup>(147)</sup>
- Biceps and quadriceps muscle endurance has been assessed by the twenty repetition maximum test (20 RM) using a MultiGym device, This test determined the maximal amount of weight the patient could lift exactly 20 times in a row before the muscle became too fatigued to continue.<sup>(148)</sup>

### **Statistical analysis of the data**

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0.

Qualitative data were described using number and percent. Quantitative data were described using minimum and maximum, mean and standard deviation and median.

Comparison between different groups regarding categorical variables was tested using Chi-square test. When more than 20% of the cells have expected count less than 5, correction for chi-square was conducted using Fisher's Exact test.

The distributions of quantitative variables were tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk test and D'Agstino test, also Histogram and QQ plot were used for vision test. If it reveals normal data distribution, parametric tests was applied. If the data were abnormally distributed, non-parametric tests were used.

For normally distributed data, comparisons between two groups were done using independent t-test. For abnormally distributed data, comparison between the two groups were done using Mann Whitney test. Correlations between two quantitative variables were assessed using Spearman coefficient.

Univariate and Multivariate linear regression was assessed.

Significance of the obtained results was judged at the 5% level.

## RESULTS

This prospective descriptive case control study was conducted on 30 patients with stable chronic obstructive pulmonary disease, admitted to the chest disease department in Alexandria main university hospital from September 2013 to April 2014. Diagnosis and grading severity of COPD was performed according to Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD guidelines 2013) without any selection bias.

Also, 12 healthy subjects were included as a control group.

### Personal data of the 2 studied groups:

Mean±SD age of the patients was 59.57±7.80 years, whereas that of control group was 57.0 ± 10.41 years with no statistically significant difference between the 2 groups.

According to the gender 93.3 %of the studied patients were males (n=28) while 6.7 % were female (n=2). In the control group 83.3% were males (n=10) while 16.7% were females (n=2), with no statistically significant difference between the 2 groups. **Table (III)**

**Table (III): Comparison between the two studied groups according to demographic data**

	Cases (n=30)		Control (n=12)		Test of sig.	p
	No	%	No	%		
<b>Gender</b>						
Male	28	93.3	10	83.3	$\chi^2=0.995$	FE p=0.565
Female	2	6.7	2	16.7		
<b>Age (years)</b>						
40 - <55	5	16.7	4	33.3	$\chi^2=1.947$	MC p=0.376
55 - <65	16	53.3	4	33.3		
≥65	9	30.0	4	33.3		
Min. – Max.	40.0 – 70.0		40.0 – 70.0			
Mean ± SD.	59.57±7.80		57.0 ± 10.41		t=0.874	0.387
Median	62.50		58.0			

p: p value for comparing between the two studied groups

$\chi^2$ : Chi square test

FE: Fisher Exact test

t: Student t-test

\*: Statistically significant at  $p \leq 0.05$

**Anthropometric data:**

Regarding grades of obesity based on BMI, 8 patients with COPD were underweight, 15 patients were in the normal range of weight, while the remaining 7 patients were classified as overweight. Control group showed normal range of weight in 50% of them and overweight pattern in the remaining 50%.

Mean  $\pm$  SD values of body mass index (BMI) of patients with COPD was  $21.26 \pm 4.14$  kg/m<sup>2</sup> whereas it was  $24.88 \pm 1.69$  kg/m<sup>2</sup> in the control group with statistically significant lower value in patients with COPD compared to control group (p=0.005). (Table IV, Figure 11)

Mean  $\pm$  SD values of weight were statistically significant lower (p=0.002) in patients compared to control group with values  $59.57 \pm 11.71$  kg,  $70.08 \pm 6.82$  kg respectively. (Table IV, Figure 12)

Mean  $\pm$  SD values of height of patients with COPD was  $167.68 \pm 8.10$  cm whereas it was  $168.72 \pm 6.01$  cm in the control group with no statistically significant difference between the patients and the controls (p=0.689). (Table IV)

**Table (IV): Comparison between the two studied groups according to anthropometric data**

	Cases (n=30)		Control (n=12)		Test of sig.	p
	No	%	No	%		
<b>BMI</b>						
Under weight	8	26.7	0	0.0	$\chi^2=5.106$	<sup>MC</sup> p=0.072
Normal weight	15	50.0	6	50.0		
Over weight	7	23.3	6	50.0		
Min. – Max.	14.70 – 29.70		22.50 – 28.40		Z=2.800*	0.005*
Mean $\pm$ SD.	21.26 $\pm$ 4.14		24.88 $\pm$ 1.69			
Median	21.30		24.50			
<b>Weight in lb</b>						
Min. – Max.	92.0 – 194.0		142.0 – 191.0		Z=3.273*	0.001*
Mean $\pm$ SD.	131.11 $\pm$ 25.90		155.87 $\pm$ 15.13			
Median	128.50		152.50			
<b>Weight in kg</b>						
Min. – Max.	42.0 – 88.0		64.0 – 86.0		Z=3.164*	0.002*
Mean $\pm$ SD.	59.57 $\pm$ 11.71		70.08 $\pm$ 6.82			
Median	58.50		68.50			
<b>Height in cm</b>						
Min. – Max.	153.0 – 185.0		159.0 – 182.0		t=0.404	0.689
Mean $\pm$ SD.	167.68 $\pm$ 8.10		168.72 $\pm$ 6.01			
Median	167.25		168.0			

BMI :body mass index.

p: p value for comparing between the two studied groups

Z: Z for Mann Whitney test

t: Student t-test

\*: Statistically significant at p  $\leq$  0.05

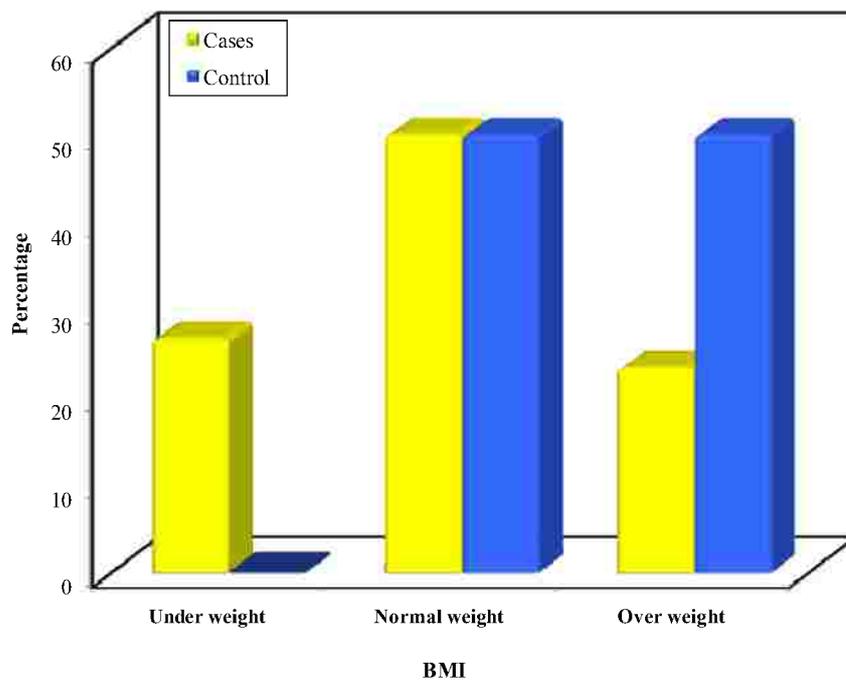


Figure (11): Comparison between the 2 studied groups according to BMI

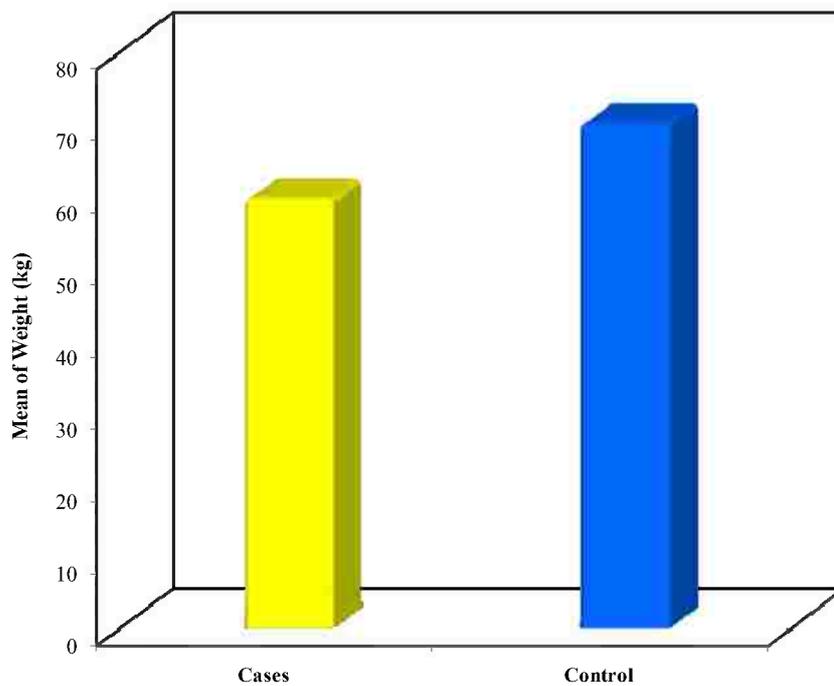


Figure (12): Comparison between the 2 studied groups according to the weight (kg)

**Smoking history:**

Mean  $\pm$  SD of duration of smoking in the studied COPD group was  $35.57 \pm 8.50$  years with a Mean  $\pm$  SD smoking index of  $66.13 \pm 35.0$  pack year index. (Table V)

**Table (V): Distribution of the studied cases according to smoking history(risk factor) (n=30)**

	No	%
<b>Smoker</b>		
Current smoker	13	43.3
Ex smoker	17	56.6
<b>Duration of smoking (years)</b>		
Min. – Max.	20.0 – 50.0	
Mean $\pm$ SD.	$35.57 \pm 8.50$	
Median	37.0	
<b>Severity of airway obstruction (according to FEV1% of predicted)</b>	<b>No.</b>	<b>%</b>
Mild	1	3.3
Moderate	16	53.3
Severe	9	30.0
Very severe	4	13.3
<b>Smoking index (pack year index)</b>		
Min. – Max.	20.0 – 100.0	
Mean $\pm$ SD.	$66.13 \pm 35.0$	
Median	60.0	

**Demogaphic data:**

Out of 30 patients with COPD, 11 patients that are 36.7% were not working while the rest 19 patients 63.3% were working. Most common occupations were: farmers 16.7% (n=5) followed by 13.3% (n=13.3) drivers, while the others were (2) carpenters, (2) waiters, (2) builders that was 6.7%.(Table VI)

**Table (VI): Distribution of the studied cases according to occupation (n=30)**

	No	%
<b>Occupation</b>		
Not working	11	36.7
<b>Working</b>	<b>19</b>	<b>63.3</b>
Farmer	5	16.7
Driver	4	13.3
Carpenter	2	6.7
Waiter	2	6.7
Builder	2	6.7
Electertian	1	3.3
Captain	1	3.3
Businessman	1	3.3
Painter	1	3.3

**Spectrum of complaints:**

All patients with COPD complaint of dyspnea and cough while 14 of them that are 46.7% reported easy fatigability. wheezes as a chest complaint was present in 26.7% that are 8 patients.

**Pattern of CST use :**

All the studied patients were on CST with different routes and regimens as following:

13 Patients (43.3%) were on interrupted ICS, while 10 Patients (33.3%) were on combined ICS and systemic CST regimen and finally 7 patients (23.3%) were on systemic CST regimen. Mean  $\pm$  SD of duration of CST use was  $5.83 \pm 3.56$  years. **(Table VII)**

**Table (VII): Distribution of the studied cases according to patients complaints & use of corticosteroid (n=30)**

	No	%
<b>Dyspnea</b>	30	100.0
<b>Cough</b>	30	100.0
<b>Wheezes</b>	8	26.7
<b>Easy fatigability</b>	14	46.7
<b>CST</b>	30	100.0
<b>CST route</b>		
Interrupted ICS	13	43.3
Interrupted ICS + systemic	10	33.3
Interrupted Systemic	7	23.3
<b>CST duration (years)</b>		
Min. – Max.	2.0 – 15.0	
Mean $\pm$ SD.	$5.83 \pm 3.56$	
Median	5.0	

CST : corticosteroids therapy ICS : inhaled corticosteroids

**Vital signs:**

Mean  $\pm$  SD of systolic blood pressure in the studied patients was  $120.67 \pm 7.85$  mmHg while that of the diastolic blood pressure was  $78.17 \pm 5.33$  mmHg. Mean  $\pm$  SD of the heart rate in the studied patients was  $75.33 \pm 10.75$  beat per minute while of respiratory rate was  $13.83 \pm 1.70$  breaths per minute. (Table VIII)

**Table (VIII): Vital signs of the studied cases (n=30)**

Vital signs	Min. – Max	Mean $\pm$ SD.	Median
Systolic BP (mmHg)	110.0 – 130.0	$120.67 \pm 7.85$	120.0
Diastolic BP(mmHg)	70.0 – 85.0	$78.17 \pm 5.33$	80.0
HR /min	60.0 - 95.0	$75.33 \pm 10.75$	73.0
Resp.rate/min	12.0 – 18.0	$13.83 \pm 1.70$	14.0

HR: heart rate

BP: blood pressure

**Physical findings:**

By order of frequency, hyperinflation of chest and use of accessory muscles of respiration were the 2 most commonly encountered physical findings, both of them were found in 28 patients that is 93.3% of all studied cases. Wheezes were detected in 22 patients that is 73.3% of studied cases. Warm extremities and fine tremors existed in 17 patients that are 56.7% of studied cases. Finally 15 patients that are 50% of studied cases demonstrated pursed lip breathing. (Table IX)

**Table (IX): Distribution of the studied cases according to findings of clinical examination (n=30)**

Physical findings	No	%
Pursed lip breathing	15	50.0
hyperinflation	28	93.3
Use accessory ms of resp.	28	93.3
Wheezes	22	73.3
Warm extremities	17	56.7
Fine tremors	17	56.7

**Hematological profile:**

Mean  $\pm$  SD of hemoglobin concentration was  $14.27 \pm 1.61$  g/dl. Mean  $\pm$  SD of RBCs count was  $4.89 \pm 0.52$  million RBCs/mcl. Mean  $\pm$  SD of hematocrit value was  $44.74 \pm 4.88\%$ . Mean  $\pm$  SD of WBCs count was  $8.08 \pm 1.89$  cell/mm<sup>3</sup>. Mean  $\pm$  SD of platelets count was  $239.33 \pm 74.0$ /cmm. **(Table X)**

**Table (X): Hematological profile in the studied patients**

	<b>Min. – Max</b>	<b>Mean <math>\pm</math> SD.</b>	<b>Median</b>
<b>Hb</b>	11.10-16.90	$14.27 \pm 1.61$	14.30
<b>RBC</b>	4.16 – 5.90	$4.89 \pm 0.52$	4.98
<b>Hematocrit</b>	35.30 – 56.10	$44.74 \pm 4.88$	43.85
<b>WBCs</b>	2.91 – 10.91	$8.08 \pm 1.89$	8.64
<b>Platelet</b>	131.0-452.0	$239.33 \pm 74.0$	236.50

HB: hemoglobin  
WBC: white blood cell  
RBC: red blood cell

**ECG tracings:**

ECG tracings showed normal findings in all studied patients. **(Table XI)**

**Radiological findings:**

All studied patients showed evidence of hyperinflation on plain chest x rays except one patient who demonstrated normal chest X ray findings. **(Table XI)**

**Table (XI): Distribution of the studied cases according to ECG and CXR (n=30)**

	<b>No</b>	<b>%</b>
<b>ECG</b>		
Normal	30	100.0
<b>Chest x ray</b>		
Normal	1	3.3
Hyperinflated chest	29	96.7

## Results

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### Arterial gasometry (on room air):

Day time arterial gasometry in the 30 studied patients showed : Mean  $\pm$  SD of pH was  $7.36 \pm 0.02$ . Mean  $\pm$  SD of PaCO<sub>2</sub> was  $53.4 \pm 6.28$  mmHg. Mean  $\pm$  SD of PaO<sub>2</sub> was  $77.4 \pm 4.65$  mmHg. Mean  $\pm$  SD of SaO<sub>2</sub> was  $90.53 \pm 3.14\%$ . Mean  $\pm$  SD of HCO<sub>3</sub> was  $29.16 \pm 2.78$  mmol/L. (Table XII)

**Table (XII): Arterial blood gases of the studied cases (n=30)**

	Min. – Max	Mean $\pm$ SD.	Median
<b>pH</b>	7.33 – 7.44	$7.36 \pm 0.02$	7.35
<b>PCO<sub>2</sub></b>	39.0– 66.0	$53.4 \pm 6.28$	53.5
<b>PaO<sub>2</sub></b>	68.0 – 87.0	$77.4 \pm 4.65$	77.0
<b>SaO<sub>2</sub></b>	85.4 – 96.0	$90.53 \pm 3.14$	90.55
<b>HCO<sub>3</sub></b>	24.30 – 35.0	$29.16 \pm 2.78$	28.7

PaO<sub>2</sub>: arterial partial pressure of oxygen

PaCO<sub>2</sub>: arterial partial pressure of carbon dioxide

HCO<sub>3</sub>: bicarbonate

Sat O<sub>2</sub>% : saturation of oxygen in arterial blood

### MMRC score

Regarding the assessment of the degree of dyspnea, verified by the MMRC scale<sup>(112)</sup>, which is based on the rates of different activities that lead to dyspnea, ranging from '0' (individual is not troubled with shortness of breath, unless subjected to vigorous exercise) to '4' (individual shows substantial shortness of breath when leaving the house or even when changing clothes). The individuals determined their score on the scale as the score that best related to their dyspnea, with higher scores referring to higher incapacity. The MMRC scale was applied in the form of an interview by the examiner, it was observed that 7 of the studied patients (23.3%) showed score 4, 10 patients (33.3%) demonstrated score 3 while 9 patients (30%) scored 2 and finally 4 patients (13.3%) scored 1.

Mean  $\pm$  SD of MMRC score in studied patients was  $2.67 \pm 0.99$ . (**Table XIII**)

### BODE index

The BODE Index was calculated using the following variables: BMI, degree of airway obstruction with FEV1% of predicted, dyspnea through the MMRC scale and ability to exercise by walking distance in 6MWT. The subjects received scores according to the results obtained in each of the four variables (0–3 for FEV1, dyspnea and walking distance in 6MWT, 0–1 for BMI) and these results were added up to a total score ranging from 0 to 10. The individuals' classification was divided into quartiles, where: Quartile 1 is the score from 0 to 2; Quartile 2 from 3 to 4; Quartile 3 score from 5 to 6; and Quartile 4 from 7 to 10. The higher the score, the greater was the severity and the likelihood of mortality for individuals with COPD.

With regard to the BODE Index classification, it was found that 33.3% of the patients were classified as Quartile 4, 23.3% as Quartile 3 and 26.66% of the patients as Quartile 2, and finally 16.6% of patients were classified as Quartile 1.

Mean  $\pm$  SD of BODE index was  $5.23 \pm 2.79$ . (**Table XIII**)

### Spirometric data

Mean  $\pm$  SD of FEV1% of predicted was  $51.98 \pm 16.75$ , while of FVC% was  $54.94 \pm 15.62$  and of FEV1/FVC % was  $31.27 \pm 11.85$ . Regarding severity of obstruction based on FEV1 % of predicted, studied patients were stratified as following: 4 patients (13.3%) were very severe, 9 patients (30%) showed severe obstruction, while 16 patients (53.3%) were of moderate severity and finally 1 patient (3.3%) was mild. (**Table XIII**)

### CRP:

As a marker of systemic inflammation, patients displayed a Mean  $\pm$  SD CRP value of studied patients was  $7.54 \pm 6.58$  mg/dl. (**Table XIII**) Normal reference concentration in healthy human serum is usually lower than 1 mg/dl.

**Table (XIII): MMRC, BODE index, C reactive protein and PFT values in the studied patients (n=30)**

<b>MMRC score</b>		
	<b>No.</b>	<b>%</b>
Score 1	4	13.3
Score 2	9	30.0
Score 3	10	33.3
Score 4	7	23.3
Min. – Max	1.0 – 4.0	
Mean ± SD.	2.67 ± 0.99	
Median	3.0	
<b>BODE index</b>		
	<b>No.</b>	<b>%</b>
Quartile1(Score from 0 to 2)	5	16.6
Quartile 2 (Score from3 to 4)	8	26.6
Quartile 3( Score from 5 to 6)	7	23.3
Quartile 4(Score from 7 to 10)	10	33.3
Min. – Max	1.0 – 10.0	
Mean ± SD.	5.23 ± 2.79	
Median	6.0	
<b>FEV<sub>1</sub> %pred</b>		
Min. – Max	23.0 – 81.0	
Mean ± SD.	51.98± 16.75	
Median	53.93	
<b>FVC % pred</b>		
Min. – Max	29.10 – 90.0	
Mean ± SD.	54.94 ± 15.62	
Median	52.30	
<b>FEV<sub>1</sub>/FVC %</b>		
Min. – Max	19.0 – 65.0	
Mean ± SD.	31.27 ± 11.85	
Median	27.60	
<b>severity of obstruction based on FEV<sub>1</sub>%predicted</b>		
	<b>No.</b>	<b>%</b>
Mild	1	3.3
Moderate	16	53.3
Severe	9	30.0
Very severe	4	13.3
<b>CRP mg/dl</b>		
Min. – Max	0.42 – 23.31	
Mean ± SD.	7.54±6.58	
Median	5.66	

**MMRC** : Modified Medical Research Council, **CRP**: C reactive protein.

**Peak oxygen consumption:**

VO<sub>2</sub> peak was statistically significant lower in patients with COPD (Mean ± SD was 22.21 ± 5.01 mL/kg/min) compared to control group (Mean ± SD was 37.87 ± 6.45 mL/kg/min). (Table XIV, Figure 13)

**6 MWT:**

Statistically significant lower 6 MWT was found in patients with COPD (Mean ± SD was 233.33±94.58 meters) compared to control group (Mean ± SD was 577.33 ± 74.24 meters). (Table XIV, Figure 14)

**Table (XIV): Comparison between the two studied groups regarding peak oxygen consumption and 6 minute walking distance test**

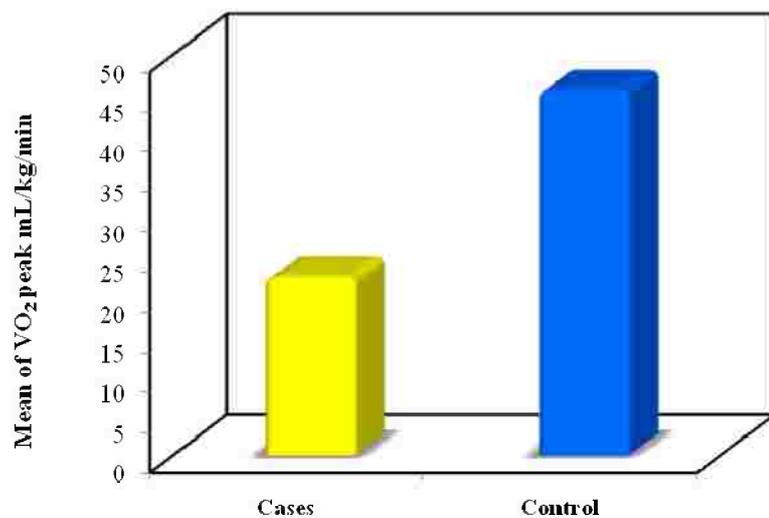
	<b>Cases (n=30)</b>	<b>Control (n=12)</b>	<b>Test of sig.</b>	<b>p</b>
<b>VO<sub>2</sub> peak</b>				
Min. – Max.	11.86 – 32.57	25.02 – 45.49		
Mean ± SD.	22.21 ± 5.01	37.87 ± 6.45	t=8.422*	<0.001*
Median	21.88	38.78		
<b>6MWT(meters)</b>				
Min. – Max.	66.0 – 396.0	460 – 685.0		
Mean ± SD.	233.33±94.58	577.33 ± 74.24	Z=5.014*	<0.001*
Median	245.0	583.50		

p: p value for comparing between the two studied groups

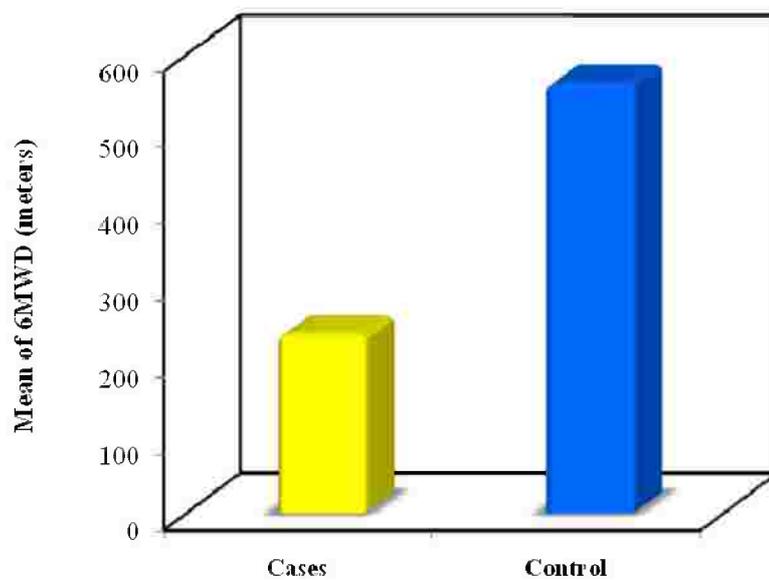
Z: Z for Mann Whitney test

t: Student t-test

\*: Statistically significant at p ≤ 0.05



**Figure (13): Comparison between the 2 studied groups according to mean of VO<sub>2</sub> peak**



**Figure (14): Comparison between the 2 studied groups according to mean value of 6MWT (meters)**

**Respiratory and peripheral skeletal muscles functional assessment:**

**Respiratory muscles**

- P<sub>lmax</sub> was statistically significant lower in patients with COPD (Mean ± SD was -58.47±15.35 cm H<sub>2</sub>O) compared to control group (Mean ± SD was -92.17 ± 13.03cm H<sub>2</sub>O). **(Table XV, Figure 15)**
- P<sub>Emax</sub> was statistically significant lower in patients with COPD (Mean ± SD was 85.39±27.06 cm H<sub>2</sub>O) compared to control group (Mean ± SD was 121.17 ± 15.32 cm H<sub>2</sub>O). **(Table XV, Figure 16)**

**Peripheral skeletal muscles**

- Hand grip strength was statistically significant lower in patients with COPD (Mean ± SD was 22.40±7.61 kg) compared to control group (Mean ± SD was 42.25 ± 10.17 kg). **(Table XV, Figure 17)**
- There was no statistically significant difference in biceps muscle strength between patients with COPD (Mean ± SD was 6.02 ± 1.50 kg) compared to control group (Mean ± SD was 6.98 ± 1.36 kg), as p=0.078. **(Table XV)**
- 20 RM of biceps muscle was not statistically significant different in patients with COPD (Mean ± SD was 4.36 ± 1.28 kg) compared to control group (Mean ± SD was 5.25 ± 1.03 kg), as p=0.051. **(Table XV)**
- Quadriceps muscle strength was statistically significant lower in patients with COPD (Mean ± SD was 9.27±3.65 kg) compared to control group (Mean ±SD was 14.19 ± 4.57 kg). **(Table XV, Figure 18)**
- 20 RM of quadriceps muscle was statistically significant lower in patients with COPD (Mean ± SD was 5.38 ± 2.92 kg) compared to control group (Mean ± SD was 11.46 ± 3.69 kg). **(Table XV, Figure 18)**

## Results

**Table (XV): Comparison between the two studied groups regarding respiratory and peripheral skeletal muscles function assessment ( strength and endurance).**

	Cases (n=30)	Control (n=12)	Test of sig.	p
<b>PI max (cm H2O)</b>				
Min. – Max.	-32.0 - -90.0	-118.0 - -78.0		
Mean ± SD.	-58.47±15.35	-92.17 ± 13.03	t=6.688*	<0.001*
Median	-59.0	-88.0		
<b>PE max (cm H2O)</b>				
Min. – Max.	40.80-140.0	98.0 – 140.0		
Mean ± SD.	85.39±27.06	121.17 ± 15.32	t=4.292*	<0.001*
Median	80.0	122.0		
<b>Hand grip strength (Kg)</b>				
Min. – Max.	12.0-34.0	22.0 – 54.0		
Mean ± SD.	22.40±7.61	42.25 ± 10.17	Z=4.196	<0.001*
Median	22.50	46.0		
<b>Biceps ms strength (Kg)</b>				
Min. – Max.	3.50 – 9.25	4.50 – 9.25		
Mean ± SD.	6.02 ± 1.50	6.98 ± 1.36	Z=1.762	0.078
Median	6.0	7.25		
<b>20 RM of Biceps ms (kg)</b>				
Min. – Max.	2.0 – 6.25	3.0 – 6.50		
Mean ± SD.	4.36 ± 1.28	5.25 ± 1.03	Z=1.955	0.051
Median	4.50	5.75		
<b>Quadriceps strength (kg) ms</b>				
Min. – Max.	3.0 – 15.0	9.0 – 24.0		
Mean ± SD.	9.27±3.65	14.19 ± 4.57	Z=2.899*	0.004*
Median	10.0	13.50		
<b>20 RM of Quadriceps ms (kg)</b>				
Min. – Max.	1.50 – 10.50	6.0 – 16.50		
Mean ± SD.	5.38 ± 2.92	11.46 ± 3.69	Z=3.902*	<0.001*
Median	6.0	12.50		

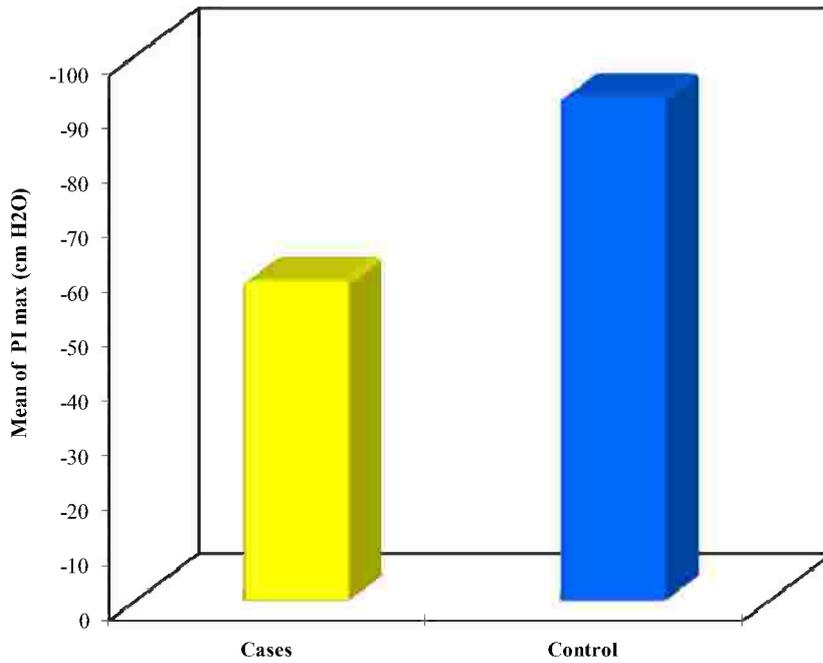
p: p value for comparing between the two studied groups

Z: Z for Mann Whitney test

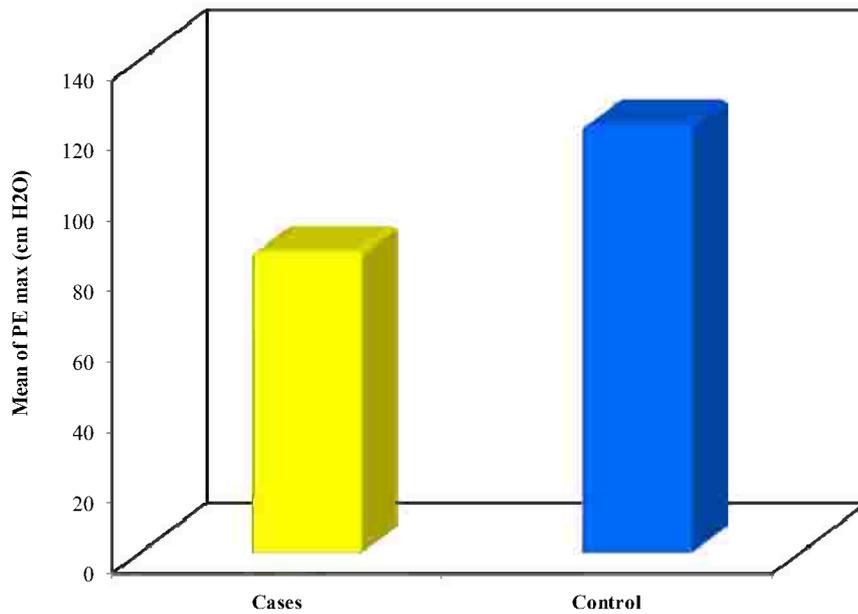
t: Student t-test

\*: Statistically significant at  $p \leq 0.05$

20RM: 20 repetition maximum.



**Figure (15): Comparison between the 2 studied groups according to mean of PI max (cm H<sub>2</sub>O)**



**Figure (16): Comparison between the 2 studied groups according to mean of PE max (cm H<sub>2</sub>O)**

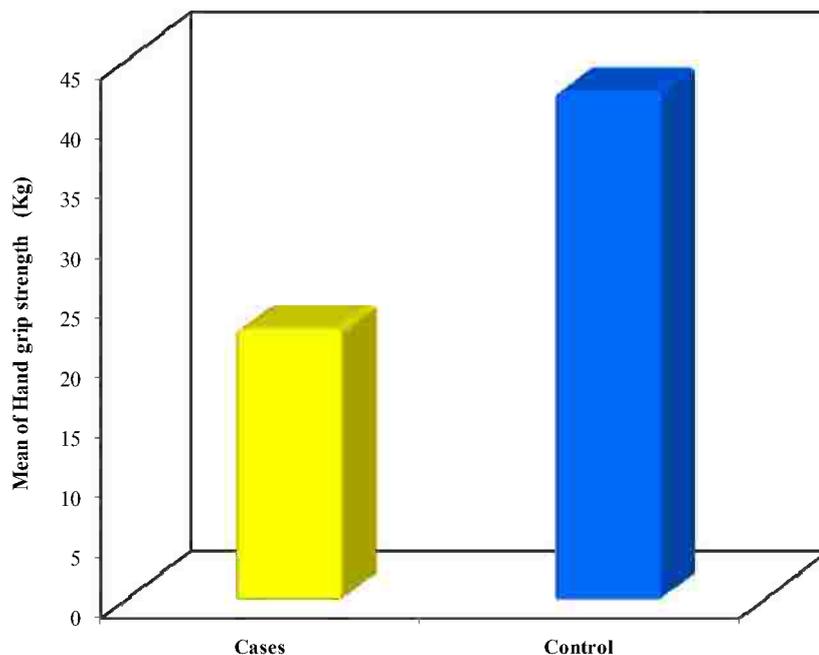


Figure (17): Comparison between the 2 studied groups according to mean of hand grip strength (kg)

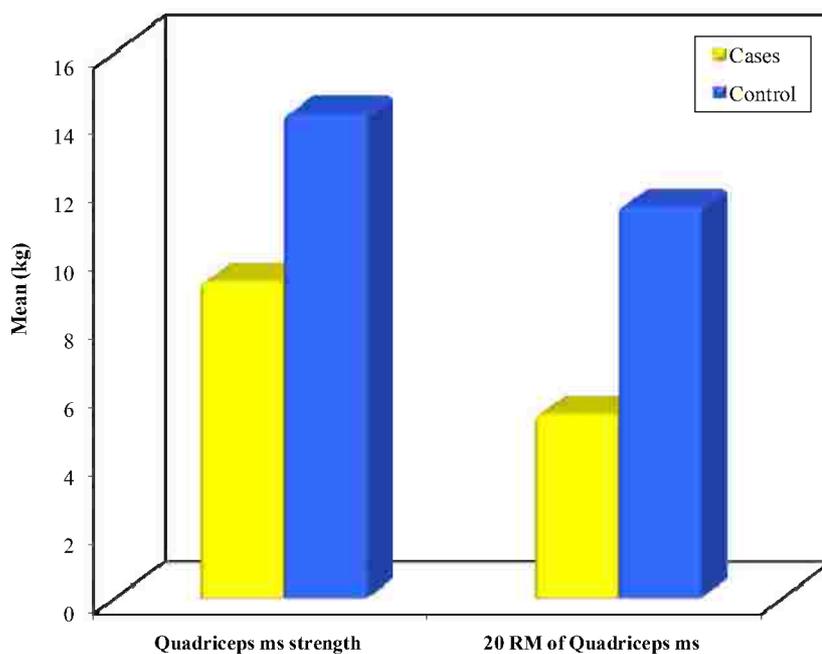


Figure (18): Comparison between the 2 studied groups according to mean of quadriceps strength (kg) and 20 RM of quadriceps muscle (kg)

**Correlation studies**

**Correlation of MMRC and different functional parameters:**

- Statistically significant correlation was found between MMRC and each of peakVO2 ( r = - 0.670, p=<0.001 ) and 6MWT ( r = 0.773, p <0.001).

**Correlation of FEV1% of predicted to different parameters:**

- Statistically significant correlation was found between FEV1 % of predicted and each of MMRC ( r = -0.735, p=0.001), peakVO2 ( r =0.581, p=0.001) and 6MWT ( r =0.635, p <0.001).

**Correlation between FEV1% and respiratory and peripheral skeletal muscles function assessment parameters:**

- Statistically significant positive correlation was found between PImax and FEV1% of predicted in studied patients with COPD with (rs =0.726, P=<0.001). **(Table XVI, Figure 19)**
- Statistically significant positive correlation was found between quadriceps muscle strength and FEV1% of predicted in studied patients with COPD with (rs =0.364, P=0.048). **(Table XVI, Figure 20)**

**Table (XVI): Correlation between peripheral skeletal muscles function assessment (strength, endurance) and FEV1% of predicted in COPD group**

	FEV1% of predicted	
	r <sub>s</sub>	p
<b>PI max (cm H<sub>2</sub>O)</b>	0.726*	<0.001*
<b>PE max (cm H<sub>2</sub>O)</b>	0.015	0.935
<b>Hand grip strength (Kg)</b>	0.045	0.812
<b>Biceps ms strength (Kg)</b>	0.139	0.465
<b>Biceps ms endurance ( kg)</b>	0.288	0.123
<b>Quadriceps ms strength (kg)</b>	0.364*	0.048*
<b>Quadriceps ms endurance (kg)</b>	0.116	0.543

r<sub>s</sub>: Spearman coefficient

\*: Statistically significant at p ≤ 0.05

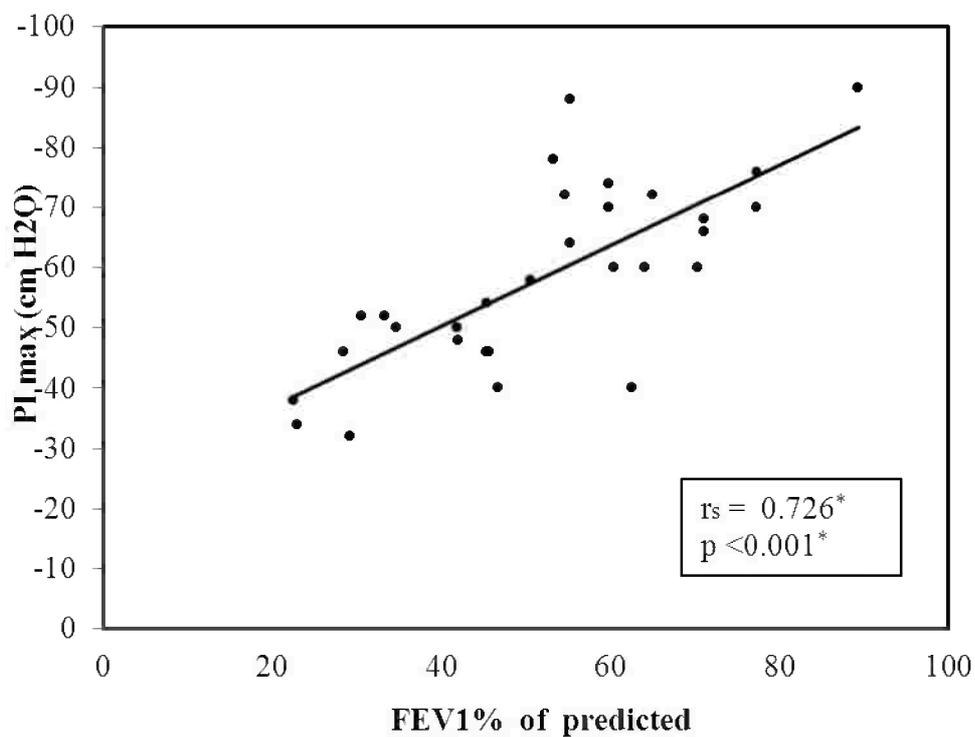


Figure (19): Correlation between FEV1% of predicted and PI max (cm H<sub>2</sub>O)

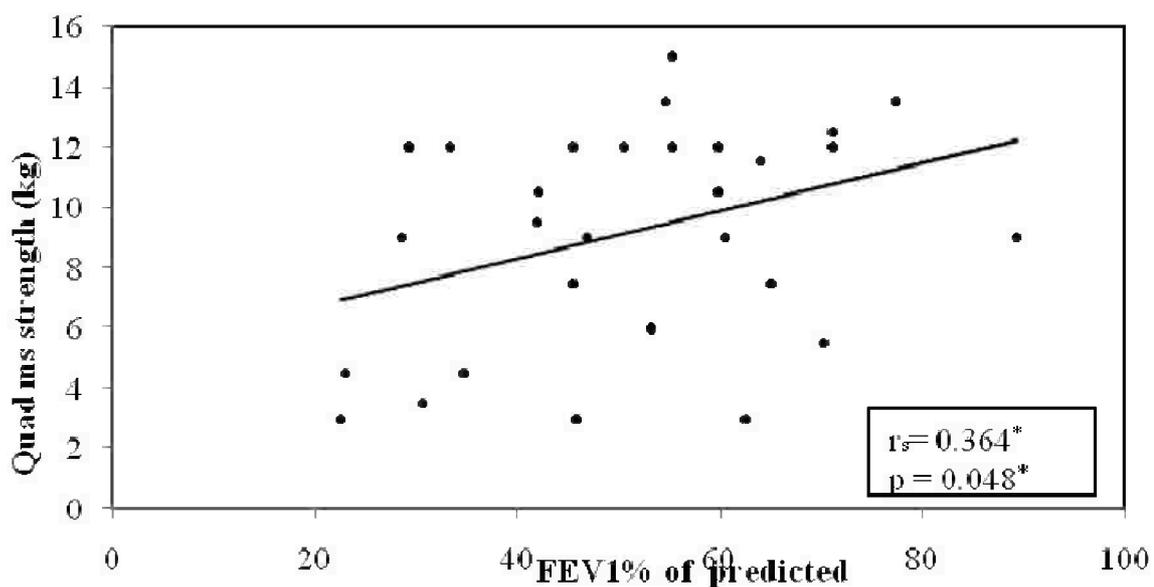


Figure (20): Correlation between FEV1% of predicted and quadriceps muscle strength (kg)

**Correlation between smoking grade of severity according to FEV1% of predicted and different skeletal muscles functional assessment parameters:**

- Statistically significant negative correlation was found between PImax and smoking grade according to FEV1% of predicted in studied patients with COPD with ( $r_s = -0.839$ ,  $P < 0.001$ ). (Table XVII, Figure 21)
- Statistically significant negative correlation was found between quadriceps muscle strength and smoking grade according to FEV1% of predicted in studied patients with COPD with ( $r_s = -0.365$ ,  $P = 0.048$ ). (Table XVII, Figure 22)

**Table (XVII): Correlation between respiratory and peripheral skeletal muscles function assessment (strength, endurance) and smoking grade of severity according to FEV1% of predicted in COPD group:**

	smoking grade (according to FEV1% of predicted)	
	$r_s$	<b>P</b>
<b>PI max (cm H2O)</b>	-0.839*	<0.001*
<b>PE max (cm H2O)</b>	0.135	0.478
<b>Hand grip strength (Kg)</b>	0.112	0.556
<b>Biceps ms strength (Kg)</b>	-0.155	0.413
<b>Biceps ms endurance ( kg)</b>	-0.289	0.121
<b>Quadriceps ms strength (kg)</b>	-0.365*	0.048*
<b>Quadriceps ms endurance (kg)</b>	-0.110	0.563

$r_s$ : Spearman coefficient

\*: Statistically significant at  $p \leq 0.05$

No statistically significant correlations between FEV1% and any of smoking duration or index(  $r = 0.050$   $p = 0.793$   $r = -0.285$   $p = 0.127$  respectively).

No statistically significant correlations between CST therapy duration and any of PI max or quadriceps strength or endurance with ( $r = 0.285$ ,  $P = 0.127$ ,  $r = 0.138$ ,  $P = 0.468$ ,  $r = 0.010$ ,  $P = 0.960$ ,  $r = 0.052$ ,  $P = 0.783$  respectively).

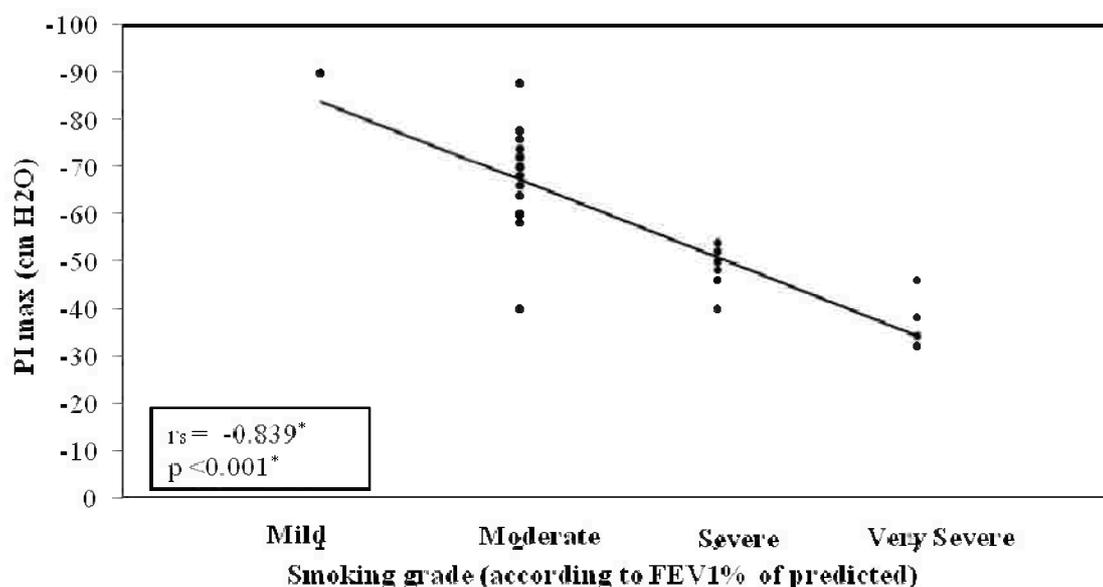


Figure (21): Correlation between smoking grade (according to FEV1% of predicted) and PI max (cm H<sub>2</sub>O)

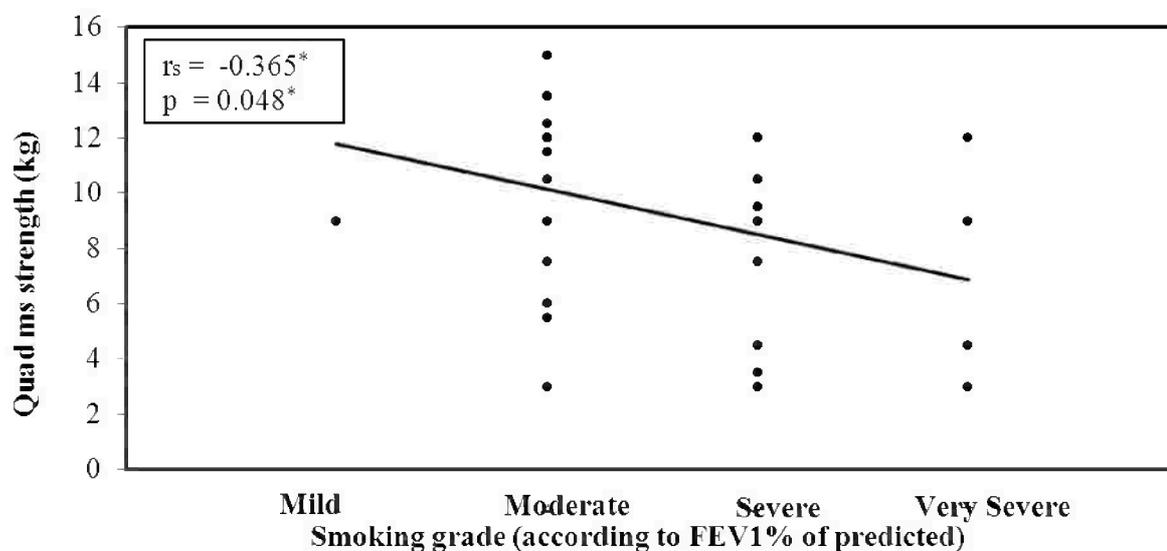


Figure (22): Correlation between smoking grade (according to FEV1% of predicted) and quadriciceps muscle strength (kg)

**Correlation between BODE index and different parameters of peripheral skeletal muscles function assessment**

- Statistically significant negative correlation was found between PImax and BODE index in studied patients with COPD with ( $r_s = -0.868$ ,  $P = <0.001$ ). (Table XVIII, Figure 23 )
- Statistically significant negative correlation was found between quadriceps muscle strength and BODE index in studied patients with COPD with ( $r_s = -0.482$ ,  $P = 0.007$ ). (Table XVIII, Figure 24)

**Table (XVIII): Correlation between BODE index and respiratory and peripheral skeletal muscles function assessment (strength and endurance) in COPD group**

	BODE index	
	$r_s$	<b>p</b>
<b>PI max (cm H<sub>2</sub>O)</b>	-0.868*	<0.001*
<b>PE max (cm H<sub>2</sub>O)</b>	0.051	0.790
<b>Hand grip strength (Kg)</b>	-0.186	0.325
<b>Biceps ms strength (Kg)</b>	-0.321	0.084
<b>Biceps ms endurance ( kg)</b>	-0.344	0.063
<b>Quadriceps ms strength (kg)</b>	-0.482*	0.007*
<b>Quadriceps ms endurance (kg)</b>	-0.255	0.175

$r_s$ : Spearman coefficient

\*: Statistically significant at  $p \leq 0.05$

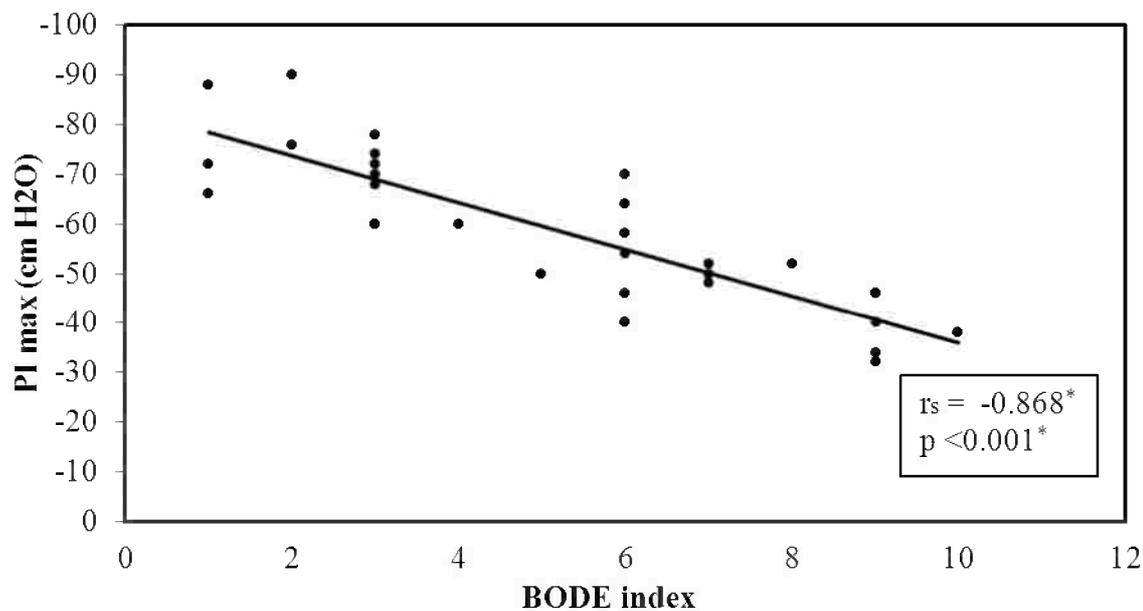


Figure (23): Correlation between BODE index and PI max (cm H<sub>2</sub>O)

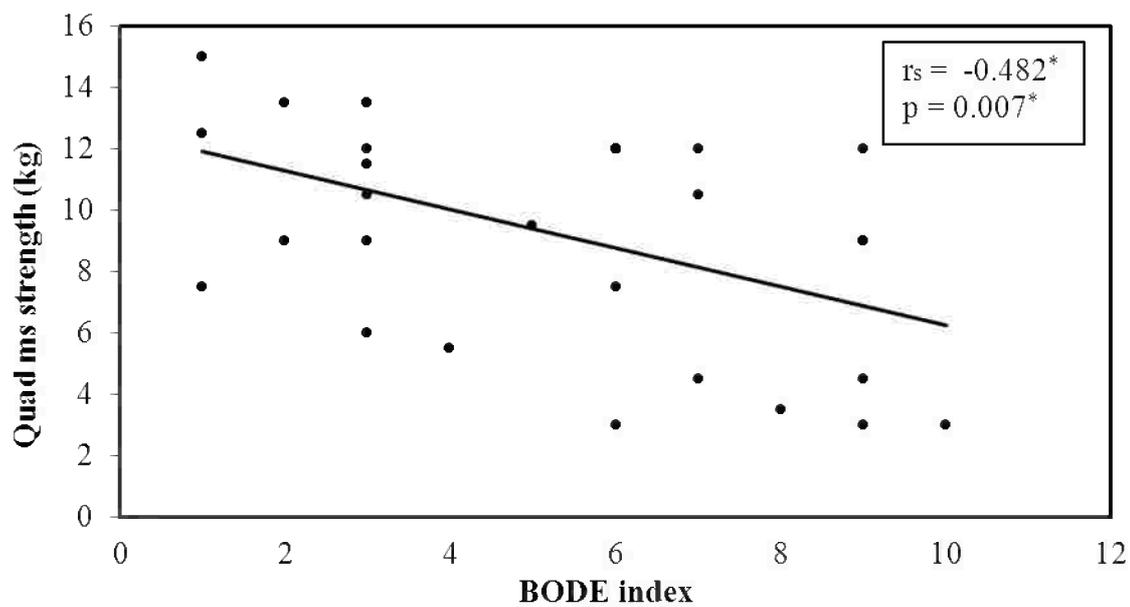


Figure (24): Correlation between BODE index and quadriceps muscle strength (kg)

**Correlation between BMI and different parameters of peripheral skeletal muscles function assessment:**

- No statistically significant correlations existed between BMI and any of skeletal muscle functions parameters assessed in our study. (Table XIX)

**Table (XIX): Correlation between peripheral skeletal muscles function assessment (strength, endurance) with BMI in cases group**

	BMI	
	$r_s$	p
PI max (cm H <sub>2</sub> O)	-0.150	0.428
PE max (cm H <sub>2</sub> O)	-0.037	0.844
Hand grip strength (Kg)	0.065	0.733
Biceps ms strength (Kg)	0.019	0.920
Biceps ms endurance ( kg)	-0.095	0.618
Quad ms strength (kg)	0.092	0.629
Quad ms Endurance (kg)	0.171	0.367

$r_s$ : Spearman coefficient

**Correlation between mMRC and different parameters of skeletal muscles function assessment**

- Statistically significant negative correlation was found between PImax and mMRC in studied patients with COPD with ( $r_s = -0.842$ ,  $P = <0.001$ ). (Table XX, Figure 25)
- Statistically significant negative correlation was found between quadriceps muscle strength and mMRC in studied patients with COPD with ( $r_s = -0.374$ ,  $P = 0.042$ ). (Table XX, Figure 26)

**Table (XX): Correlation between mMRC and respiratory, peripheral skeletal muscles function assessment (strength and endurance) in COPD group**

	mMRC	
	$r_s$	p
PI max (cm H <sub>2</sub> O)	-0.842	<0.001*
PE max (cm H <sub>2</sub> O)	0.090	0.635
Hand grip strength (Kg)	-0.122	0.521
Biceps ms strength (Kg)	-0.328	0.076
Biceps ms endurance ( kg)	-0.336	0.069
Quadriceps ms strength (kg)	-0.374*	0.042*
Quadriceps ms endurance (kg)	-0.094	0.621

$r_s$ : Spearman coefficient

\*: Statistically significant at  $p \leq 0.05$

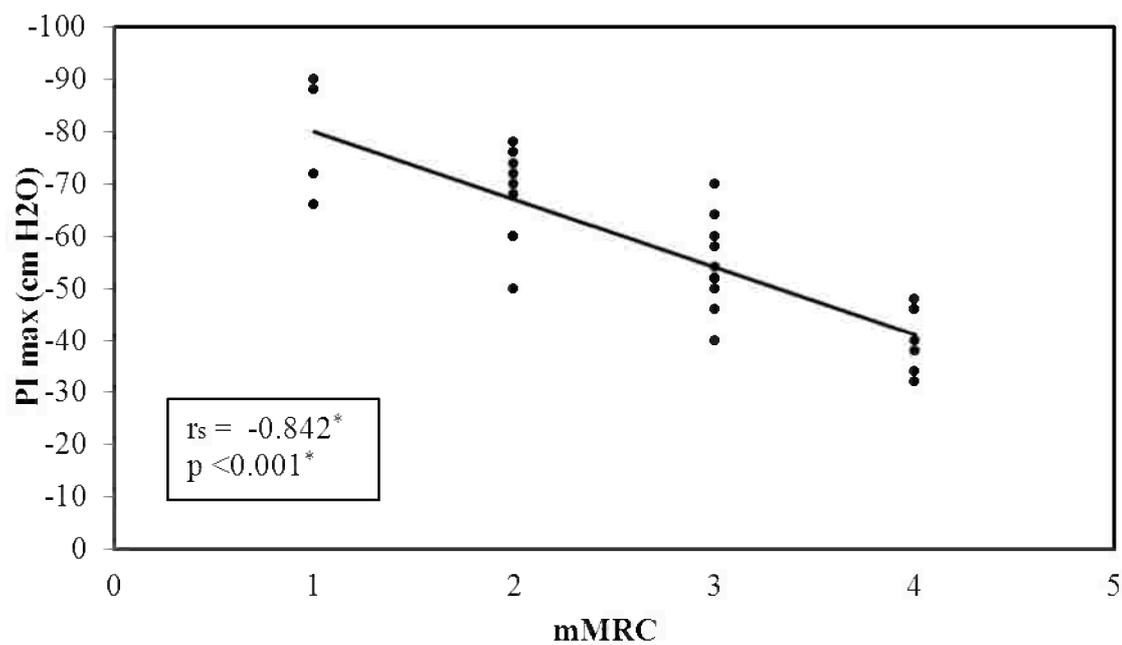


Figure (25): Correlation between mMRC and PI max(cm H<sub>2</sub>O)

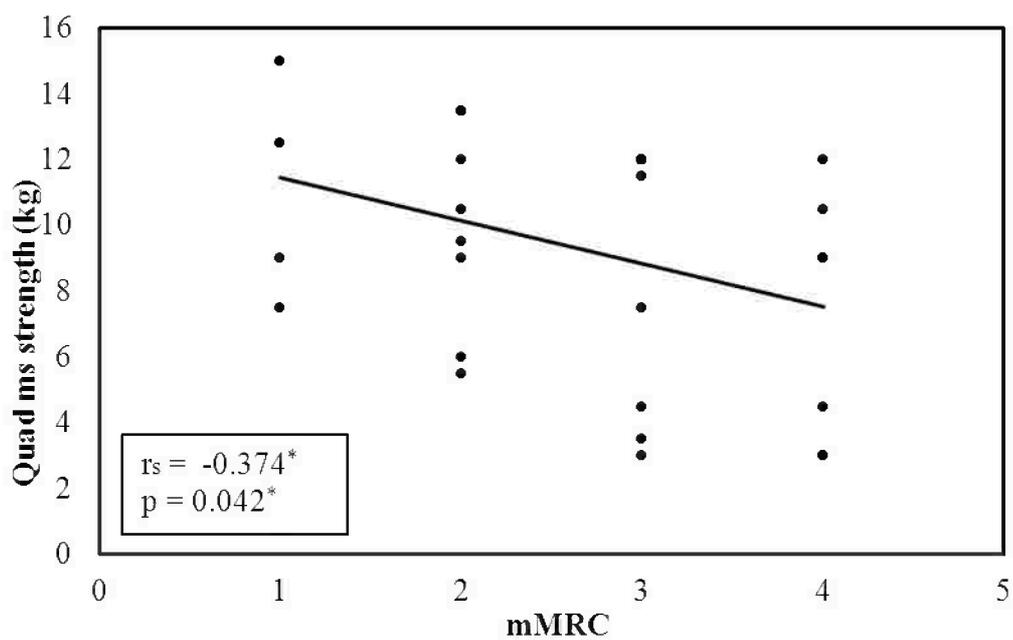


Figure (26): Correlation between mMRC and quadriceps muscle strength (kg)

**Correlation between peak VO<sub>2</sub> and different parameters of respiratory and peripheral skeletal muscles function assessment:**

- Statistically significant correlation was found between peak VO<sub>2</sub> and each of PI max, hand grip strength and quadriceps muscle strength in the studied patients with COPD ( p= <0.001, p=0.001, p=0.005 respectively ). (Table XXI)

**Table (XXI): Correlation between skeletal muscles function assessment (strength and endurance) with peak VO<sub>2</sub> in COPD group**

	peak VO <sub>2</sub>	
	r <sub>s</sub>	p
<b>PI max (cm H<sub>2</sub>O)</b>	0.623	<0.001*
<b>PE max (cm H<sub>2</sub>O)</b>	0.257	0.170
<b>Hand grip strength (Kg)</b>	0.557	0.001*
<b>Biceps ms strength (Kg)</b>	0.338	0.068
<b>Biceps ms endurance ( kg)</b>	0.362	0.056
<b>Quad ms strength (kg)</b>	0.502	0.005*
<b>Quad ms Endurance (kg)</b>	0.345	0.062

**Correlation between 6 MWT and different parameters of respiratory and peripheral skeletal muscles function assessment:**

- Statistically significant correlation was found between 6 MWT and each of PI max, and quadriceps muscle strength in the studied patients with COPD ( p= <0.001, p=0.005 respectively ). (Table XXII)

**Table (XXII): Correlation between 6 MWT and skeletal muscles function assessment (strength and endurance) within COPD group:**

	6 MWT	
	r <sub>s</sub>	p
<b>PI max (cm H<sub>2</sub>O)</b>	0.784	<0.001*
<b>PE max (cm H<sub>2</sub>O)</b>	0.049	0.796
<b>Hand grip strength (Kg)</b>	0.256	0.172
<b>Biceps ms strength (Kg)</b>	0.207	0.274
<b>Biceps ms endurance ( kg)</b>	0.183	0.334
<b>Quad ms strength (kg)</b>	0.496	0.005*
<b>Quad ms Endurance (kg)</b>	0.315	0.090

**Correlation between CRP and different parameters of respiratory and peripheral skeletal muscles function assessment:**

- No statistically significant correlation existed between CRP and any of skeletal muscle functions parameters assessed in our study. (Table XXIII)

**Table (XXIII): Correlation between peripheral skeletal muscles function assessment (strength, endurance) with CRP in COPD group:**

	CRP	
	$r_s$	<b>p</b>
<b>PI max (cm H<sub>2</sub>O)</b>	-0.055	0.773
<b>PE max (cm H<sub>2</sub>O)</b>	-0.303	0.104
<b>Hand grip strength (Kg)</b>	-0.031	0.870
<b>Biceps ms strength (Kg)</b>	-0.042	0.827
<b>Biceps ms endurance ( kg)</b>	-0.194	0.304
<b>Quad ms strength (kg)</b>	-0.055	0.774
<b>Quad ms Endurance (kg)</b>	-0.138	0.466

$r_s$ : Spearman coefficient

**Correlation between PaO<sub>2</sub> and different parameters of respiratory and peripheral skeletal muscles function assessment:**

- No statistically significant correlation existed between PaO<sub>2</sub> and any of skeletal muscle functions parameters assessed in our study. (Table XXIV)

**Table (XXIV): Correlation between peripheral skeletal muscles function assessment (strength, endurance) with PaO<sub>2</sub> in COPD group**

	PaO <sub>2</sub>	
	$r_s$	<b>p</b>
<b>PI max (cm H<sub>2</sub>O)</b>	-0.27	0.157
<b>PE max (cm H<sub>2</sub>O)</b>	0.075	0.698
<b>Hand grip strength (Kg)</b>	- 0.012	0.951
<b>Biceps ms strength (Kg)</b>	0.32	0.09
<b>Biceps ms endurance ( kg)</b>	0.369	0.05
<b>Quad ms strength (kg)</b>	0.229	0.232
<b>Quad ms Endurance (kg)</b>	- 0.004	0.985

$r_s$ : Spearman coefficient

**Correlation between FEV1% of predicted and CRP:**

- No statistically significant correlation existed between FEV1 % of predicted and CRP assessed in our study. (Table XXV)

**Table (XXV):Correlation between FEV1% predicted and CRP:**

	FEV1% of predicted	
	r <sub>s</sub>	p
CRP	-0.077	0.686

r<sub>s</sub>: Spearman coefficient

**Univariate regression analysis for quadriceps muscle strength (kg)**

- Statistically significant positive correlation was found between quadriceps muscle strength and FEV1% of predicted in studied patients with COPD with (rs =0.364, P=0.046).(Table XXVI, Figure 27 )
- Statistically significant negative correlation was found between quadriceps muscle strength and BODE index in studied patients with COPD with (rs= -0.482, P=0.007 ).(Table XXVI, Figure 28)
- Statistically significant negative correlation was found between quadriceps muscle strength and MMRC in studied patients with COPD with (rs = -0.374, P=0.042). (Table XXVI, Figure 29)

**Table (XXVI): Univariate regression analysis for Quadriceps muscle strength (kg)**

	Quadriceps ms strength (kg)	
	r	p
FEV1% of predicted	0.364*	0.046*
CRP	-0.055	0.774
BODE	-0.482*	0.007*
MMRC	-0.374*	0.042*
BMI	0.092	0.629
PaO <sub>2</sub>	-0.181	0.340

r<sub>s</sub>: Spearman coefficient

\*: Statistically significant at p ≤ 0.05

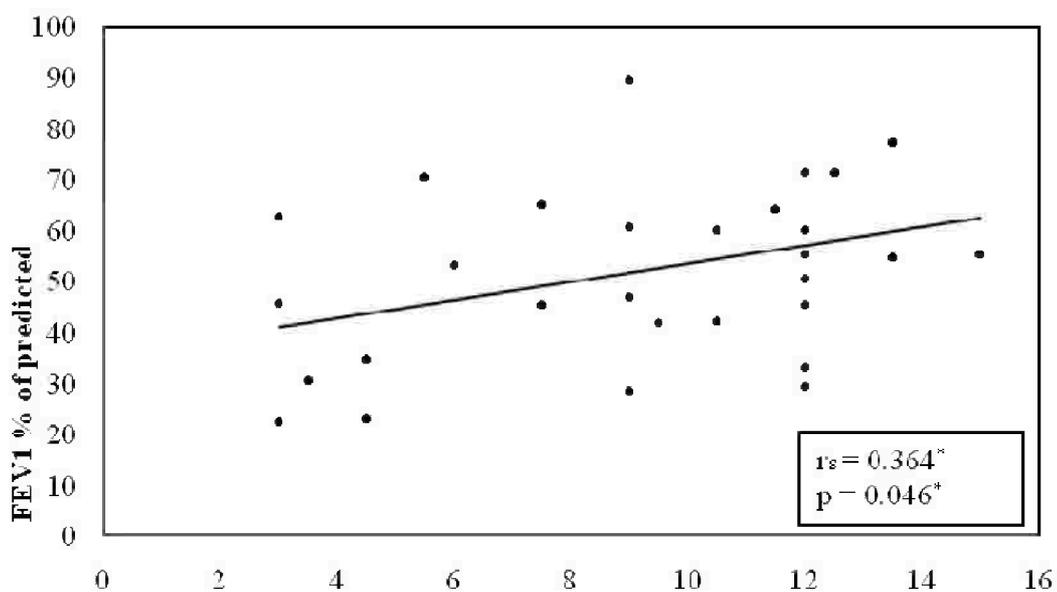


Figure (27): Correlation between quadriceps muscle strength (kg) and FEV1% of predicted

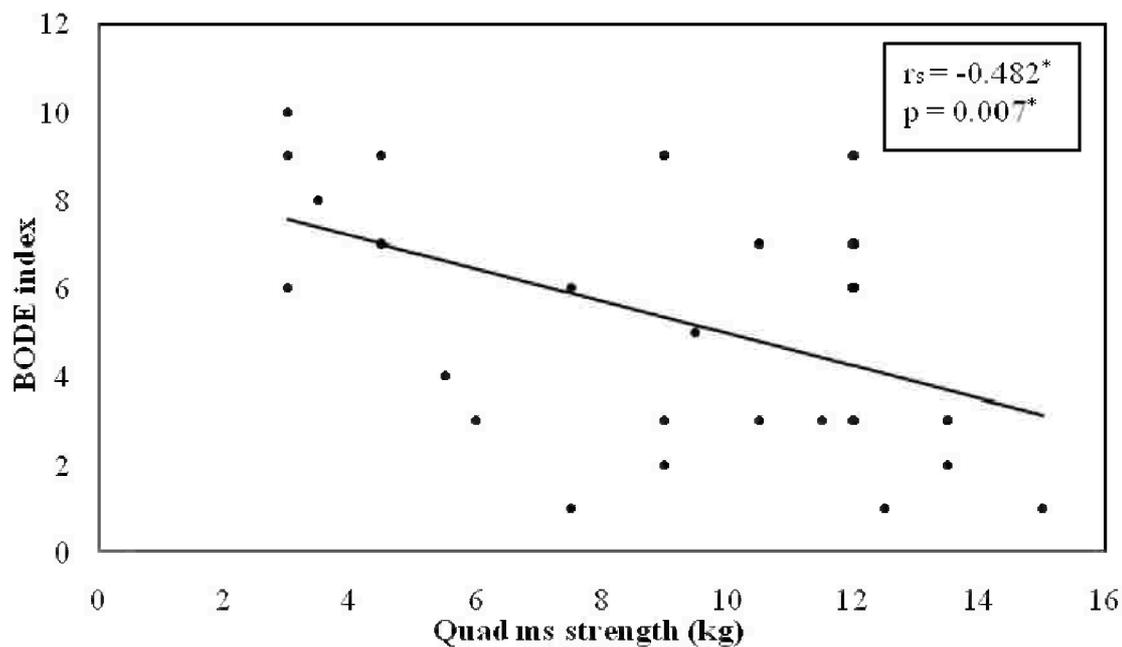


Figure (28): Correlation between quadriceps muscle strength (kg) and BODE index

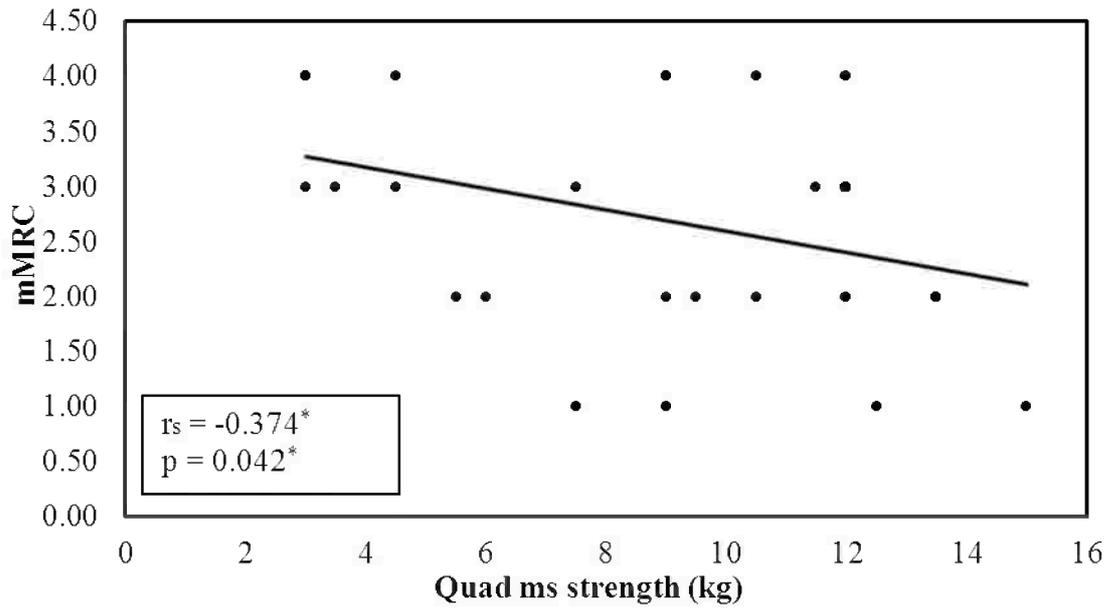


Figure (29): Correlation between quadriceps muscle strength (kg) and MMRC

**Multivariant stepwise regression analysis for inspiratory muscle strength:**

- Multivariant stepwise regression analysis revealed that inspiratory muscle strength ( as dependent variable ) is mainly related to BODE index ( $p < 0.001$ )

**Table (XXVII): Multivariate linear regression analysis for inspiratory muscle strength ( $PI_{max}$ )**

	<b>B</b>	<b>t</b>	<b>p</b>
<b>BODE</b>	4.727	8.94*	<0.001*
<b>Peak VO2</b>	-0.074	-0.521	0.607
<b>6MWD</b>	-0.123	-0.633	0.532
<b>mMRC</b>	0.283	1.019	0.317
<b>FEV1 % of predicted</b>	-0.090	-0.516	0.610

**Multivariant stepwise regression analysis for quadriceps muscle strength:**

- Multivariant stepwise regression analysis revealed that quadriceps muscle strength ( as dependent variable ) is mainly related to BODE index ( $p = 0.022$ )

**Table (XXVIII): Multivariate linear regression analysis for quadriceps muscle strength**

	<b>B</b>	<b>t</b>	<b>p</b>
<b>BODE</b>	-1.783	2.446*	0.022*
<b>Peak VO2</b>	-0.214	-0.922	0.357
<b>6MWT</b>	0.219	0.935	0.358
<b>mMRC</b>	3.020	1.746	0.093
<b>FEV1 % of predicted</b>	-0.028	0.465	0.646